Endocrine Abstracts

April 2019 Volume 62
ISSN 1479-6848 (online)

Society for Endocrinology Endocrine Update 2019

Society for Endocrinology

published by bioscientifica

Online version available at
www.endocrine-abstracts.org

Endocrine Abstracts

Volume 62
April 2019

Society for Endocrinology: Endocrine Update 2019

08–10 April 2019

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Society for Endocrinology

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OC1

Virilisation at puberty – a new subtype in the spectrum of NR5A1 mutations

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Case history
A 14.5-year-old girl was brought forward by her mother to the paediatric endocrine clinic in view of virilised genitalia, absent breast development and primary amenorrhoea. Her genital appearance had changed gradually throughout childhood though she never disclosed this to her parents. She was otherwise healthy with no significant family history of note. On examination, she had fused labioscrotal folds containing 10–12 ml testis. There was no obvious vaginal dimple and she had a 7 cm clitoral-penile structure with hypospadias, stage 4 pubic hair and stage 2 breast development. At 17 she was referred to UCLH adult DSD service for gonadectomy.
Investigations
Tests included an endocrine profile, synacthen test, 3-day human chorionic gonadotropin (HCG) test, a urine steroid profile and pelvic ultrasound. Genetic tests included a karyotype and testing for disorders of sexual development (DSD) mutations.
Results and treatment
Bloods showed the following: AMH of 24.7 pmol/l (females 3.0–46.6; males 9.4–331.8), inhibin B 65 ng/l (females <341; males 25–325), DHEAS 6.76 umol/l (females 1.2–6.7; males 2.8–10.0), 17-hydroxyprogesterone 2.8 nmol/l (0.3–6.3), testosterone 8.5 nmol/l, oestradiol 51 pmol/l, LH 2.8 IU/l and FSH 10.4 IU/l. TFTs, synacthen test, 3-day HCG test and urinary steroid profile were normal. Karyotype was 46XY. A variant mutation of NR5A1 gene was found. No Mullerian structures were observed on pelvic ultrasound and testes were present in the labioscrotal folds bilaterally. She was referred to a clinical psychologist and following prolonged consultations opted for feminising therapy after given the options of masculinising/feminising surgery or let nature take its course. She was started on a gonadotropin-releasing hormone agonist and later started on oestradiol valerate 1 mg, which was eventually increased to 2 mg in view of fatigue. She is due to have gonadectomy later on this year with examination under anaesthesia and cystoscopy. Subsequent surgeries will involve clitoral reduction and vaginoplasty.
Conclusion and points for discussion
Virilisation at puberty is a feature of several forms of 46XYDSD of which NR5A1 mutations are a relatively recently recognised subtype. This is a difficult clinical scenario as the natural history of gender identity is not well described as individuals grow older. Gamete preservation in DSD is often not routinely offered but is likely to become an important part of management. It is important not to rush with irreversible gender assigning medical and surgical therapy. Hormonal blocking therapy may be the most appropriate treatment until the patient has received prolonged psychological therapy and is more mature to decide regarding gender assigning treatment.

DOI: 10.1530/endoabs.62.OC1

OC2

Abstract Unavailable.

OC3

A case of Birt-Hogg-Dubé syndrome presenting with a rare oncocytic non-secretory phaeochromocytoma

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Case history
Birt-Hogg-Dubé syndrome (BHDS) is a rare autosomal dominant disorder caused by heterozygous pathogenic variants in the *FLCN* gene encoding *folliculin* on chromosome 17p11, first described clinically in 1975. It is a '*hamartomatous*' disorder usually manifesting with pulmonary cysts, benign cutaneous tumours and conferring a high risk of renal malignancy. A 43 year old man had a 34 x 22 mm right adrenal nodule discovered incidentally on a CT CAP. Relative percentage washout was reassuring at 77%. Relevant past medical history included a recent hemithyroidectomy with histology diagnostic of a follicular adenoma. A diagnosis of multiple sclerosis was made at the age of 22 following episodes of retrobulbar neuritis, on the basis of an MRI showing multiple areas of high signal in the periventricular area. In terms of family history; the patient's mother also had a diagnosis of multiple sclerosis in addition to a spontaneous pneumothorax requiring drainage and a sublingual lipoma. The patient's maternal grandparents had multiple (poorly characterised) malignancies. Clinical examination showed an absence of BHDS-related skin lesions. Blood pressure was 144/90.
Investigations
There was no evidence of endocrine functionality. 24-hour urinary free cortisols (228 and 118 nmol) (50–300), 24-hour urinary normetadrenaline (0.2 umol x 2) (0.0–3.8), 24-hour urinary metadrenaline (0.1 umol x2) (0.0–2.2), plasma renin 6.0 mU/l (5.4–60) and aldosterone 127 pmol/l (90–720). Interval imaging showed the adrenal nodule had grown to 51 x 40 mm prompting a laparoscopic right adrenalectomy.
Results and treatment
Histologically the morphological and immunohistochemical findings were felt to be somewhat ambiguous. Given the positivity with markers for CD56 and synaptophysin and the negative SF1 immunohistochemistry a diagnosis of oncocytic pheochromocytoma was made. PASS score 7/20. A PET CT showed bilateral multiple pulmonary cysts in a predominantly basal distribution. Sequencing of the *FLCN* gene showed the patient to be heterozygous for a pathogenic variant c.1285dupC, p.(His429ProfsTer27) confirming BHDS.
Conclusions
Oncocytic variant pheochromocytoma is very rare histological subtype where the tumour cells have an eosinophilic granular cytoplasm. Only 6 cases have been reported in the literature. Only one other case of an adrenal oncocytic tumour has been reported in a patient with BHDS; this was also non-secretory. We present the first reported case of BHDS associated with multiple non-functioning endocrine tumours. Under current *ESE* guidance the initial adrenal nodule is classified as radiologically benign despite the histological diagnosis.

DOI: 10.1530/endoabs.62.OC3

OC4

A novel PHEX mutation, p.(Trp749Ter), is associated with hypophosphataemia and rhabdomyolysis in adulthood

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Case History
X-linked hypophosphataemia (XLH) manifests as rickets in infancy or childhood, and is caused by mutations of the phosphate-regulating neutral endopeptidase (*PHEX*) gene, which leads to excess production of the fibroblast growth factor-23 (FGF-23) hormone. We present a case illustrating that mutation of *PHEX* can also

cause hypophosphataemia presenting in adulthood. The proband is a 56-year-old male, who was referred with persistent hypophosphataemia (serum phosphate ranging between 0.44–0.79 mmol/l, normal 0.80–1.50 mmol/l). He is of normal stature (height 1.78 m) with no osteomalacic symptoms or lower limb deformities. His 22-year-old daughter was also found to be hypophosphataemic (serum phosphate 0.42–0.61 mmol/l) following an episode of exercise-induced rhabdomyolysis. She is of normal stature with no prior rickets.
Investigations
Biochemical investigations in the proband showed: a normal serum calcium of 2.38 mmol/l (normal 2.20–2.60); eGFR of >90 ml/min per 1.73 m^2; borderline elevated serum parathyroid hormone of 7.2 pmol/l (normal 1.1–6.9); normal serum 25-hydroxyvitamin D of 91 nmol/l (normal >50); normal serum 1,25-dihydroxyvitamin D of 116 pmol/l (normal 43–144); low tubular maximum of phosphate/glomerular filtration rate (TmP/GFR) of 0.53 (consistent with a renal tubular phosphate leak); and elevated serum FGF-23 of 117 RU/ml (normal <100). The proband's affected daughter was also found to have a renal tubular phosphate leak (TmP/GFR of 0.58) and a borderline elevated serum FGF-23 of 95 RU/ml. Her rhabdomyolysis was considered to be due to the hypophosphataemia as a muscle biopsy revealed no other metabolic cause. The finding of renal phosphate loss and FGF-23 excess in the proband and his daughter suggested an underlying genetic aetiology.
Results
DNA sequence analysis of known phosphate-regulating genes (*PHEX*, *FGF23*, *DMP1*, *ENPP1* and *SLC34A3*) in the proband revealed a novel germline p.(Trp749Ter) *PHEX* mutation, which is predicted to cause the loss of the PHEX carboxyl-terminus Trp749 residue. Homology modelling using the crystal structure of the related human neutral endopeptidase (NEP) enzyme showed the Trp749 residue to form part of an evolutionarily conserved carboxyl-terminus tetrapeptide motif, which is required for stabilising the catalytic domain of neutral endopeptidases. Thus, the p.(Trp749Ter) mutation would be predicted to disrupt PHEX catalytic activity.
Conclusion and points for discussion
These findings demonstrate that mutation of the *PHEX* gene can cause hypophosphataemia in the absence of rickets, and indicate that *PHEX* mutational analysis should be considered in hypophosphataemic adults harbouring a renal tubular phosphate leak and FGF-23 excess.

DOI: 10.1530/endoabs.62.OC4

OC5

A case of SDHC mutation with two neuroendocrine tumours. Is it just a coincidence?

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Case history
63 year man with two trans-temporal incomplete resections of a glomus jugulare tumour (HNPGL) in 1993 and 2000 with regular surveillance scans for residual disease. Eight years later, an MRI demonstrated an incidental pituitary macroadenoma with cavernous and sphenoid sinuses invasion. The patient was asymptomatic but, his biochemistry revealed a markedly raised prolactin of 43,000 mIU/l with no other pituitary hormone deficiency. Cabergoline was commenced and the macroprolactinoma demonstrated an excellent response, with normalization of serum prolactin within one year. Family history revealed that his brother was also diagnosed with a glomus vagale tumour and his cousin with pituitary tumour. The patient was referred to a clinical geneticist. Our patient was found to be positive for missense *SDHC* mutation as a variant of uncertain significance. Further genetic testing demonstrated that his brother and sister also had *SDHC* mutation. Interestingly his cousin with NFPA did not.
Result and treatment
Biochemical screening showed a raised plasma 3-methoxytyramine (3MT) 1014 pmol/l (0–180) but normal metanephrine and normetanphrine. His whole body MRI scan showed stable residual HNPGL with no other lesion detected. We questioned if the isolated rise in 3MT could be a drug induced phenomenon as the patient was concurrently treated with dopamine agonist (cabergoline) and 3MT is a metabolite of the neurotransmitter dopamine. Carbergoline was temporarily stopped; his repeated 3MT was 1965 and 2185 pmol/l at 2 and 4 weeks of ceasing cabergoline respectively. Most HNPGLs are functionless but the isolated high 3MT level was suggestive of metastatic disease. Functional imaging with (123)I-MIBG and (68)Ga-DOTATATE PET/CT were performed to exclude multifocal disease. (68)Ga-DOTATATE PET/CT demonstrated avid uptake at his residual neck disease and another focus of uptake in his sacrum. Biopsy of the lesion was not possible given its size and location. He received fractionated radiotherapy for his skull base and sacral lesions. Follow-up in the next 3 year remains stable with Ga-68 PET/CT demonstrated reduced uptake in the sacrum with stable HNPGL and 3MT around 700 pmol/l.
Discussion
We are reporting a very interesting patient who harbors *SDHC* germ-line mutation with metastatic HNPGL and pituitary tumour. *SDHC* mutation is typically benign and non-functioning but a recent publication of metastatic disease has been reported. The relationship of pituitary tumour and *SDHC* remains un-defined, as loss of heterozygosity study is not available. The other interesting phenomenon is the rise in 3MT with dopamine agonist withdrawal.

DOI: 10.1530/endoabs.62.OC5

OC6

Effective novel therapy in the use of managing refractory hypoglycaemia in a patient with metastatic insulinoma

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Case history
22 year old female presented with left sided hemiparesis following a generalised seizure; the blood glucose was 1.2 mmol/l. Corrective treatment restored cerebral function. In the preceding 6 months, she had symptoms of drowsiness on waking which corrected with sugary drinks and described tiredness with lethargy. There had been no reported change in appetite or bowel habits however, there had been a degree of weight loss during this period. During hospital admission, 20% dextrose infusion was required to maintain euglycaemia.
Investigations
Blood samples during a spontaneous hypoglycaemic episode (1.5 mmol/l) demonstrated elevated insulin level 392 pmol/l (18–173 pmol/l) and C-peptide 3913 pmol/l (370–1470 pmol/l) with a negative sulphonylurea screen. CT scan revealed 3 indeterminate bilobar hepatic lesions which were further characterised as metastatic disease on MRI with an exophytic lesion identified in the pancreatic body. Gallium DOTATATE demonstrated avidity of pancreatic and hepatic lesions in keeping with a pNET (Insulinoma) in the body/tail and 4 DOTATATE-avid hepatic metastases. EUS was not tolerated and liver biopsy was performed.
Results and treatment
Histology from the liver biopsy showed a metastatic well-differentiated neuroendocrine tumour with a Ki-67 proliferation index 1% (G1). Genetic testing was negative for mutations in MEN1, AIP and CDKN1B. Diazoxide (up to 400 mg/day) was commenced without any benefit and hypoglycaemia remained refractory despite increased doses of Octreotide (200 mcg TDS) and depot Lanreotide (120 mg) injections. She required continuous 20% Dextrose infusion throughout this prolonged admission (10 weeks). Everolimus was commenced with addition of oral Dexamethasone for appetite stimulation which rapidly restored euglycaemia. Following a distal pancreatectomy, partial splenectomy and two segment liver resections she has remained normoglycaemic whilst withdrawing medications.
Conclusion
This case highlights the challenge of managing refractory hypoglycaemia in an unusually young presentation of metastatic insulinoma. There were large volume metastases and marked hyperinsulinaemia. Everolimus is a protein kinase inhibitor (mTOR) used in several cancers including pNETs. Through inhibition of the PI3K/AKT/MTOR pathways everolimus can normalise blood glucose levels by inhibition of gluconeogenesis and reduction of insulin secretion. Our patient remained dextrose dependent, despite SSA, prednisolone and diazoxide, until the introduction of everolimus which had rapid and sustained effects in achieving glucose control. Other treatments considered included pasireotide, PRRT, Chemo/Radio Embolisation and cytotoxic chemotherapy but the response to everolimus allowed safe discharge until surgical resection of disease was undertaken.

DOI: 10.1530/endoabs.62.OC6

OC7

An aldosterone crisis

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Case history
A 26 year-old lady was admitted directly from the endocrine clinic with severe hypertension (BP 180/130 mmHg) and bilateral papilloedema. Six weeks prior to admission she had undergone resection of a 24 cm right upper quadrant lesion that

was pre-operatively felt to be of hepatic origin. She was normotensive pre-operatively. Histology confirmed this to be an adrenal phaeochromocytoma with deficient SDH immunostaining. Pre-operative biochemical assessment had not been performed but there was no evidence of any blood pressure abnormality or variation pre- or peri-operatively. Two weeks post-operatively she began to experience episodes of palpitations, sweating and hypertension and had attended the emergency department of her local hospital on a number of occasions and been commenced on doxazosin.
Investigations
She was hypokalaemic on admission (K 3.2 mmol/l, Na 19 mmol/l) and given the large size of the original lesion and absence of a crisis during the original surgery, renovascular mediated hypertension was considered. Renin, aldosterone and a renal MRA were requested.
Results and treatment
She was admitted to the High Dependency Unit for invasive blood pressure monitoring and treatment. The MRA confirmed an infarcted right kidney with a patent accessory renal artery. A DMSA demonstrated only a 5% contribution from the right kidney. Hyper-reninaemic hyperaldosteronism was subsequently confirmed (renin 18.3 nmol/l per h NR 0.5–3.5 nmol/l per h, aldosterone 1,014 pmol/l NR 150–550 pmol/l). She was discharged on losartan which was subsequently switched to candesartan. The blood pressure proved difficult to control and she was referred for renal artery embolization. On the day of the procedure she was found to be pregnant and the procedure was postponed. The pregnancy was considered high risk, the candesartan was discontinued and the blood pressure proved difficult to control with a further admission required to treat papilloedema. Genetic analysis subsequently confirmed she carried an underlying *SDHB* mutation (c.72+1G>T).
Conclusions and points for discussion
This is an unusual and interesting case of acute secondary hyperaldosteronism. We will discuss the risks of renal injury during phaeochromocytoma surgery, the complex medical management of this case outside and during a pregnancy and the results of the renal artery embolization.

DOI: 10.1530/endoabs.62.OC7

OC8

Adenoma to carcinoma progression of a deoxycortisol-secreting adrenal cortical carcinoma in a 71 year old man presenting with hypokalaemia

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Case history
We present a 71 year old man, with a 3 year history of problematic hypertension (BP exceeding 190/100 on treatment), incidentally found to be hypokalaemic (K 1.8 mmol/l) during investigations for leg weakness. He had no clinical features to suggest an endocrinopathy. Investigations at his local centre revealed hypokalaemia dating back over 3 years.
Investigations
Biochemistry:
Na 142 mmol/l (135–145 mmol/l)
K 1.8 mmol/l (3.5–5.5)
Plasma metadrenaline <180 pmol/l (<1000 pmol/l)
Plasma normetadrenaline <270 pmol/L (<600 pmol/L)
24 h UFC 81 nmol/24 h (<146 nmol/24 h)
Cortisol day profile: normal diurnal rhythm
Aldosterone <70 pmol/l (90–405 pmol/l)
Renin 6 mU/l (5.4–60 mU/l)
11-deoxycortisol 20 nmol/l (7–13 nmol/l).
Urinary steroid profile: An ACC is indicated by high concentrations of metabolites of 11-deoxycortisol, tetrahydro-11-deoxycortisol (456 ug/l) and 11-deoxycorticosterone, tetrahydrocortocosterone (93 ug/l).
Imaging: Triple-phase adrenal protocol CT: 6.5 cm right adrenal mass with unenhanced attenuation of 25 HU and enhancement washout of 57%. Metomidate PET-CT: 67 × 44 mm mass with heterogeneous uptake (TOF SUVmax 31.4) (Sharp IR SUVmax 41.5). Areas of low attenuation and photon deficiency are seen within this mass suggesting necrosis. ^{18}FDG PET-CT: 65 mm right adrenal mass with heterogeneous tracer uptake with a focus of high peripheral uptake (corresponding to the photon-deficient area on Metomidate PET-CT). (SUV-max=7.3). No evidence of disseminated disease.
Histology: Immunohistochemistry shows tumour cells positive for adrenal cortical markers and negative for chromogranin. The proliferation index in the solid area corresponding to the area of high FDG uptake, is up to 15%, with a background proliferation index of 3%. This favours an oncocytic adrenocortical tumour with a solid area of malignant transformation in keeping with oncocytic adrenocortical carcinoma. No histological features of necrosis were seen to explain the photopenic region on metomidate PET-CT.
Results and treatment
The patient underwent a laparoscopic adrenalectomy. Five months post operation, there is no radiological or biochemical evidence of disease recurrence.
Conclusions and discussion
We present a case of a rare 11-deoxycortisol secreting oncocytic adrenocortical carcinoma with features suggestive of adenoma-carcinoma progression in a patient with a 3 year history of hypertension and hypokalaemia. This case demonstrates the clinical utility of molecular imaging in adrenal tumours, as two distinct areas on CT were seen, which had reciprocal avidity for metomidate and FDG PET and correlated with a discrete nodule with malignant transformation within a larger oncocytic neoplasm on histological review.

DOI: 10.1530/endoabs.62.OC8

OC9

Osteoporosis with a raised serum testosterone – an unexpected finding

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Case history
A 20-year-old man was referred to the metabolic bone clinic following a left sided neck of femur fracture (sustained after a simple fall whilst roller skating). He was otherwise well with no past medical history; systemic enquiry was unremarkable. A DEXA scan revealed osteoporosis (*Z* scores: total hip −2.97; lumbar spine −3.1), and bone turnover markers were significantly raised. Unexpectedly, the patient was found to have an elevated serum testosterone level (37.4 nmol/l (8–29)). Serum TSH was also mildly raised (8.41 mU/l (0.35–5.5)). He was therefore referred for endocrine review.
Investigations
Although serum total testosterone was again raised (31.0 nmol/l), SHBG was markedly increased (145 nmol/l (10–57)) yielding a calculated free testosterone of just 0.22 nmol/l, with LH 9.3 U/l (1.5–6.3) and FSH 5.6 U/l (1.0–10.1). Further investigations included:
- serum prolactin 42 mU/l (45–375).
- serum TSH 8.41 mU/l, free T4 (fT4) 52.7 pmol/l (10–19.8), free T3 (fT3) 29.5 pmol/l (3.5–6.5); assay interference was excluded.
- TRH test: TSH (mU/l): 0 minutes, 6.46; 30 minutes, 11.19; 60 minutes, 7.81.
- Alpha subunit: 5.9 IU/l (<1.0).
- Octreotide (100 mcg s.c.) suppression test: 74% reduction in serum TSH at 300 minutes.
- Pituitary MRI: 35x29x13 mm macroadenoma, compressing the optic chiasm.

Results and treatment
The patient was commenced on Lanreotide ATG 120 mg s.c. every 28 days. After three injections, his TFTs had improved but remained abnormal. In preparation for surgery, subcutaneous octreotide (200 mcg tds) and propylthiouracil (200 mg tds) were substituted, with resultant normalisation of serum fT3. An endoscopic endonasal approach revealed a vascular tumour, which precluded safe transsphenoidal resection. Subsequent angiography demonstrated a 'tumour blush' but no prominent intratumoural arteries. At craniotomy a gross total resection was achieved. Immuno-histochemical staining was strongly positive for TSH and negative for all other pituitary hormones (MIB-1 3.6%). Following surgery, the patient developed central hypothyroidism and continues on levothyroxine replacement. He is otherwise eupituitary. Postoperative imaging demonstrated no evidence of residual or recurrent tumour.
Conclusion and points for discussion
This case illustrates several challenges that may be encountered in the investigation and management of TSH-secreting pituitary adenomas:
1. Paucity of symptoms despite markedly raised serum fT4 and fT3 with target organ damage.
2. Masking of hypogonadism in the presence of dramatically elevated SHBG levels.
3. Limitation of octreotide suppression test in predicting depot SRL responsiveness.
4. Requirement for multimodal medical therapy to control thyrotoxicosis prior to surgery.
5. Surgical challenge presented by prominent tumoural vascularity.

DOI: 10.1530/endoabs.62.OC9

OC10

An occult cause of thyrotoxicosis

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Case History

A 46 year old lady presented with deranged thyroid function (TSH 0.05, T4 19.7). She reported palpitations, mild eye irritation, sweats and weight loss. Examination revealed a resting tremor and regular pulse (72 bpm). A small goitre with bruit was present, but no evidence of thyroid eye disease. Block-and-replace regime of carbimazole and levothyroxine was commenced for Graves' disease. Thyroid peroxidase antibodies were <1. After one year of euthyroidism treatment was stopped, but she relapsed into hyperthyroidism. The patient opted for total thyroidectomy. The histology report was 'consistent with treated Graves' disease.' Four days following surgery she developed palpitations and tremor; blood tests confirmed hyperthyroidism.

Investigations

Ultrasound of the neck confirmed total thyroidectomy with no residual thyroid tissue. Thyroid uptake with SPECT CT and I131 scan of the thyroid area were unremarkable. The elusive source of thyroid hormone prompted consideration of ectopic production. Pelvic ultrasound revealed a 'complex mixed cystic/solid mass, ovarian in origin'. TSH receptor antibodies were negative, but CA125 elevated at 76.9. I131 scan of the abdomen and pelvis demonstrated 2 foci of uptake- in the bladder and the left ovary.

Results and treatment

Histology from unilateral salpingo-oopherectomy and omental washings demonstrated follicular thyroid carcinoma arising in struma ovarii. Levothyroxine re-commenced after surgery achieved euthyroidism. Thyroglobulin was <5 with no histological evidence of intraepithelial invasive neoplasia, so adjuvant therapy was not necessary.

Conclusions and points for discussion

Struma ovarii is a specialised or monodermal teratoma with thyroid tissue comprising more than 50% of the overall tissue. It accounts for 5% of all ovarian teratomas. Whilst approximately 95% are benign, malignant transformation can occur, most commonly papillary carcinoma, followed by follicular carcinoma. The majority of struma ovarii are asymptomatic however 5–8% present with hyperthyroidism. Our patient presented with hyperthyroidism which was treated as presumed antibody-negative Graves' disease. Patient preference for total thyroidectomy, rather than radioiodine, meant a thyroid uptake scan was not performed which would have demonstrated low thyroid uptake prompting investigation for ectopic hormone production. Thyroid histology supported a diagnosis of Graves', however clinical history may have affected interpretation. Initial I131 scan was limited to the neck and thorax thus missing the struma ovarii. Whilst some malignant struma ovarii cause abdominal signs (ascites, abdominal swelling) our patient had no localising features. This case demonstrates the need to suspect rare causes of excess thyroid hormone production in antibody-negative hyperthyroidism.

DOI: 10.1530/endoabs.62.OC10

Poster Presentations

P01

Where is the problem - Ectopic ACTH or ACTH-secreting Pituitary Adenoma?

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Case History
This is a 73 year old lady with known Type 2 Diabetes Mellitus who presented to Acute Medicine with a 2-week history of diarrhoea and acute confusion on a background of a 4-month history of gradual cognitive and functional decline. She was treated for low-respiratory tract infection with acute kidney injury on a background of age-related functional decline. CT brain was organised.
Investigations
CT Brain: Large enhancing soft tissue dense lesion at skull-base causing bone destruction. Differentials are brain metastasis, chronic sinusitis or chordoma.
MRI Brain: Enhancing skull-base mass centred at the clivus extending into the sphenoid sinus but sparing the pituitary.
CT Chest/abdomen/Pelvis: No evidence of any suspicious lesion
Pituitary Hormone profile: LH <0.3 u/L (15.9–54.0), FSH 1.7 u/L (23–116.3), TSH 0.53 mu/L (0.55–4.78), fT3 2.9 pmol/L (3.5–6.5), fT4 16.9 pmol/L (10–18.7), Prolactin 200 mu/L (60–620), IGF1 8.8 nmol/L (4.6–28.3), Cortisol 1258 nm0 l/L (119–619)ACTH 105 ng/l (0–46).
Results and further Investigations
The patient was started on Levothyroxine 50 microgram OD.
Urinary cortisol 1607 nmol/24 hr (0–146). Overnight dexamethasone suppression test: Cortisol 1373 nmol/L (119–619). She then had potassium 2.6 mmol/L needing IV potassium replacement. Low-dose dexamethasone suppression test: Baseline cortisol: 1274 nmol/L and 48 hr post cortisol: 1864 nmol/L. Skull-base MDT outcome at tertiary centre: Chordoma or Plasmacytoma and patient was to be seen as outpatient. Marked clinical deterioration with pneumonia, hypoxia and worsening in swallow. Nasogastric tube was trialled for feeding and medications, but without much success. Metyrapone was commenced but only minimal doses were given due to administration difficulties. The patient was also having significant epistaxis from the mass invading the skull base bones, further complicating nasogastric tube usage. The patient unfortunately died after being palliated.
Conclusion and points for discussion
The patient did not have any cushingoid features clinically and deteriorated rapidly. She had uncontrolled blood glucose, hypokalaemia, high cortisol and high ACTH, high UFC, non-supressed cortisol with ODST and low dose dexamethasone suppression test and she had a skull base mass with no other primaries. Is this ectopic ACTH from a chordoma or is this an ACTH-dependent pituitary adenoma with an odd presentation? Should we have given Metyrapone earlier? Would an early transfer as an inpatient to neurosurgery change the outcome? This case highlights the difficulties in pursuing endocrinological investigations and administration of drugs in a complicated setting.

DOI: 10.1530/endoabs.62.P01

P02

Pituitary hyperplasia due to untreated hypothyroidism

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Case history
A 51-year old female presented to emergency with occipital headache for 5 days on a background of recurrent headaches for over a year. She had been diagnosed with Hashimoto's disease at the age of 30 and given levothyroxine, which she discontinued 5 years ago due to aversion to take medications. She had noticed cold intolerance and low energy. At presentation her body mass index was 25.26 kg/m^2 and the physical exam was unremarkable; specifically, there was no goiter, blood pressure was 99/71, heart rate was 70 bpm and her temperature was 36.5°C.
Investigations
A CT scan of the head was done for headaches that showed a 9 mm hypodense sellar lesion and the baseline pituitary hormone testing drawn at 10:30 AM in emergency showed: TSH = 496.8 mIU/L, prolactin = 44.4 ug/L (N = 5.2–27 ug/L), IGF-1 = (N = 81–238 ug/L), and cortisol = 131 nmol/L (N = 120–500 nmol/L before 930AM). MRI of the sella showed a mildly expanded sella turcica with a homogeneously enhancing enlarged pituitary measuring 1.3 cm × 1.7 cm × 1.4 cm.
Results and treatment
Based on the investigations, a diagnosis of pituitary hyperplasia secondary to primary hypothyroidism was made and levothyroxine was initiated. She remained poorly compliant with levothyroxine and at 9-month follow-up her TSH had decreased to 13.9 mIU/L, MRI demonstrated a normal-sized homogeneous pituitary gland that measured 7.5 mm in maximal height. At 18 months TSH was 4.11 mIU/L, T4 13.5 pmol/L, prolactin 10.6 ug/L and pituitary MRI was stable.
Conclusions and points for discussion
A diffusely enhancing sellar mass may be due to pituitary hyperplasia or inflammatory/infiltrative disorders. In primary hypothyroidism, lack of feedback to the hypothalamus leads to increased TRH secretion and thyrotroph hypertrophy[1]. Pituitary hyperplasia is reported in 25–81% of patients with untreated primary hypothyroidism and can develop within weeks of the onset of hypothyroidism[2,3]. Clinical features may include signs of hypothyroidism, optic nerve compression, headaches, menstrual irregularity and galactorrhea; goiter is uncommon[4]. Hyperprolactinemia is thought to be due to the stimulatory effect of TRH on lactotrophs or inhibition of dopamine effect on prolactin release[4]. Thyrotroph hyperplasia can resemble an adenoma radiographically, which may result in inappropriate treatment with dopamine agonists or surgery[3,4]. Thyroid hormone replacement rapidly shrinks hyperplasia[1,4,5]; however, surgery is indicated in compressive symptoms or nonresponse to levothyroxine therapy[4,6,7].

DOI: 10.1530/endoabs.62.P02

P03

Secondary Takotsubo syndrome induced by Phaeochromocytoma

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Case history
We present the case of a 70-year-old female who presented to the Emergency Department with sudden onset inter-scapular and upper abdominal pain. She had been experiencing intermittent headaches, palpitations and constipation which had not previously been investigated. The only past medical history was of hypothyroidism. She had no significant family history. There was a discrepancy in the blood pressure between both arms. Admission blood pressure was elevated at 146/88 mm Hg on the left and 120/80 mm Hg on the right.
Investigations
Admission ECG showed ST depression in the inferolateral leads. Troponin T was elevated (488 ng/l; normal <14) but other baseline bloods were normal. An urgent CT aortic angiogram was arranged which showed no evidence of dissection but an incidental left adrenal partially cystic mass of 7.4 × 7.3 cm. Echocardiogram revealed no left ventricular hypertrophy but a severely hypokinetic basal inferior segment with severe mitral regurgitation. Urgent angiogram showed normal coronary arteries. Interestingly, repeat troponin T assay 48 hours later had reduced markedly to 246 ng/l. Endocrinology review was sought and further investigations revealed elevated plasma metadrenaline >9000 pmol/l (normal range <510), normetadrenaline >40000 pmol/l (<1180), and 3-methoxytyramine 1732 pmol/l (<120). 24 hour urinary catecholamines were also significantly raised, with volume 1856 ml, normetadrenaline 95.1 umol/24 h (normal <3.3), metadrenaline 21 umol/24 h (0.1–1.2) and methoxytyramine 5.36 umol/24 h (normal <2). Aldosterone-renin ratio and 1 mg overnight dexamethasone suppression test were normal. MIBG scan showed increased uptake in the left adrenal gland consistent with a diagnosis of phaeochromocytoma.
Results and treatment
Phenoxybenzamine was initiated and titrated to 30 mg twice daily which improved her symptoms. She went on to have a successful laparoscopic adrenalectomy with no perioperative complications. Histology confirmed adrenal phaeochromocytoma with necrotic area and no obvious malignancy. Patient is awaiting a repeat echocardiogram, cardiac MRI and genetic work up.
Conclusions and points for discussion
Takotsubo syndrome mimics an acute coronary syndrome with ischaemic ECG changes, myocardial enzyme elevation, chest pain and echocardiographic abnormalities. Coronary angiogram is usually normal. Increased catecholamine release due to phaeochromocytoma is a recognised trigger, although rare. Other cardiovascular manifestations of phaeochromocytoma include myocardial infarction, arrhythmia and cardiac failure. Secondary takotsubo syndrome due to phaeochromocytoma should be considered especially in the context of normal coronary arteries and treatment resistant hypertension.

DOI: 10.1530/endoabs.62.P03

P04

Phaeochromocytoma presenting as an adrenal haemorrhage

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Case history
We present the case of a 72-year-old lady who presented to the surgical team with sudden onset abdominal (flank) pain. On initial assessment, she was significantly

hypertensive (213/110 mmHg) and tachycardic (pulse 98 bpm) but afebrile. She was not on any anticoagulation. On physical examination, her abdomen was tender with mild guarding and retroperitoneal tenderness.
Investigations
Admission blood tests showed a normal haemoglobin (149 g/l), normal clotting profile, renal function, liver function tests and calcium. Serum amylase was not raised. Urine dip stick showed no evidence of infection with no blood. Urgent CT scan of the abdomen revealed a 4.8 cm right adrenal mass with acute haemorrhage (with no evidence of extravasation or active bleeding). Urgent endocrine review on the same day raised the possibility of phaeochromocytoma, hence patient was initiated on phenoxybenzamine. Further investigations revealed elevated 24-hour urinary normetadrenaline (10.65 mmol/24 hr; reference interval 0.1–3.3) and metadrenaline (2.31 umol/24 hr; reference interval 0.1–1.2) but normal methoxytyramine level. Plasma normetadrenaline was elevated at 7287 pmol/L (120–1180) and metadrenaline at 596 pmol/l (80–510). Aldosterone and renin were normal (446 pmol/L and 39 mu/l respectively; ratio 12) as was the overnight dexamethasone suppression test (9 am cortisol 38 nmol/L after 1 mg dexamethasone at 11 pm). MIBG scan showed a focal area of increased uptake in the region of the right adrenal gland with no other lesions.
Results and treatment
Patient was closely followed up in Endocrine clinic and phenoxybenzamine was titrated up to 30 mg twice daily. Propranolol was added later to the regimen. Her blood pressure significantly improved (126/66 mmHg). Consequently, she underwent a laparoscopic adrenalectomy and tissue biopsy confirmed phaeochromocytoma. Patient has been referred for a full genetic work up.
Conclusions and points for discussion
Spontaneous adrenal haemorrhage is considered to be a rare phenomenon. There are very few cases in literature where the first presentation of phaeochromcytoma is a haemorrhagic adrenal gland presenting as an acute abdomen. Adrenal phaeochromocytoma rupture leading to intraperitoneal haemorrhage and shock can be fatal. Proceeding to surgery with an occult phaeochromocytoma can be catastrophic, therefore a high index of suspicion is required for pre-operative acute diagnosis. Urgent involvement of a multidisciplinary team is advised. Our case demonstrates that imaging is the most useful investigation for diagnosis, whilst medical optimisation followed by elective surgery is the best definitive treatment.

DOI: 10.1530/endoabs.62.P04

P05

A rare cause of hyponatraemia

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Case history
We describe a case of 35 year old female who presented with abdominal pain, nausea and lower backache. She was initially treated with Trimethoprim for a urinary tract infection. 5 days later, she re-attended hospital with feeling more unwell, ongoing lower abdominal pain and vomiting. On examination, she was haemodynamically stable. She had suprapubic tenderness on abdominal palpation, and the rest of her systemic examination was normal.
Investigations
Biochemistry showed significant hyponatraemia of 122 mmol/l. Her inflammatory markers and renal function were normal. Her Chest X-ray did not show any abnormalities. Cortisol and Thyroid function tests were also satisfactory. Abdominal CT scan showed dilated bowel loops suggestive of ileus. She was started on intravenous fluids (0.9% saline) and her sodium dropped to 115 mmol/l. His serum osmolality was 251 mmol/kg, urine osmolality 383 mmol/kg and urinary sodium was 78 mmol/l. He required an infusion of 1.8% Hypertonic saline on the intensive care unit. Her sodium incremented to 121 mmol/l in 24 hours.
Results and treatment
Although patient's clinical history suggested dehydration, her serum and urine biochemistry revealed a degree of fluid overload with SIADH. This prompted the team to investigate for porphyria given the abdominal symptoms. Fluid restriction was commenced along with a urinary porphyria screen. Her sodium improved transiently with fluid restriction, but dropped again in the next few days to 115 mmol/l. She started having more back pains then. By that time, her urinary porphobilinogen/creatinine ratio result came back elevated at 93.1 µmol/mmol (NR 0-15), confirming the diagnosis of Acute Intermittent Porphyria. She was treated with IV Haeme arginate (Hemin) for 4 consecutive days and glucose loading. This improved her serum sodium gradually.
Conclusions and points for discussion
Hyponatraemia is common in acute intermittent porphyria, due to SIADH or gastrointestinal/renal sodium loss. The diagnosis of AIP is challenging due to non-specific symptoms, a wide list of differentials and unfamiliarity of many clinicians with appropriate testing and interpretation of results. Our case highlights the importance of keeping a high index of suspicion for acute porphyrias, in the evaluation of young patients with unexplained hyponatraemia and abdominal pain. Early diagnosis and treatment of symptomatic AIP can prevent long-term and life-threatening complications. Avoiding exacerbating factors (medications, diet and hormonal changes) plays an important role in preventing future attacks, and also in treating acute attacks. Advice from specialist porphyria services is available to clinicians 24/7.

DOI: 10.1530/endoabs.62.P05

P06

Unexpected free thyroid hormone results in a case of an incidental pituitary macroadenoma

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Case history
We present the case of a 64 year old man with an incidental finding of pituitary macroadenoma (1.1×0.8×0.5 mm). He had a past medical history of obstructive sleep apnoea, asthma, osteoarthritis, hypertension, retinal detachment and cataract.
Investigations
Blood tests.
Results and treatment
Pituitary function tests showed markedly elevated prolactin 4272 mIU/L (86–324), elevated free tri-iodothyronine (fT3) 18.2 pmol/L (3.1–6.8) and free thyroxine (fT4) 42.5 pmol/L (12.0–22.0) with a non-suppressed thyroid stimulating hormone (TSH) 1.08 mIU/L (0.27–4.20). Macroprolactin was not present in significant amounts. Repeat free thyroid hormones showed similarly elevated levels and a normal TSH. The patient was clinically euthyroid with no evidence of goitre or thyroid orbitopathy. There was no past medical or family history of thyroid disease, intercurrent (non-thyroidal) illness and medication usage including thyroxine, heparin, amiodarone. As the clinical picture was consistent with prolactinoma rather than a TSHoma or thyroid hormone resistance, we suspected assay interference. This was confirmed when free thyroid hormones were measured at another laboratory using different assays. The initial thyroid function tests were analysed with a Roche cobas analyzer and repeat tests showed free T3 3.25 pmol/L, free T4 10.4 pmol/L and TSH 0.81 Miu/L with an Abbott Core Immunoassay Analyzer.
Conclusions and points for discussion
We present a case of incidental prolactinoma and discordant thyroid function tests. It is important to consider the clinical context. Although TSH-oma and thyroid hormone resistance may have fit the biochemical picture, absence of overt manifestations of thyrotoxicosis made assay interference more likely. Correctly identifying assay interference avoided unnecessary further investigations.

DOI: 10.1530/endoabs.62.P06

P07

Hyperglycemic Diabetic ketoacidosis precipitated by an SGLT-2 inhibitor in a non-insulin dependant type 2 diabetic

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Case history
We present the case of a 51-year-old female of South-East Asian origin presenting with a four-day history of feeling progressively unwell with vomiting, reduced oral intake and urinary symptoms. Her past medical history was T2D (HbA1c 98 mmol/mol March 2018). Drug history on admission was Metformin 500 mg twice daily, Gliclazide 160 mg twice daily, Ramipril 1.25 mg once daily and Dapagliflozin 10 mg once daily. The initiation date of Dapagliflozin and Ramipril coincided with the start of her symptoms.
Investigations
Blood tests (biochemistry, haematology), blood cultures, urine culture.
Results and treatment
The patient was septic on admission with a metabolic acidosis (pH 7.28, lactate 1.7 mmol/L, HCO3 14.8 mmol/L, glucose 21.5 mmol/L, base excess −10.8 mmol/L) with blood ketones 5.6 mmol/L. Anti-GAD antibody negative with a random paired insulin C-peptide 350 pmol/L and glucose 5.3 mmol/L. She was started on a fixed rate insulin infusion 5.8 units/hour and the Dapagliflozin stopped. Blood and urine cultures were positive for Escherichia coli fully sensitive to co-amoxiclav (treatment started).
Conclusions and points for discussion
Dapagliflozin is a sodium glucose cotransporter 2 inhibitor (SGLT-2i). SGLT-2i's improve glycaemic control and weight loss through increased urinary excretion of glucose. The association with DKA has been reported in insulin dependent T2D. Our patients elevated HbA1C and poor compliance should raise suspicion for

likely insulin deficiency. This coupled with the use of an SGLT-2i increased her risk of developing DKA. Her urinary tract infection further compounded her stress response and progression into DKA. In patients with poor glycaemic control and a long duration of diabetes, consideration should be given to initiating insulin before an SGLT-2i.

DOI: 10.1530/endoabs.62.P07

P08

Immunotherapy: the cause or the cure?

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Case history
A 57 year old man is referred due to repeated admissions with confusion, malaise, hypotension and hyponatraemia. He has a background of metastatic melanoma (brain, liver, lung) for which he had received surgery, whole brain radiotherapy and combined immunotherapy (Ipilimumab and Nivolumab). At the time of referral he was on a maintenance regimen of Nivolumab, the dose of which had been increased just prior to the aforementioned admissions. There was no past medical history of note nor any family history of endocrinopathies.
Investigations
Sodium ranged between 133 to 145 mmol/L prior to the increase in Nivolumab, afterwards it declined to a nadir of 125 mmol/L (at which point the urine osmolality was 361 mmol/kg and urine sodium was 80 mmol/L). Potassium remained within normal range throughout these episodes, as did his eGFR. Short synacthen results: Cortisol 76, 196, 274 mmol/L (time zero, 30 mins and 60 mins, respectively). ACTH15 ng/L TSH 1.08 mU/L, FreeT4 8.5 pmol/L, FreeT3 2.1 pmol/L LH 5.9 IU/L, FSH 11.9 IU/L, Testosterone 14.0 nmol/L, SHBG 72 nmol/L, Free Testosterone (calculated) 158 pmol/L, Prolactin 22 mIU/L MRI pituitary: Isointense/high T1 3 mm nodule behind the attachment of the pituitary stalk with enhancement of the pituitary stalk. High T1 nodules, three in the right temporal lobe, one in left posterior putamen and one in right medial thalamus in keeping with known brain metastases. Historic CT chest and abdomen: No evidence of adrenal abnormality.
Results and treatment
Following the short synacthen results he was initiated on the replacement dose of hydrocortisone (10 mg, 5 mg, 5 mg). This led to a prompt and profound improvement in his symptoms and sodium. Following the receipt of the ACTH result he was started on levothyroxine (50 mcg once daily). The Nivolumab was continued according to the schedule.
Conclusions and points for discussion
Melanoma rarely metastasizes to the pituitary gland, however the MRI appearance in the context of this patient, is suggestive. Given the site of the lesion, we would have expected hyperprolactinaemia.
Hypophysitis has been associated with a number of immunotherapies including Nivolumab, Ipilumumab and other immune checkpoint inhibitors. The timing of the presentation and anterior hypopituitarism is supportive of hypophisitis, although imaging did not show the characteristic changes.
We considered the following possibilities:
1) The coexistence of a pituitary metastasis with radiologically-inapparent hypophysitis
2) Pituitary metastasis which is selectively impairing the hypothalamic signalling to the anterior pituitary whilst sparing the dopaminergic inhibition, the timing with Nivolumab being coincidental
3) Pituitary metastasis with coexistant anterior hypopituitarism due to radiotherapy.

DOI: 10.1530/endoabs.62.P08

P09

Chronic diarrhoea - a rare endocrine cause

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Case history
A 59-year-old male presented to gastroenterology with a two years of high volume persistent watery diarrhoea. He gave a past medical history of poorly controlled, insulin treated diabetes mellitus present for 8 years. He reported abdominal pain and diarrhoea that persisted despite fasting. A colonoscopy with biopsy were reported as normal. Diarrhoea, malaise, fatigue and weight loss persisted.
Investigations
Stool culture and faecal elastase were unremarkable. CT imaging revealed a large pancreatic mass involving the body and tail of the pancreas and liver lesions were noted. Tissue diagnosis confirmed an ENETS grade 2 pancreatic NET with strong synaptophysin expression, weak chromogranin A, Cytokeratins positive and Ki67 of 6%. Initial biochemistry: Na 128, K 2.8, Urea 9.1, Creatinine 142. Severe metabolic acidosis pH of 7.14 to 7.19, bicarbonate of 19 with worsening renal function was also noted. Gut peptides revealed Glucagon 48 (0–49 pmol/L), Gastrin 13 (0–39 pmol/L), P Polypeptide >500 (0–299 pmol/L), Somatostatin >1000 (0–149 pmol/L), VI Polypeptide (ViP) 102(0–29 pmol/L), Chromogranin A 130.5(0–6 nmol/L). Octreoscan confirmed avidity with disease limited to the pancreas and liver.
Results and treatment
Management required urgent electrolyte replacement, octreotide, initially given subcutaneously and correction of the acidosis with bicarbonate infusions. Diarrhoea persisted with bowel movements up to 8–10 times. Lanreotide autogel 120 mg injection was also started. Glucocorticoids were commenced to improve syndrome functionality. VRIII was used to maintain normoglycaemia. Transferred to HDU for central line access. To improve his nutritional status total parenteral nutrition was also commenced via PICC line. Electrolytes improved and gradually doses of Octreotide and steroid were weaned. He was sent home self-managing the octreotide, insulin and with ambulatory TPN in the community and for peptide receptor radionuclide therapy. To date he has received two cycles of treatment with Lutetium DOTATE with good response in terms of reduction of VIP levels, cessation of diarrhoea and reduction in tumour load.
Conclusions and points for discussion
ViPOMA is a rare pancreatic neuroendocrine tumour with an annual incidence of 1/10 million. It is also known as pancreatic cholera or the Verner Morrison syndrome or WDHA (watery diarrhoea hypokalaemia and achlorhydria) syndrome.Treatment is to initially prevent death from dehydration but also includes octreotide which inhibits the actions of ViP. Surgery offers cure where disease is localised. Peptide receptor radionuclide therapy which has also been shown to be highly effective.

DOI: 10.1530/endoabs.62.P09

P10

Metabolic encephalopathy secondary to diabetic ketoacidosis

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Case presentation
A 35-year-old man presented to the emergency department (ED) in a confused and agitated state. His past medical history was significant for poorly controlled type 1 diabetes, complicated by background diabetic retinopathy. He was taking basal/bolus insulin and had a history of diabetic ketoacidosis (DKA) eleven years prior. He also had multiple sclerosis however disengaged with neurology services and was non-compliant with interferon therapy. Prior to admission he worked as a caretaker in a school, smoked ten cigarettes per day, took excess alcohol and smoked cannabis twice per week. Following initial investigations, he was found to be in DKA. Unfortunately, despite timely and appropriate management his neurological symptoms and behavioural disturbance persisted.
Investigations
Biochemistry revealed DKA (pH 7.17, blood ketones 8 mmol/L and blood glucose 26 mmol/L). Alcohol levels were undetectable, urine and serum toxicology screens were negative. Excluding ketosis, acidosis and hyperglycaemia there were no significant abnormalities in other biochemical or haematological investigations. HbA1c was 70 mmol/mol (8.5%). Analysis of cerebrospinal fluid (CSF) on the second day of admission revealed an elevated protein at 61 mg/dl with normal glucose 6.3 mol/L, erythrocytes 86 u/L and leucocytes 1/uL. Serum and CSF extended viral PCR was negative. Neuroimaging revealed temporal lobe abnormalities consistent with an encephalopathic process. The patient underwent extensive investigation looking for evidence of autoimmune, infective, metabolic, toxic and paraneoplastic encephalopathy, with no obvious cause demonstrated. Temporal lobe biopsy showed marked astrocytic gliosis without evidence of vasculitis, inflammation, infarction or neoplasia. Electroencephalogram was consistent with an encephalopathic process. A diagnosis of metabolic encephalopathy secondary to DKA was reached.
Results and treatment
In addition to his initial treatment for DKA followed by basal/bolus insulin, the patient was also given high dose intravenous thiamine and a reducing regimen of chlordiazepoxide. He received empiric antiviral treatment and folic acid supplementation. Subsequent treatment was largely supportive, involving a multidisciplinary team of occupational therapy, physiotherapy, social care and neuropsychology. Despite neuro-rehabilitation, the patient's cognitive function remained impaired up to 18 months post presentation and he ultimately required residential care.
Conclusion and points for discussion
DKA poses a serious and significant neurological risk to patients with diabetes mellitus. To our knowledge this is the second case report of metabolic encephalopathy

as an acute complication of DKA. The aims of this report are to highlight metabolic encephalopathy as a complication of DKA and to explore the current research in diabetic related brain injury.

DOI: 10.1530/endoabs.62.P10

P11

A rare case of co-existing Thyroid Hormone Resistance and Graves' disease

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Case history
A 52 year old lady presented to her GP with a 2 year history of headaches, anxiety and loose stools. The GP found lid retraction and fine tremor but no goitre. Her heart rate was 100. Her GP sent blood for thyroid function tests and results showed a TSH of <0.03 mu/l and free T3 of >30.8 pmol/l. She was started on propranolol 40mg thrice daily and referred to endocrinology. In clinic she described palpitations whilst watching TV and sweatiness. She had suspected she had lost weight over two years. She had no eye symptoms. Her only past medical history was depression and she was only on propranolol. Her sister and son had been diagnosed with Thyroid Hormone Resistance (THR). On examination she had mild smooth enlargement of her thyroid and no thyroid bruit. Her heart rate was 72 bpm. She had mild lid retraction and mild proptosis of her right eye with no diplopia. Her propranolol was decreased to 40 mg twice daily and she was started on carbimazole 30 mg once daily.
Investigations
TFTs on follow-up three months later in clinic demonstrated an improved T3 of 11.0 pmol/l and her TSH remained suppressed at <0.03 mu/l. Ultrasound of the thyroid showed overall appearance in keeping with Graves' disease and an 8 mm nodule in the right lobe. A thyroid uptake scan showed borderline diffuse enlargement of the thyroid with diffuse symmetrical uptake throughout. Thyroid receptor antibodies were raised at 0.8 U/l (0–0.4). Alpha subunit levels were normal at 1.15 iu/l (0–3).
Results and treatment
The carbimazole dose was slowly titrated downwards and 4 years later was stopped. This lady's symptoms settled within a few months of starting carbimazole. Her TSH rose into the reference range within 5 months of treatment starting and remained in range. Her free T3 remained elevated and seemed to respond to the changes in carbimazole dose, settling at $\sim$10 pmol/l once treatment had finished. Her free T4 remained $\sim$30 pmol/l throughout.
Conclusion and points for discussion
This lady has strongly suspected Thyroid Hormone Resistance (genetic testing results awaited) and this case demonstrates the challenges when THR presents alongside Graves' disease. TSH at presentation was suppressed despite the THR due to the extreme thyroid hormone levels overcoming the thyroid hormone resistance. TFTs need to be taken in context and elevated levels accepted with the dosage of carbimazole titrated according to the patient's symptoms.

DOI: 10.1530/endoabs.62.P11

P12

Macro-TSH as a cause of spuriously raised TSH in a euthyroid patient

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Case history
A 28-year-old gentleman was referred with symptoms of memory fog, difficulty with concentration, mood disturbance and fatigue. His thyroid function tests had been stable but abnormal for over 8 years, with a normal FT4 between 17–19 pmol/l (12–22 pmol/l), FT3 5.6 pmol/l (3.1–6.8 pmol/l) and an elevated TSH between 12–16 mu/l (0.27–4.2 mu/l). He had no family history of thyroid disease. He was clinically euthyroid. His weight had remained stable over the years and he had a pulse rate of 70 bpm. Clinical examination of his thyroid was normal.
Investigations
Further investigations showed that his thyroid peroxidase antibody titre was negative, and his SHBG concentration and anterior pituitary function tests were normal. A differential diagnosis of assay interference or thyroid hormone resistance was considered. A sample was sent to the reference laboratory at Addenbrooke's Hospital, Cambridge.
Results and Treatment
Blood results from Addenbrooke's Hospital showed good agreement with local assay methods, however, there was low PEG recovery in the DELFIA assay indicating the possible presence of macro (antibody-bound) TSH. There was a comment that TSH results may be unreliable in this patient. This fitted with the clinical impression, and he was discharged with a recommendation that his FT4/FT3 should be used to assess his thyroid status if there was any future concern. Alternative causes for his symptoms were explored.
Conclusion and points for discussion
This patient's raised TSH was due to assay interference from macro-TSH. Macro-TSH is caused by combinations of TSH and anti-TSH autoantibodies forming macrocomplexes. It has low bioactivity. Macrocomplexes as a cause of assay interference have been best described with respect to prolactin (macroprolactin). This phenomenon is less familiar with TSH, but is not that uncommon. Estimates of prevalence range from 0.6% in a study of 463 samples sent for routine analysis and found to have a TSH$>$10 mu/l, to 1.62% in 681 samples from patients with subclinical hypothyroidism. As TFTs (particularly TSH) are checked in many millions of the UK population annually, this is probably an under-recognised phenomenon. It is important to be aware of macro-TSH to prevent patients undergoing inappropriate investigations and treatment.

DOI: 10.1530/endoabs.62.P12

P13

Extensive intracranial calcification in a patient with hypoparathyroidism

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Case history
A 74 years old gentleman with no medical illness presented with loss of consciousness in March 2018. CT head did not show acute cortical infarct but there was florid symmetrical calcification involving the basal ganglia, thalami, cerebellar lobes and subcortical white matter within the parietal-occipital lobes bilaterally. Fahr's disease was suspected and an outpatient MRI was requested.
Investigation and Results
2 weeks later, a routine blood investigation with patient's GP note a corrected calcium level of 1.39 mmol/l. Patient was asymptomatic and was admitted for calcium replacement. Vitamin D level was 43, albumin 44, phosphate 1.31, magnesium 0.92 and parathyroid hormone 0.4. In-patient MRI showed bilateral basal ganglia and subcortical white matter calcification, consistent with the findings from the previous CT.
Diagnosis and Treatment
Diagnosis of primary hypoparathyroidism was made. Brain calcification on CT and MRI is most likely due to hypoparathyroidism. Calcium tablets and alfacalcidol was started and the patient's corrected calcium level gradually improved and normalised. The patient was also referred to the cardiology team because of trifascicular heart block on ECG. 24 hours tape showed runs of VT. Diagnosis of tachy-brady syndrome was made and he will likely need a pacemaker if a repeated 24 tape after correction of his calcium level still show arrhythmias. He is also seeing ophthalmology and awaiting cataract surgery. The patient was last seen in the clinic a week ago and his calcium level is in the normal range with calcium and alfacalcidol supplement. His ECG was normal with no heart block. USG KUB did not show nephrocalcinosis.
Conclusion and points for discussion
Hypoparathyroidism must be suspected in a patient with basal ganglia calcifications and calcium level should be checked.

1. There are several features that are unique to chronic hypoparathyroidism. These include the presence of basal ganglia calcifications, cataracts, dental abnormalities, and ectodermal manifestations.
2. Acquired hypoparathyroidism is most often the result of post-surgical or autoimmune damage to the parathyroid glands.
3. Persistent hypocalcemia with a low or inappropriately normal parathyroid hormone level and hyperphosphatemia is, in the absence of hypomagnesemia, virtually diagnostic of hypoparathyroidism.
4. The goals of therapy in patients with hypoparathyroidism are to relieve symptoms, to raise and maintain the serum calcium concentration in the low normal range ((2.0 to 2.1 mmol/l)), and to prevent iatrogenic development of kidney stones.

DOI: 10.1530/endoabs.62.P13

P14

A case of maternal and fetal virilisation

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A baby was born at 32 weeks with a birth weight of 1.59 kg. Mother had complex medical history including diabetes mellitus, chronic hypertension, nephropathy, maculopathy, ischaemic stroke on aspirin, hyperthyroidism and polycystic ovarian syndrome. Antenatal scan showed ambiguous genitalia with clitoromegaly and mother had bilateral adnexal multi-separated cysts. Baby was born by emergency lower segment cesaerean section due to pre-clampsia and biopsy of mother adnexal mass was performed. On examination, baby had clitoromegaly 0.9 cm×0.6 cm and prominent labial minora. Anogenital distance 0.9 cm. No gonads palpable, labial fusion, rugae, nor hyperpigmentation. Anus was patent and other systemic review unremarkable. Urgent karyotype confirmed 46XX. Electrolytes, glucose and newborn screening were normal. Hormonal profile showed normal 17a-OH progesterone (17OHP). Testosterone (TA) ↑4.6 nmol/l. DHEAS was slightly elevated. Ultrasound pelvis showed uterus,cervix and normal bilateral adrenal glands. Mother was also virilised with clitoromegaly and hirsutism over chin, thigh and pubic region. During pregnancy, TA ↑27 nmol/l, DHEAS normal, sex hormone binding globulin (SHBG) >180 nmol/l. In view of maternal virilisation with ↑TA, ↑SHBG but normal DHEAS and bilateral maternal adnexal mass, baby virilization could be due to pregnancy luteoma or hyperrectio luteinalis (HL) or rarely androgen secreting ovarian tumor. On the other hand, baby's condition like P450 oxidoreductase deficiency could cause both baby and maternal virilization but this could not explain maternal bilateral adnexal mass and baby also did not have any skeletal features. Other differential diagnosis such as congenital adrenal hyperplasia (CAH) is less likely as this could not explain maternal features. Histology of mother adnexal mass came back to be corpus luteal cyst of pregnancy. Further discussion with pathologist confirmed it was more compatible with hyperrectio luteinalis. Hence we monitored baby and her mother's blood serially. Baby DHEAS gradually normalized and her TA dropped to 2.1 nmol/l in 1 month and gradually normalised. Mother's TA also fell from 29 nmol/l post-partum to 0.54 nmol/l in 1 month then gradually normalised. HL is a benign, pregnancy related cystic enlargement of the ovaries. Most (66%) occurred in primiparity. Comorbidities include PCOS and thyroid problem. Most had elevated androgen (84%). 30% had maternal virilization and rarely 3.5% had fetal virilization because of the timing of androgen exposure and protective mechanisms such as ↑maternal SHBG, progesterone competing for androgen binding sites, conversion of maternal androgen to estrogen. Nevertheless, HL will resolve after baby delivery and hence warrant a conservative approach.

DOI: 10.1530/endoabs.62.P14

P15

ARDS and life threatening renal failure secondary to severe hypercalcaemia

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Case history
A 54 year old Polish gentleman was admitted to a large northern teaching hospital, with life threatening hypercalcaemia, requiring renal replacement therapy. He presented with extreme fatigue and lethargy, with a significant reduction in mobility and exercise tolerance. Further initial history was hampered by language barrier and an increasingly moribund patient.
Investigations
Base line blood work up revealed stage 3 AKI, with a liver bone profile showing a calcium of 5.06. PTH was then requested showing a level over 300. patient was then referred to the endocrine team. Despite aggressive fluid replacement and IV bisphosphonate treatment, his renal function continued to decline requiring renal replacement. Unfortunately even with renal replacement and falling calcium levels- he developed increased shortness of breath and new oxygen demands- requiring mechanical ventilation. His CXR showed severe ARDS. After a period on ICU he was successfully weaned off the ventilator and stepped down to a ward. Repeat PTH was still nearly 300 and it was thought most likely to be a case of parathyroid malignancy.
Results and treatment
Imaging and uptake scans proved inconclusive- a biopsy did not show any malignancy, and a diagnosis of primary hyperparathyroidism was made. He underwent total Parathyroidectomy- and has had a good recovery- with PTH levels falling to undetectable post-surgery. It later became apparent from his English speaking daughters that he had been taking calcium supplements back in Poland for some time. It is not clear the dose or frequency of the supplements, or whether they were taken in excess. The effects of this supplementation may or may not have contributed to his hyperkalaemia.
Conclusion
It is rare to see such hypercalcaemia and such elevated PTH levels with primary PTHism. We wondered if the initial fluids were the driving force of the ARDS or the hyperkalaemia itself. More evidence is needed to aid treatment and develop fluid regimes in such cases.

DOI: 10.1530/endoabs.62.P15

P16

Solitary myofibroblastoma of the forearm presenting with ectopic β-human Chorionic Gonadotrophin production.

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A 57-year-old woman was referred due to elevated urine & serum human chorionic gonadotrophin (β-hCG) concentrations found at routine pre-operative assessment. She was asymptomatic and was not pregnant. Her past history included a long standing benign 7 cm×5 cm myofibroblastic mass in her left forearm asthma, rotator cuff tear and a uterine fibroid. Her medications were cyclical norethisterone, lansoprazole, frusemide & inhalers. The left forearm mass was not associated with any neuromuscular or vascular compromise. Clinically, she was eupituitary with intact visual fields. Her serum β-hCG level was elevated to 202 IU/l (non-pregnant values <5 IU/l) and serial dilutions as well as PEG precipitation had shown no evidence of analytical interference. Her pituitary profile was normal other than slightly raised gonadotrophins (FSH 27 IU/l (post menopausal range >30 IU/l), LH 21 IU/l (post menopausal range >30 IU/l) and oestradiol 145 pmol/l (post menopausal range <183 pmol/l). A CT Chest, Abdomen & Pelvis and MR pelvis only showed multiple benign fibroids with no suggestion of a germ cell tumour. Endometrial biopsy showed no evidence of malignancy. MR left forearm done at yearly intervals over 3 years showed a stable soft tissue mass encasing the anterior & posterior compartment. An initial biopsy was suggestive of benign mesenchymal lesion. β-hCG staining carried out 3 year later was positive. Ki67 showed no proliferation.
Discussion
β-human chorionic gonadotrophin is chiefly produced by the placental trophoblasts & is mainly used to diagnose pregnancy. Ectopic β-hCG can also be elevated in certain conditions such as pituitary human chorionic gonadotropin (hCG) production, trophoblastic disease, choriocarcinoma, teratomas, germ cell tumours, and sarcomas. β-hCG is also described in literature as an oncogene and depicts worse outcomes in colorectal cancers. As a tumour marker it is also used for its prognostic value and monitoring of therapeutic response to treatment. Ectopic β-hCG secretion has rarely been reported in benign mesenchymal tumours and usually seen in more high grade sarcomas. Excisional surgery in this case would result in major loss of function of her left arm due to extensive locally invasive nature. Thus it is currently being monitored with regular scans. Whether β-hCG positivity in the absence of local proliferation and distant malignant disease and should prompt surgery remains to be determined.

DOI: 10.1530/endoabs.62.P16

P17

Self-diagnosis of De la Chapelle syndrome

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Case history
A 30 years old male Caucasian had his saliva tested on a self-funded commercial DNA testing to identify his ancestral roots. The markers for Y chromosome were found to be absent and further evaluation revealed him to have 46 XX karyotype.This was consistent with the diagnosis of De la Chapelle syndrome or XX male syndrome. Fluorescence *in situ* hybridization (FISH) studies confirmed the presence of SRY (sex determining region Y) gene which was responsible for his male phenotype. In view of the symptoms of hypogonadism he was referred to our endocrinology clinic for further investigations and management. He described himself as generally fit and well but struggled to manage his weight despite going to the gym regularly. He had a difficult time with bullying at school. Puberty was achieved at around age 14 but he had concerns over the years regarding his development in comparison to other boys of a similar age. On examination he was obese with BMI of 49.9 kg/m^2. He had sparse pubic and axillary hair and bilateral gynaecomastia. Scrotal sac was small with only left testis palpable which was about 3 ml in size. The right testis was absent and his penis was small. Rest of the systemic examination was unremarkable.
Investigations
Testosterone level 6.2 nmol/l (normal range: 8.0–30.0); Follicle stimulating hormone (FSH) – 20.3 IU/l (normal: 1.0–12.0), Luteinising Hormone (LH) – 9.9 IU/l (normal: 1.0–9.0). Oestradiol was 122 pmol/l (normal: <160). Thyroid function test, prolactin and insulin like growth factor (IGF-1) were normal. Testicular ultrasound showed small left testis measuring 25×10×22 mm but right testis was absent in the scrotal sac as well as inguinal canal. MRI pelvis confirmed that there was no testicular tissue along the course of the right inguinal canal or within the right sided retroperitoneum.
Treatment
He was commenced on topical testosterone with Testogel 50 mg daily which markedly improved his hypogonadal symptoms as well as his serum testosterone. He had an improvement in energy levels, libido and facial hair growth.

Conclusions and Discussion points
De la Chapelle syndrome is a rare cause of hypogonadism. Commerical DNA testing is becoming increasingly common. (1) Is there a need to regulate this industry? (2) What is the best management strategy to address all the issues in XX male syndrome?

DOI: 10.1530/endoabs.62.P17

P18

A rare cause of hypercalcemia and nephrolithiasis

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We present a 67 years old male originally from Cyprus who presented with Hypercalcemia. He had renal calculi twice and required Laparoscopic procedure. In his family history his 3 siblings had confirmed raised calcium and PTH and 2 other siblings had renal calculi. One of his brother, had surgery for primary hyperparathyroidism twice but no parathyroid adenoma was found and his calcium remained high. Patients' calcium was 2.81 mmol/l (2.15–2.50), 25 HVD 82 nmol/l (75–200), 1,25 hydroxy vitamin D was 119 pmol/l (43–143) and PTH on 2 occasions was <0.7 pmol/l (1.1–6.9). He had hypercalciuria. His parathyroid imaging was normal. His genetic test did not identify mutations in dominant HPT panel. He had Homozygous mutations in CYP24A1C.1186C>T_p.Arg396Trp. CYP24A1 is an enzyme that inactivates vitamin D. Loss-of-function mutations in this enzyme is rare but clinically, two distinct phenotypes have been recognised from this mutation: 1) Infants with CYP24A1mutations present with infantile idiopathic hypercalcaemia, often precipitated byrophylactic vitamin D supplementation. 2) A separate phenotype of nephrolithiasis, hypercalciuria and nephrocalcinosis often presents in adulthood. CYP24A1 mutation should be suspected when a classical biochemical profile of high active vitamin D metabolites, high or normal serum calcium, high urine calcium and low parathyroid hormone is detected. 65% of patients with hypercalciuric nephrolithiasis may have a positive family history with polygenic or monogenic inheritance. CYP24A1 mutation is now included as a new monogenic etiology of hypercalciuric nephrolithiasis with hypercalcemia and normal/low PTH. 25-OH-D3:24, 25-(OH)2D3 ratio greater than 50, and usually greater than 80, is indicative of inactivating CYP24A1 mutations. Restriction of vitamin D and sun protection might protect affected patients. Vitamin D supplementation can be deleterious in these patients. Ketoconazole/fluconazole, a nonspecific inhibitor of P450 enzymes can reduce 1, 25-(OH) 2D3 levels by inhibiting 1α-hydroxylase, the enzyme responsible for its production. Although CYP24A1mutations are rare, early recognition can prompt definitive diagnosis, ensure treatment and avoid parathyroidectomy. We suggest that it is clinically important to identify patients with this phenotype.

References

Schlingmann KP1, Kaufmann M, Weber S, Irwin A, Goos C *et al.*; Mutations in CYP24A1 and idiopathic infantile hypercalcemia. *N Engl J Med.* 2011365(5): 410-21. A. Molin R. Baudoin M. Kaufmann J. C. Souberbielle *et al.*; CYP24A1 Mutations in a Cohort of Hypercalcemic Patients: Evidence for a Recessive Trait. *The Journal of Clinical Endocrinology & Metabolism*, 100(10), 1 October 2015.

DOI: 10.1530/endoabs.62.P18

P19

Two novel mutations in the Calcium Sensing Receptor (CASR) gene in patient s with biochemical investigations suggestive of Familial Hypocalciuric Hypercalcemia (FHH)

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Case history
Case 1: 18-year-old female referred with asymptomatic hypercalcaemia (adjusted calcium 2.69 mmol/l), phosphate 0.96 mmol/l, parathyroid hormone 2.6 pmol/l and total 25 hydroxyvitamin D 37 nmol/l. No evidence of end organ damage. Initial calcium: creatinine clearance ratio 0.0033 but the patient had a vitamin D 24 nmol/l. Case 2: A 53-year-old female referred with asymptomatic incidental hypercalcaemia (adjusted calcium 2.73–2.87 mmol/l), raised parathyroid hormone (7.4 pmol/l), normal vitamin D. Parathyroid imaging at the time suggested parathyroid hyperplasia as an underlying cause. Bone densitometry showed osteoporosis at the spine. The patient was diagnosed with primary hyperparathyroidism and discharged. She was referred back to the endocrinology clinic four years later.

Investigations
Ultrasound scan (USS) thyroid and parathyroid, nuclear medicine (NM) parathyroids, repeat calcium: creatinine ratio and subsequent genetic testing for FHH.

Results and treatment
Case 1: Normal USS and NM parathyroid scan, calcium: creatinine clearance ratio 0.0106 (normal vitamin D). Genetic testing revealed a G to A nucleotide substitution in Exon 7 of calcium-sensing receptor gene (CASR) (c. 1979G>A) which is predicted to result in replacement of the amino acid cysteine with tyrosine at residue 660 (p. Cys660Tyr). Case 2: US thyroid and parathyroid - all four parathyroids similar in size with measurements of right superior 4×4×3 mm, right inferior 4×3×3 mm, left inferior 4×3×2 mm and left superior 5×4×3 mm. Parathyroid hyperplasia more likely than adenoma. Genetic analysis of CASR (Exons 2–7) found a C to G nucleotide substitution in exon 7 of CASR (c. 2617C>G), which is predicted to result in replacement of the amino acid arginine with glycine at residue 873 (p. Arg873Gly).

Conclusions and points for discussion
We present two cases of FHH with novel mutations in the CASR gene - namely nucleotide substitution in Exon 7 of CASR. Neither variant is present on the Online Mendelian Inheritance in Man (OMIM), Mutation Discovery or 1000 genome databases. FHH is an autosomal dominant genetic condition characterised by usually moderate hypercalcaemia associated with inappropriate PTH and urinary calcium excretion. The patient in case 2 presented with likely parathyroid hyperplasia with FHH. It is often an incidental finding, but rarely patients may experience symptoms of hypercalcaemia (thirst, fatigue, weakness. We have not been able to study other members of the family tree for ethical reasons. Further research is needed to characterize the mutated gene function.

DOI: 10.1530/endoabs.62.P19

P20

Hypercalcemia in pregnancy in a patient with previous miscarriages

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Case history
36 years old, 14 weeks pregnant lady was referred to endocrinology department by GP urgently with corrected Calcium CCa of 2.97 mmol/l and normal parathyroid hormone (PTH). Her symptoms were urinary frequency and nausea. She had 3 previous miscarriages and 2 normal births. She was on folic acid and vitamin D supplements. There was family history of type 2 diabetes and B12 deficiency. Her 6 family members had normal calcium levels.

Investigations
She had high CCa (2.64–2.97 mmol/l) with normal PTH (3.2–5.2 pmol/l) and low phosphate (0.66–0.93 mmol/l). Her vitamin D, renal function and electrolytes including Mg were normal. Her urinary calcium was 1.24 mmol/l in 24 hours.

Results and treatment
Calcium Creatinine Clearance Ratio of 0.0044 was in favour of Familial Hypocalciuric Hypercalcemia but on other hand negative family history made it difficult to diagnose without further investigation. She had her genetic screening for FHH and her case was discussed with genetic lab to prioritise her test and get results in 1–2 weeks (usually takes 8 weeks). Nuclear medicine team at Oxford advised not to do SETSTAMIBI in pregnancy rather consider MRI scan. Opinion was sought from endocrinologists at Hammersmith Hospital about starting her on cinacalcet in order to reduce hypercalcemia related risk in pregnancy and decision was made not to give it as there was no outcome study on its effect in pregnancy. She was seen by ENT, Obstetrician and obstetric anaesthetist so she could have timely parathyroidectomy in case of negative genetic tests. Her genetic screening was heterozygous positive for CASR which gave her a diagnosis of FHH type 1. She was monitored during rest of her pregnancy which remained uneventful. She delivered normally in May 18 and her daughter's calcium levels post birth remained normal at 2.4 mmol/l. Patient was continually involved in decision making throughout the management of her hypercalcemia in pregnancy.

Conclusions and points for discussion
Hypercalcaemia during pregnancy is not very common and can result in foetal morbidity and miscarriages. If it is due to primary hyperparathyroidism, guidelines suggest parathyroidectomy if CCa is >2.75 mmol/l which is considerably lower than usual cut off of 3 mmol/l in non-pregnant patients. If surgery is needed the best time is the second trimester as general anaesthesia is safer. When a pregnant patient is diagnosed with hypercalcaemia all the efforts should be done to make the right diagnosis as quickly as possible and plan the management properly.

DOI: 10.1530/endoabs.62.P20

P21

An atypical presentation of subclinical spontaneous pituitary apoplexy

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Case history
A 34-year-old man attended the emergency department with a history of sudden onset severe headache associated with vomiting, neck stiffness mild photophobia not relieved with analgesia. He reported a past medical history of hypertension treated with angiotensin-converting enzyme inhibitor (ACEi). There was no focal neurology, and his observations were unremarkable - blood pressure 121/64 mmHg, heart rate 54 beats per minute, respiratory rate 14 breaths per minute. His visual acuity was well preserved - right eye 20/32 -3/7 and left eye 20/20 -2/9.
Investigations
Computed tomography (CT) head, magnetic resonance imaging (MRI) pituitary, routine biochemistry and haematology. His blood tests revealed an adrenocorticotropic hormone (ACTH) 417 ng/L, follicular stimulating hormone 4.8 IU/L (1.3 – 19.3), luteinising hormone 2.2 IU/L (1.2–8.6), insulin-like growth factor 1 22.8 nmol/L (13 – 50), serum prolactin (PRL) 9 miU/L (56 – 278), free thyroxine 3.8 pmol/L (8.4–19.1), thyroid-stimulating hormone 3.07 miU/L (0.38–5.33).
Results and treatment
Initial CT head reported an expanded sella turcica with the suggestion of an exogenous mass. A dedicated MRI pituitary confirmed a large supra-sellar mass lesion consistent with a pituitary macro-adenoma elevating and compressing the central part of the optic chiasm. There was bilateral mass effect on the cavernous sinuses with encasement of the cavernous portion of the internal carotid artery suggesting early invasion of the cavernous sinuses bilaterally with the possibility of a haemorrhagic component. The patient was initiated on oral hydrocortisone 10/5/5 mg which was later converted to prednisolone 5 mg once a day; levothyroxine 75 mcg once a day was also started. The patient was referred for urgent neurosurgical intervention as per the Society of Endocrinology guidance for management of Pituitary Apoplexy.
Conclusion and points for discussion
Spontaneous pituitary apoplexy (PA) typically presents with partial or complete pituitary hormone deficit (usually ACTH deficiency). As seen in our patient, isolated low serum prolactin might be the only manifestation. It is essential to exclude pituitary lesions in patients with borderline clinical signs and symptoms. Initial management involves the assessment of hypothalamic-pituitary-adrenal axis and indications for urgent surgical decompression. Spontaneous pituitary apoplexy is a rare and life-threatening endocrine emergency. It is caused by infarction of the pituitary gland (haemorrhagic or ischemic) and is most commonly associated with an existing macroadenoma. Early recognition and a high degree of suspicion are particularly important in patients with no known underlying pituitary adenoma. Timely identification of PA will reduce morbidity and mortality in these patients.

DOI: 10.1530/endoabs.62.P21

P22

A rare variant of Hashimoto's thyroiditis

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Hashimoto's thyroiditis (HT) is the most common inflammatory condition of the thyroid gland. In addition to the classic variant of HT, several other subtypes have been identified, such as the fibrous variant (HTFV).
Case history
A 38 years old man noticed a rapidly enlarging lump in his neck month ago. This resulted in discomfort with choking sensation and mild dysphagia. He mentioned weight loss, tiredness and night sweats. He was a smoker and drank alcohol in moderation. He had no other past medical history. On examination he had palpable hard thyroid mass. The USS of the neck showed diffusely enlarged thyroid gland, with uniform alteration in echotexture. There was strikingly mixed reflectivity. The thyroid capsule was intact, with no infiltration into the overlying muscles. The most likely diagnosis was thought to be amyloid goitre. Patient had a core biopsy of the thyroid. CT scan of the neck and thorax confirmed diffusely enlarged thyroid with heterogenous enhancement with no retrosternal extension. There was no significant tracheal deviation or narrowing. His Thyroid function tests showed primary hypothyroidism with FT4 of 6.2 pmol/l (10.8–25.5), FT3 1.7 pmol/l (3.1–6.8) and TSH of >100 mU/l (0.27–4.20). His C reactive protein was 71 mg/l (0–5). He had high titres of Thyroid peroxidase antibodies 1779 IU/ml (0–109) and TSH receptor antibodies were negative. The core biopsy showed marked fibrosis with lymphocyte, eosinophil infiltartes. Immunochemistry showed B and T lymphoid infiltrates with a large population of plasma cells. Features were suggestive of Reidel's thyroiditis but there was no significant expression of IgG4 within the plasma cells. This is usually high in Reidel's thyroiditis. A diagnosis of Fibrous variant of Hashimoto's thyroiditis was made and that would fit with high TPO antibodies. The fibrosclerotic process is the key feature of several thyroid diseases like Reidel's thyroiditis (RD). Differential diagnosis between HTFV and RT is based on histological criteria established by Beahrs *et al*. In HTFV the fibroinflammatory process involves a part or whole gland and it does not include the adjacent tissues. In conclusion, this case shows that the differential diagnosis between HTFV and RD is difficult due to the partial clinical and morphological overlapping and the poor efficacy of conventional cytology as well as presurgical biopsy.
Reference
G. Iannaci, R. Luise, P. Sapere, V. *et al*. Fibrous Variant of Hashimoto's Thyroiditis as a Diagnostic Pitfall in Thyroid Pathology. Case reports in Endocrinology 2013.

DOI: 10.1530/endoabs.62.P22

P23

Pancreatic lesions in von Hippel–Lindau (vHL) disease: A diagnostic and management challenges

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vHL disease is commonly inherited in an autosomal dominant fashion. Pancreatic lesions in vHL are generally asymptomatic or associated with mild nonspecific symptoms.
Case history
A 40 year old Asian female was seen in genetic/endocrine clinic for Predictive vHL mutation. She was married to her first cousin and had a 19 years old daughter. Her sister was diagnosed with vHL in Canada. She presented with Renal cell carcinoma and renal cysts. Her mother died at the age of 57 due to kidney problems in Pakistan. Patients' genetic test showed mutation in vHL gene. Her abdominal USS showed multiple cysts of different sizes throughout the pancreas. MRI pancreas showed numerous simple cysts with no contrast enhancement. Findings were suggestive of multiple cystadenomas. Her 19 years old daughter was also vHL mutation positive. Her USS showed multiple cysts in pancreas and a 1.5 cm solid mass in the head of pancreas. MRI scan showed a well defined heterogenous 2.6 cm mass in the head of pancreas suggestive of neuroendocrine tumour (NET) and rest of the cysts were cystadenomas. FDG PET scan of the same lesion showed 3 cm increased uptake suggestive of a NET. She had surgical resection. There are a number of different pancreatic pathologies associated with vHL disease. True cysts are the most common and are multiple. Serous Cystadenoma (SCAs) are well-delineated usually multiloculated lesions. NETs are typically nonfunctional, multiple, and located throughout the pancreas. Lesions are usually hypervascular. These may behave malignant may present with metastases. Metastatic Renal Cell Carcinoma and Pancreatic adenocarcinomas are rare findings in vHL.
Recommended follow-up for suspected NETs in vHL by Libutti *et al*.
≤ 1 cm Follow up every 12 months with CT or MRI
1–3 cm Case-by-case assessment
>3 cm If symptomatic or functional or increasing size offered resection
Treatment recommendations for NETS in vHL
Prognostic criteria:
Ø Tumor size $\geq$ 3 cm
Ø Mutation in exon 3
Ø Tumor doubling time $\leq$ 500 d
None of the criteria
Ø Followed by CT/MRI every 2–3 yr
1 criterion: Followed by CT/MRI every 6–12 months
2 or 3 criteria: Consider surgical intervention
Treatment strategy in patients with the metastatic disease is still controversial.
Conclusion
Pancreatic lesions in vHL are common (60%). Asymptomatic lesions can often be identified prior to the development of other manifestations of the disease. Incidence of simple cysts 47%, SCAs 11% and NETs 15%. NETs may undergo malignant transformation. Patients with small NETs should be followed up and larger lesions should be resected.

DOI: 10.1530/endoabs.62.P23

P24

First paraganglioma identified on surveillance screening in an asymptomatic SDHA germline mutation carrier

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Case history
We present the case of a 72-year-old female who was referred to the endocrinology service following the identification of a pathogenic germline mutation in the *SDHA* gene (c.91C>T, p.Arg32*) as part of a genetic panel for hypertrophic cardiomyopathy. There was no personal or family history of phaeochromocytoma or paraganglioma (PPGL), gastrointestinal stromal tumours or pituitary adenoma.
Investigations
Our patient was reviewed in our specialist *SDH* clinic and underwent surveillance screening including assessment of metanephrine levels and non-contrast MR imaging (skull base to pelvis). She reported no symptoms of catecholamine excess and was normotensive (BP 134/62 mmHg, HR 78 bpm) on 150 mg Irbesartan. 24 hour urinary metanephrines were within the reference range: normetadrenaline 1681 nmol/24h (<4400 nmol/24h), metadrenaline 795 nmol/24h (<2000 nmol/24h) and 3-methoxytyramine 950 nmol/24h (<2500 nmol/24h). Non-contrast MRI revealed a 3 × 3.6 cm lesion at the left carotid bifurcation, consistent with a carotid body paraganglioma. No other *SDH*-related lesions were identified on imaging.
Results and treatment
Due to the patients' comorbidities of cardiomyopathy and primary hyperparathyroidism and the identified lesion being non-secretory, a decision was made for active surveillance. She underwent an interval MRI at six months follow-up which revealed an unchanged appearance of the paraganglioma. She will undergo a further surveillance MRI at a one-year interval from the preceding scan. In the interim, she is undergoing assessment and optimisation by the cardiology team.
Conclusions and points for discussion
It is now widely accepted that patients who carry *SDH* mutations should undergo surveillance screening. The aim of surveillance programmes is for early identification of tumours, recurrence, and metastases to allow timely intervention. As genetic testing is becoming more accessible, cascade genetic testing is leading to the identification of increasing numbers of asymptomatic familial carriers. These asymptomatic individuals should be entered into surveillance screening programmes to allow early detection of PPGLs and other associated lesions. The modality and frequency of this surveillance however is still controversial. *SDHA* mutations are less common than *SDHB* and *SDHD* mutations and therefore there are fewer reported cases and a limited understanding of the best surveillance for these individuals. To our knowledge, we report the first case of a surveillance screen detected PPGL to be found in an asymptomatic individual with previously identified *SDHA* mutation status. Previous literature has debated the need for surveillance screening in *SDHA* carriers due to estimated low penetrance rates. This case highlights the importance of at least an initial surveillance screening in all newly identified *SDHA* mutation carriers.

DOI: 10.1530/endoabs.62.P24

P25

Elevation in free T3 following levothyroxine treatment – the clue to a diagnostic challenge

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Case History
We present a 3-week-old baby who presented to a District General Hospital with prolonged unconjugated hyperbilirubinaemia and evolving developmental delay.
Investigations
Initial thyroid function demonstrated a TSH at 2.41 mIU/l (0.8-5.4), free T3 at 7.39 pmol/l (3.40–7.60) and free T4 at 9.9 pmol/l (11.0–23.6). The TFT was repeated using an alternative assay with FT4 at 11.8 pmol/l (11.5–28.3), FT3 at 9.20 pmol/l (3.00–9.30) and TSH at 3.1 mIU/l (0.72–11.0). On referral to the regional paediatric endocrine centre, the low T4 was investigated via a TRH stimulation test. TSH peak reached 5.24 mIU/L with a baseline at 1.94 mIU/L. T4 at the time of testing was 10.9 pmol/l (11.0–23.6). Given the modest rise in TSH in conjunction with a low T4, the patient was treated for secondary hypothyroidism with 25 micrograms levothyroxine. However, remaining pituitary function was normal. Ultrasound scan of the thyroid was normal. T4 normalised to 14.1 pmol/l, with TSH = 0.03 mIU/L and T3 at 7.35 pmol/l. Repeat thyroid function 4 months later showed a similar pattern of TSH and T4 on levothyroxine 37.5 micrograms but a supraoptimal T3 (8.12 pmol/l). Concerns over developmental delay lead to an MRI, which showed a normal pituitary gland but neuronal hypomyelination. Further investigations included plasma amino, organic acids and biotinidase, urine oligosaccharides, CSF cell count, amino acids, viruses, lactate, glucose and protein all of which were normal. Thyroid peroxidase antibodies were negative.
Results and Treatment
The FT3 was normalised following reduction in the levothyroxine dose but suboptimal T4 and TSH. In view of the combination of hypomyelination and supraoptimal FT3 with normal FT4 on levothyroxine, genetic analysis was performed revealing a pathogenic hemizygous base change in exon 4 of SLC16A2 consistent with Allen-Herndon-Dudley Syndrome (AHDS). This mutation results in a deleterious alternation in the transporter protein monocarboxylate transporter 8 (MCT8), leading to developmental delay as the brain is starved of T3. Following on from a recent multicentre interventional trial (NCT02060474 and NCT02396459) using the thyroid hormone analogue TRIAC (3, 5, 3'-triiodothyroacetic acid), our patient was commenced on an escalating dose of TRIAC in an attempt to prevent further neurological deterioration.
Conclusions and Discussion
Unusually this diagnosis of AHDS was reached through the combination of high-normal FT3 which rose on levothyroxine treatment, developmental delay and hypomyelination. Normally, AHDS is diagnosed on presentation with high FT3.

DOI: 10.1530/endoabs.62.P25

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A rare case of dual cerebral venous sinus thrombosis secondary to Thyroid storm

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Background
Evidence suggested a hypercoagulable state in the context of hyperthyroidism. We presented a case of cerebral venous thrombosis (CVT), a rare but potentially fatal complication of the already high mortality thyroid storm.
Case History
A 16year old boy with Asperger's syndrome was admitted with one-month history of non-specific illness and weight loss followed by 2 weeks of progressive frontal headaches and vomiting, weakness in left arm and left leg for few days. He previously attended A&E twice with headache and vomiting. Examination revealed a dense left-sided hemiparesis with upper motor neurone signs, prominent exophthalmos, a temperature of 38C and sinus tachycardia.
Investigations
Thyroid biochemistry evidenced severe thyrotoxicosis: TSH < 0.01 mU/L [0.35–3.50], FT4 56 pmol/L [8-21] and FT3 > 46.1 pmol/L [3.8–6.0]. *Burch-Wartofsky*score was calculated at 55 suggestive of probable thyroid storm. CT head showed features in-keeping with dural venous sinus thrombosis. Lupus anticoagulant (DRVV ratio) was positive (but normalised 10 months after presentation). PNH, Homocysteine, Methionine, Protein C, Protein S, Antithrombin mutation, Factor V leiden mutation, JAK2 mutation, Prothrombin time, APTT and Vasculitis antibodies were all normal. His factor VIII was high at 428% [59–200%].
Management
He was treated with Propylthiouracil, Propranolol, IV hydrocortisone and therapeutic anticoagulation with Dalterparin 12500 units followed by warfarin. High frequency of seizure activity within 24 hours of admission prompted an escalation of treatment to *Lugol's iodine* in addition to high dose antiepileptic medications (Phenytoin, Levetiracetam). The patient's neurology was completely resolved by his first follow-up appointment. He was also maintained in a euthyroid state on Carbimazole. He was treated with Warfarin for 12 months and then changed to aspirin. It was felt that CVT was primarily driven by the hyperthyroid state.
Discussions
Thyroid storm can be triggered by infection, post-surgery, post radioiodine and delayed treatment. The background of Asperger Syndrome in this case might have caused delayed presentation and diagnosis leading to thyroid storm. The hypercoagulable state in hyperthyroidism is multifactorial due to the increased activity of factor VIII (as in this case), Von Willebrand factor, fibrinogen and tissue plasminogen activator. There have been 19 cases of CVT with hyperthyroidism reported. One other case has been reported of antiphospholipid syndrome and Grave's leading to cerebral venous and arterial thrombosis. It is

hypothesised that anticardiolipin antibodies may cross-react with thyrotropin receptor stimulating antibodies. Thus, we should have a low threshold for checking venous thromboembolism in hyperthyroidism.

DOI: 10.1530/endoabs.62.P26

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A rare cause of human acidosis: lessons from the milking shed

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Case history
A 27-year-old woman presented with a 48 hour history of lethargy, nausea and myalgia. Twelve days earlier she had given birth to her first child. Her daughter was born at term following an uncomplicated pregnancy. She had no abdominal pain or vaginal discharge and her episiotomy wound was well healed. She had no significant past medical history, took no regular medications and did not drink alcohol. There was no significant family history. On arrival in the emergency department, she was tachycardic (119 bpm) and tachypnoeic (28 breaths per minute) with a normal temperature, blood pressure and oxygen saturations.
Investigations
She underwent detailed biochemical assessment including arterial blood gas analysis.
Results and treatment
Arterial blood gas analysis revealed a severe metabolic acidosis (pH 6.99, bicarbonate 2.2 mmol/L) with partial respiratory compensation (P_aCO_2 1.2kPa). The anion gap was raised at 30.5 (sodium 139 mmol/L, potassium 4.7 mmol/L, chloride 111 mmol/L). Causes of a raised anion gap metabolic acidosis were considered. She denied ethanol or other toxin ingestion and blood alcohol, paracetamol and salicylate levels were undetectable. Renal function was normal (urea 4.9 mmol/L) as were lactate (1. 2 mmol/L) and glucose (4.4 mmol/L). There was, however, significant ketonuria (4+ on dipstick) and ketonaemia (capillary beta-hydroxybutyrate 6.6 mmol/L). On direct questioning, it transpired that she had adopted a diet virtually absent in carbohydrates since delivery and her infant was exclusively breastfed. A diagnosis of starvation and lactation-induced ketoacidosis was made. Given the severity of her acidosis, she was admitted to the intensive care unit for invasive monitoring and received parenteral B vitamins, glucose and 8.4% sodium bicarbonate. Breastfeeding was temporarily discontinued and a dietician review was obtained. The acidosis resolved within 24 hours and she was discharged 48 hours later. Her acid-base status remained normal in convalescence and she was able to continue breastfeeding whilst adhering to an unrestricted diet. Urinary organic acid analysis confirmed the diagnosis with elevations of 3-hydroxybutyric acid and acetoacetic acid only.
Conclusions and points for discussion
Ketoacidosis associated with lactation is a common occurrence in dairy cattle (incidence exceeding 10%) but has been described in only a handful of human cases, almost exclusively in association with a low carbohydrate diet. Years of selective breeding to maximise milk yields, necessitating ambitious feed intakes, explains its increased prevalence in cattle and provides an excellent opportunity to discuss peri-partum comparative physiology.

DOI: 10.1530/endoabs.62.P27

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Alemtuzumab induced thyrotoxicosis in a patient undergoing autologous haematopoietic stem cell transplant for multiple sclerosis

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Case History
A 37 year old female underwent an elective autologous stem cell transplant (ASCT) for multiple sclerosis (MS), with cyclophosphamide and anti-thymocyte (ATG) conditioning. She had previously received two doses of alemtuzumab, with the last dose 12 months prior to ASCT. Baseline thyroid function was normal pre atemluzumab. 3 months prior to dose 2 (18 months post first dose), subclinical hyperthryoidism was present with a raised TSH antibody (0.08 unit/ml). There were no further thyroid function tests (TFTs) done in the interim before ASCT. During the ASCT the patient became persistently tachycardic, with subsequent evidence of right heart strain and peripheral oedema. These symptoms were initially thought secondary to the conditioning regimen. No other cause was detected. TFTs subsequently revealed a severely thyrotoxic state. On retrospective enquiry, the patient identified palpitations, heat intolerance and dry eyes for the month pre ASCT. Fine peripheral tremor, mild proptosis, lid lag, and mild smooth goitre were present.
Investigations
Pre alemtuzumab: Thyroid stimulating hormone (TSH) 0.4 milliunit/L, free T4 (FT4, thyroxine)15 pmol/L. 3 months prior to second dose alemtuzumab: TSH 0.08 milliunit/L, FT4 14.6 pmol/L, free T3 (FT3, tri-iodothyronine)5.3 pmol/L. TSH antibody 1.5 unit/mL. Day 7 post stem cell transplant: TSH 0.00 milliunit/L, FT4 47.9 pmol/L, FT3 46.1 pmol/L, TSH antibody >30 unit/ml, TPO (thyroid peroxidase) antibody 239 IU/mL. Thyroid ultrasound showed diffuse hypervascularity, in keeping with Graves' disease.
Results and treatment
Carbimazole was delayed until neutrophil regeneration post ASCT. After one month of carbimazole (40 mg OD) the patient's thyroid function was as follows: TSH <0.01 milliunit/L, FT3 10.6 pmol/L, FT4 17.5 pmol/L, TSH antibody >30 unit/ml, TPO antibody 159.
Conclusions and points for discussion
This lady presents a likely case of alemtuzumab induced autoimmune thyroid disease, with progression from subclinical hyperthyroidism to frank thyrotoxicosis within 15 months. The development of thyroid autoimmunity months or years after alemtuzumab is a frequent and unpredictable complication, which requires ongoing biochemical surveillance for a least 4 years after therapy. The use of Alemtuzumab is significant amongst the transplant community, and in patients with MS. Therefore vigilance is required. This is especially important in patients who might undergo procedures such as ASCT, where symptoms of thyroid dysfunction may be wrongly attributed to conditioning or neutropenic sepsis. In MS patients the need for full thyroid function testing pre transplant is essential.

DOI: 10.1530/endoabs.62.P28

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Normotensive primary hyperaldosteronism as a prelude to atrial fibrillation: potentially curable by endoscopic radiofrequency ablation?

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Case History
In 2011, an asymptomatic 63-year-old professor was found to have isolated hypokalemia. He was normotensive and his only past medical history was hypercholesterolaemia. Investigations were suggestive of Primary Hyperaldosteronism (PHA): aldosterone 1055 pmol/L, renin mass 10 mU/L, Na^+137 mmol/L, K^+3.2 mmol/L, bicarbonate 31 mmol/L. A CT scan was reported as normal, but a 12mm nodule was subsequently noted contiguous with the left adrenal. A metomidate PET CT showed high uptake in this nodule, and likely a unilateral cause of PHA.
Results and treatment
His hypokalaemia was controlled by amiloride, but over the next few years he became progressively more hypertensive, and plasma renin was suppressed. In 2017 he developed palpitations, associated with dyspnoea and occasional dizziness. A Kadir device fitted by the cardiologists confirmed a diagnosis of paroxysmal atrial fibrillation (pAF). Echocardiogram was essentially normal, including the size of the left atria. The incidence of pAF is 7-12 fold higher among patients with PHA than with essential hypertension. However he was not keen to undergo adrenalectomy. In 2018, he enrolled in a feasibility study of endoscopic ultrasound-guided radiofrequency ablation of left-sided aldosterone producing adenomas (APA). 3 months post ablation his biochemistry (on Amiloride 10 mg) is as follow: aldosterone 5020 pmol/L, renin 2.37 ng/l, bicarbonate 30 mmol/L, K^+4.2 mmol/L. Reassuringly there has been a significant reduction in the number of symptomatic pAF episodes he is now experiencing. He reports only 2 episodes in the 3 months post-procedure, compared weekly episodes pre-procedure. A repeat metomidate PET CT is awaited, to ascertain whether there is evidence of improvement on radiology.
Points for discussion
We present an unusual case of PHA where hypokalaemia (without hypertension) was the predominant feature for many years. The unconventional management plan was driven by the patient's limited disease burden from his hypertension (he only required one antihypertensive medication), and his aversion to surgery. Ablation of APAs have been successfully performed via percutaneous and

retroperitoneal approaches, usually for patients unfit for surgery. This is the first case where an endoscopic approach has been used. Its safety and efficacy is currently being assessed via the FABULAS Study; and has the potential to revolutionise the future management of PHA. This minimally invasive procedure has a significantly shorter recovery time compared to laparoscopic adrenalectomy. More excitingly, it could potentially open the door to offer definitive treatment for patients with bilateral disease: by surgical removal of the right adrenal and endoscopic RFA of left sided APAs.

DOI: 10.1530/endoabs.62.P29

P30

A dangerous master of disguise – An undiagnosed phaeochromocytoma presenting with pulmonary haemorrhage

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Case history
A 39 year old female had a first admission to her local hospital with cough and haemoptysis. She reported palpitations for the previous 6 months and had been previously investigated with an echocardiogram which showed a normal LV function. There was no other past medical history. During this first admission CT Pulmonary Angiogram (CTPA) demonstrated ground-glass opacifications. She was hypertensive and so a 24 hour urine sample was collected for metanephrines but at that time no result was available. She was treated for suspected community acquired pneumonia and discharged. She re-attended A&E 6 weeks later and had a second admission. She again presented with haemoptysis but also breathlessness and type 1 respiratory failure with a blood pressure of 107/84 mmHg. A repeat CTPA identified bilateral pulmonary haemorrhage. She was admitted to ITU, intubated and ventilated. The initial working diagnosis was pulmonary vasculitis treated with high dose steroids.
Investigations
The troponin I on admission was 1196 ng/l ($<$40) and 927 ng/l the following day. Echocardiogram demonstrated a significantly reduced LV function and global basal akinetic segments. The urine metadrenaline result became available and was elevated. Plasma metanephrines were urgently processed and demonstrated extremely high levels (plasma metadrenaline $>$ 9000 pmol/L, normetadrenaline $>$ 40,000 pmol/L and 3-methoxytyramine 386 pmol/L). A CT chest/abdomen/pelvis revealed a large 8.2 cm solitary heterogeneous mass arising from the right adrenal gland. The patient was referred and transferred to a tertiary centre for management of phaeochromocytoma crisis. FDG PET demonstrated intense glycolytic in the right adrenal mass with no evidence of other sites of disease.
Results and treatment
After adequate alpha-blockade, she underwent successful open right adrenalectomy. The histology confirmed a 9 cm infiltrating and locally aggressive phaeochromocytoma with a Ki67 of 10% and a clear resection margin. Genetic testing did not reveal any disease causing variant.
Conclusions and points for discussion
Phaeochromocytoma can be challenging to diagnose and can present with haemodynamic compromise and LV dysfunction which may mimic cardiomyopathy or acute coronary syndrome. Haemoptysis and pulmonary haemorrhage is a rare presentation of phaeochromocytoma crisis, first described in 1975 and rarely since. Cases are often misdiagnosed initially as pulmonary vasculitis. Phaeochromocytoma should therefore be regarded as a rare differential in respiratory crisis as well as a cause of unexplained cardiogenic shock, acute LV dysfunction or troponin leak especially in a young patient.

DOI: 10.1530/endoabs.62.P30

P31

Hypercalcemia: a diagnostic challenge

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A 44 year old man attended our endoscopy unit for gastroscopy to further investigate ongoing epigastric pain. He was incidentally found to be very hypertensive so gastroscopy was cancelled. Hypertension was treated. He had past medical history of hypertension and Gout. Routein blood tests showed renal impairment with significantly raised calcium 3.19 mmol/l. Hypercalcemia was treated with iv bisphosphonates. MEN 2a, was considered as a unifying diagnosis for high calcium and hypertension. Further work up showed normal PTH, vitamin D, alkaline phosphate and auto antibody screening. 24 hour urinary calcium excretion and urinary calcium to creatinine ratio was normal. PTHrP was undetectable. Thyroid functions and cortisol were in normal range. Urine and plasma catecholamines were normal. Provisional diagnosis of MEN2a was discarded due to negative endocrine work up. Serum and urine protein electrophoresis, bone turnover markers like P1NP and plasma CTX were also in normal range. Serum phosphate was intermittently raised. Although there were no symptoms but serum ACE level was done and were found to be high normal, 55 iu/l (15–55 iu/l). Repeat ACE level was normal and CT TAP did not show any abnormality. HRCT thorax was further performed which excluded any interstitial/granulomatous lung disease. FDG PET showed high intensity FDG activity within gastric pylorus. Gastroscopy showed reactive gastritis.Later on 1–25 dihydroxy vitamin D was checked and was found to be significantly high, 196 pmol/l (5–55 pmol/l). Patient was not on any sort of vit D preparation. Radiological work up was negative for any malignancy and granulomatous disorder which could produce 1–25 hydroxy vitamin D. Finally the reason for hypercalcemia was considered to be due to CYP24 A1 mutation. This rare disorder is due to inactivation mutation in CYP24 A1 gene. This leads to production of a defective 24 hydroxylase enzyme which is responsible for degradation of 1–25 hydroxy vitamin D. Patients with this mutation can present with any symptoms associated with hypercalcemia but additional feature of severe hypertension has been described. PTH and 25 hydroxy vitamin D are usually normal. 24–25 dihydroxy vitamin D level is usually low and finally diagnosis can be confirmed with genetic testing. Our patient is awaiting genetic testing. Longterm treatment of hypercalcemia with condition is considered with glucocorticoid or azole, antifungal medications. Our patient is currently on glucocorticoid and we plan to switch him to antifungals after confirmation of diagnosis with genetic testing.

DOI: 10.1530/endoabs.62.P31

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Pan-hypopituitarism induced by additive effect of cranial radiotherapy (CRT) and Nivolumab

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Case history
A patient with malignant melanoma with multiple cerebral metastases and a left adrenal metastasis was treated with CRT (30Gy, 10 fractions). This was followed by 12 cycles of Nivolumab, after which the left adrenal lesion was managed with cyberknife (30Gy, three fractions) and Nivolumab was continued thereafter. The patient developed worsening deafness, became unsteady on his feet and complained of feeling generally unwell. At this time an MRI brain was performed showing increased signal intensity in the deep white matter, which was thought to be subsequent to the radiation. The patient was commenced on steroids at this time, though they were later withdrawn due to intolerable effects of mood instability. The patient was referred to for an endocrinology opinion 2 years after the CRT and Nivolumab treatment commenced, as the patient was feeling increasingly fatigued, had lost around 10 kg in weight and had begun experiencing gait and balance abnormalities. He also described reduction in libido, lack of erections and increasing gynaecomastia.
Investigations
0900 h blood results:
Cortisol 62 nmol/l, ACTH 8 pg/l
Testosterone 2 nmol/l, LH 2, FSH 5
T4 6.2 pmol/l, THS 3.42 nU/l
Prolactin 250 mU/ml
Imaging: MRI showed stable appearances of the known cerebral metastases and no pituitary abnormality.
Results and treatments
Commenced on 5 mg prednisolone OD, levothyroxine 75 µg OD, and testogel, with significant symptomatic improvement.
Conclusions and points for discussion
Both cranial radiotherapy and nivolumab have effects on the pituitary. Pituitary abnormalities after radiotherapy depend on the dose and duration, with growth hormone deficiency being most common. Pan-hypopituitartism would be unusual 2 years after 30Gy to the whole brain. Nivolumab is a monoclonal IgG that blocks Programmed Death Receptor 1 (PD1 Ab) and has shown activity in multiple

cancers. Whilst the CTLA-4 inhibitor causes pan-hypopituitarism in up to 20% of patients, nivolumab only affects the pituitary in about 1 in 1000 and then usually results in isolated ACTH deficiency. Therefore this case is unusual, and we hypothesis that the prior radiotherapy may have modified the immune mediated effects of nivolumab, perhaps by inducing neo-antigen expression in the pituitary.

DOI: 10.1530/endoabs.62.P32

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A case of thyrotoxic periodic paralysis

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Case history
Thyrotoxic periodic paralysis (TPP) which was first described in 1902 is characterised by episodes of painless muscle weakness, hypokalaemia and thyrotoxicosis without any total body potassium deficit. It predominantly affects people of Asian descent between 20 and 40 years old with a 2 percent incidence compared to 0.2 percent in non-Asian descent. The pathogenesis of TPP is related to an increase Na+/K+-ATPase activity in the skeletal muscle leading to an influx of potassium into cells. Here we present a rare case of TPP and his progress. A 22 year old Caucasian gentleman presented to Emergency Department (ED) with quadriplegia. He was found to have severe hypokalaemia (1.6 mmols/l) in the context of a normal magnesium/calcium. Despite no signs and symptoms of hyperthyroidism, his thyroid function test (TFT) showed a free T4 of 51 and TSH of <0.01. He was commenced on 30 mg carbimazole once a day. However, he represented 2 days later with paraplegia and his potassium was 2.6 mmols/l. On both occasions, his symptoms improved within 6–8 hours independent of intravenous potassium treatment.
Results and treatment
16 weeks into his treatment; he remains asymptomatic with no associated symptoms of thyrotoxicosis and further episode of hypokalaemia. His antibodies were positive (both thyroid peroxidase antibodies and TSH receptor antibodies). Thyroid uptake scan showed evidence of generalised overactive thyroid with no focal lesion. With carbimazole treatment, his thyroid function normalised. He eventually underwent a near total thyroidectomy around 8 months into treatment. Currently, he is doing well on 125 micrograms of levothyroxine.
Conclusions and points for discussion
Intravenous (IV) potassium during a crisis is crucial for accelerated recovery. The main concern is rebound hyperkalaemia as the patient is not depleted in total potassium. Beta-blockers such as oral propranolol prevent adrenergic stimulation of Na+/K+-ATPase activity by reducing the influx of potassium into cells. Potassium supplements between attacks as prophylaxis are not useful. Once the thyrotoxicosis is under control, offer definitive treatment options such as radioactive iodine therapy or thyroidectomy to avoid future relapses.
Clinical questions:
A) Considering his hyperthyroidism was fully asymptomatic and only presented with paralysis and the potential genetic cause for TPP, is there any place for family screening?
B) In our case, we offered thyroidectomy as soon as he was euthyroid on medication, was that the right choice, or should we have waited for longer or alternatively with no eye involvement offer him radioactive iodine?

DOI: 10.1530/endoabs.62.P33

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A case of 'Camouflaged Insulinoma & Diazoxide quandary'

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Case history
A 74 years old lady with background of hypertension and asthma had multiple admissions with funny turns, dizziness and double vision for at least 2 years. She was seen by various medical specialties including cardiology, stroke medicine and rheumatology before she was noticed to have a capillary glucose of 1.2 mmol/l. Whipple's triad was demonstrated during evaluation. Supervised fasting confirmed biochemical evidence of endogenous hyperinsulinaemia with inappropriately high level of serum Insulin & C-peptide during hypoglycaemia and a negative Sulphonylurea screen.
Investigations
Biochemistry during supervised fast: Plasma Glucose-1.9 mmol, Plasma Insulin-7.6 mU/l, C-Peptide-746 pmol/l & negative Sulfonylurea screen. CT and MRI pancreas (2015 & 2018) - No pancreatic lesions or malignancy Ocreoscan NM scan with SPECT (July 2018): No evidence of Octreotide avid lesion Endoscopic Ultrasound (September 2018): 1.5 cm mass (with classic appearance of insulinoma) seen tucked between splenic vein and artery. It appeared to be wrapped around a non-dilated pancreatic.
Treatment
Although patient was successfully managed initially with dietary modification, symptoms progressed and Diazoxide was started with excellent results. She unfortunately developed severe peripheral oedema and weight gain necessitating reduction in dose of Diazoxide. As a result, she developed persistent hypoglycaemia. Despite lowering the dose of Diazoxide, she developed clinical features of heart failure (BNP>2400, Echo - Preserved ejection fraction) and eventually she decided to stop Diazoxide because of debilitating symptomatic fluid overload. This is when we localalised the tumour with EUS. At this point, she was setting alarm every hour during night to check for (& treat) hypoglycaemia. The fluid overload resolved and BNP normalized after stopping Diazoxide. She was then started on a trial of SC Octreotide despite negative Octreotide scan, which had a dramatic effect on her symptoms and blood sugar control. She has not had a single hypo since been on Octreotide for the last 3 months. She is now waiting for surgery.
Conclusion and points of discussion
1. Although endogenous Insulin over secretion is rare, it should be considered in the differential diagnosis of patients presenting with symptoms suggesting hypoglycemia.
2. Capillary glucose should be tested in ALL unwell patients or with symptoms suggestive of hypoglycaemia
3. Glucose should be assayed by ALL blood gas analyzers (in retrospect, our hospital blood gas machine did not check for Glucose which potentially contributed to the delay in diagnosis)
4. Diazoxide can cause refractory (reversible) heart failure
5. Octreotide can still be effective in managing hypoglycaemia with Insulinoma despite negative Octreoscan

DOI: 10.1530/endoabs.62.P34

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Abstract Unavailable.

P36

A case of meningioma associated with long-term use of cyproterone acetate

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Case history
A 58 year old woman presented to her GP when her family members noted prominence of her left eye. She had a background history of polycystic ovary syndrome (PCOS). Her main symptom of PCOS was hirsutism. She had been treated initially with the combined oral contraceptive pill 'Dianette' (ethinyloestradiol/cyproterone) but had also been treated intermittently with varying doses of 25–100 mg cyproterone acetate (CPA) 10 days/cycle. Post menopause she took 25mg daily CPA for 4 years. In total she took CPA for 34 years.
Investigations
She underwent MRI brain which showed a left sphenoid wing meningioma with a soft tissue component in the middle cranial fossa, a separate focus of meningioma in the right olfactory groove and proptosis.

Results and treatment
Patient underwent craniotomy, resection and orbital reconstruction with calvarial bone grafting. Histology was consistent with a WHO Grade 1 (benign) meningioma with extensive bony infiltration. The tumour showed extensive strong nuclear positivity for progesterone receptor (>90% nuclei) but oestrogen receptor. Follow up MRI showed complete macroscopic soft tissue clearance of the meningioma. The management plan is to monitor for recurrence for 10 years.
Conclusions and points for discussion
Meningiomas are among the most common tumours of the central nervous system. 70% express progesterone receptors but less than 30% express oestrogen receptors. Meningioma is a rare side effect of progestogen therapy. The relationship appears to be related to the dose and duration of therapy. In a cohort study the incidence of meningioma was 11× higher in those taking >25 mg daily of CPA (which has progestogenic activity), with an incidence rate of 60/100,000 person years. There were no cases amongst low dose users. Progestin-associated meningiomas were also more frequently multiple meningiomas. Duration of treatment ranged from 2 to 27 years. None of the reported cases had a fatal outcome. Most case reports have been in women, although there have also been some in men, and there have been 9 case reports in transsexual women. Cyproterone acetate is a commonly used medication in women with PCOS and lower doses (e.g. 12.5–25 mg/day 10 days/cycle or 25 mg alternate days in post-menopausal women) are effective in controlling hirsutism. We recommend using the lowest efficacious dose of CPA in treating androgenic symptoms and to frequently assess the ongoing need for treatment, in order to minimise the rare but recognised risk of meningioma associated with this therapy.

DOI: 10.1530/endoabs.62.P36

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A unique case of Graves' disease and Low Platelets

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Case history
A 38 years old Afro-Caribbean gentleman presented in June 2018 with symptoms of hyperthyroidism. He is a smoker and takes alcohol occasionally. Examination revealed fine tremors, tachycardia, moderate sized goitre with no thyroid bruit and right sided proptosis. Thyroid workup revealed suppressed TSH, raised free T4 and TRAb of 9.75 IU/L suggesting Graves' Thyrotoxicosis. He was started on 20 mg of Carbimazole (CBZ)OD with Propanolol. After initiating carbimazole for one month, he was admitted with thrombocytopenia on July 2018. He was hemodyanamically stable with no bleeding manifestations. He was then discussed with haematology team, where suggestion was Graves' disease or its treatment is contributing to thrombocytopenia. Carbimazole was switched to Propylthiouracil (PTU)100 mg TDS during the admission after which platelet count showed improvement. He was readmitted with thrombocytopenia in August 2018 when he was symptomatically and biochemically improving from hyperthyroidism. His propylthiouracil was stopped. He was referred to haematologist and was investigated in detail for causes of thrombocytopenia and was diagnosed with immune thrombocytopenia (ITP). He was started on steroids. He has had two further admissions with bleeding manifestations and persistent thrombocytopenia.
Investigations:
- 4/05/18: Start of CBZ, T4 >100 pmol/L, TSH<0.01 mIU/L, TRAb 9.75 IU/L, Platelet 72
- 13/07/18: First admission CBZ stopped PTU started, T4 83.7, TSH<0.01, TRAb 9.35, Platelet 9
- 25/07/18: Discharged Platelet 30
- 04/08/18: Second admission PTU Stopped and steroid started, T4 66.1, TSH< 0.01, TRAb 8.34, Platelet 10
- 22/08/18: Discharge on steroid, T4 40.3, TSH<0.01, TRAb 5.49, Platelet 101
- 22/10/18: Third admission, Refractory ITP, T4 30.8, TSH 0.01, Platelet 2
- 09/11/18: Therapy for refractory ITP, Steroids, Eltrombopag, T4 17.2, TSH 0.01, Platelet 5
- 07/01/18: Rutiximab started, T4 10.6, TSH 0.11, TSH <0.4, Platelet 2

Results and treatment
He was treated with anti-thyroid drugs only for first 2 months. His anti-thyroid drugs were stopped initially with a view of contributing to thrombocytopenia. After being diagnosed with ITP, he has been repeatedly on steroids that showed improvement in his thyrotoxic state, but minimal improvement in platelets. In December 2018 admission he was started on Rituximab along with steroids for refractory ITP.
Conclusions and points for discussion
Our patient's Graves' disease responded to steroids, thus leading to marked reduction in T4, TRAb levels and clinical improvement, in the absence of antithyroid drugs. Because of the strong fundamental autoimmune mechanism underlying both diseases, it is known that the treatment of associated autoimmune thyroid disorder contributes to the remission of ITP, which was not in our case. I would like discuss the following:
1. Role of steroid in Graves'? Is the response transient/permanent?
2. Best long term plan in this patient Radioiodine Vs Thyroidectomy?
3. What could be done differently as opposed to our approach?

DOI: 10.1530/endoabs.62.P37

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Genetic sequelae of a thyroidectomy

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Case history
A 28-year-old female was investigated for hypocalcaemia. Her calcium level was checked because her mother was found to be hypocalcaemic post thyroidectomy for recurrence of Graves disease. Further detailed history taking revealed that the patient's grandmother often complained of hand cramps on kneading dough. The patient's aunt was believed to have a parathyroid disorder; no further details were available. On further investigation, it was apparent that her mother's hypocalcaemia pre-dated the thyroidectomy and was long standing. The patient had a history of seizures between the ages of 5–8 years during which her calcium levels were not available. She also had a history of paraesthesiae in her hands and feet. The patient's Trousseau sign was negative at 3 minutes and there were no abnormal phenotypic findings on examination.
Investigations
Her corrected calcium varied between 1.87 and 2.07 mmol/l (2.2–2.6 mmol/l). Her PTH level was 2.9 pmol/l (1.3–9.3 pmol/l) when her serum calcium was 2.01 mmol/l, thus confirming hypoparathyroidism. Her 25-OH Vitamin D level was 38.1 nmol/l and her serum magnesium levels were normal. As she had a family history in keeping with a likely monogenic cause for her hypoparathyroidism, sequence analyses of *AIRE, GATA3, CASR, GCM2, GNA11*and *PTH*genes were undertaken.
Results and treatment
Before the mutational analysis results, the patient had been commenced on alfacalcidol, which did not have an effect on her calcium levels at relatively high doses. The mutational analysis revealed that she was heterozygous for *CASR* c.452C>T p.(Thr151Met). This variant has been described in a Norwegian kindred of 61 individuals, segregating with hypocalcaemia. The change was absent in normal controls. This confirmed a diagnosis of autosomal dominant hypocalcaemia (ADH).
Conclusions and points for discussion
ADH is a rare disorder due to pathogenic gain of function mutations in the calcium sensing receptor (*CASR*), increasing sensitivity of the CASR to extracellular ionised calcium. In the kidney, less calcium is reabsorbed regardless of the calcium level, therefore patients are hypercalciuric. Patients do not often respond to alfacalcidol and the treatment may exacerbate the hypercalciuria, making them prone to nephrocalcinosis and nephrolithiasis. Although high quality evidence is lacking, asymptomatic patients can be monitored in the long term, without active treatment. Diagnosing monogenic calcium disorders is also of value for members of the family, as it can result in avoidance of unnecessary investigations and treatment.

DOI: 10.1530/endoabs.62.P38

P39

Hypophysitis secondary to pembrolizumab use in primary lung carcinoma with brain and adrenal metastasis: An evaluation of hormone replacement and future management

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Case history
A 72 year old male was diagnosed with primary lung adenocarcinoma grade T4N2M1b with adrenal and brain metastasis 1 year previously. On diagnosis his

tumour was strongly positive for PDL-1 expression. This patient was started on dexamethasone 8 mg once a day that was weaned down to 4mg twice daily and then slowly weaned off steroids whilst receiving whole brain radiation. He was started on pembrolizumab therapy and had received ten cycles of treatment when he began experiencing worsening headaches and generalised malaise. He was referred to the endocrinology team with a 0900 h cortisol level of 33 nom/l, TSH 0.34 miU/l, fT3 2.9 pmol/l and fT4 10.9 pmol/l; with a rising prolactin and low testosterone count. This acute change in his pituitary function was likely associated with pembrolizumab. Since this diagnosis he has been treated with levothyroxine and hydrocortisone and his pembrolizumab therapy was held for review.

Investigations

Initial investigations by the oncology team revealed a 9am cortisol level of 135 nmol/l, fT4 16 pmol/l and TSH 0.46 miu/l pre-initiation of pembrolizumab. After cycle ten prolactin level went from 320 mu/l to 1085 mu/l, 0900 h cortisol level of 33 nmol/l, fT4 10.4 pmol/l and TSH 0.23 miu/l Testosterone 5.3 nmol/l, sex hormone binding globulin 79 nmol/l, free androgen index 6.7, ILGF-1 was 15.6 nmol/l. CT head and MRI head showed multiple frontal lobe metastasis with no pituitary involvement and CT abdomen confirmed steady disease in left adrenal metastasis. Visual fields remained intact in this patient and he had no changes in his blood pressure control.

Results and treatment

Symptoms improved on 125 micrograms of levothyroxine and hydrocortisone (20 mgs in the morning and 10 mg in the evening). Thyroid function improved and his levothyroxine was weaned. He remains on hydrocortisone replacement. Initially his pembrolizumab therapy was held and after 3 weeks it was restarted. Current prolactin is 1305 mu/l and testosterone remains low.

Conclusions and points for discussion

$<0.1\%$ of those on pembrolizumab suffer from endocrinopathies. The level of adverse effects does not correlate with the number of treatment cycles. Predicting endocrinopathies is difficult in practice and requires regular monitoring. Pembrolizumab improves prognosis and in our opinion hypophysitis should not deem a patient unsuitable for further treatment. An important differential is pituitary metastasis. Testosterone replacement and treating hyperprolactinemia should be reviewed.

DOI: 10.1530/endoabs.62.P39

P40

Hypopituitarism and hyperprolactinemia secondary to a sella/suprasellar mass consistent with metastatic lung adenocarcinoma

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Case history

A 68 year old woman was referred to Endocrinology with a history of vomiting, extreme fatigue of acute onset and non-specific visual changes. She had a history of primary hypothyroidism and an adenocarcinoma of the lung with bone metastases initially been treated with pemetrexed and cisplatin chemotherapy. The patient subsequently required palliative radiotherapy for metastatic spinal cord compression and was started on denosumab. Imaging shortly before her referral to Endocrinology was suggestive of local disease recurrence for which palliative radiotherapy was arranged.

Investigations

Initial investigations by the Oncology team revealed a 0900 h cortisol of 108 nmol/l, FT4 11.5 pmol/l and TSH 0.11 miu/l. A full pituitary screen and MRI of the brain were subsequently performed.

Results and treatment

Following the initial investigations the patient was commenced on hydrocortisone 20 mg on waking and 10 mg in the early evening. Her levothyroxine was increased from 50 µg to 75 µg daily. The results of a full pituitary profile were as follows: FT4 14.9 pmol/l, FT3 3.4 pmol/l, TSH 0.05 miu/l, FSH 2.8 u/l, LH <0.1 u/l, prolactin 3786 mu/l (84% macroprolactin recovery), oestradiol <92 pmol/l, testoterone <0.5 nmol/l, cortisol 321 nmol/l, IGF 1 85 ng/ml. An MRI brain revealed a lobulated sellar and suprasellar lesion with oedema of the optic chiasm. Visual field testing revealed a bitemporal hemianopia.The case was reviewed in a pituitary MDT and the imaging felt to be consistent with pituitary metastases. Treatment with hydrocortisone, monitoring for diabetes insipidus and consideration of radiotherapy was recommended. The patient subsequently reported polyuria and polydipsia. Investigations were consistent with diabetes insipidus and treatment with desmopressin was commenced.

Conclusions and points for discussion

This patient's hypopituitarism and hyperprolactinaemia were attributed to pituitary metastases. The hyperprolactinaemia was felt to result from stalk compression rather than a pituitary tumour. Pituitary metastases are rare but most commonly associated with malignancies of the breast and lung. Their presentation can relate to mass effect and/or hormonal dysfunction. The symptoms of hypopituitarism can mimic those associated with malignancy and oncological treatments. Certain monoclonal antibodies carry a risk of hypophysitis of auto-immune aetiology. Regular monitoring of pituitary function could be considered in at risk patients and symptoms of hypopituitarism should be promptly investigated. Identification of the likely cause of hypopituitarism will guide management. In the case of pituitary metastases, whole brain radiotherapy and surgical decompression can be considered.

DOI: 10.1530/endoabs.62.P40

P41

An Interesting case of Transient Graves' Ophthalmopathy on the background of Hashimoto's Thyroiditis

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Case History

A 30 year old woman presented with the history of swollen painful eyes for 4 weeks while visiting Italy. She had a background of Hashimoto's Thyroiditis since 2010 and was treated with levothyroxine 100 mcg once daily. She was given a course of oral steroids for 2 weeks and her thyroxine dose was reduced to 25 mcg once daily in Italy. Since then, her orbital swelling began to improve. She was a non-smoker. On examination, she was noted to have bilateral mild proptosis and lid-lag. She had normal visual acuity and visual fields were normal to confrontation. There was no diplopia noted. She had a palpable goitre with bruit.

Investigations

Her thyroid function test showed TSH 0.01, FT3 5.5, FT4 15.9, TPO antibodies 415 and TSH receptor antibodies were 11.4. Her levothyroxine was then stopped. She was referred to Ophthalmology and subsequently had MRI orbits which was normal.

Result and treatment

Her proptosis completely resolved. She subsequently became hypothyroid again (TSH 12.58, FT4 10.9, TSH receptor antibodies 2) and was restarted on levothyroxine.

Discussion

Hashimoto's and Graves' diseases represent the main two types of autoimmune thyroid disease. Thyroid-associated eye disease is more common in patients with Graves' disease and may affect $\sim$25% of these patients. Up to 6% patients with Hashimoto's may also be affected by thyroid-associated eye disease.[1] However, presentation of Graves' Ophthalmopathy with subclinical hyperthyroidism in patients with Hashimoto's Thyroiditis has not been previously reported. There is a strong association of TSH receptor antibodies and Graves eye disease.[2] This can be seen in our case as the resolution of Ophthalmopathy correlated with the fall of Thyroid receptor antibodies.

References

1. Kahaly GJ *et al*. Thyroid stimulating antibodies are highly prevalent in Hashimoto's thyroiditis and associated orbitopathy. J Clin Endocrinol Metab. March 10, 2016.
2. Khong JJ, McNab AA, Ebeling PR, Craig JE, Selva D. Pathogenesis of thyroid eye disease: review and update on molecular mechanisms. Br J Ophthalmol. 2016 Jan; 100(1):142–50.

DOI: 10.1530/endoabs.62.P41

P42

Severe hypercalcaemia in a young patient

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Case History
16-year-old fit and well lady was referred to endocrinology clinic by GP due to severe hypercalcaemia. She is being investigated for secondary amenorrhea. She is not taking any regular medication. There is a history of hypercalcaemia in the family, her mother has hypercalcaemia and paternal grandfather had hypercalcaemia. She had no signs and symptoms of hypercalcaemia.
Investigations
Corrected Calcium: 3.28 mmol/l, Phosphate: 0.60 mmol/l, 25 OH vitamin D: 28 nmol/l, Cortisol: 225 nmol/l. Normal Synacthen test, Parathyroid hormone: 4.1 pmol/L, Normal Gut Hormone profile. Normal Prolactin, Ultrasound Parathyroid is normal. Parathyroid MIBI scan is normal, Ultrasound of abdomen showed no urolithiasis
Results and treatment
IV Fluid and IV Pamidronate were given and repeat calcium after treatment was 2.73 mmol/l. However, follow-up blood showed that she had persistent hypercalcaemia (>3 mmol/l). Therefore, PO Cinacalcet was given but she is not taking regularly. As a result, her calcium level is persistently above 3 mmol/l. We tried multiple attempt to do 24-hour urinary calcium/creatinine clearance, but patient did not give the sample. However, just recently she provided 24-hour urine sample which showed 24-hour urine calcium level 0.9 mmol/l and 24-hour urinary calcium: creatine ratio 0.011 mmol/mmol. Because of strong family history of hypercalcaemia and patient has hypercalcaemia with biochemical test suggestive of neonatal hyperparathyroidism, genetic test was requested which showed heterozygous sequence change in calcium sensing receptor gene C.554G>A, p.(Arg185Gln). Her mother was also seen in our endocrinology clinic and diagnosed as Familial hypocalciuric hypercalcemia (FHH) which is evidenced by hypercalcaemia (>3 mmol/l) and hypocalciuria (24 hr Urinary Calcium is 2.6 mmol/24 hr and calcium creatinine clearance ratio is 0.006 mmol/mmol). She also had same mutation as her daughter and her USG Neck and Parathyroid MIBI scan were normal.
Conclusion and points for discussion
Patient's 24-hour urinary calcium: creatine ration is borderline to diagnose familial hypocalciuric hypercalcemia. Calcium level of both patient and her mother is higher than expected in familial hypocalciuric hypercalcemia. Same genetic mutation found in both patient and her mother are associated with neonatal hyperparathyroidism. We advised to continue with oral hydration and cinacalcet 60 mg BD. In this rare mutation in calcium sensing receptor gene, should we observe calcium level, or should we consider parathyroidectomy?

DOI: 10.1530/endoabs.62.P42

P43

Thyroid storm - from clinic to intensive care

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Case history
A 46-year-old female patient presented to A&E with a three day history of diarrhoea and vomiting, after three months of progressive weight loss. Her past medical history included chronic autoimmune thrombocytopaenia and Graves' disease, which had been diagnosed four years earlier and treated with a brief course of propylthyuracil (PTU). She was clinically *in extremis*, with signs of severe cardiovascular and respiratory compromise and reduced responsiveness.
Investigations
Her investigations included standard biochemistry and full blood count, arterial blood gas, septic screen, urgent thyroid function tests and a bedside echocardiogram.
Results and treatment
Her baseline investigations revealed severe metabolic acidosis, neutrophilia, hyperglycaemia (17 mmol/l) and raised ketones. She was profoundly thyrotoxic, with a FT4 of 74 pmol/l, FT3 of 31 pmol/l and a fully suppressed TSH. She had echocardiographic evidence of global cardiomyopathy. She was diagnosed with a combination of diabetic ketoacidosis (new diagnosis of diabetes mellitus) and thyroid storm. She was intubated and transferred to intensive care on inotropic support, while anti-thyroid treatment was commenced with a combination of high-dose PTU (1,500 mg/day), propranolol, hydrocortisone and potassium iodate. Her haemodynamic instability, driven by thyrotoxicosis, was so severe that she required additional support by means of a cardiac pump and extra-corporeal membrane oxygenation (ECMO). She was also placed on a fixed rate insulin infusion, which readily controlled her glucose levels. Her clinical course was further complicated by the development of hepatitis, mandating a switch to carbimazole, and ischaemic bowel. She underwent three operations for ischaemic bowel and intra-abdominal bleeding.
Outcome and points for discussion
Thyroid hormone levels improved within six days, and returned to normal nine days after treatment initiation. Effective biochemical control was accompanied by a rapid improvement in cardiac contractility, ushering in a return to haemodynamic stability. After a prolonged intensive care stay, she was eventually discharged to her home on carbimazole and long-acting insulin. Thyroid storm remains the endocrine emergency with the highest mortality. Rapid control of thyroid function is essential but can be challenging. Modern, invasive means of cardiorespiratory support may have a role in severe cases, buying vital time until the thyroid function can be sufficiently controlled.

DOI: 10.1530/endoabs.62.P43

P44

Pituitary metastasis masquerading as a non-functioning pituitary macroadenoma

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Case History
A female, aged eighty-three was admitted for an elective urology stent procedure. She had a background history of a non-functioning pituitary adenoma diagnosed 3 weeks before admission. This was found after investigation for headache and diplopia. The pituitary lesion was described as 18 × 17 × 14 mm in size and mixed solid/cystic in nature. There was no chiasmal compression. During that admission her case was discussed with neurosurgery and it was felt that she was not a good surgical candidate. During this elective admission for her stent she was unwell with severe headache and confusion. Pituitary function tests showed a prolactin of 900 mU/L (59-619 mU/L), TSH 0.07 mU/L, T4 17 pmol/L, IGF-1 12.7 nmol/L, LH 0.5 U/L, FSH 3.8 U/L, 9 am cortisol 570 nmol/L. An urgent CT scan was arranged to rule out pituitary apoplexy. It showed an interval increase in the size of the pituitary adenoma. We then organised a pituitary MRI scan that surprisingly showed an aggressive sella mass with surrounding invasion suggestive of pituitary metastasis. A subsequent staging scan was arranged to look for a primary that showed disseminated systemic disease with an unknown primary.
Investigation
Staging CT showed multiple lung metastasis with enlarged mediastinal and retroperitoneal nodes. There was a mass within the pancreas and associated thrombus within SMV/portal vein. There was also an abnormality within the right lobe thyroid highly suspicious of malignancy. All these findings were in keeping with metastatic disease.
Treatment
Considering the aggressive nature of the tumour with systemic metastasis and the rapid progression of metastatic lesion within pituitary, she was palliated.
Conclusion
It was debated when she re-presented whether there would be further benefit from re-scanning her given her previous medical management plan. However symptom progression led us to believe it would yield useful information. Symptomatic pituitary metastases are rare, not well documented and associated with poor prognosis. It may be difficult to differentiate adenoma from metastasis clinically and radiologically. Previous studies have reported that only 7% of pituitary metastases are symptomatic. In contrast to the adenoma, metastases are more likely to be located in the posterior pituitary in part due to the fact that this region of the gland is supplied by the systemic circulation. Literature review showed breast cancer followed by lung and thyroid cancer being the most frequent primary origin of metastases.Although rare, pituitary metastases may be the initial presentation of cancer.

DOI: 10.1530/endoabs.62.P44

P45

Delivery of a diagnosis

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Case history
A 32 female was referred to a tertiary maternity unit due to hypercalcaemia and a diagnosis of primary hyperparathyroidism (PHPT). She had learning difficulties,

2 previous C-sections and was a smoker. She presented 5 years earlier to her local hospital with abdominal and leg pains, nausea, constipation and fatigue. She had undergone 2 parathyroidectomies but remained hypercalcaemic and had been managed medically with Cinacalcet when she conceived an unplanned pregnancy.

Investigations

At the initial diagnosis of PHPT:

- Corrected calcium 3.05 mmol/l
- PTH 8.5 pmol/L
- Vitamin D 15.4 nmol/l
- Normal prolactin and metanephrines
- 24-hour calcium was 4.2 mmol/24hr (2.5–7.5) felt to be consistent with PHPT
- Normal renal ultrasound scan
- Parathyroid localization with ultrasound and Mibi scan showed no adenoma

Results and treatment

Neck exploration removed 2 inferior parathyroid glands felt to be hyperplastic but histologically normal. After surgery, she remained hypercalcaemic and symptomatic. Repeat urinary calcium levels were lower but there were concerns about the collection and Vitamin D deficiency. Imaging again showed no evidence of an adenoma. Repeat parathyroidectomy removed a right superior parathyroid adenoma but the hypercalcaemia persisted and Cinacalcet was started. At the antenatal clinic at 20 weeks gestation, corrected calcium-3.05 mmol/l, PTH 5.0 pmol/l, Vitamin D 24.4 nmol/l and Hammersmith spot Urinary Calcium: Creatinine ratio 0.004. The hypercalcaemia in pregnancy was managed conservatively with good hydration, requiring a couple of admissions for intravenous fluids due to vomiting. The pregnancy was otherwise uncomplicated. At 37 weeks gestation, calcium levels appeared to be rising and she underwent an elective C-Section delivering a male infant weighing 2.4 kg. In light of the maternal PHPT, the paediatric team was alerted to the risk of hypocalcaemia. However, at 12 days of age corrected calcium-3.46 mmol/l, PTH 3.4 pmol/l and Vitamin D 28.7 nmol/l.

Conclusions and points for discussion

The baby's results suggest a diagnosis of Familial Hypocalciuric Hypercalcaemia (FHH), rather than PHPT. Genetic analysis is awaited.

1. FHH is an important differential diagnosis of PHPT and should be excluded. It has a benign course and does not require surgical management.
2. FHH should be reconsidered if hypercalcaemia persists after surgery.
3. Hypercalcemia among family members suggests the diagnosis of FHH.
4. Vitamin D deficiency may worsen hypocalciuria and hyperparathyroidism making the differentiation between PHPT and FHH challenging.
5. Urine calcium: creatinine ratio <0.01 is accepted as a differentiating feature of FHH but there is overlap with higher levels and genetic testing should be performed to prevent patients from undergoing inappropriate surgery due to misdiagnosis.

DOI: 10.1530/endoabs.62.P45

P46

Thyroid Dysfunction induced by Alemtuzumab; a monoclonal antibody used in the treatment of multiple sclerosis

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Case History

Case 1: A 37-year-old lady with relapsing-remitting multiple sclerosis was initiated on Alemtuzumab and symptoms of sweats and heat intolerance arose. Hyperthyroidism was confirmed with free T4 30.1 pmol/l (12–22) and suppressed TSH. Symptoms settled without antithyroid medication and within 2 months T4 had fallen to 10.2 pmol/l with TSH 6.95 mIU/L. After a further 6 weeks T4 was 9.8 with TSH 20.35 and levothyroxine was initiated. Anti-TPO was raised at 442 U/mL, with TSH receptor antibodies (TRAb) of <0.3I U/L. The patient did not complain of any swelling in the neck and the thyroid examined normally throughout. Case 2: A 27-year-old female with relapsing-remitting multiple sclerosis had two periods of alemtuzumab treatment through 2016 and 2017. In 2018, she developed symptoms of sweating, feeling faint and palpitations. T4 rose to 65.5 pmol/L with suppressed TSH, improving at 6 weeks to a T4 of 11.4 pmol/L, but TSH remained suppressed without treatment. Within another 8 weeks TSH was measurable at 6.04 mIU/L with T4 falling to 7.4 pmol/L and levothyroxine 50micrograms was started. TRAb were markedly raised at 85.4 IU/L.

Results and treatment

Neither case received antithyroid medication and both cases eventually became hypothyroid and were started on Levothyroxine. Given that alemtuzumab is strongly associated with autoimmune thyroiditis (40%), watchful-waiting is the way forward in cases like this. Treatment should be initiated early in those with ophthalmoplegia, those with acutely enlarging goitre and those with prolonged symptoms. TSH receptor antibodies are an important test as graves thyroid disease is less likely to self-resolve.

Conclusions and points for discussion

These cases highlight firstly the need for awareness of the impact of alemtuzamab on thyroid function, given its frequent use and its reported 40% incidence of associated thyroid dysfunction. Secondly, there is a need for awareness of the variable clinical and immunological presentation induced by alemtuzamab. Both our cases had a symptomatic hyperthyroid phase, of short duration and self-limiting progressing rapidly to a hypothyroid phase. In Case 1, anti TPO antibodies were strongly positive with unmeasurable TRAb, whereas Case 2 had significantly raised TRAb with a much smaller anti TPO rise. Additionally, variation in TRAb bioactivity both between patients and over time in individual patients treated with alemtuzamab has been recently described. In summary, our cases demonstrate a need for careful thyroid monitoring in alemtuzamab treated patients. The significance of thyroid antibody results in predicting clinical course or guiding treatment decisions needs to be more clearly determined.

DOI: 10.1530/endoabs.62.P46

P47

Two cases of ectopic ACTH in advanced NETs

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Case history

Patient 1, a 78 year old male, was diagnosed five years ago with a metastatic NET with octreotide avid disease including ileocolic/right common iliac nodal metastases and a solitary segment VII liver lesion. He elected for watchful waiting and was asymptomatic. Interval imaging showed gradual local disease progression. He was diagnosed with motor neurone disease resulting in unilateral arm weakness. He re-presented four years after diagnosis with progressive weakness rendering him bed bound, peripheral oedema, hypertension, hypokalaemia, hyperglycaemia, Cushingoid facies and new onset hypothyroidism. Patient 2, an 83 year old female, was diagnosed in 1984 with a metastatic pancreatic NET resulting in biliary obstruction, and bone metastases. She underwent gastric and biliary bypass with choledochoduodenostomy; histology showed a low grade pancreatic NET with little mitotic activity. She had no further treatment and was lost to follow up in 2009. In 2018, 34 years following diagnosis, she developed gradual deterioration in health culminating in admission to hospital with increasing shortness of breath and peripheral oedema. On admission she was hypokalaemic, hypocalcaemic and hyperglycaemic.

Investigations

Patient 1: random cortisol 1436 nmol/L, urinary cortisol >1650 nmol/24h, ACTH 359 ng/L, no suppression on LDDST. CT showed enlarged smooth adrenal glands with no associated adrenal mass and progression at the known sites of disease. Patient 2: random cortisol 6363 nmol/L, urinary cortisol >23450 nmol/24h, ACTH 3879 ng/L; no suppression on LDDST. CT revealed bilateral adrenal gland enlargement and progression at the known sites of disease. MRI pituitary showed a normal pituitary gland.

Results and treatment

Patient 1 was commenced on ketoconazole and metyrapone, however the former was stopped due to a fungal lung infection requiring treatment with voriconazole. Cortisol fell on high dose metyrapone and lanreotide and he is now on a "block and replace" regime with gradual functional recovery. Patient 2 was initially treated with metyrapone, but due to rapid deterioration she was admitted to ITU for an etomidate infusion. Despite a rapid fall in cortisol she continued to decline. Active treatment was withdrawn and the patient was palliated, as per her wishes.

Conclusions

Although Cushing's due to ectopic ACTH is often due to small, frequently occult primary NETs, these cases serve as a reminder that it can also develop in advanced previously non-functioning NETs. A high index of suspicion is needed for the early symptoms to try to prevent rapid decline.

DOI: 10.1530/endoabs.62.P47

P48

Partial cranial diabetes insipidus in breast cancer: invisible pituitary metastases or uncanny coincidence

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Case history
PD is a 57-year-old female teacher who presented to her GP in October 2017 with lethargy, dyspnoea and anaemia. Bone marrow biopsy followed by a CT scan of her chest and abdomen confirmed lobular breast cancer with peritoneal and bone metastases (ER+/HER2−). The patient also had an MRI scan of her head to assess for intracranial metastatic disease which was negative at the start of December 2017. She was commenced on letrozole, palbociclib and denosumab. A fortnight after commencing treatment for the breast cancer, the patient was admitted by the GP with intractable thirst –symptoms began September 2017 (predated breast cancer diagnosis).
Investigations
Other causes of polyuria were excluded (diuretics; thyroid biochemistry, bone profile, renal profile, anterior pituitary hormone profile, glucose – all fine). The patient proceeded to have a water deprivation test in December 2017. The results are shown in Table 1.

Table 1 Results from water deprivation test.

Water Deprivation Test			
Spec No	Time (mins)	Serum Osmolality mosmol/Kg	Urine Osmolality mosmol/Kg
1	0	306	354
2	2H	308	
3	4H	308	411
2 microgram	DDAVP given		
4	6H		601
7	7H		644
8	8H		703
9	9H	289	
10	10H		725

Following confirmation of partial cranial diabetes insipidus (DI), reimaging of the posterior pituitary was requested in January 2018 which again demonstrated no intracranial or pituitary pathology.
Results and treatments
The test demonstrates partial cranial DI as there is failure to fully concentrate urine to >750 mosmol/Kg with a serum osmolality >295 mosmol/Kg and improvement of the urine osmolality to 601 mosmol/Kg following administration of DDAVP. The patient was subsequently commenced on regular desmopressin with resolution of symptoms and normal electrolytes.
Conclusions and points for discussion
This is an interesting case of partial cranial diabetes insipidus on a background of metastatic breast cancer without intracranial metastases on radiological surveillance. Serial pituitary MRI scans over 12 months demonstrated no pituitary/intracranial pathology. The patient had good biochemical and symptomatic resolution following treatment. While idiopathic cranial DI is possible, onset of symptoms coincided with development of breast cancer making this less likely.

DOI: 10.1530/endoabs.62.P48

P49

A challenging case of transient hypercortisolism presenting with diabetic ketoacidosis: could this be cyclical Cushing's syndrome?

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A 49-year-old female was admitted to with diabetic ketoacidosis (DKA) and newly diagnosed diabetes. Her only significant medical problem was malignant hypertension with poorly controlled blood pressure (BP) on four antihypertensive agents. She reported no exogenous glucocorticoid or liquorice ingestion. She also complained of a 6-month history of lethargy, weight gain, and a two-month history of easy bruising, lower-limb weakness, increasing polyuria and polydipsia. There was no history of a headache, palpitations, flushing or diaphoresis. She had a BMI of 41 kg/m^2 with evidence of easy bruising, abdominal striae, and lower limb proximal myopathy. There was no evidence of androgen excess. Following resolution of DKA she underwent routine blood tests, overnight low-dose dexamethasone suppression test (LDDST), 24-hour urine free cortisol (UFC), adrenal computed tomography (CT), 24-hour urine metanephrines, magnetic resonance imaging pituitary. Significant findings were an IFCC-HbA1C (glycated haemoglobin) 102 mmol/mol on admission (30 mmol/mol 6 months earlier) and an overnight LDDST with a non-suppressed cortisol level 163 nmol/L (normal < 50 nmol/L). Total urine cortisol was 472 nmol in 24hours, confirming hypercortisolemia. Adrenal CT revealed a 2.6 cm right-adrenal adenoma (absolute washout =69%). 24-hour urine metanephrines (repeated), plasma aldosterone-renin-ratio and androgens were all within normal range; adrenocorticotropic hormone (ACTH) level 15.9 ng/L (0–46 ng/L). An MRI pituitary confirmed no evidence of visible adenoma. She was discharged on insulin, metformin 500 mg twice daily and regular anti-hypertensives. Insulin was eventually stopped two months following discharge. The HbA1C has remained in the non-diabetic range with a well-controlled BP. Repeat outpatient overnight LDDST (twice) showed serum cortisol levels of 65 and 37 nmol/L. Multiple UFCs have been normal for 12 months since hospital discharge. A repeat CT-adrenals confirmed unchanged appearances of the right adrenal mass. This patient had convincing history, signs and investigation results of hypercortisolism likely leading to development of life-threatening malignant hypertension and DKA. Glucose intolerance associated with Cushing's syndrome is usually only mild to moderate in severity and marked hyperglycaemia with ketosis is very rare. Cyclical Cushing's is a poorly understood phenomenon and the mechanisms causing such abnormality have yet to be discovered. This condition has recently been recognised as occurring much more frequently than initially thought. A high index of suspicion of the syndrome is required in patients with symptoms or signs of Cushing's syndrome but with normal cortisol values. This patient remains under endocrine follow up with periodic UFC measurements.

DOI: 10.1530/endoabs.62.P49

P50

Nature's price for Cushing's disease: A blind eye and a hole in the (pituitary) Middle

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Case history
A 61 year old male with a background of diabetes mellitus Type 2 and congestive cardiac failure (CCF) was diagnosed with Cushing's disease in 2014 following identification of severe osteoporosis through investigations for non-traumatic vertebral fractures causing paraplegia.
Investigations
He had high ACTH and cortisol levels which failed to suppress on low and high dose dexamethasone suppression tests, hypogonadotrophic hypogonadism and MRI imaging identified a pituitary macroadenoma with sphenoid and cavernous sinus invasion a CT scan of his chest/abdomen/pelvis was normal.
Results and treatment
He underwent transpheniodal surgical de-bulking in May 2015 (histology compatible with an ACTH staining pituitary adenoma with Ki67 index of 15%) followed by radiotherapy. He remained on hydrocortisone (HC) post-operatively, but this was withdrawn in February 2016 following a normal short synacthen test (SST). Serum cortisol levels began to rise once again to 1204 in February 2018. MRI demonstrated increase in size of the residual adenoma and metyrapone was started and titrated to 1g TDS. Due to his multiple comorbidities, with deteriorating glycaemic control, raised BMI and progressive CCF symptoms he was deemed high surgical risk and so chemotherapy with temozolomide was being considered. He presented to A&E 6 weeks later with headache, double vision and right-sided ptosis. He was found to have 3rd, 4th and 6th cranial nerve palsies, with a temporal field defect and MRI demonstrated significant enlargement of the tumour with central necrosis. During this admission his glycaemic control improved leading to recurrent hypoglycemia, resulting in reduced insulin requirements and his symptoms of CCF improved without further treatment. His metyrapone dose was down-titrated and eventually stopped and two weeks later HC was reintroduced. Unfortunately in November 2018, ACTH and cortisol levels started to rise and HC was once again discontinued. Repeat MRI showed worsening of the appearances of the intracranial lesion(s), raising concerns of development of a second neoplasm.
Conclusions and points for discussion
This is a fascinating case, which demonstrates the challenges of managing Cushing's disease due to an aggressive pituitary adenoma. During the period of surveillance nature offered a respite for his severe hypercortisolaemia when central tumour necrosis rendered him cortisol deficient but at the cost of severe ophthalmological complications (ptosis and unilateral partial blindness). He is currently off metyrapone and hydrocortisone whilst awaiting investigations to further characterise the unusual appearances of the intracranial lesions and to plan further treatment for these.

DOI: 10.1530/endoabs.62.P50

P51

Steroid cell ovarian tumour presenting with severe hyperandrogenism

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A 69-year-old woman was referred with a 2 year history of frontal balding, deepening voice and weight loss. Past medical history included primary hypothyroidism, osteoarthritis, varicose veins and menopause at age of 50 years. Current medications included levothyroxine. She was otherwise very well and enjoyed heightened physical endurance – regularly cycling >60 miles with a group of male friends. On examination she was virilised with male pattern alopecia, marked facial hirsutes, clitoromegaly and had a lean muscular build but no other abnormalities. Testosterone was elevated at 46.9 nmol/l (0.1–1.4). This was cross analysed for interference and confirmed with mass spectrometry. Dihydrotestosterone was 1.2 nmol/l (post-menopausal range <0.62); 17 hydroxyprogesterone was 16 nmol/l; SHBG 93 nmol/l (18–144); DHEAS 1.2 umol/l (0.7–11.5); androstenedione 8.7 nmol/l (1–11.5); FSH 17.7 IU/l (post-menopausal range 26.7–133.4), LH 4.6 IU/l (post-menopausal range 5.2–62), estradiol 256 pmol/l (post-menopausal range <183) indicating probable shunting of the androgens to oestrogen. There was no suppression of her androgens after standard low dose dexamethasone testing. MRI of the adrenals and pelvis revealed a heterogeneous 40 mm left ovarian mass, with normal adrenal appearance, and no evidence of distant disease. She underwent bilateral salpingo-oophorectomy. Histology and immunohistochemistry of the left ovarian lesion was consistent with a malignant steroid cell tumour with infiltration of the capsule but Ki 67 index of only 3%. There was positive staining for calretinin, inhibin and CD99. Following surgery her testosterone level is undetectable, her oestrodiol has also fallen and her physical appearance is gradually improving. Her case has been reviewed in a supraregional MDT and she is being closely monitored with serial serum testosterone and imaging. Ovarian steroid cell tumours are rare sex cord-stromal tumours with malignant potential. They account for <0.1% of all ovarian tumours. They are divided into three main subtypes including stromal luteoma, Leydig cell tumours, and steroid cell tumour NOS (not otherwise specified), which have uncertain cell lineage. Steroid cell NOS comprise more than 50% of steroid cell tumours, and may produce testosterone (most commonly), estradiol or cortisol. Up to 43% may be malignant and so long term monitoring is recommended. However, there are very limited numbers of cases reported and so long term prognosis and the duration of optimal follow up are not yet clear.

DOI: 10.1530/endoabs.62.P51

P52

A rare case of pituitary extraventricular neurocytoma presenting with visual field defects

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Case report
Central neurocytomas are well-differentiated rare central nervous system tumours. These tumours when identified in brain parenchyma or spinal cord are termed as extra ventricular neurocytomas. We report a case of 40 year old lady with mild hypertension who presented with long standing history of intermittent headaches which got worse 2 months before presentation, mainly affecting her forehead and left retro-orbital region. She also noted blurring of vision in her left eye. She had long standing weight gain with menstrual irregularities. On physical examination, she had BMI of 50 but no other signs of growth hormone or cortisol excess. Visual fields on confrontation method revealed subtle bitemporal defects which were later confirmed on formal neuro visual fields test.
Investigations
Her pituitary function tests done before surgery showed non-functioning type with ACTH 19 ng/l (normal 0–46), TSH 1.9 Mu/l (normal 0.35–0.55), Prolactin 286 mu/l (normal: 59–619), IGF1:109 ng/ml (normal: 63.4–223.0), FT4 14.9 pmol/l (normal: 10–20), Cortisol 395 nmol/l (normal: 200–500). Both CT and MRI scans showed expanded pituitary gland with 18×29×23 mm sellar and suprasellar lesion with significant compression of optic chiasm which also appeared pre-fixed. Radiologically it was reported as macroadenoma.
Results and treatment
Her case was discussed in our Pituitary multidisciplinary team meeting.It was though thatgiven the size of lesion, there was high potential for significant supra-sellar remnant necessitating re-do surgery which was discussed with patient prior to proceeding for first surgery. She underwent trans-sphenoidal subtotal resection due to unusual shape of lesion. Histology confirmed WHO grade 2 extraventricular neurocytoma which was Chromogranin A, CD56 and Synapto-physin positive. There was no hormonal staining. Overall appearance was of pituitary neuronal tumour with no convincing accompanying adenomatous component. The Ki-67 labelling index was variable and focally elevated to around 1–6%. Post-surgical MRI after 3 months showed sizeable remnant with visual fields not fully recovered to normal. Genetic analysis has been requested, including AIP gene mutation. Her pituitary profile after surgery was normal. She is planned to have further pituitary surgery.
Conclusions and points for discussion
Our case highlights a challenging case of Pituitary extraventricular neurocytoma which presented as a macroadenoma with significant chiasmal compression and visual field defects. The outcome of re-do surgery remains to be seen. Since chemotherapy and radiotherapy is proven to have positive outcomes after surgery, a detailed MDT discussion will be important for further management plan.

DOI: 10.1530/endoabs.62.P52

P53

Abstract Unavailable.

P54

Iatrogenic euglycaemic DKA following polypharmacy overdose

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Case history
A 39 year old male patient presented via ambulance to our unit with a deliberate mixed overdose. He had a past medical history of type 2 diabetes mellitus, depression and hypertension. He had ingested an uknown amount of atenolol, dapagliflozin, ramipril, co-codamol with both cocaine and benzodiazepines detected in urine toxicology. On arrival to hospital, the patient had fluid refractory hypotension, with a systolic blood pressure of 70mmHg and HR 45BPM. Given the concern of beta blocker toxicity he received an IV glucagon bolus with a good, although transient, haemodynamic effect. He was therefore commenced on a continuous glucagon infusion with a satisfactory and sustained haemodynamic response. Overnight, he began vomitng and became increasingly acidotic (H+ 70), despite BP 100/60 and passing good volumes of urine. U+ES, LFTs and lactate were all improving. Bedside ketone monitoring was not available on site. Laboratory ketones showed 'positive+++'.
Investigations
On admission biochemistry revealed:
1. AKI (serum creatinine was 236 from baseline of 85) K+4.2
2. acidosis with H+50.4
3. paracetamol level was below the treatment line
4. salicylate and alcohol were undetectable
5. Lactate 4.0 mmol/l
Overnight bloods were repeated that showed a worsening acidosis, H+70, improving renal function (creatinine 120), normal liver function tests and a lactate of 1.0 mmol/l.
Results and treatment
This patient developed ketoacidosis without significant hyperglycaemia. At this point, the glucagon infusion was stopped, and patient was started on the National DKA protocol, with fixed rate insulin infusion and IV fluids. The patient remained haemodynamically stable on cessation of glucagon, the acidosis resolved rapidly with the commencement of IV insulin. The patient was fit for discharge two days later.
Conclusions and points for discussion
There is a lack of information and guidance available on the toxicology of the relatively novel SGLT2 inhibitors. In this situation, the overdose was confounded by acute renal failure (likely ACEi related) and refractory hypotension (secondary

to beta-blockade). The euglycaemic DKA that ensued was likely secondary to both dapaglifolozin overdose and the concomitant administration of glucagon. Interestingly, insulin can be a therapeutic option in beta blocker overdose. In this case, routine glucose monitoring was not sufficient to ensure no adverse effect, in a diabetic patient receiving glucagon following beta-blocker and SGLTi overdose. The authors postulate bedside blood ketone monitoring could have prevented the development of euglycaemic DKA.

DOI: 10.1530/endoabs.62.P54

P55

Ectopic insulin production complicating pancreatic neuroendocrine tumour (pNET)

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Case history
58 year old male presented in April 2016 with haematemesis. Octreotide-avid pancreatic mass with liver metastases was identified. Liver biopsy demonstrated well differentiated Grade 2 NET (Ki-67 10–13%). He progressed on Somatostatin analogue therapy, and subsequently Sunitinib, following which he underwent four cycles of Peptide Receptor Radionuclide Therapy (PRRT) with partial response. In May 2018, there was radiological progression. He reported episodes of symptomatic hypoglycaemia, and was commenced on Everolimus. He developed recurrent hypoglycaemia despite supplemental enteral feeding.
Investigations
Fasting insulin and c-peptide levels were elevated at 239 pmol/l and 1762 pmol/l during confirmed hypoglycaemia, consistent with endogenous insulin secretion. Intra-arterial calcium-stimulated venous sampling (ASVS) demonstrated a baseline insulin level of 34.2 mU/l in the hepatic artery, peaking at 239.9 mU/l, compared to a rise from 55.3 mU/l to 102.8 mU/l in the gastroduodenal artery. This confirmed the liver metastases as the source of endogenous insulin secretion. The pancreatic gradient of less than 2 ruled out insulin secretion from the pancreatic primary, therefore excluding metastatic insulinoma.
Results and treatment
He had ongoing hypoglycaemia despite diazoxide, dexamethasone and octreotide. He proceeded to embolisation of the right liver lobe in August 2018 with resolution of hypoglycaemia. In October 2018, the hypoglycaemia recurred secondary to disease progression within the left liver lobe. His left liver lobe was successfully embolised with resolution of hypoglycaemia, which has since been sustained. He commenced further systemic therapy with Capecitabine and Temozolomide.
Conclusions and points for discussion
In summary, ectopic insulin secretion can occur in apparently non-functioning pNET, and in this case widespread metastatic disease preceded symptoms, with subsequent rapid onset of symptomatic hypoglycaemia in the absence of significant disease progression. Endogenous insulin excess was confirmed by ASVS, thus presenting an alternative mechanism of hypoglycaemia in advanced NET, distinct from the previously proposed mechanism of GLP-1/glucagon secretion[1]. Localised therapy with embolisation is an effective therapy, and achieved resolution of hypoglycaemia in this case.
Reference
1) Roberts RE *et al*. GLP-1 and glucagon secretion from a pancreatic neuroendocrine tumor causing diabetes and hyperinsulinemic hypoglycemia. *J Clin Endocrinol Metab*. 2012 Sep; 97(9):3039-45.

DOI: 10.1530/endoabs.62.P55

P56

Paraganglioma of the seminal vesicle

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Case history
A 49-year-old male with hypertension (on doxazosin, amlodipine and perindopril), obesity (BMI 40 kg/m^2) and recent DVT (on warfarin) presented with a few months' history of episodic headaches, palpitations, light-headedness and sweats accompanied by facial pallor, occurring around twice weekly without warning. Symptoms were often worse when upright. Spontaneous recovery followed. He did not have a family history of endocrine disease. Clinical examination was unremarkable except for obesity.
Investigations
Urinary normetadrenalines were elevated on several occasions (between 9.37–21.09 umol/24h – normal <4) after stopping interfering medications. Chromogranins A and B were negative. Urinary 5HIIA and urine free cortisol were normal. CT scans did not show any adrenal or paraspinal abnormalities, but an enlarged 'lymph node' was demonstrated adjacent to the right seminal vesicle. Subsequent MIBG scans did not demonstrate paraspinal or adrenal abnormalities - no adrenal or extra adrenal parganglioma (PGL) was demonstrated. However, a ^{68}Ga-DOTATE PET scan showed a 1.8$\times$2.6 cm paraganglioma adjacent to right seminal vesicle. Genetic analysis revealed no mutations in FH, SDHAF2, SDHB, SDHC, RET, MAX, TMEM127 or VHL genes. Following preoperative alpha blockade with phenoxybenzamine the PGL was removed through robotic surgery. Subsequent histology confirmed a benign functioning PGL. Follow up post-operative 24 urine metanephrines are awaited.
Conclusions and points of discussion
PGL of the genitourinary tract are uncommon with the bladder and urethra being most commonly affected. Seminal vesicle PGL are extremely rare with only 4 cases reported in the literature. Apart from the typical symptoms of catecholamine excess, they present with lower urinary tract symptoms, haematuria or haemospermia. As evidenced above, such lesions may be challenging to localise on standard imaging and specialised scans such as ^{68}Ga-DOTATATE scans may need to be utilised. Surgery remains the treatment modality of choice and robotic surgery was successful in our patient.

DOI: 10.1530/endoabs.62.P56

P57

Alirocumab and the management of dyslipidaemia associated acute pancreatitis

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Case history
A 59-year-old lady with a background of type 2 diabetes, hypercholesterolemia and hypertension presented with a 3-week history of progressively worsening central abdominal pain and vomiting. Her drug history included bezafibrate and atorvastatin on which she was unable to meet her cholesterol and lipid targets and hence were stopped two weeks prior to her admission. The plan had been to start once fortnightly Alirocumab, a PCSK9 inhibitor; which had been delayed due to a lack of availability. Examination revealed xantholasma and abdominal distension with generalised abdominal tenderness.
Investigations
Blood results were initially returned as 'lipaemic' and could not be reported. Once the patient had been initiated on a fixed rate insulin infusion, subsequent bloods showed WCC 12.2, Hb 109, Triglycerides 111.80, Cholesterol 32, CRP 48 and amylase 16. The patient's LFTs were also deranged on admission with an ALT of 83, ALP 289 and a normal bilirubin of 8. The patient underwent a CT abdomen which showed peri-pancreatic inflammatory fat stranding suggestive of acute pancreatitis. In addition it revealed a markedly enlarged liver with appearances consistent with severe hepatic steatosis. In light of this she underwent an abdominal US which showed no evidence of portal or hepatic vein thrombosis and a normal gallbladder without evidence of biliary obstruction.
Results and treatment
She was kept NBM, and jointly managed with the surgeons for acute pancreatitis, secondary to dyslipidaemia. Her hypertriglyceridemia was treated with a fixed rate insulin infusion, dietetic input and the reintroduction of bezafibrate. Restarting atorvastatin was considered, however was precluded by her raised LFTs. Throughout her 9 day admission her triglycerides improved to 13.5 with an HDL of 11.2 and LDL of 0.56. She was successfully initiated on subcutaneous Alirocumab soon after discharge.
Conclusions and points for discussion
The association between dyslipidaemia and acute pancreatitis is well established both as a precipitant and as an epiphenomenon. Dyslipidaemia is commonly secondary to diabetes and obesity, and statins and fibrates are the key pharmacological treatment options. Alirocumab is a monoclonal antibody that binds circulating PCSK9 and blocks its interactions with surface LDLR. It is approved for high risk patients who fail to attain LDL-cholesterol goals despite maximum tolerated medical therapy, including those with a history of pancreatitis. In this case, since the initiation of Alirocumab the patient's lipid profile has improved significantly and she has not experienced further episodes of pancreatitis.

DOI: 10.1530/endoabs.62.P57

P58

In a bind: abnormal thyroid function tests

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Case history
A 44 year old black African woman was referred to the endocrinology clinic for investigation of abnormal thyroid function tests. She had initially presented with palpitations and sweats. She had no significant past medical history and was not taking any prescribed medications or over the counter preparations. On examination, she was clinically euthyroid and did not have any abnormal findings of note.
Investigations
Biochemical investigations revealed a normal TSH of 3.75 iU/ml (0.38–5.33 iU/ml) with a raised free T4 of 24.2 pmol/l (7.0–16.0 pmol/l) and a normal free T3 of 5.6 pmol/l (3.8–6.0 pmol/l). TSH-receptor antibodies were not detected and anterior pituitary hormones were normal. Measurement of thyroid function tests using a second assay at another laboratory yielded similar results, excluding assay interference. Thyroxine binding globulin level was normal at 17.0 ug/ml (14.0–31.0 ug/ml).
Results and treatment
Her total T4 was found to be raised at 195.0 nmol/l (69.0–141.0 nmol/l) by immunoassay, raising suspicion of familial dysalbuminaemic hyperthyroxinaemia (FDH). Radioligand binding assay demonstrated enhanced binding of the patient's albumin to T4, confirming FDH. Furthermore, mutational analysis of the albumin gene ALB revealed a heterozygous change for c.725G > A, (p.Arg242His).
Conclusions and points for discussion
Approximately 99.98% of circulating T4 is protein bound. FDH is an autosomal dominant condition of euthyroid hyperthyroxinaemia caused by mutations in the gene encoding albumin that increase the affinity of albumin for T4. Analogue fT4 assays, commonly used to measure free T4 in clinical practice, work on the assumption that approximately 10% of thyroxine is bound to albumin; in FDH abnormal albumin protein binds up to 30% of thyroxine. 'True' free thyroxine levels remain normal; hence the patient is clinically euthyroid. In addition, as T3 is mostly unbound, it remains normal. The condition does not require treatment. Screening of relatives should be offered. Patients with FDH may be mistakenly treated for thyrotoxicosis, and so a high degree of suspicion is warranted in patients presenting with a raised free T4 in the context of a normal TSH and free T3. Depending on the mutation, the levels of T4 can be 1.2 to 15 times the upper levels of normal. The mutation found in our patient is associated with a milder hyperthyroxinaemia compared to other mutations. FDH has been reported predominantly in Caucasian and Hispanic subjects with only three other cases described in individuals of African (Somali) origin. To our knowledge, this is the first report of the Arg242His mutation in a person of African origin.

DOI: 10.1530/endoabs.62.P58

P59

Treatment of low bone density with a thiazide-like diuretic in idiopathic hypercalciuria

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Case History
A 64 year old lady with osteoporosis was referred for parental antiresorptive therapy due to a history of oral bisphosphonate intolerance. She was screened for osteoporosis at age 53 after her mother suffered a hip fracture, DEXA showing an L2-L4 T score of −2.5 and mean femur −2.2. She was given a trial of alendronate, but stopped due to indigestion. On Calcium and Vitamin D supplementation, the DEXA after 4 years showed improvement of both the spine and femur densities, but after another 5 years, there was a loss in BMD of 0.9% in the spine and 8.2% in the hip. There was no history of previous fragility fractures, she had never taken steroids and did not have rheumatoid arthritis. She was a current smoker. Her menarche was at age 10 and menopause at age 50. Her mother also had a history of kidney stones. Clinical examination did not suggest the presence of any endocrinopathy or other secondary cause of osteoporosis.
Investigations
Full blood count, renal, and liver profiles were within normal limits. Bone profile showed, CoCa 2.41 mmol/l, Phosphate 0.89 mmol/l, PTH 4.9 pmol/l and 25(OH) VitD 116 nmol/l. TFTs and Protein electrophoresis were unremarkable. 24hr urine calcium showed marked hypercalciuria of 9.25 mmol in total (NR 2.5–7.5).
Treatment
FRAX score suggested a 10 year probability of major osteoporotic fracture of 22% and hip fracture of 5.1%; treatment was recommended. The patient was not keen to start parental bisphosphonates, but agreed to take indapamide MR 1.5 mg od. Two years later, bone mineral density in 2018 showed a 5.7% and 7.9% improvement in the density of the spine and mean femora respectively. Based on WHO classification, she is currently in the osteopaenic range.
Conclusions and points for discussion
This case illustrates the importance of looking for secondary causes of osteoporosis, as targeting the underlying cause could be the best treatment option. Studies have shown that administration of a thiazide, as indapamide, with bisphosphonate therapy is associated with a greater reduction in hypercalciuria and improvement in bone density than with bisphosphonate therapy alone. Recent secondary analyses highlight the lower fracture risk in patients using thiazide diuretics compared with other antihypertensive drugs. Studies in individuals with hypercalciuria to examine the efficacy of thiazides, or thiazide-like diuretics, alone or in combination with bisphosphonates in improving bone density and reducing fracture risk are indicated.

DOI: 10.1530/endoabs.62.P59

P60

Hypophosphatemic osteomalacia due to Fanconi's syndrome in a patient with HIV and Hepatitis B coinfection

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Case history
A 56 year old man presented with a few months history of diffuse bone pain affecting his arms, legs, ribs and particularly his left hip. Past medical history included well controlled HIV infection, hepatitis B co-infection, peripheral neuropathy associated with HAART, lipoatrophy, Kaposi's sarcoma, ADHD, type 2 diabetes mellitus, and a history of previous Fanconi's syndrome associated with Tenofovir Disoproxil Fumarate (TDF) 8 years ago. At his initial presentation, his HIV and Hepatitis B treatment comprised of Darunavir, Ritonavir, Raltegravir, Entecavir, Lamivudine and Adefovir. On presentation, this was soon switched to Darunavir, Ritonavir, Dolutegravir, Emtricitabine and Tenofovir alafenamide fumarate (TAF). The latter was discontinued afterwards due to persistent diffuse bone pain.
Investigations
Phosphate was low at 0.59 mmol/l and ALP was elevated at 236 IU/l. Adjusted calcium, magnesium, PTH, bicarbonate, potassium were within normal range. GFR 58 ml/min/1.73 m^2, TmP/GFR: 0.19 (0.8–1.35), urinary aminoacids: elevated, urinary protein: elevated, protein electrophoresis: no paraprotein. A whole-body Tc-99m MDP bone scan showed appearances consistent with multiple rib fractures, asymmetric periarticular activities at both hips, asymmetric focal activity at the left inferior pubic ramus, right TMT joint regions and left shoulder. MRI pelvis demonstrated subchondral fractures within both femoral heads, worse on the left with large joint effusion, active synovitis and fractures of the left inferior and superior pubic rami.
Results and treatment
Hypophosphataemia with low TmP/GFR, proteinuria, glucosuria and aminoaciduria was suggestive of proximal renal tubulopathy and multiple insufficiency fractures were consistent with hypophosphatemic osteomalacia secondary to Fanconi's syndrome. The patient improved with phosphate and alfacalcidol supplementation with subsequent normalisation of phosphate levels and gradual resolution of diffuse pain. Repeat imaging showed healing of the fractures with persistent activity in the left hip joint and residual bone oedema, due to degenerative joint disease. He is awaiting left hip replacement.
Conclusions and points for discussion
Hypophosphatemic osteomalacia due to acquired Fanconi's syndrome has been described in TDF and Adefovir use. Ritonavir co-administration has been reported as a risk factor. TAF has pharmacology similar to TDF with lesser nephrotoxicity. In our patient, it is likely that adefovir was the offending agent, however, the patient continued to have tubular dysfunction despite discontinuation of adefovir and TAF. It is unclear whether he had persistent low grade residual tubulopathy from previous TDF use. Published reports suggest that tubular recovery may take months and may not be complete.

DOI: 10.1530/endoabs.62.P60

P61

A challenging case of cerebral salt wasting syndrome superimposed on central diabetes insipidus following pituitary tumour apoplexy

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Case history
An 84-year old man with known non-functioning pituitary macroadenoma was admitted with productive cough and headache. Clinical assessment revealed evidence of pneumonia and antibiotic treatment was initiated. However subsequently the patient's GCS dropped to 12. Left-sided 6th nerve palsy was present, but patient drowsiness precluded visual-field examination. CT brain showed pituitary tumour apoplexy due to haemorrhage, confirmed on MRI. His condition initially improved with intravenous hydrocortisone.
Investigations
Pituitary hormonal profile revealed panhypopituitarism (random cortisol 125 nmol/L, free T4 4.0 pmol/L, TSH 2.9 mU/L, testosterone $<$1.0 nmol/L, undetectable prolactin and LH/FSH). By day 3 the patient developed polydipsia and polyuria. Overnight water deprivation test confirmed central diabetes insipidus (DI). He was commenced on oral hydrocortisone, levothyroxine, desmopressin and topical testosterone. On day 7, serum sodium dropped to 128 mmol/L. He was initially clinically euvolaemic. Paired serum and urine osmolality were 237 and 752 mmol/L respectively. Urine sodium was elevated (129 mmol/L). Hyponatraemia was initially ascribed to over-replaced DI. Desmopressin dose was reduced and his fluid intake was restricted to 1–1.5 litres/day. Urine output remained high (3–3.5 litres/day), he became progressively dehydrated and serum sodium dropped to 107mmol/L. A diagnosis of cerebral salt wasting (CSW) was made based on clinical hypovolaemia; high urine sodium; and failure of hyponatraemia to improve despite fluid restriction and desmopressin dose reduction.
Results and treatment
The patient received boluses of hypertonic saline (2.7%) for four days in medical high dependency, and serum sodium rose to 120 mmol/L. Thereafter he was maintained on isotonic saline with Slow Sodium tablets to replace urinary sodium loss. Fludrocortisone was added to curtail natriuresis. Serum sodium gradually normalised, and saline infusion, Slow Sodium and fludrocortisone were weaned. He was transferred for rehabilitation six weeks after admission with sodium stable at 135–140 mmol/L.
Conclusion and points for discussion
CSW is a rare cause of hyponatraemia in patients with acute brain injury. The biochemical features of CSW are indistinguishable from syndrome of inappropriate anti-diuretic hormone secretion (SIADH) or over-replacement of desmopressin in DI. Coexistence of CSW with central DI has been described in case reports. In this scenario the diagnosis of CSW may be delayed, as hyponatraemia could be ascribed to desmopressin over-replacement. A useful diagnostic distinction is the patient's clinical volume status; however assessment can be unreliable if volume deficit in CSW is subtle. Management of CSW involves saline infusion guided by serum sodium and fluid balance monitoring. Fludrocortisone can be a useful adjunct treatment.

DOI: 10.1530/endoabs.62.P61

P62

A case of a TSH-secreting pituitary macroadenoma in a previously well thirty year old woman

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Case History
A thirty year old female presented to hospital after a first seizure. She had no significant past medical history. She had a one week history of recurrent frontal headaches and had noticed irregular periods. There were no clinical features of acromegaly. CT and MRI brain imaging showed a 5 cm mass arising from the pituitary fossa, extending into the suprasellar cistern and anterior cranial fossa. There was evidence of mass effect on the optic nerves and optic chiasm with oedema and mass effect affecting the right inferior frontal lobe.
Investigations
Blood tests showed a raised fT3 (13.6 pmol/L), raised fT4 (41.0 pmol/L) and elevated TSH (5.48 mu/L). These results were corroborated by a separate assay. The SHBG was normal at 115 nmol/L. The alpha-glycoprotein hormone subunit was elevated at 2.42 Iu/L. Prolactin was elevated at 963 miu/L. LH (10.3 iu/L), FSH (9.2 iu/L), GH (3.9 ug/L), cortisol (231 nmol/L), calcium (2.37 mmol/L) and PTH (1.92 pmol/L) were all in the normal range. IGF-1 was raised at 61.2 nmol/L. Short synacthen test caused serum cortisol level to rise to 447 mmol/L at one hour from a baseline of 240 mmol/L. These investigations were highly suggestive of a TSH-secreting macroadenoma.
Results and treatment
The patient was discharged on hydrocortisone, propranolol, carbimazole and levetiracetam. She returned to receive her first dose of octreotide 20 mg. Within one week, her thyroid function had normalised. Once euthyroid, the neurosurgical plan was for a multi-stage operation to remove the tumour. She underwent trans-sphenoidal surgery to remove the intra-sellar portion and frontal craniotomy one week later to remove the supra-sellar component. Histology has confirmed pituitary adenoma with focal TSH and GH expression. During surgery it was impossible to fully remove the tumour and subsequently her TSH and fT3/fT4 have risen. Post-operative imaging shows full resection of the sella component but remaining suprasellar tumour. She has received two further doses of octreotide to normalise her thyroid function prior to further surgery later this month.
Conclusions and points for discussion
TSH-secreting pituitary adenomas are rare, with an estimated incidence of one per million. They tend to present due to mass effect rather than hyperthyroidism as the patient gradually becomes accustomed to elevated thyroid hormone levels. This case exemplifies this as the presentation was with a seizure. This case demonstrates successful use of octreotide to normalise thyroid status prior to surgery, the complexity of surgery for large macroadenomas, and the atypical presentation of TSH-omas.

DOI: 10.1530/endoabs.62.P62

P63

Prednisolone replacement makes steroid optimisation easier in patients on mitotane

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Case history
A 66 year old lady presented with abdominal pain, new onset diabetes and hypertension. She was diagnosed with Cushing's syndrome and was found to have a large heterogeneous left adrenal mass of 11.4 $\times$ 9.3 cm in size with no disease elsewhere. She underwent a left open adrenalectomy and the histology confirmed an adrenocortical carcinoma (Weiss score of 7) with focal vascular invasion, no extra-capsular spread and clear resection margins. Following surgery she was commenced on 4 mg of prednisolone as steroid replacement. With her low-moderate risk of recurrence different management options were discussed including adjuvant mitotane treatment. Two months postoperatively, mitotane was started with a plan to escalate the dose.
Investigations
We have shown previously that once-daily prednisolone can be used as steroid replacement instead of three times a day hydrocortisone. Most patients require between 3 to 4 mg of prednisolone per day which can be adjusted according to the 8-hour prednisolone level aiming for 15 mcg/l to 25 mcg/l. Keeping in mind that mitotane leads to CYP3A4 induction of which prednisolone is one of its substrate, we carried out three prednisolone day curves (at 1, 2 and 7 months after starting Mitotane) with parallel ACTH measurements to find the optimal prednisolone replacement dose using ACTH as marker of adequate replacement.
Results and treatment
Our results showed that prednisolone levels at different time points correlate well with ACTH levels. With increasing duration of Mitotane treatment, increasing prednisolone doses were required to achieve normalisation of ACTH at 8 hours. Cortisol binding globulin levels predictably increased from 55.7 mg/L to 158.9 mg/L within two months of Mitotane treatment. Our patient required 20 mg of prednisolone at 7 months of treatment.
Conclusions and points of discussion
Mitotane increases cortisol clearance and increases cortisol binding globulin concentration. There is no reliable laboratory marker to guide the optimal dose of steroid replacement. Hydrocortisone needs to be given three times daily and the dose adjustment can be difficult in this scenario. Clinical symptoms, 24-hour urinary free cortisol levels and serial ACTH measurements are being used. With once-daily prednisolone as steroid replacement, a single 8-hour ACTH level can be used to adjust the prednisolone dose with patients receiving Mitotane.

DOI: 10.1530/endoabs.62.P63

P64

5-year survival in poor prognosis adrenocortical carcinoma without mitotane treatment

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Case history
52 year old gentleman presented in 2013 with a 1 year history of abdominal pain. Imaging to screen for gallstones identified a large adrenal mass which was radiologically suspicious for adrenal carcinoma with probable inferior vena cava (IVC) involvement.
Investigations
Overnight dexamethasone suppression test (ONDST) failed to suppress cortisol (324 nmol/l) with undetectable ACTH (<5 ng/l). Failure of suppression on low dose dexamethasone suppression test (cortisol [nmol/l]: T=0, 324; T=48h, 286; ACTH [ng/l]: T=0, <5; T=48h, <5) confirmed a cortisol-producing tumour. Urinary fractionated metanephrines were 2.46 umol/24h (normal <3.47), ruling out phaeochromocytoma.
Results and treatment
A 28 cm right adrenal tumour was resected en bloc with a section of IVC and partial hepatectomy. Recovery was complicated by post-operative cardiac arrest and prolonged ITU stay. Histopathology was suggestive of a malignant tumour with Weiss score of 9, with viable tumour confirmed in the main adrenal vein/IVC. Post-operatively the patient required steroid replacement due to contralateral adrenal suppression. Short synacthen test (SST) showed cortisol 130 (T=0 m), 129 (T=30 m) and 136 (T=60 m). In view of the high risk of recurrence the patient was offered post-operative mitotane therapy which he has consistently declined, so has been followed up with clinical, biochemical and radiological monitoring. ONDST has consistently suppressed cortisol fully (<20), however, the patient developed Cushingoid features with weight gain and hypertension. Serial cross-sectional imaging has shown no evidence of macroscopic disease recurrence at 5 years post-resection. Since 2015, 24-hour urine collection has shown elevated adrenal androgens and cortisol metabolites suggestive of adrenal Cushing's, presumed secondary to microscopic disease not visible on imaging. He remains steroid-dependent on replacement prednisolone. Most recent SST showed baseline ACTH 92.8, cortisol 214 (T=0 m), 246 (T=30 m) and 244 (T=60 m).
Conclusions
Case series suggest very poor prognosis for large adrenocortical carcinomas with vascular invasion at presentation, and routine management would involve post-operative mitotane for this reason. However, there is a risk of selection bias in case series from tertiary referral centres, as advanced disease may prompt referral. Our patient declined conventional therapy but remains free of macroscopic disease recurrence at 5 years. He appears to have active cortisol precursor production causing elevated urinary metabolites and Cushingoid features, but persistently suppressed peak cortisol on SST and fully suppressed cortisol on ONDST. Mindful consideration is given to achieving ACTH suppression with steroid replacement to reduce the risk of overt disease recurrence, balanced against the adverse metabolic effects of rendering him Cushingoid.

DOI: 10.1530/endoabs.62.P64

P65

Pituitary abscess with meningitis: a rare presentation

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Case history
A 42-year-old lady was referred from neurology clinic after being assessed for symptoms of headaches, dizziness, transient visual problems and paraesthesia over her limbs for 2 months. On review, she complained of amenorrhoea and was noted to be pale, however, her neurological examination including visual fields to confrontation and ocular movements were normal. Subsequent investigations were consistent with pan-hypopituitarism and she was promptly commenced on hydrocortisone.
Investigations:
LH: 1.0 U/L (2.0–13.0)
FSH: 4.7 U/L (3.0–10.0)
Estradiol: <44.0 pmol/L
TSH: 0.04 mU/L (0.35–5.5)
Free T4: 10.0 pmol/L (10–20)
Prolactin: 684 mU/L (59–619)
Cortisol: 20 nmol/L (200–500)
Sodium: 124 mmol/L (133-146)
She had an urgent MRI scan which revealed 18 × 14 mm pituitary mass with minor optic-chiasmal compression and unusual signal characteristics (Image 1.0/1.1).

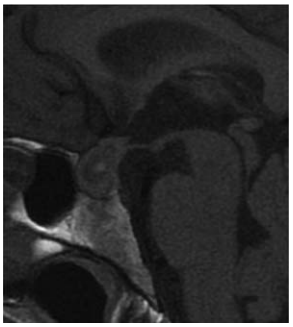

Image 1.0

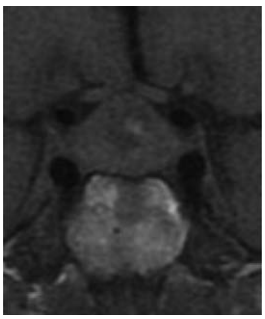

Image 1.1

Results and treatment
Two weeks later she presented to emergency with worsening headache, persistent vomiting and visual blurring. She was noted to have slightly reduced visual acuity in the left eye, however, visual fields were normal. Urgent CT scan did not reveal acute haemorrhage and she was being considered for elective surgery and a high-resolution MRI Pituitary was planned. Whilst admitted she developed a severe headache, photophobia and vomiting. Lumbar puncture revealed raised intracranial pressure & lymphocytic pleocytosis.
CSF results:
Opening pressure: 43 cm H_2O
Protein: 1.2 g/L (0.08–0.32)
WCC: 2000 (P 35%, L 65%)
Culture/Virology/AFB/Mycobacterium spp. PCR: Negative
She was then started on i.v. Ceftriaxone & Acyclovir and review of her images at regional Pituitary MDT raised suspicion of infective pathology. She was being considered for urgent trans-sphenoidal debulking/decompression, however, she subsequently improved clinically and repeat imaging showed shrinkage of the pituitary lesion with infundibular thickening. She also developed cranial diabetes insipidus and was managed with oral desmopressin. She was managed conservatively for a pituitary abscess and completed an 8-week course of antibiotics. Repeat imaging at 2 and 7 months showed complete resolution of the lesion (Image 2.0/2.1) and she remains on pituitary hormone replacement.

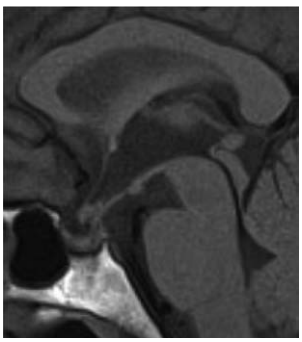

Image 2.0

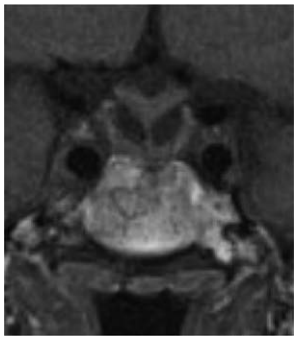

Image 2.1

Conclusions and points for discussion
A pituitary abscess is a rare cause for a sellar mass which may present without classical symptoms of infection. Atypical imaging characteristics should raise the index of suspicion.
What are the prospects of recovery of pituitary function?
What should be the follow-up surveillance?

DOI: 10.1530/endoabs.62.P65

P66

Treatment of low bone density with a thiazide-like diuretic in idiopathic hypercalciuria

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Case History
A 64 year old lady was referred for parental antiresorptive therapy due to a history of oral bisphosphonate intolerance. She had been screened for osteoporosis at age 53 after her mother had suffered a hip fracture, DEXA scan showed an L2-L4 T score of −2.5 and a mean femur −2.2. She was given a trial of alendronate, but had stopped due to indigestion. The DEXA scan at 4 years showed improvement of both the spine and femur densities on Calcium and VitaminD Supplementation. 5 years later, there had been a loss in BMD of 0.9% in the spine and 8.2% in the hip. There was no history of previous fragility fractures, she had never taken steroids and did not have rheumatoid arthritis. She was a current smoker. Her menarche was at age10 and she had reached menopause at age50. Her mother had a history of kidney stones starting at age19. Clinical examination did not suggest the presence of any endocrinopathy or other secondary cause of osteoporosis.
Investigations
Her full blood count, renal, and liver profiles were within normal limits. Bone profile showed, Corrected Ca 2.41 mmol/L, Phosphate 0.89 mmol/L, PTH 4.9 pmol/L and 25(OH)Vit D 116 nmol/L. TFTs and Protein electrophoresis were unremarkable. 24hr urine calcium showed marked hypercalciuria of 9.25 mmol in total (NR 2.5–7.5).
Treatment
FRAX score suggested a 10 year probability of major osteoporotic fracture of 22% and hip fracture of 5.1%; starting treatment was recommended. The patient was not keen to start parental bisphosphonates, but she agreed to take indapamide MR 1.5 mg od. Two years later, bone mineral density in 2018 showed a 5.7% and 7.9% improvement in the density of the spine and mean femora respectively and based on WHO classification, she is currently in the osteopaenic range.
Conclusions and points for discussion
This case illustrates the importance of looking for secondary causes of osteoporosis, as targeting the underlying cause could be the best treatment option. Studies have shown that administration of a thiazide with bisphosphonate therapy is associated with a greater reduction in hypercalciuria and improvement in bone density than with bisphosphonate therapy alone. Recent secondary analyses highlight the lower fracture risk in patients using thiazide diuretics compared with other antihypertensive drugs. Studies in individuals with hypercalciuria to examine the efficacy of thiazides, or thiazide-like diuretics, alone or in combination with bisphosphonates in improving bone density and reducing fracture risk are indicated.

DOI: 10.1530/endoabs.62.P66

P67

Adrenal insufficiency and iatrogenic Cushing's syndrome in an asthmatic patient on inhaled corticosteroids and antidepressants

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Case history
A 45-year-old female with a background of depression presented with asthma exacerbation. She was taking paroxetine and mirtazapine for depression. Over the preceding six months the patient's asthma control had deteriorated, resulting in overuse of inhaled beclometasone. On questioning, the patient reported a four stone weight gain in four months with generalised weakness, dizziness and fatigue during simple activities. On examination, the patient appeared overtly Cushingoid.
Investigations
Overnight dexamethasone suppression test revealed 11pm cortisol of 48 and 8am cortisol of less than 27 nmol/L, excluding Cushing's disease. Early morning cortisol, repeated without dexamethasone suppression, measured 27 nmol/L and short synacthen test supported the diagnosis of adrenal insufficiency. Pituitary profile revealed suppression of further hormones, with normal imaging. Our investigations indicated severe hypothalamic-pituitary adrenal axis suppression with concurrent iatrogenic Cushing's Syndrome.
Results and treatment
The patient was commenced on hydrocortisone and counselled on her diagnosis. Along with education on inhaler technique and appropriate use, her drug control was optimised. According to the GP, signs and symptoms had developed rapidly over a few months. Overuse of inhaled corticosteroids (ICS) is common, reported in up to 50% of patients and therefore may only provide partial explanation for such severe and rapid progression in this patient. Cytochrome (CYP) 34A is the enzyme responsible for steroid metabolism. It is well documented that concurrent use of an ICS and CYP34A inhibitors, such as antivirals and antifungals, results in rapid development of steroid-related side effects. It is rarely described in patients on commonly prescribed antidepressants. Paroxetine is a strong inhibitor of CYP450 enzymes, with laboratory studies suggesting a moderate inhibitory effect on CYP34A. Additionally, as mirtazapine is also metabolized by the CP34A enzyme, competitive inhibition may result. This drug interaction, whilst significant due to the commonality of such prescriptions, may be under-appreciated. To our knowledge, there is one just existing case in the literature reporting such interaction.
Conclusions
Whilst there are systemically safer ICS available, current national guidelines recommend the least costly drug that is suitable for an individual should be prescribed. This can be problematic with concurrent use of CYP450 inhibitors, which is often overlooked. Therefore, practitioners should be aware of the issues discussed and be able to recognize early presentation of side effects. Additionally, education on inhaler technique and appropriate use could prevent exacerbation of this drug interaction.

DOI: 10.1530/endoabs.62.P67

P68

The double edge sword steroid facilitated diagnosis of primary thyroid lymphoma

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Introduction
Primary thyroid lymphoma (PTL) is a rare cause of malignancy, accounting for $<5\%$ of thyroid malignancies and $<2\%$ of extra-nodal lymphomas. Most thyroid lymphomas are non-Hodgkin's lymphomas of B-cell origin. Patients with Hashimoto's thyroiditis are at greater risk for developing PTL. Early diagnosis is important as treatment and prognosis of PTL depend upon the histology and stage of the tumour at diagnosis. We report a rare case of primary thyroid lymphoma in a patient presenting with a rapidly enlarging thyroid goitre highly suspicious of anaplastic thyroid carcinoma posing as a diagnostic histological challenge due underlying Hashimoto's thyroiditis which was unmasked after a short course of oral steroids.
Case report
A 51 years old female was referred by GP with increasing painless swelling over the right side of neck over a period of 3 weeks. She did not have any difficulty in

swallowing or breathing. There was no history of any weight loss or night sweats. Her TSH was 9.57 mIU/L with a normal free T3, T4 and positive thyroid peroxidase antibody suggestive of subclinical hypothyroidism secondary to Hashimoto's thyroiditis. The scan showed a large mass on the right side of the thyroid gland measuring 4.8 × 4.6 × 3.7 cm, encasing the common carotid artery with complete compression and thrombosis of the internal jugular vein. There were multiple lymph nodes on the right side of neck. Initial imaging was highly suspicious of anaplastic thyroid cancer which carries a poor prognosis. She was referred to our thyroid surgeon and had a fine needle aspiration which unexpectedly only showed inflammatory/reactive picture with no clear signs of malignancy. She was given oral steroids for 4 days, which decreased the size of the neck swelling followed by a core biopsy. The resultant histology showed clearance of the inflammatory picture whilst unraveling histological features of a high grade lymphoma. A diagnosis of B cell lymphoma was confirmed by the Haematologist. From a haematological perspective, giving steroids prior to diagnostic biopsy for suspected lymphoma is strongly discouraged as steroids can partially treat high-grade lymphomas, induce necrosis and render the biopsy uninterpretable.

Conclusion

This case highlights the unexpected paradoxical role of steroids in unmasking the histopathological diagnostic dilemma of PTL which carries a more favourable prognosis compared to anaplastic thyroid carcinoma whilst shrinking the mass.

DOI: 10.1530/endoabs.62.P68

P69

It's not all primary hypertension

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Case history

48 year old man presented in the endocrinology clinic for further evaluation of hypertension (HTN). He had a hospital admission 2 months ago with worsening dyspnoea and markedly elevated BP (236/149 mmHg). He denied any visual disturbances or chest pain. There were no symptoms to suggest any endocrinopathy. His PMH included previous inguinal hernia repair. He was not on regular medications and he had no allergies. He lived with his family, worked as a manager and he was a smoker. There was a family history of HTN in his father but no other cardiovascular conditions. On examination, he appeared overweight but he had no stigmata of any endocrine conditions. Respiratory and cardiovascular examination were unremarkable

Investigations

During his hospital admission, he was investigated for end organ damage and underlying secondary causes. These included baseline blood tests, chest x-ray, ECHO, urine dipstick, fundoscopy, ARR and 24-h-urine catecholamines, HBA1c and lipid profile.

Results and Treatment

Investigations revealed evidence of end-organ damage (LVH pattern with left strain on ECG, LVH on ECHO, Grade 3 retinopathy on fundoscopy, Creatinine:117) and hyperreninemic hyperaldosteronism (Renin: 20.4-H, Aldosterone: 760-H, ARR: 37. 24 urine metadrenalins: 1.4 (< 1.2), normetadrenalins: 4.5 (< 2.9) 3-methoxytyramine 1.7 (< 1.3). In addition, he was diagnosed with impaired glucose regulation and hyperlipidaemia. He was commenced on Ramipril, amlodipine, bisoprolol and Furosemide. In view of the above, he had a CT with contrast to visualize the adrenals and renal arteries. This showed a 13mm myolipoma on the right adrenal, normal kidneys with no masses and bilateral slightly beaded renal arteries suggestive of fibromuscular dysplasia (FMD). He repeated urine collection for catecholamines three times and were all negative. At follow up, he remained on 4 different antihypertensive agents, with moderate control of his HTN. He has been referred to the Vascular team for further evaluation.

Conclusions and points of discussion

FMD is a non-inflammatory, non-atherosclerotic disorder that leads to arterial stenosis, occlusion, aneurysm and dissection and is more common in women. Its exact prevalence is unknown and although the disease is thought to be rare, recent studies have suggested that it may be underdiagnosed. In our case, demographics, personal and family history would suggest a likely diagnosis of essential hypertension. However, in light of evidence of accelerated hypertension, further assessment of secondary causes was warranted. Hyperreninemic hyperaldosteronism with hypertension is indicative of renovascular disease. In the abscence of more common causes, FMD should remain in the differential diagnosis and appropriate imaging considered.

DOI: 10.1530/endoabs.62.P69

P70

How low can you go? Isolated hypothyroxinaemia in pregnancy

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Case history

A 40-year-old, primaparous woman was referred at 24 weeks' gestation to Obstetric Medicine for review of abnormal thyroid function tests (TFTs).

Investigations

One year prior to pregnancy, TFTs included a thyroid stimulating hormone (TSH) level of 0.95 mU/l (local non-pregnant reference range 0.3–4.2 mU/l) and a free thyroxine level (fT4) of 7.3 mU/l (local non-pregnant reference range 9.0–23.0 mU/l). At 18 weeks' gestation, routine TFTs showed a TSH of 1.00 mU/l (local reference range for 2nd trimester 0.6–2.8 mU/l) and a fT4 of 7.3 mU/l (local reference range for 2nd trimester 9.0–14.3 mU/l). She was prescribed 25 mcg thyroxine based on these results, and also took pregnancy multivitamins. She denied all symptoms of hypopituitarism and had a mid-day cortisol of 219 nmol/L. MRI pituitary showed a slightly enlarged gland, consistent with pregnancy. Thyroid assay interference was excluded by analysis at the supra-regional assay service.

Results and treatment

All results were reassuring, but with ongoing diagnostic uncertainty, 25–50 mcg thyroxine was continued. However her TSH remained normal, and fT4 remained < 8.0 mU/l. It was later concluded that she had isolated hypothyroxinaemia (IH). Healthy twin boys were delivered by caesarean section at 37 + 5 weeks' gestation. At delivery her thyroxine was stopped; post-partum TFTs remained normal (TSH 0.52 mU/l, fT4 9.4 mU/L).

Conclusions: *What is IH?*

IH is defined by a fT4 below the lower limit of the trimester-specific reference range. It complicates 1–2% of pregnancies, with significant geographical variation (1).

What is the role of iodine supplementation?

IH is associated with iodine deficiency. Individual iodine status is difficult to assess, as urinary iodine has significant intra-individual variability (2); therefore cases of IH may benefit from empirical iodine supplementation.

What is the role of pituitary axis assessment?

Pituitary dysfunction can very rarely present as isolated hypothyroxinaemia. In pregnancy, thorough clinical assessment is essential, but routine intracranial imaging or biochemical assessment of the pituitary is not justified in all women with IH.

Is there a role for thyroxine treatment?

IH is not associated with adverse pregnancy outcomes so routine treatment with thyroxine is not recommended (3,4). If there is no clinical suspicion of pituitary dysfunction, it is reasonable to cease thyroxine treatment.

References

1. Dong & Stagnano-Green, Thyroid 2018.
2. Wainwright & Cook, Annals of Clin Biochem. 2018.
3. Lazarus *et al*. Eur Thyroid J 2014.
4. Alexander *et al*. Thyroid 2017.

DOI: 10.1530/endoabs.62.P70

P71

Late effects of cancer treatment: it's not always the pituitary

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A 21 years old male, diagnosed with ALL in 2003 (aged 9), completed treatment in June 2009 (aged 15). Chemotherapeutic agents included doxorubicin, daunorubicin, cytarabine, mercaptopurine, methotrexate, asparaginase, vincristine, dexamethasone (7 mg for 3.5 years). He didn't receive any cranial irradiation. He underwent endocrine assessment aged 15 because of delayed puberty and had testosterone replacement for 4 years (September 2012 till January 2016). He also had history of sepsis at age of 16 weeks and has an autistic spectrum disorder. He was diagnosed with veno-occlusive disease (VOD) with splenomegaly and thrombocytopaemia in 2012. Recently he underwent TIPS which was not successful likely due to an occluded portal vein, and has evidence of cirrhosis on liver biopsy. He was referred to endocrinology team with low FT4 and normal TSH and low IGF1 to determine (summarised below). Examination revealed no evidence of hypopituitarism clinically and normal pubertal development.

Investigations
Cortisol(random)138 (133–537 nmol/l)
Testosterone 19.5 (7.6–31.4 nmol/l)
SHBG 51 (16–55 nmol/l)
FT4 9.6 (12–22 pmol/l)
FT3 4.5 (4.0–6.8 pmol/l)
TSH 1.72 (0.27–4.2 mIU/l)
TBG 9.2 (14–31 μg/ml)
IGF-1 9.0 (15.5–67 nmol/l)
IGF BP3 1.2 (2.8–6.4 mg/l)
Prolactin 171 (86–324 mIU/l)
Thyroid assay interference studies (Cambridge) DELFIA assay showed TSH 1.42 mU/l (0.4–4.0), FT4 10.7 pmol/l (9.0–20), calculated FT4 10.0.
FT3 CENTAUR 4.76 pmol/l (3.5–6.5), Total T4 44.6 nmol/L (69–141), TBG 9.2 μg/ml (14–31).
They showed no evidence of assay interference, demonstrated low total T4 and TBG, and commented that some fT4 assays can cause fT4 low depending on methods. Short synacthen test 9am cortisol 168, 30 minutes 415, 60 minutes 485.
Points for discussion
Severe VOD has been reported after 6-thioguaninine and indeed this agent was not used after 2003. There is a rarer association of thioguanine with portal hypertension reported in literature. This patient is unusual in that the VOD occurred sometime after completion of chemotherapy. In this patient synthetic function of the liver has been affected by severe VOD, resulting in low IGF1 concentration and abnormal TFTs. This could have been interpreted as pituitary disease however he had no treatment that affects pituitary function, here other reasons for his endocrine abnormalities were explored and liver disease was determined to be the cause. These data additionally demonstrate how inter-current illness and intensive treatment such as in the management of haematological malignancy can affect pubertal development. The need for testosterone replacement should be reviewed when patients have recovered to ensure they are not treated inappropriately, particular in patients such as this where no gonadotoxic agents were used.

DOI: 10.1530/endoabs.62.P71

P72

Challenges in managing a young lady with recurrent unexplained hypoglycaemia

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Case history
A 23-year-old Caucasian nurse presented with six months of frequent recurrent symptomatic hypoglycaemic episodes with capillary blood glucose ranging between 1.2 and 3.5 mmol/l and symptoms improving after a carbohydrate snack or a drink. The episodes were more likely to occur during fasting state and after excess physical activities. A careful history excluded intake of any off-prescription medications, dfrugs or psychosocial problem.
Investigations
FBC, U&E, LFTs, bone profile, prolactin, IGF-1, LH, FSH, free T4, TSH, random and 0900 h cortisol, short synacthen test, 72-hour fasting, 5 hour OGTT, mixed meal test, coeliac screening, plasm metanephrines, IGF1:IGF2 ratio, insulin antibodies, fasting gut peptides, amino acids carnitines, ammonia, lactate, glycogen storage disorder genetic testing. Urine metabolic and organic acid screening, 24-hour urine 5HIAA, sulphonylureas screening. MRI pancreas, small bowel, abdomen, neck. CT thorax.
Results and treatment
All above routine and other investigations, urine tests, pituitary hormone profile and radiological investigations were normal. During the first 72-hour fasting, she developed symptomatic hypoglycaemia (plasma glucose 1.8 mmol/l) and concomitant levels of insulin (10 mmol/l) and C-peptide (<94 pmol/l) were appropriately suppressed. Blood sulphonylurea screen during hypoglycaemia was negative. During the second 72-hour fasting, her lowest plasma glucose level was 2.3 mmol/l, and concomitant levels of insulin (11 mmo/l) and C-peptide (125 pmol/l) were appropriately supressed. Corresponding hydroxybutyrate levels were high >3000. IGF-2: IGF-1 ratio (4.0) and insulin antibodies (4.8 Mg/l (<5)) were normal. During the mixed meal test, her blood glucose was at its lowest (3.3 mmol/l) at 150 minutes post meal without any symptoms. A diagnosis of idiopathic hyperketotic hypoglycaemia resulting from some rare yet unidentified enzymatic defects in her glucose metabolism pathway was made. She has been enrolled in the 100,000-genome project. Despite a trial of dietary interventions she continued to suffer from hypoglycaemic episodes significantly affecting her work and quality of life. Therefore, oral hydrocortisone (total 20 mg a day) was initiated on a trial basis on which she showed a significant improvement.
Conclusions and points for discussion
Hypoglycaemic disorders are common especially in young women, where a common diagnosis is reactive hypoglycaemia. However, this case highlights the challenges in investigating and managing hypoglycaemia where a cause is not obvious after extensive investigations. When faced with any rare insulin-independent cause of hypoglycaemia a pragmatic approach to management with diet and, if necessary, pharmacotherapy is crucial in improving symptoms and quality of life.

DOI: 10.1530/endoabs.62.P72

P73

A curious case of hypernatraemia

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This case pertains to a 58 year old female who attended hospital with right leg pain. Past medical history included metastatic uterine cancer (lung, bone, and brain), and bipolar disorder treated with sodium valproate and lithium. Prior to admission the patient lived at home with her husband, mobilised independently, and communicated with a mild expressive dysphasia secondary to brain metastases. The patient was admitted under orthopaedics and diagnosed with a pathological right femur fracture. During pre-operative assessment it was noted that the patient was acutely confused and drowsy with new onset tachycardia and shortness of breath. CTPA showed multiple PEs and increased burden of metastatic disease, chest XR showed nil focal, and CT head was similar to previous with some white matter oedema. The patient was treated clinically with antibiotics for pneumonia and treatment dose clexane. The patient continued to deteriorate overnight with decreased GCS and episodes of twitching (seizure activity) isolated to the upper limbs. EEG showed no status but mild encephalopathy. Neurology advised starting on leviteracetam and a course of dexamethasone. On day 4 of admission blood tests showed a sodium of 165 (previously within range). Fluid balance showed a 5 litre per 24 hours urine output with poor oral intake resulting in a deficit of approximately 4 litres per day. Urine and serum osmolalities were sent to the laboratory and treatment with intravenous fluids was commenced. A titration of dextrose, 0.18% saline, and normal saline were used variably over the next 11 days to return sodium levels to normal range. During this period the patient was taking 7-8 litres of fluid per day, initially intravenous and then orally, maintaining a positive fluid balance of approximately 1L per day. Urine osmolality = 172 mOsm/kg Serum osmolality = 327 mOsm/kg Endocrinology advised a trial of low dose desmopressin for long-term management of urine output. This reduced urine output to 2 l per day thus reducing the patient's oral intake requirements. The patient had a successful surgery with IVC filter *in situ* 12 days post admission. It transpired that prior to admission the patient's family had been assisting the patient in drinking 8 litres of water per day. At point of admission, an unintentional water-deprivation test revealed the underlying diagnosis of diabetes insipidus. The debate remains as to what the underlying pathology was. A) Nephrogenic diabetes insipidus secondary to lithium or B) neurogenic diabetes insipidus secondary to brain metastases?

DOI: 10.1530/endoabs.62.P73

Clinical Update

Workshop A: Disorders of the hypothalamus and pituitary

WA1

A rare case of diabetes insipidus and breathlessness…

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Langerhans cell (LCH) histiocytosis occurs in 1 per 560,000 adults with variable manifestations. It has a high rate of misdiagnosis due to its variable presentation and rarity. It is even more rare that it presents with simultaneous and multiple endocrine dysfunction early in the course of disease. We report a case of Langhans Cell Histiocytosis in an adult male presenting with central Diabetes Insipidus, Hypergonadotrophic Hypogonadism and pulmonary disease. A 36 year old male presented with new onset polyuria, polydipsia, nocturia associated with weight loss and generalised lethargy. Systemic enquiry revealed exertional dyspneoa, dry cough, two episodes of spontaneous epistaxis and left leg pain resulting limp on walking. Chest examination revealed bilateral crackles in lung bases. Investigations showed compensated hypergonadotrophic hypogonadism, marginally elevated prolactin, normal thyroid function and IGF 1. Short Synacthene Test was normal. Water Deprivation Test suggested Central Diabetes Insipidus. His ESR was elevated at 51. Vasculitis screen, immunoglobulin and compliment were normal. Pituitary MRI revealed absent bright spot. Chest X ray showed nodularity on upper lobes and CT chest confirmed upper lobar nodularity, cystic changes and fibrosis. Skeletal survey was normal. Diagnosis was confirmed by lung biopsy. A diagnosis of multisystem Langhans Cell Histiocytosis with Central DI and Hypogonadism was made. He was started on desmopressin and testosterone replacement. Langhans Cell Histiocytosis should be considered as a diagnosis in any case presenting with Cental Diabetes Insipidus with multiorgan involvement.

DOI: 10.1530/endoabs.62.WA1

WA2

Hypopituitarism due to Hypothalamic-Pituitary sarcoidosis- an index event of a systemic condition

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We report a 38 years old male who was referred to the endocrine clinic with 3 months history lethargy, lack of libido and reduced shaving frequency. He was previously fit and well with no past medical history however he and his wife has been trying for pregnancy for 2 years. He didn't smoke, has no history of opioids use and drink 10 units of alcohol a week. His investigation showed panhypopiturism with profound low serum testosterone of <0.5 nmol/l (8.33–30.19), SHBG 33.2 nmol/l (13.5–71.4), lH <0.1 iu/l (0.57–12.07) FSH 0.6 iu/l (0.95–11.95), 0900 serum Cortisol of 51 nmol/l, TSH 1.12 miu/l (0.35–4.94), Free T4 5.9 pmol/l (9.0–19.0) and Insulin-like growth factor 1 9.9 nmol/l (8.3–29.2). MRI Pituitary gland showed 4 mm focus of subtly reduced enhancement in the left half of the pituitary fossa and 6 mm nodule infundibulum in keeping with neoplastic, infectious and granulomatous infiltration. CT Thorax abdomen showed extensive bilateral hilar and mediastinal lymphadenopathy with nodularity and fibrosis in the upper lobes which is typical of pulmonary sarcoidosis. Serum calcium was normal however serum Angiotensin converting Enzyme (ACE) came back elevated at 146 iu/l (10–75).

Diagnosis

Hypothalamic-Pituitary sarcoidosis and pulmonary sarcoidosis. He was started on Hydrocortisone, levothyroxine and topical testosterone as treatment for anterior pituitary dysfunction. His symptoms improved significantly. He has been referred to respiratory team for further evaluation and treatment of pulmonary sarcoidosis.

Discussion

Although patients with sarcoidosis have only 5% clinical involvement of the nervous system, the hypothalamus is the most frequently involved of all the endocrine glands. This case shows that in the absence of obvious systemic features of sarcoidosis, hypopituitarism was the index event leading to the diagnosis of a systemic disease. Treatment involves replacing hormones. Role of high dose systemic steroid to restore pituitary function is not established however there is some evidence of regression of radiological features.

DOI: 10.1530/endoabs.62.WA2

WA3

A case of Isolated left Abducens Nerve paresis and Pituitary macroadenoma

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A 64 years old female presented with frontal headache and sinusitis like features. Later she got double vision when she woke up in the morning. No eye pain or vision loss. No weakness in the limbs. No neck pain. On examination: BP, heart rate and other observations within normal limits. No postural hypotension. Diplopia on left lateral gaze, very limited abduction of left eye. Other cranial nerves intact. Normal visual fields. No signs of Cushing's. No motor or sensory deficit. No signs of meningism. CT head showed pituitary adenoma and then Pituitary MRI revealed 11 mm Pituitary macroadenoma with extension into left posterior aspect of cavernous sinus. Short synacthen test showed normal response. Prolactin, thyroid functions within normal limits. FSH, LH elevated appropriately for post-menopausal state. Vacuitis screen negative, HbA1C 38. It is unusual for Pituitary adenoma to involve Abducens nerve and spare other cranial nerves in the cavernous sinus. Pituitary adenoma is non functioning in this case but question is if this patient needs pituitary surgery if Abducens nerve paresis is due to Pituitary adenoma.

DOI: 10.1530/endoabs.62.WA3

WA4

Pineal Gland Tumor presenting with Panhypopitutarism & Diabetes Insipidus

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21 year old man presented to the emergency department with hypotensive shock. He had been seeing the GP with complains of poor appetite, intermittent vomiting, increased thirst and postural dizziness for the last 6 months. Previous medical history included tonsillitis, gastritis and learning difficulties. The working differential was severe gastroenteritis with hypovolemic shock, and so he was given immediate fluid resuscitation. He remained hypotensive, and so was given empirical steroids to good effect. The following day, he developed polyuria prompting endocrinology review. Examination revealed scarcity of facial hair,small volume testes (Tanner stage 3) but no visual field defect to confrontation. Investigation then confirmed diabetes insipidus (which is likely to have been unmasked by glucocorticoid treatment) and panhypopituitarism. The presenting serum sodium was 156 mmol/l (133–146 mmol/l), serum osmolality 320 mmol/kg (275–295 mmol/kg) with urine osmolality 187 mmol/kg (40–1200 mmol/kg). Cortisol was 83 nmol/l (101–536 nmol/l),Growth Hormone 0.26 ug/l, IGF1 3.2 nmol/l (11.3–56.6), Testosterone <0.4 nmol/l (8.6–29), lH, <0.2 IU/l (3–8 IU/l), FSH <0.2 IU/l (<8 IU/l), Prolactin 1102 mIU/l (53–360 mIU/l). FT4 7 pmol/l (8–21),TSH 0.37 mU/l (0.35–3.5) and similar TFTs noted 1 year earlier on electronic record. Autoimmune screen and serum tumor markers including hCG were normal. CXR was unremarkable. MRI showed wide spread abnormal signal around the pineal gland extending anteriorly to the hypothalamus and optic chiasm suggestive of a pineal gland germ cell tumour with local invasion. Subsequent analysis of the cerebral spinal fluid showed elevated hCG 10.83 IU. The patient was initiated on hydrocortisone, levothyroxine, desmopressin and testosterone and discussed at the regional pituitary neuro-oncology MDT. Craniotomy and open biopsy confirmed the presence of a pineal gland germinoma. He then received 24Gy radiotherapy in 15 fractions and remains extremely well at 20 months follow up but has become partially sighted. Pineal gland tumors represent around 1% of all primary intracranial tumours and can be subdivided into germ cell and non germ cell types. These typically manifest in adolescence with endocrine dysfunction, disruption of growth and puberty. These tumours are remarkably radiosensitive but optimal treatment varies according to pathology requiring a tissue diagnosis wherever possible. In this case, three clues to the eventual diagnosis might have been spotted earlier. Vomiting beyond 2 weeks should prompt a search for underlying causes. Prolonged delay of growth and puberty should prompt a detailed physical evaluation and a basic endocrine assessment. Finally, a low T4 in the context of low or normal TSH i.e secondary hypothyroidism, should also prompt an endocrine referral.

DOI: 10.1530/endoabs.62.WA4

WA5

Abstract Unavailable.

WA6

Recurrence of Pituitary Apoplexy in non-functioning pituitary adenoma

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79 year old gentleman was reviewed as new patient in the Endocrine clinic. He was diagnosed with Pituitary Apoplexy of a Non-functioning Adenoma in 1998. He was under surveillance and the tumour remained relatively stable with no complications until 2008.

Surgical history

There was a gradual increase in the size of the adenoma over 5 years. He underwent Transphenoidal adenectomy in Feb 2014 as the tumour was draped over the optic chiasm. Intra-operatively, the tumour consisted of tough fibrous tissue. He had a large remnant tumour post-surgery. He re-presented in March 2016 with sudden onset headache and was diagnosed with Pituitary apoplexy and necrosis. He underwent further surgery and had similar intra-operative finding of tough fibrous tumour which was technically difficult to resect. Post-surgery MRI showed marked reduction in size of the adenoma but had remnant suprasellar tumour elevating optic chiasm.

Changes in hormone profile

The 9am Cortisol levels remained in the normal range and the Short Synacthen tests repeated over the years always showed good response. He was started on Levothyroxine in 2013 but was stopped as he did not tolerate it. He had a transient episode of thyroiditis in 2014–2015 with positive TSH receptor antibodies. He was diagnosed with Hypogonadotrophic Hypogonadism in 2010 and he is on testosterone replacement. The IGF1 has remained low since 2013 but not currently on replacement. This is an interesting case of the long term complications of Non-functioning Pituitary Adenoma including pituitary apoplexy. There is a slow progression to panhypopituitarism but the ACTH and cortisol production are still preserved. This case also demonstrates the challenges in managing thyroid dysfunction in patients with pituitary disease in the community and secondary care.

DOI: 10.1530/endoabs.62.WA6

WA7

Opioids - yet another cause for Adrenal Insufficiency

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Opioids –Yet another Cause for Adrenal Insufficiency. Opioid prescriptions have almost doubled in the last decade in the UK. Opioid related hypogonadotropic hypogonadism is a well-recognised clinical entity. Opioid therapy as a cause of adrenal insufficiency is an under-recognised endocrinopathy with potentially lifethreatening adverse effects. We present the case of a 57 year old lady referred to the endocrine clinic with symptoms of generalised fatigue and weakness. Her only medication was moderately high dose of morphine sulphate which she has been on for chronic back pain. Her 9 AM cortisol was 113 nmol/l (200–500 nmol/l). A subsequent Short Synacthen test (SST) showed basal cortisol of 32, 30 min level at 526 and 60-min level at 649 nmol/l. Her ACTH level was undetectable at <5 ng/l. Her other pituitary bloods were unremarkable except for FSH (21.4 U/l) and LH (1.3U/l) with estradiol (<44 pmol/l) levels. Her MR pituitary imaging was normal. Treatment with hydrocortisone 5 mg three times a day has not led to an improvement of symptoms. Opioids suppress the HPA axis via kappa and delta receptors resulting in suppression of CRH release and thus affecting ACTH levels. It appears as though there is a female gender preponderance to this effect of opioids. One study showed patients on higher doses of opioids equivalent to morphine 62 mg daily or more showed a blunted response to SST. The fact that she was on a smaller dose of morphine and the fact that we cannot ascertain the actual onset of ACTH deficiency might explain the normal response to ACTH. The optimum management and long term outcome of patients with this condition is not currently known.

DOI: 10.1530/endoabs.62.WA7

WA8

Pituitary apoplexy in a non-functioning pituitary adenoma: A case of favorable outcome in conservative management approach

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Introduction

Pituitary apoplexy presents as a medical emergency, and usually occurs in people with pituitary macroadenomas. Immediate multidisciplinary expertise and timely intervention is needed to mitigate the associated morbidity. There is controversy regarding the role and the timing of neurosurgical intervention versus conservative management approach to obtain best visual and endocrine outcomes. Here we present a case of a man presenting with pituitary apoplexy and managed conservatively to achieve remarkable improvement in vision and tumor size.

Case History

A 54 year old man with a history of nonfunctioning pituitary adenoma was referred to our care when he presented with acute severe headache, diplopia and visual disturbance. He was known to have a pituitary tumor that had been incidentally detected in 2013, and followed with annual imaging that had shown a gradual increase tumor size, not requiring intervention. On acute presentation with apoplexy he had bitemporal hemianopia with right sided 3rd and 6th cranial nerve palsies.

Investigations

Magnetic Resonance Imaging (MRI) of pituitary revealed subacute bleeding into the pituitary macroadenoma which bulged into suprasellar cistern and touched the optic chasm with minimal elevation, and extended into the right cavernous sinus. His serum sodium was 128 and the pituitary profile suggested panhypopituitarism with cortisol 61 nmol/L, TSH 0.73 miU/mL, Free T4 <5.2 pmol/L, LH 0.4 IU/L, FSH 1 IU/L, Testosterone <0.4 nmol/L and Prolactin 5 mIU/L. The diagnosis of pituitary apoplexy was made.

Management

He was started immediately on hydrocortisone 40 mg per day, thyroxine and testosterone replacement. He was managed conservatively, with frequent visual function assessments, which showed substantial improvement within few days without further deterioration of cranial nerve palsies. The 3rd and 6th cranial nerve palsies improved gradually while visual fields had recovered completely by sixth week. Repeat MRI after 6 weeks showed that the tumor height had decreased from 22 mm to 13 mm with no contact on the optic chiasm and complete resolution of the hemorrhage. On three month follow up, he is well with fully recovered vision but still has panhypopituitarism requiring anterior pituitary replacement therapy.

Discussion

This case illustrates the positive outcome of conservative management of pituitary apoplexy resulting in favorable neuro-ophthalmic outcome and reduction in tumor size. Thus conservative approach is permissible if vision is improving as outlined in the pituitary apoplexy guidelines (1).

Reference

1. Rajasekaran S. *et al*. UK guidelines for the management of pituitary apoplexy. Clin Endocrinol(Oxf).2011;74:9–20.

DOI: 10.1530/endoabs.62.WA8

WA9

Non-functioning pituitary adenoma with pituitary apoplexy

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A 60-year-old gentleman known to suffer from atrial fibrillation (on warfarin therapy), hypertension and beta-thalassemia trait presented to the endocrine clinic for follow-up of hypothyroidism for which he was started on levothyroxine by his general practitioner about 2 years before. Serial thyroid function tests revealed a progressive reduction in thyroid stimulating hormone (TSH) levels in the setting of a decline in free thyroxine (fT4) levels. The patient denied any history of headaches, visual disturbances or symptoms suggestive of any relevant hormone deficiency, other than a long-standing history of easy fatiguability and mild weight loss. There was no

past surgical history. He was married with three children and was an ex-smoker. On examination, the parameters were stable with no postural hypotension. He had very sparse body hair. However, systemic examination was otherwise unremarkable. A full pituitary hormone profile confirmed panhypopituitarism as outlined below:
TSH 0.645 mIU/L (0.3–3) ↓
fT4 10.3 pmol/L (11–18) ↓
10 am cortisol 21 nmol/L (119–618) ↓
FSH 2.4 U/L (0.7–11.1)
LH 1.1 U/L (0.8–7.6)
Prolactin 339 mU/L (53–360)
Oestradiol 79.7 pmol/L (0–206)
Testosterone < 0.69 nmol/L (4.47–29.57) ↓
GH <0.05 ug/L (0–3)
IGF-1 20 ng/Ml (41–189) ↓
ACTH 20 pg/mL (10–48)
Serum osmolality 297 mOsmol/kg
Urine osmolality 502 mOsmol/kg
An MR of the pituitary showed a large pituitary macroadenoma containing large areas of haemorrhage. The adenoma itself had a craniocaudal diameter of 2.8 cm, an anteroposterior diameter of 2.4 cm and a transverse diameter of 2.3 cm. The haemorrhage within the adenoma measured 2 cm × 1.7 cm × 1.7 cm. Superiorly, the adenoma was compressing the optic chiasm, also invading the left cavernous sinus in close proximity to the left internal carotid artery. Formal Goldmann perimetry showed a relative temporal visual field defect. He was commenced on lifelong hydrocortisone replacement therapy at 10mg-5mg-5mg. A hydrocortisone emergency pack was given together with a steroid card. The patient was re-assessed within a few days from the MRI. He denied any headaches, other than few hours of mild to moderate headaches (severity scaled 6 out of 10) occurring a few days after his MRI had been carried out. There was no diplopia or extraocular muscle weakness. Warfarin therapy was immediately stopped. He underwent transsphenoidal resection of the pituitary adenoma. There were no perioperative or postoperative complications. On follow-up, he remained clinically well and his visual fields improved.

DOI: 10.1530/endoabs.62.WA9

WA10

Abnormal TFTs - a macro-cause for concern

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Prolactinomas are the most common hormone-secreting pituitary tumors. They typically present with hypogonadism, decreased libido, infertility, and gynaecomastia in men. We present an interesting case of a 44-year-old gentleman who was referred to our endocrine clinic for 'abnormal thyroid function tests' with a low T4 despite a normal TSH (TSH 2.01, T4 7.5, T3 3.9). He reported a few years' history of increasing weight gain and lethargy, generalized aches and pains, occasional frontal headaches and low libido. His visual fields were normal to confrontation. There were no clinical features suggestive of cortisol excess. TFTs suggestive of central hypothyroidism (CH) led to a full pituitary profile as follows: Prolactin 131,000, Macroprolactin negative. Oestradiol <100, LH 0.5, FSH 1.4, testosterone 1.1, SHBG 11, GH<0.05, IGF1 12.3, random cortisol 278. MRI pituitary confirmed a large macroadenoma with expansion into the left cavernous sinus and suprasellar extension causing displacement of the optic chiasm. A diagnosis of pituitary macroprolactinoma was made with evidence of secondary hypothyroidism and hypogonadism. He was started on Cabergoline 250 mcg weekly uptitrated to 500 mcg 3× week over a period of few months with reduction in prolactin levels from 131000 o 12566 (see attached graph 2). Insulin tolerance test to further assess his anterior pituitary function revealed a baseline cortisol of 225 with peak cortisol 284, baseline GH <0.05 with peak GH 0.06 consistent with secondary cortisol and GH deficiency. He was started on Hydrocortisone 10 mg, 5 mg, and 2.5 mg. Levothyroxine was started few weeks after this. A repeat MRI 3 months since start of treatment showed reduction in size of lesion particularly the suprasellar and left parasellar components with no displacement of the optic chiasm.
Learning points:
- Treatment with dopamine agonists is usually well tolerated and effective in normalizing the prolactin level and shrinking the tumor mass of even large prolactin-secreting tumors.
- We wish to highlight the importance of identifying the spectrum of 'abnormal' thyroid function and having a high suspicion to consider a pituitary pathology with a picture suspicious of central hypothyroidism. Our case had a mildly low free T4, with normal TSH that led to a diagnosis of a macroprolactinoma with anterior hypopituitarism.
- Patients with central hypothyroidism usually display mild to moderate non-specific symptoms and signs similar of primary hypothyroidism.
- In patients at risk for combined pituitary hormone deficiencies potential concomitant central adrenal insufficiency must be excluded before starting levothyroxine therapy due to the risk of precipitating an adrenal crisis.

DOI: 10.1530/endoabs.62.WA10

WA11

Parasellar meningioma: an insidious impersonator

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The patient is a 45 year old gentleman known case of HIV seropositivity (well-controlled, undetectable viral load) and polycystic kidney disease, who was referred to our Endocrine clinic by the Infectious disease specialists in view of a 4 year history of erectile dysfunction (ED – preceded diagnosis of HIV) and a low testosterone level. During the first consultation, the patient reported occasional lethargy and long term nausea which was attributed to his retroviral treatment. He denied any vomiting or headaches. The only neurology of note was right abducens nerve palsy, stable since diagnosis 10 years prior. (Magnetic resonance (MR) imaging of the head at time of initial presentation had been reported as showing no positive findings.) Clinical examination was otherwise unremarkable. A full pituitary profile taken after the initial endocrine consultation was suggestive of hypopituitarism (low serum total testosterone, cortisol and free thyroxine concentrations. In light of the biochemical investigations, an urgent MR pituitary was organised which showed an extensively infiltrating right parasellar lesion, which was most in keeping with a parasellar meningioma. A retrospective evaluation of his past imaging studies demonstrated that the lesion had already been present in the first MR study. Formal visual perimetry was overall normal. A standard short synacthen test (SST) performed after the results of the initial pituitary profile showed adequate cortisol response. He was subsequently started on testosterone and levothyroxine replacement therapy which brought about an improvement in his hypopituitary symptoms and biochemistry. At this point, definitive treatment of this gentleman's meningioma is still being carefully evaluated within a multi-disciplinary team. Given the size and the location of the meningioma and the possible inherent complications of surgery, radio-therapy appears to be the favoured treatment option. This case report highlights the diagnostic pathway in the investigation of hypopituitarism whilst bringing to the fore mimickers of pituitary tumours.

DOI: 10.1530/endoabs.62.WA11

Workshop B: Disorders of growth and development

WB1

Ectopic posterior pituitary syndrome with hypopituitarism and pubertal delay

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A 19 year old Bangladeshi male attended ED with a fractured finger. He was noted to have a severely delayed bone age of 13.5 years, and no facial hair. He had moved to the UK aged 11 and could recall little information regarding his childhood or his parents. He had no significant medical co-morbidities, and in particular no history of mumps, measles or testicular injury. He reported being the shortest in his class, and being unable to keep up with his classmates in physical activity. He had never had nocturnal penile tumescence. On assessment in the endocrinology clinic, he had no dysmorphic features and his voice was unbroken. He was 146 cm tall, and weighed 38.3 kg (BMI 18). His target height was 170 cm, based on an estimated mid-parental height. He was Tanner stage 1, with a testicular volume of 2.5 ml and a penile length of 2.5 cm. He had no facial, pubic or axillary hair. An MRI pituitary scan demonstrated pituitary hypoplasia with hypoplastic pituitary stalk and an ectopic posterior pituitary gland posterior to the optic chiasm. Initial blood tests demonstrated hypopituitarism: TSH 4.04 mIU/L (NR 0.27–4.20 mIU/L), LH <0.3 IU/L (NR 1.7–8.6 IU/ L), FSH 0.6 IU/L (1.5–12.4 IU/L), SHBG 80 nmol/L (NR 15–48 nmol/L), free testosterone <0.1 nmol/L (9.9–27.8 nmol/L), androstenedione <1.1nmol/L (NR 1.4–9.1 nmol/L), DHEAS <0.4 umol/L (NR 2.2–15.2 umol/L), cortisol 54 nmol/L (NR 171–536 nmol/L), prolactin 430 mIU/L (NR 86–324 mIU/L). The results from a short synacthen test confirmed adrenal insufficiency. He was diagnosed with congenital hypopituitarism with pubertal delay secondary to pituitary hypoplasia. He was commenced on oral hydrocortisone, levothyroxine and Adcal D3. When reviewed three months later, he reported significant improvement in his energy levels, and was initiated on Growth Hormone therapy which was gradually up-titrated. Prior to optimisation of therapy, baseline medical photographs and bone turnover markers were measured. In order to identify a growth spurt - and therefore the optimal time to initiate testosterone replacement - his height was measured every 4 weeks. After one year of treatment, he had grown by 5 cm, and he was commenced on testosterone replacement therapy. After 8 months of treatment, his testosterone level reached 15.2 nmol/L with a stable PSA and Hb. At three years since diagnosis he reports good energy levels, mood and sexual function. His testosterone level is now satisfactory at 17.5 nmol/L. Ectopic posterior pituitary is due to abnormal development of the pituitary gland and stalk, resulting in hypopituitarism. This diagnosis should be considered as part of the differential in the adolescent presenting with hypopituitarism.

DOI: 10.1530/endoabs.62.WB1

WB2

Rare case of panhypopituitarism with normal testosterone

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A 16 year old boy presented to his GP with a two month history of polyuria and polydipsia. He was reviewed by his GP and diabetes mellitus was ruled out. At the time of presentation three months later, he had a three week history of headache and vomiting. His glasses prescription had changed and he had increasing diplopia. The optician found bilateral papilloedema and he was referred to the eye clinic for further assessment. Due to abnormal gaze palsies, he was admitted to the neurosurgery ward. On examination, blood pressure 131/85 mmHg. There were upward and lateral gaze palsies with convergence retraction nystagmus. He underwent CT head which showed a 3 cm soft tissue mass engulfing the pineal gland and a smaller hyperdense mass in the infundibular recess of the third ventricle associated with hydrocephalus. MRI confirmed these findings and the smaller mass is inseparable from the pituitary stalk. During his admission, it was noted he was passing excessive amount of urine and drinking 4-6l of fluids daily. He was referred to Endocrinology for work up for diabetes insipidus (DI). He had completed his pubertal development and testes volume was 20 mls bilaterally. Serum osmolality was 303 mmol/kg (275–295), urine osmolality 136 mmol/kg and urine sodium 23 mmol/l. Blood tests showed normal sodium level, FT3 2.8 pmol/l(4–7), FT4 8 pmol/l (10–25), TSH 2.71 mu/l (0.51–4.94), prolactin 1011 mu/l (45–375), IGF-1 17.9 nmo/l (22.5–53.8), testosterone 28.5 nmol/l(4.1–32.9), undetectable LH and FSH. Short synacthen test was abnormal. Testosterone level was inappropriately normal for low levels of LH. Further tests revealed alpha fetoprotein 391 kU/l (0–10), B-HCG 19 u/l(0–5). CSF cytology revealed no malignant cells but raised AFP 982 microg/L (0–3) and HCG 79 IU/L (0–2). The biopsy is in keeping with a germinoma. He was confirmed to have a pineal HCG secreting germ cell tumour causing panhypopituitarism. He was commenced on hydrocortisone, levothyroxine and desmopressin. He is now under the care of oncology for chemotherapy and radiotherapy. Intracranial germinomas account for 0.5–2.0% of all intracranial tumours. Suprasellar involvement will cause endocrinopathies with DI being the most common presenting feature. Most HCG secreting germ cell tumours are diagnosed by young adolescence therefore present with precocious puberty. In older patients, symptoms depend on location of tumour with pituitary hormone deficiency. This is an unusual case with low gonadotropins but normal testosterone which is likely due to stimulating effect of B-HCG on LH receptors.

DOI: 10.1530/endoabs.62.WB2

WB3

Hamartoma of hypothalmus presented as precocious puberty and Epilepsy in 10-year old girl

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Background
Hamartoma of the hypothalamus represents a well-known but rare cause of central precocious puberty and gelastic epilepsy. Due to the delicate site in which a tumour is located, surgery is often difficult and associated with considerable risks.
History
10-year old girl presented with early menstrual cycles. The condition started at age of one year when her parents noticed that their child has developed abnormal vaginal bleeding. Her cycles were regular, each cycle lasted for 3 days. Her parents also noticed that she has developed breast, axillary and pubic hair at the age of five, and seven respectively. The parents also gave a history of difficulty in speech especially articulation and abnormal generalized body movements (epilepsy) since childhood for which she is on medications. She also had attacks of an inappropriate laugh.
Diagnosis and Treatment
Her lab tests consisted with central precocious puberty, MRI shows suprasellar mass and she had been put on leuprolide and antiepileptic medicines until surgery planned. Her surgery was done with complete resection, with histopathology showing hamartoma. After surgery, there was complete remission of seizure.
Conclusion
The treatment of hypothalamic hamartoma (HH) associated with generalized epilepsy (GE) has been found to improve seizures and behavioural disturbances with an acceptable morbidity rate by using a variety of surgical approaches. Partial resection of a tumour may be sufficient to reduce seizure frequency and to improve behaviour and quality of life with few side effects.

DOI: 10.1530/endoabs.62.WB3

Workshop C: Disorders of the thyroid gland

WC1

Toxic Thyroid Adenoma in the context of Subclinical Hyperthyroidism

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Subclinical hyperthyroidism is defined as low serum thyroid stimulating hormone (TSH) in the setting of normal levels of free T4 (fT4) and free T3 (fT3). Treatment for subclinical hyperthyroidism can be considered when TSH is persistently <0.1, particularly in (i) the presence of hyperthyroid symptoms, (iii) individuals aged >65 years, (iii) the presence of heart disease or osteoporosis. We present a case of a 34-year-old lady who was referred to endocrine outpatient clinic in view of neck swelling and subclinical hyperthyroidism. At presentation, the patient complained of recent weight loss and episodic palpitations. She had regular menses and denied any history of diarrhoea, tremor, anxiety, night sweats or hair loss. Neck examination revealed a palpable right thyroid nodule. There were no thyroid bruits. She was clinically euthyroid and there were no signs of dysthyroid eye disease. Thyroid profile sampling confirmed subclinical hyperthyroidism: TSH 0.013 mIU/L (0.3–3), fT4 16.07 pmol/L (11–18), fT3 6.5 pmol/L (3.5–6.5). TSH Receptor Antibody (TRAb) and anti-thyroid peroxidase antibody (TPOAb) titres were normal (TRAB 0.64 U/l [<1.8]; TPOAb $<$ 10.0 iu/ML [0.0–50.0]). An ultrasound of the thyroid confirmed the presence of a 24×12 mm well-defined nodule in the right thyroid lobe, with internal vascularity on Doppler. An US guided aspiration had already been performed confirming a benign nodule (Thyroid Bethesda category 2). An NM Thyroid scan confirmed the occurrence of a large, well-defined focus of avid tracer uptake corresponding to the right thyroid nodule. The rest of the thyroid gland was hardly evident. This was consistent with a diagnosis of toxic adenoma in the context of subclinical hyperthyroidism. The patient was started on Carbimazole 5 mg daily on account of her symptomatology, rendering her euthyroid within a few weeks, and treatment options were discussed at length. The patient opted for thyroid lobectomy and has been referred for surgery.

DOI: 10.1530/endoabs.62.WC1

WC2

Medics maddened by Myxoedema

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We present a case of recurrent troublesome hypothyroidism with three pathologies to vex her medical attendants. This 75 year old lady was treated for Grave's thyrotoxicosis elsewhere when she was 55 years old. She had positive TSH receptor antibodies and high uniform uptake of radioactive iodine. She presented to us age 65 with relapsed thyrotoxicosis and was maintained on carbimazole 5 mg OD for 8 years which was then stopped. She had been off medication for 2 years when she presented to A&E with hypothermia and bradycardia in February 2017 and was found to be hypothyroid (TSH 7.6, fT4 – 17). She started 25 mcg of levothyroxine and was discharged. Readmitted Jan 2018 with similar signs still on thyroxine 25 mcg (TSH 1.7, fT4 19.2). Treated as possible urosepsis and discharged. Third admission March 2018 with bradycardia and hypothermia but normal TFT. Endocrine advice was not sought during any of these admissions. She had a catastrophic admission to ITU April 2018 with low GCS, hypothermia, bradycardia (TSH 2.5, fT4 14, fT3 2.9). Endocrinology involved with a diagnosis of myxoedema coma. Confirmed compliance, absence of food and drug interaction and of malabsorption symptoms. ECG showed sinus bradycardia. Treated with tri-iodothyronine intravenously, levothyroxine increased to 100 mcg OD with hydrocortisone cover till panhypopituitarism was excluded. Pituitary MR was normal. She recovered dramatically with improved TFT (TSH 1.4, fT4 24.6, fT3 4.1). Four months later she maintained her improvement clinically (TSH undetectable, fT4 27.9, fT3 5.7). Between clinics her worried GP arranged admission in November 2018 with bradycardia, hypothermia and mental slowing (TSH 0.02, fT4 27.2). Gradually increased thyroxine dose to 300 mcg as inpatient over 3 weeks monitoring for signs of thyrotoxicosis. She slowly improved AMTS score, body temperature rose over 36 degrees Celsius and pulse crept over 60/minute. Discharged on 300 mcg thyroxine (TSH <0.01, fT4 33.3, fT3 6.1). In clinic Jan 2019 still bradycardic 60/min, still cold so thyroxine increased to 350 mcg. She posed a challenge heightened by the fact that despite supressed TSH, high fT4 and fT3 she was clinically still hypothyroid. Thus this lady exhibited poor T4 to T3 conversion, isolated TSH deficiency and subsequently both central and peripheral thyroid hormone resistance. Management relied on clinical rather than laboratory assessment for titration of thyroxine in transforming a cold, pale, confused and bradycardic patient slowing to her death into a warm and quick-witted one.

DOI: 10.1530/endoabs.62.WC2

WC3

When TFTs just don't add up

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A 31-year-old man originally from Ukraine attended the clinic having been started on Carbimazole 20 mg by his GP. His symptoms included intermittent palpitations, sweating and poor sleep and they had improved since starting anti-thyroid therapy. He was originally diagnosed with thyrotoxicosis in Germany in 1999 but was not treated and he re-presented in 2005. This time he was started on Carbimazole but stopped treatment on his own accord after a month because his symptoms improved. There was no family history of thyroid disease. He was a non-smoker and may have been exposed to radiation following the Chernobyl disaster. He was clinically euthyroid on examination. Thyroid function tests: TSH 8.29 mIU/L, FT4 22.8 pmol/L and FT3 6.7 pmol/L (see reference ranges in Table). Carbimazole was stopped and he underwent an MRI scan to investigate for TSHoma which was unremarkable. The rest of the pituitary screen also were in normal limits. A plan to investigate for TSH hormone resistance fell through due to appointment DNAs. After some time he re-attended having commenced carbimazole for elevated free thyroid hormones (fT4 57 pmol/L and TSH 0.01 mU/L). With carbimazole treatment blood tests improved with TSH 2.36 mIU/L, FT4 27 pmol/L and FT3 7.4 pmol/L. TSH-receptor antibody was mildly elevated at 2.5 IU/L consistent with auto-immune thyrotoxicosis. Genetic testing for TSH-resistance showed no causative mutation. Carbimazole was continued and titrated at follow-up appointments and subsequent biochemistry is shown below:

Biochemistry

	10/2015	12/2015	03/2016	09/2016	01/2017	07/2017	11/2017	09/2018
TSH (0.27–4.2 mIU/l)	3.06	4.08	2.7	2.63	1.3	1.93	2.24	2.33
FT4 (10–23 pmol/l)	23.9	23.5	26.0	27.3	29.0	29.0	27.1	20.5
FT3 (3.1–6.8 pmol/l)	6.8	6.5	5.2	6.3	6.0	7.3	8.1	6.5

The differential for elevated FT4 and normal TSH includes:

- Thyroxine replacement therapy
- Drug-induced
- TSH-oma
- Thyroid hormone resistance
- Non-thyroid illness
- Assay interference

We organised for the thyroid tests to be performed on an alternative platform (Abbott Architect, as opposed to ROCHE).

The values on the Abbott platform were very different, indicating that there is assay interference seen with the Roche assay.

	Roche	Abbott
TSH	1.93	1.42
FT4	29	19.7
FT3	7.3	5.3

We believe he has true thyroid disease, managed as Graves' disease with carbimazole. Assay interference should be considered when thyroid results are confusing.

DOI: 10.1530/endoabs.62.WC3

WC4

A case of Subclinical Hyperthyroidism

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An 88-year old female was referred to the Endocrine clinic for abnormal thyroid function tests. She had been complaining of intermittent palpitations, being generally unwell, with low mood and some degree of weight loss (3 kg within the last 6 months). Her past medical history includes: osteoporosis, atrial fibrillation, poor mobility and falls. There is no family history of thyroid disease. She is currently on Duloxetine, AdCal-D3 and Alendronic acid. On examination, her heart rate was 78/min and irregularly, irregular. She was normotensive and did not display any overt clinical features of hyperthyroidism – no tremors, no palmar erythema, no proximal myopathy, no features of thyroid eye disease and no goitre.

Investigations

The most recent thyroid function tests showed a TSH level of 0.1 mU/l (normal range: 0.27–4.20 mU/l), Free T4 of 21.3 pmol/l (normal range: 11–25 pmol/l), TRAb <0.9 U/l and TPO <9 U/ml. Her TSH levels have been persistently low (0.02–0.43 mU/l) but has never been completely suppressed. She also had a normal Free T4 for the last 3 years (0.02–0.43 pmol/l).

Management

Radio Iodine therapy was arranged and low dose Bisoprolol was started for symptomatic atrial fibrillation.

Discussion

Subclinical hyperthyroidism (SH) is a mild form of hyperthyroidism. It is characterised by elevated levels of TSH with normal thyroid hormone levels. SH can either be exogenous or endogenous. Example of exogenous subclinical hyperthyroidism would be secondary to levothyroxine and of endogenous subclinical hyperthyroidism would be multinodular goitre or Graves' disease. Diagnosis of SH is dependent upon ruling out pituitary/hypothalamic disease, drug effects, non-thyroid illness and exogenous thyroid hormone use. Multi-nodular goitre of the thyroid is the most common cause of SH followed by Graves' disease. Treatment for SH is recommended when TSH levels are persistently lower than 0.1 mU/l in individuals over 65 years of age; in patients with cardiac risk factors, heart disease or osteoporosis; in post-menopausal women who are not on oestrogen or bisphosphonates; and in patients with hyperthyroid symptoms. Treatment for SH is based on the aetiology of the thyroid dysfunction and follows the same principles as for the treatment of overt, clinical hyperthyroidism.[1]

Reference

1. Ross DS, Burch HB, Cooper DS, Greelee MC, Laurberg P, Maia AL *et al*. 2016 American thyroid association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis, *Thyroid,* 2016; 26(10): 1343-1421.

DOI: 10.1530/endoabs.62.WC4

WC5

Interpretation of abnormal thyroid function tests

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Background

In the majority of cases, the results of TFTs are straightforward. In significant subgroup of patients, the interpretation of TFTs is more challenging, either because. The results appear discordant with the clinical picture (e.g. normal TSH in a patient with suspected thyrotoxicosis), Or measurements appear to contradict each other (e.g. raised TH concentrations, but with non-suppressed TSH).

Case presentation

29 year old Caucasian female complains of Tiredness, insomnia. amenorrhoea and goitre. Initially diagnosed at T3 Thyrotoxicosis (2009) and treated with Carbimazole. Clinically she was euthyroid with palpable smooth thyroid. TFT showed f T4 19.4, Free T3 7 TSH 15.24.

TPO Abs <30.

Her TFTs (Table 1)

T4	T3	TSH
25		2
30	9	1
9	7	15

US Thyroid

Thyroid gland upper limit of normal in size. Isthmus appears slightly enlarged. Significantly increased Doppler flow noted.

MRI Pituitary

Bulky pituitary gland but no significant abnormal.

External Assay

TFTs (referred) but no evidence for assay interference.

Delfia TFT

TSH: 30.8 mU/L (0.40–4.0) fT4: 13.7 pmol/L (9–20) fT3: 7.0 pmol/L (3.0–7.5). Total T4: 139.0 nmol/L (69–141) TBG: 23.8 ug/mL (14–31)

Centaur TFT

TSH: 23.33 mU/L (0.35–5.5) fT4: 14.6 pmol/L (10–19.8) fT3: 6.0 pmol/L (3.5–6.5).

Normal a subunits

Genetics showed Mutation in TH receptor b gene (THRb). Patient was treated with Cabergoline, 0.5 mg weekly. Continued on Carbimazole 15 mg. patient's follow up: periods returned, weight stabilised and symptoms resolved.

Discussion

Causes of elevated total T4 with non-suppressed thyroid stimulating hormone:

- Raised serum binding proteins
- Familial dysalbuminaemic hyperthyroxinaemia
- Anti-iodothyronine/anti-TSH antibodies
- Non-thyroidal illness (including acute psychiatric disorders)
- Neonatal period
- Iatrogenic: thyroxine replacement therapy, drugs (for example, amiodarone, heparin)
- TSH secreting pituitary tumour
- Resistance to thyroid hormone

Amongst the various discordant TFT patterns one of the most challenging distinctions to make is between Resistance to thyroid hormone due to a loss-of-function mutation in the human THRB gene (TRb RTH) And a TSH-secreting pituitary adenoma (TSHoma/thyrotropinoma).

Types of THR:

- Generalised (GRTH)- variable presentations.
- Selective pituitary resistance (PRTH)- thyrotoxicosis.

– 85% of RTH are caused by mutations of TRB gene.

THRB gene sequencing confirms the diagnosis in 85% of cases.

Treatment

- Usually no treatment is required.
- In PRTH:

1) Chronic suppression of TSH with T4, tri-iodothyroacetic acid, octreotide or Dopamine agonist.
2) Thyroid ablation with radioiodine or surgery.

DOI: 10.1530/endoabs.62.WC5

WC6

Isolated Thyroxinaemia

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A 54 year old male was referred by GP for abnormal TFT. Thyroid function was done routinely. TSH 3.0 (normal 0.5 to 4.5), FT4-25.2. GP repeated the TFT twice, and both of them were similar. There were no clinical features of Thyrotoxicosis. On examination, his heart rate was 78/min regular, wt 79 kg, no thyroid enlargement, no tremor. Cardiovascular examination was unremarkable. He is fit and well gentleman. He does not take any regular medication. No history of taking any other over the counter medications also. He is a smoker for 30 years. No family history of thyrotoxicosis. After 3 months his TFT was repeated and it showed TSH-1.6 and FT4-27.7. Anti TSH receptor Ab was negative. Repeat TFT after 6 months was also similar. In both occasions patient was asymptomatic with high FT4.

Questions:

1) What is the probable diagnosis?
2) How should we manage this case with Asymptomatic isolated Thyroxinaemia?

DOI: 10.1530/endoabs.62.WC6

WC7

Carbamazepine induced low FT4

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This is 66 year old lady was referred by GP for Abnormal TFT. Her TFT was done routinely and showed TSH-2.7, FT4-9.8. Patient did not have symptoms of hypothyroidism, or did not have any weight gain. On examination, thyroid was

not enlarged. In view of Low FT4, she was started on Levothyroxine 25 mcg once daily. After taking the medications she felt warm and unsteady and noticed tremour on both hands. The repeat TFT came back as normal. TSH-2.9, FT4-14.2.. In view of pts symptoms the thyroxine was stopped. Repeat TFT showed normal TSH and low FT4. Looking back at her TFT over the last few years it has shown normal TSH and low FT4. No previous thyroid problems She is known to have epilepsy and hypertension. She is on Lamotrigine, Carbamazepine, Amlodipine and bendroflumethiazide.

Questions

1) Is this low FT4 secondary to Carbamzepine?

2) How to manage this case?

DOI: 10.1530/endoabs.62.WC7

WC8

TSHoma: an elusive finding

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Introduction

TSHomas are rare pituitary tumors that secrete an abnormal amount of a hormone called thyroid-stimulating hormone (TSH). Alternatively given the name thyrotropinoma, only makes up to 1%–2% of all pituitary adenomas. Patients often remain misdiagnosed for years. Many patients undergo treatments that end up destroying the thyroid gland. This case report is to emphasize the rarity of the condition and the importance of diagnosing it early and accurately to ensure timely management and relief of symptoms before perpetual damage is done.

Case description

We present to you a case of a 56 year old lady who presented with anxiety, generalized tiredness and sleeplessness. Blood tests showed: Prolactin levels: 738 mIU/l (l < 440 mIU/l), TSH 6.7 (normal 0.27–4.5 mIU/l), T4 36.1 (11–23 pmol/l), T3: 9.15 (3.1–6.8 pmol/l). She was clinically asymptomatic apart from thyroid swelling. She gave a history of previously being treated for prolactinoma followed subclinical hypothroidism having had cabergoline and levothyroxine in the past. Having raised T3 and T4 with raised TSH ringed bells for a high suspicion of TSHoma. Associated Prolactin levels were < 1000 mIU/l and was thought to be likely secondary to disconnection hyperprolactenemia (stalk effect). TRH stimulation test to rule out secondary and tertiary causes of thyroid hormone abnormalities was performed which showed flat profile with TSH levels in the range of 5.7–8.11 mIU/L and T4 30–32 pmol/l. T3 supression test with SLR showed TSH levels in the range of 1.9 pmol/l–4.5 pmol/l. Heterophile antibody test to rule out interference with thyroid hormone assays was performed and was found to be negative. Familial dysalbuminemic hyperthyroxenemia test was also negative. Alpha subunit levels were checked showing values of 1.35–2.6 ng/ml. Based on these investigation results a formal working diagnosis of TSHoma was considered likely in contrast to Thyroid hormone resistance. MRI pituitary scan was carried out showing a pitutiary adenoma of 16 mm in size. Patient subsequently had Endoscopic Trans-sphenoidal hypophysectomy with biopsies taken. Histopathology reports confirmed atrophic but viable neoplastic cells expressing prolactin with extensive expression of TSH consistent with pleurihormonal adenoma with somatostain treatment effect.

Discussion

TSHoma is highly under diagnosed. It is important to consider the pitfalls in diagnosis where normal or low alpha sub unit levels could lead to dubious differentials. The use of advance technology i.e functional MRI scans to confirm diagnosis should be carried out early on leading to timely treatment options including radiotherapy and surgery.

DOI: 10.1530/endoabs.62.WC8

WC9

When thyroid function tests remain deranged despite treatment

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A 60 year old lady was diagnosed with thyrotoxicosis in 1985 (aged 28) five months postpartum. She underwent partial thyroidectomy in 1990 (age 32). Thyroid tests remained abnormal and in 1992, she underwent radio-iodine treatment requiring post-treatment. She remained under endocrine supervision and the TSH was found to be persistently elevated with normal free thyroid hormone levels (whilst on Levothyroxine). Issue with compliance and assay interference were considered. She was referred to our unit for an opinion and advice on best management. Her mother also had abnormal thyroid status and her sister has been referred for genetic testing, which we presume was secondary to abnormal thyroid function tests. She denied any long bone fractures, however reported worsening symptoms of feeling hot and sweaty with occasional palpitations over 12 months. She was on Tibolone which was changed to alendronic acid for osteoporosis identified on DEXA scan.

BIOCHEMISTRY

TPO-abs: 35 (0–60 mIU/L)

Anti -Thyroglobulin Abs < 15 (0–60 mIU/L)

TSH-R abs: < 0.9 (IU/L)

OTHER BLOODS:

Normal FSH, LH and serum prolactin from 2014.

SHBG: 49 (14–69 mmol/L)

Cortisol: 611 nmol/L (6–10 am: 133–537 nmol/L; 4–8 pm: 68–327 nmol/L)

Vitamin D 122 nmol/L

Anti-Tissue transglutaminase Ab: 0.3 (0-7)

Negative smooth muscle antibody, anti-nuclear antibody, anti-mitochondrial antibody, gastric parietal cell antibodies and negative Liver/kidney microsomal antibodies. Pituitary MRI showed a small Rathke's cleft cyst of the pituitary gland with no serial change over two years. Given the family history and repeated elevated TSH level and free T4, she had diagnostic testing for thyroid hormone resistance once assay interference was ruled out. Fluorescent sequencing analysis detected a heterozygous base change c.272 > T, in exon 7 of the THRbeta gene. This pathogenic variant is predicted to result in an abnormal THRbeta protein and has been previously associated with thyroid hormone resistance. Reviewing the history it is likely that prior to surgery and RAI that free hormone levels were elevated with non-suppressed TSH (data unavailable). There is no current clinical or serological evidence of Graves' or AITD. Understanding that there is THR helps with management of the case. We have been titrating thyroxine against clinical symptoms, measuring free hormones and SHBG. The patient feels most well with a generous TSH, and there may be differential tissue sensitivity to the exogenous thyroxine.

DOI: 10.1530/endoabs.62.WC9

WC10

A case of thyroid hormone resistance due to mutation in THRβ gene

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A 25 year old gentleman was referred to the endocrine clinic for evaluation of abnormal thyroid function tests. He reported symptoms of diffuse abdominal pain associated with loose stool up to six times a day with urgency, frequency and tenesmus. These symptoms had been present since childhood, becoming increasingly troublesome over the preceding two years. He also reported symptoms of tiredness, palpitations and sweating episodes. Thyroid function tests were abnormal. TSH was 0.78 mU/l (reference range 0.27–4.2 mU/l) and Free T4 29.7 pmol/l (reference range 10.5–24.5 pmol/l). He had a family history of hypothyroidism on replacement thyroxine. On examination he was found to have a BMI of 24.6 kg/m^2. His blood pressure was 156/96 mmHg with a regular pulse rate of 96 bpm. He demonstrated a fine tremor but lid lag was not detected. There were no thyroid masses felt with in the neck. His abdomen was diffusely tender, more intensely so in the left iliac fossa. Visual fields were full to confrontation and fundoscopy was normal. There was no clinical concern regarding pituitary enlargement. Repeat thyroid function tests confirmed Free T4 36.0 pmol/l, Free T3 10.4 pmol/l (reference range 3.1–6.8 pmol/l) and TSH 1.33 mUl/l. Haematology and biochemistry was unremarkable other than a microcytosis and slightly raised ALT. He was started on Carbimazole 20 mg once daily in Primary Care but this failed to improve his symptoms and this medication was stopped following Endocrine review. In view of his persistently high blood pressure, symptoms of anxiety and increased bowel frequency, Phaeochromocytoma, Conns Syndrome and Carcinoid Syndrome were excluded. The remaining 0900 h pituitary profile was normal. Extensive investigations including MRI abdomen, colonoscopy and biopsy and faecal calprotectin did not find a conclusive cause for his abdominal symptoms. In view of the persistently measurable TSH in the context of raised free T4 and T3 levels, Thyroid Hormone Resistance was suspected. Genetic studies confirmed Heterozygous THRβ pathogenic variant and confirmed the diagnosis of thyroid hormone resistance and he was started on Propranolol with normalisation of blood pressure and resolution of symptoms of tachycardia and palpitations. He continues to complain of symptoms of diarrhoea and intermittent abdominal discomfort and we wonder these symptoms may be related to raised FT4 levels.

DOI: 10.1530/endoabs.62.WC10

Workshop D: Disorders of the adrenal gland

WD1

High-risk pregnancy management due to central adrenal insufficiency and gestational diabetes

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We report a case of a 25 years old woman – with central transient hypoadrenalism after the right adrenalectomy for Cushing syndrome. She became pregnant 1 year after surgery while still taking a small dose of cortisol replacement therapy (5 mg Hydrocortisone) for partial recovery of her corticotrophic axis. Her pregnancy has been complicated by gestational diabetes, with good metabolic control under small doses of basal insulin. She increased her substitutive therapy at 26 weeks of gestation by 50% to 7.5 mg of hydrocortisone. At week 32 of pregnancy, she experienced adrenal crisis due to an upper respiratory tract infection that was managed with parenteral cortisone. Subsequently, the dose was tapered to a maintenance dose of 30 mg hydrocortisone. Further attempts to lower the maintenance dose led to the recurrence of symptoms of hypoadrenalism. Elective cesarean delivery was performed uneventfully with parenteral hydrocortisone at a stress dose maintained for 48 h postpartum. A viable macrosom, otherwise healthy fetus was born (4270 g). Treatment with glucocorticoids during pregnancy should take into account that adrenal reserve increases as pregnancy progresses. Patients on glucocorticoid replacement may need to increase their hydrocortisone dose by 50% in the last trimester of pregnancy, and by the start of the labour, the hydrocortisone dose should be increased to stress doses for 48 h postpartum. Hydrocortisone crosses the placenta in small amounts because is metabolised into the placenta by 11-beta-hydroxylase steroid dehydrogenase-2 and should be the preferred steroid during pregnancy to prevent adrenal suppression of the fetus.

DOI: 10.1530/endoabs.62.WD1

WD2

Congenital adrenal hyperplasia with testicular adrenal rest tumors

Hafiz Muhammad Zia-Ul-Hussnain, Mark Sherlock & Chris Thompson
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A 34 year old male diagnosed with congenital adrenal hyperplasia (21 hydroxylase deficiency, salt wasting variety) shortly after birth. Initial presentation was poor feeding with hypoglycemia, pigmented scrotum with elevated 17-OH progesterone. He had a right orchidopexy at age 9 for undescended testis. He was admitted multiple times with adrenal crises during his childhood. He went through puberty and achieved height of 177 cm which is 75th centile. His sister also has CAH. He did not attend our service between the age of 23 and 34 and was followed up with his local endocrinologist. He was referred back to our service at the age of 34 after attending a fertility specialist with azospermia on the background of testicular adrenal rest tumors (TARTs) diagnosed at age 30. Previous semen analysis showed oligospermia. He was receiving prednisolone 2.5 mg BD and fludrocortisone 0.1 mg OD. His most recent symptoms are ongoing fatigue, snoring at night time, back pain and hip pain. His last DXA scan showed osteopenia. His most recent 17-OH progesterone is 35.6 nmol/l (1.90–6.90), Androstenedione is 28.9 nmol/l (2.0–10.47), Direct Renin Concentration is 283.4 mIu/l (9–103.5), ACTH is 42.8 pg/ml (7.2–63.3).
Questions
1) What is the optimal management of his CAH?
2) How do we induce fertility in patients with CAH and TARTs?

DOI: 10.1530/endoabs.62.WD2

WD3

Adrenal Suppression with Inhaled Corticosteroids and concomitant use of CYP3A4 Inhibitors

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57 year old with a low 0900 h cortisol (40 nmol/l) was referred for an urgent short Synacthen test (SST). Recently during a respiratory clinic visit, he had complained of feeling very tired but there were no other symptoms to suggest adrenal insufficiency. He had a background history of ABPA, Asthma and hypothyroidism. His current medications were Symbicort Inhaler, Vitamin D3, Levothyroxine, Montelukast and Itraconazole. He had been on Symbicort for over 2 years and his Itraconazole was started about a year ago. He had achieved excellent control of his ABPA on Itraconazole. He had not received any oral steroids over the last 3 months. His initial SST was positive with cortisol of 31 nmol/l, 96 nmol/l and 160 nmol/l at 0,30 and 60 min respectively. He was started on standard hydrocortisone replacement therapy. Unfortunately, he did not have a baseline ACTH however rest of his pituitary profile was normal. He also had negative Adrenal antibodies. His adrenal glands were normal on a recent CT thorax. We did a PubMed search and found several case reports of adrenal suppression caused by concomitant use of Itraconazole and certain inhalers. On follow up clinic visit 2 weeks after starting Hydrocortisone replacement he had gained close to 5 kg in weight and his face looked very plethoric. Itraconazole is a potent inhibitor of enzyme CYP3A4 which is part of Cytochrome P450. Of the inhaled corticosteroids Fluticasone and Budesonide are very dependent on CYP3A4 enzyme pathway while Beclometasone is metabolised through a different pathway. At this point, we changed his inhaled steroid to Beclometasone. He tolerated the switch well. We reduced his hydrocortisone dose with advice to double the dose on sick days. About 4 months later he had a repeat SST with cortisol of 183 nmol/l, 343 nmol/l and 397 nmol/l at 0, 30 and 60 min respectively. At this point, his Hydrocortisone was further reduced to 5 mg once a day with a plan of stopping it in the next 2 to 3 weeks. He had a repeat SST 2 months later which was normal with cortisol's of 149, 445 and 504 at 0, 30 and 60 min respectively. This case highlights the potential hazards of inhaled steroid and certain medications such as Itraconazole. And there are other medications such as certain Macrolides, anti-retrovirals which also inhibit enzyme CYP3A4. These effects can be reduced/avoided by simply changing the inhaled steroid.

DOI: 10.1530/endoabs.62.WD3

WD4

Rare complication of congenital adrenal hyperplasia

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39Y old male who was originally treated as child with CAH secondary to 21-Hydroxylase deficiency and was put on glucocorticoids and mineralocorticoids from first week of life due to salt wasting crises. He has had very high 17-OH progesterone and adrenal androgen due to noncompliance. He developed polycythemia secondary to androgen excess, resulted in venesection. Haematologist have investigated the mutation and EPO measurement and he felt that this was probably secondary polycythemia. The main issue was that he has number of admissions with breathless and flank pain. He underwent abdominal ultrasound, which was suggestive of mass in left adrenal area and finding of bilateral multifocal adrenal nodules with central low density changes likely to represent multiple adrenal myelipomas. The was concern about alternative diagnosis of liposarcoma. A CT scan reported of bilateral adrenal lesions and there were concerns as to liver metastases. Repeat scan did not show any liver lesion. He also has ultrasound of testes, which showed heterogenous masses in both testes and their appearance suggestive of testicular adrenal rests. Case was discussed in adrenal MDT and the consensus was that bilateral adrenalectomy in this scenario would not be advisable given his poor compliance on steroids and associated risk of life threatening adrenal crises. Patient was referred to surgical colleagues to discuss the possibility of a unilateral adrenalectomy in first instance, to determine a response in the symptoms. Patient underwent laproscopic left adrenalectomy and recuperating very well. Histopathology report awaited. He was back on his usual pre-surgery steroids dosage and conversant of sick day rules. He is due to follow up in adrenal clinic next month.

DOI: 10.1530/endoabs.62.WD4

WD5

Lymphoma as a cause of bilateral adrenal gland enlargement and Adrenal insufficiency

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Lymphoma is one of the rare causes of bilateral adrenal gland enlargement that require a high index of suspicion for diagnosis. We present a case of 80-year-old lady referred by her GP for further evaluation after presenting with lower abdominal discomfort and weight loss for which she had a CT scan that revealed bilateral adrenal gland masses (60 HU) with the right adrenal gland measures

61 mm in diameter with distal ileal thickness and regional lymphadenopathy. She has no symptoms of carcinoid (i.e.: no flushes, wheeze or diarrhoea) or pheochromocytoma (i.e.: no palpitations or panic attacks) and does not appears particularly cushingoid or tanned with no postural drop in her BP (L: 135/80, S: 130/70). She is not smoker or alcohol consumer and her clinical examination revealed palpable nontender cervical lymphadenopathy but was otherwise unremarkable. Her biochemical profile revealed a random cortisol of 434 nmol/l (ACTH: 113 ng/l), chromogranin-A of 71 ug/l, normal plasma metanephrines and ARR. Her routine investigations including FBC, U+E & bone profile were all normal with mildly raised LDH level of 279 unit/l. She underwent further detailed investigations looking for the underlying cause including DHEAS, Androstenedione, testosterone, 17OH progesterone, tumour markers (CEA, Ca19-9, CA125, AFP), viral screening (HIV, HBV, HCV), immunoglobulins and serum electrophoresis which were all normal. After discussion in the endocrine MDT the consensus was to obtain a L.N biopsy which confirmed a diagnosis of diffuse high-grade NHL for which she was referred urgently for haematology colleagues and commenced on RGCVP chemotherapy. Patient had a lot of troubles with collapse /? hypotension in the last 14–21 days necessitating admission to A&E prior to starting her steroids. She is currently on Prednisolone 60 mg OD as a part of RGCVP therapy with advice to give pulse/tapering steroid in between to prevent adrenal crisis. In cases of adrenal enlargement, it is prudent to assess the functionality of the gland as well as looking for any suspicious radiological features considering both the density and the adenoma size. Clinician should always consider the causes of bilateral adrenal enlargement which require further investigations to provide the correct treatment and the differential diagnoses include: CAH, ACTH dependent Cushing's, hyperaldosteronism, infiltrative causes (e.g.: lymphoma, Leukaemia...etc) and infections (Fungi, TB...etc). Whether our patient adrenal insufficiency will resolve after successful treatment of lymphoma remains uncertain however it is felt safer to cover her with steroids at this stage.

DOI: 10.1530/endoabs.62.WD5

WD6

Adult presentation of classical Congenital Adrenal Hyperplasia with gender identity disorder

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Case history
Two Syrian refugee siblings aged 21 and 20 years, were referred. Ambiguous genitalia had been identified at birth and had been raised as males. They wished a more masculine habitus and had concerns regarding their fertility. The elder sibling had ambiguous genitalia at birth and a 46,XX karyotype. Long-term steroid treatment had been initiated and corrective genital surgery performed at 9 months of age. For unknown reasons, steroids were stopped after 9 years. He identified himself as male and underwent puberty with development of male secondary sex characteristics. There were no adrenal crises. Height was only 130 cm with male pattern pubic hair, cliteromegaly, labia majora and a vaginal opening. The younger sibling had an almost identical presentation. He was 139 cm in height, and had a micropenis of 1.5 cm and fused labia majora without a vaginal introitus.
Investigations
A diagnosis of congenital adrenal hyperplasia (CAH) was considered. In the older sibling basal and tetracosactide-stimulated cortisol levels were 109 nmol/L and 108 nmol/L, respectively. Basal 17-hydroxyprogesterone was 52 nmol/L and rose further to 456 nmol/L following stimulation, thereby confirming CAH. Baseline testosterone was 17.8 nmol/L. In the younger sibling basal and stimulated cortisol levels were 50 nmol/L and 55 nmol/L, respectively, with basal 17-hydroxyprogesterone 670 nmol/L rising to 735 nmol/L, and baseline testosterone 15.5 nmol/L. Their karyotype was 46,XX.
Results and treatment
Following the diagnosis of classic CAH, both siblings were initiated on hydrocortisone and fludrocortisone with subsequent reduction of 17-hydroxyprogesterone levels. Their testosterone levels, however, dropped below the male reference range. Due to their wish for a more masculine body habitus, testosterone replacement was initiated.
Conclusion and points for discussion
CAH is the commonest cause of sexual ambiguity in genetic females. Early diagnosis and treatment is of vital importance in order to achieve timely discussion regarding gender assignment and to institute treatments to normalize growth and pubertal development, and to prevention long-term complications. It is remarkable that these siblings survived into adulthood without suffering adrenal crises but the final heights they achieved were poor and their desire for fertility raises significant challenges. In this country we take for granted the early and appropriate management for classic CAH by a dedicated paediatric endocrinologist and multidisciplinary team. The clinical scenarios we present highlight that patients in other parts of the World with CAH may be denied essential investigation and treatment.

DOI: 10.1530/endoabs.62.WD6

WD7

A case of adrenal identity crisis

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A 78-year-old male with a background of renal cell carcinoma and bilateral adrenal metastasis presented with leg cramps and lethargy. He was on Prednisolone 10 mg od for immune therapy induced pneumonitis. Prior to commencing Prednisolone, he was on Dexamethasone 2 mg for 4 months for weight loss, nausea and vomiting. He underwent a Short Synacthen Test (SST) as his serum Na was low at 119 mmol/L (134–146). His SST showed a flat response with baseline and 30 minutes cortisol levels were low at 24 and 25 nmol/L respectively. He was diagnosed with secondary adrenal insufficiency (SAI). He was restarted on Dexamethasone before discharge as he felt better on Dexamethasone. 6 weeks later, he was readmitted with left pyelonephritis, tiredness, lethargy and weakness. His Na was low at 125, K 5.3 mmol/L (3.4–5.2), urea 8.7 mmol/L (3.4–8.0), creatinine 104 umol/L (60–126). His Na dropped further to 116. Paired serum and urine osmolalities were 247 and 384 mosm/kg respectively. His urine Na was high at 53 mmol/l. He was diagnosed with SIADH and was fluid restricted. The endocrine team advised to check renin and aldosterone. He started to experience postural hypotension and was commenced on Fludrocortisone before testing for renin and aldosterone. Na improved to 126 and K 4.69. The endocrine team advised to withhold Fludrocortisone for 24 hours before checking renin and aldosterone levels. Unfortunately, Fludrocortisone was not restarted after renin and aldosterone levels were taken. He was commenced on Tolvaptan 7.5 mg on alternate days initially and then daily as his Na continued to drop to 121. Patient was reviewed by psychologists as he continued to complain of tiredness and lethargy and was advised relaxation exercises. Renin results were not available due to technical issues. He continued to be hyponatraemic, extremely tired and intermittently hypotensive. Finally, the renin result was available and was high at 373 mIU/L (4.2–59.7) indicating Primary Adrenal Insufficiency (PAI). He was immediately commenced on IV Hydrocortisone and oral Fludrocortisone. He clinically improved and his Na normalised to 136, K 3.8. He was discharged home on oral Hydrocortisone and Fludrocortisone.
Conclusions
We describe a case of PAI incorrectly diagnosed as SAI and SIADH which resulted in inappropriate treatment and prolonged hospital stay. Our case highlights the difficulties and delays in recognising the signs and symptoms of PAI in patients who are on exogenous glucocorticoids. Prompt diagnosis and treatment may prevent severe adrenal crisis.

DOI: 10.1530/endoabs.62.WD7

WD8

CAH presenting as premature puberty with associated testicular adrenal rest tumors (TART)

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Background
Congenital adrenal hyperplasia (CAH) is one of the autosomal recessive disorders resulting from CYP 21(21-hydroxylase) deficiency. Testicular adrenal rest tumours (TARTs) are common in CAH, due to hypersecretion of ACTH. These lesions inside the testis are bilateral and multiple. TARTs may lead to structural damage and their tumours may be mistaken for Leydig cell tumour. Because of their locations; TART may cause seminiferous obstruction and infertility. History: 6-year old boy presented with the early growth of pubic hair, the condition started at age of four years when his parents noticed that their child has developed pubic hair. They also noticed that he is taller than his siblings with abnormal behaviour and deepening of the voice. There is a history of sudden death of his brother when he was 22 days old. The testicular examination was normal. Physical examination revealed the development of pubic hair (stage 4) and adult scrotum. Diagnosis and Treatment: His random 17OH progesterone was

60.80 mg/ml (increased by more than 60 folds, repeated result for 17OH progesterone showed an increase by more than 20 folds). U/S and MRI showed testicular tumours keeping with TARTs. We started the patient on HC tabs with the consultation of a urologist. Continuous follow up of these tumours were done.
Conclusion
Giving the clinical presentation, biochemical profile and MRI findings, the diagnosis is keeping with CAH complicated with TARTs. A multidisciplinary approach with the involvement of endocrinologist, pathologist and urologist is of great importance for the correct diagnosis and treatment. The aim is to draw the attention of the clinicians to the presence of the TARTs and to evaluate critically every patient with testicular tumours concomitantly with CAH. It's very important to consider treatment of CAH to prevent short stature in future.

DOI: 10.1530/endoabs.62.WD8

WD9

Corticosteroids: Time critical drug in adrenal insufficiency

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A series of 4 cases of delay in steroid treatment.
1. 35 year male, brought in by ambulance, with drowsiness and vomiting. He was known T1DM on insulin pump**,** Addison's disease on hydrocortisone. He has multiple admissions secondary to DKA. Initial assessment showed drowsiness, tachycardia, tachypnea, low saturations, hyperglycemia, ketosis and borderline acidosis. He was started on DKA protocol. His blood glucose and ketones started to improve, but he remained drowsy even 12 hours after admission. The patient was still in ED, when one of the staff nurses, who herself has Addison's disease, realized that our patient has not received any steroids since admission.At that time, first dose of IV hydrocortisone was prescribed and given. Within 45 minutes of steroid administration his GCS started to improve.
2. 17 year male attended ED at 17:20 with abdominal pain, nausea and vomiting, flu like symptoms for 2 days. Known T1DM and Addison's disease – informed reception staff of need for hydrocortisone iv. Triage and clinician review at 18:15. Blood glucose 20.05 but no acidosis or ketosis. Pt received IV fluids and stat doses of insulin, initially no hydrocortisone. Seen by medical team after 5 hours and then prescribed and administered.
3. 21 year male. Admitted from nursing home to ITU, Background: Congenital toxoplasmosis, epilepsy, Diabetes insipidus, Pituitary insufficiency. Endocrine referral from ITU next morning for 'Complex Endocrine issues'. Fluctuating level of consciousness, sodium 128 mmol/l, serum glucose readings were in low normal range. Receiving usual dose of hydrocortisone down NG tube. Impression was hypoadrenalism. He was switched to IV hydrocortisone. Pt was reveiwed next day by endocrine team, his GCS, hyponatremia and hypoglycemia were improved.
4. 65 year gentleman presented to ED with 2 days history of day gastroenteritis. On day of admission, he got up to toilet at around 03.00 am– collapsed. Found to be hypotensive and hypoglycaemic by ambulance crew. Pt had pastl history of transphemoidal surgery for a pituitary tumor. Pt was given normal saline and dextrose in ED. Seen by medical team around 14:40. Need for IV hydrocortisone was highlighted and prescribed on EP. Pt asked for IV hydrocortisone in ED and then on ward but was not given by the staff, he was told he would have to wait until 10pm as that is when the dose was prescribed for. He received his first dose at 22:00.

DOI: 10.1530/endoabs.62.WD9

WD10

Incidental finding of probable non-classical congenital adrenal hyperplasia

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A 37 year old lady presented to her GP with increasing lethergy, bloating and low mood associated with her menstrual periods. Her GP undertook a hormonal screen including androgen profile which revealed elevated 17-Hydroxyprogesterone 25.5 nmol/L (0.1–8.5). The rest of her androgen profile was normal. As a teenager she suffered with acne and hirsutism, for which she had laser therapy, but this had resolved. Periods were regular, every 28 days with 1–2 days menstruation. She underwent synacthen testing which showed a peak cortisol of 468 nmol/L and peak 17-hydroxyprogesterone 120 nmol/L. We also organised urinary steroid profiling [results pending] because diagnosis based on stimulated 17-hydroxy-progesterone levels can result in false positives. Her main concerns were lethargy and fertility. She was reassured that her symptoms were unlikely to be related to the biochemical abnormalities described. She was advised that the synacthen test demonstrated no evidence of adrenal insufficiency. She was also advised that no medication is recommended regarding fertility at present.
Discussion
This case highlights the anxiety that incidental biochemical findings can raise. She had no clinical reason to suggest non-classical congenital adrenal hyperplasia or PCOS history. This case also serves as a reminder of the utility of urinary steroid profiling as a confirmatory test given the potential for stimulated 17-hydroxyprogesterone levels to provide false positive diagnosis.

DOI: 10.1530/endoabs.62.WD10

WD11

Adrenal Insufficiency secondary to Addison's disease

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Adrenal insufficiency is a potential life-threatening condition due to lack of cortisol and early diagnosis and management is potentially lifesaving. We describe a 79-year-old lady who presented to the emergency department with new onset confusion, nausea, vomiting and decreased oral intake. Her relatives also reported a one month history of lethargy and weakness. She suffered from gastro-oesophageal reflux for which she was taking Ranitidine, and had a history of total abdominal hysterectomy and bilateral salpingoophorectomy. She was a non-smoker and a non-alcoholic and was previously independent in activities of daily living. On examination, she looked lethargic with a BP of 110/60 mmHg. There was no postural drop. The other parameters including capillary blood glucose were normal. Systemic examination was unremarkable. A complete blood count was normal. However, she had severe hyponatraemia on admission (Na 110 mmol/L). Potassium was normal. She had been admitted few months before with severe hyponatraemia requiring intensive care treatment with hypertonic saline. A CT thorax, abdomen and pelvis had been unremarkable. A morning (9am) cortisol level was taken and deemed suspiciously low (143 nmol/L). A short Synacthen test was performed, confirming hypocortisolaemia:

Time (minutes)	Cortisol (nmol/L)
0	127
30	148
60	162

Additional investigations were consistent with a diagnosis of primary autoimmune adrenal insufficiency, as evidenced by
Serum ACTH - 402++ pg/ml (10-48) ↑
Adrenal cortex antibodies - >1:10+++(<1:10) ↑
Renin – 381++ ng/L (12.6-28.0) ↑
Aldosterone – 6.0 ng/dl (2.2-35 – 30mins in upright position)
ARR – 0.2 (<19)
The patient was started on hydrocortisone replacement therapy and fludrocortisone. She was educated by the endocrine specialist nurses (including instructions regarding 'sick day rules') and provided with a steroid card. Her clinical condition improved and her serum sodium normalised.

DOI: 10.1530/endoabs.62.WD11

WD12

A case of male subfertility in congenital adrenal hyperplasia

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Our patient a 39yr old man was referred to endocrinology clinic. He described a history of being diagnosed with congenital adrenal hyperplasia after presenting with a salt wasting state at 6 weeks old. After living in Dublin as a child his family moved to Canada for 14yrs. At presentation he was taking hydrocortisone 10 mg twice daily and fludrocortisone 0.1 mg once daily. His main concern was fertility. He and his wife had been investigated in Canada. Information provided by the patient showed that in Aug 2011 FSH 2IU/L (2–8), LH <1 IU/L (2–6), were at the lower limit of detection and testosterone 26.0 nmol/L (8.4–28.7) was normal.

Two semen assessment reports from 21/4/11 and 17/9/12 confirmed azoospermia. USS testes 23/8/11 reported bilateral testicular masses felt to be testicular adrenal rests. He reported good health. Height 162 cm (2nd-9th centile) and weight 66.3 kg (25th – 50th centile). His mother was 4ft11ins and father 5ft 11ins so he measured towards the lower end of the mid parental height range. BMI 25 kg/m^2. Secondary sexual characteristics were Tanner stage 5. Testicular volume was $>$25 ml bilaterally with irregular and firm consistency felt to be in keeping with extra-adrenal rests. BP 131/83. 12/9/16 Initial testosterone was 45.5 nmol/L but when repeated 10/10/16 testosterone had fallen to 7.2 nmol/L with LH $<$ 0.2I U/L and FSH 0.6 IU/L and then 10/2/17 rose to 12.2 nmol/L, LH $<$0.2 IU/L and FSH 0.5IU/L remained suppressed. On the basis of an extremely elevated testosterone and suppressed TSH there were concerns regarding exogenous testosterone supplementation. USS 10/10/16 showed coarse testicular tissue almost completely replaced with what seemed to be most likely extra-adrenal rests. Genetic profiling supported a diagnosis of congenital adrenal hyperplasia due to 21-hydroylase deficiency. He was referred to our regional fertility clinic. On repeat testing his gonadotrophins were consistently low despite fluctuating androgen levels. At review his corticosteroid replacement regimen was changed to dexamethasone 1.5 mg at 10 pm and 0.375 mg at 8 am aiming to ensure suppression of ACTH to reduce adrenal testosterone production and resulting suppression of LH secretion. He is currently planned for a trial of gonadotrophin therapy in an attempt to stimulate spermatogenesis. He has been counselled that if medical management fails to reverse azoospermia there are reports of success with micro-TESE but Sperm Donation or adoption may be needed. This case reflects the struggle with fertility as a consequence of sub optimally controlled CAH and TART formation in male patients.

DOI: 10.1530/endoabs.62.WD12

WD13

Polyglandular autoimmune syndrome

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This was a 26 year old girl was referred for addisons disease. Her initial blood test showed low Na-123 with raised K-6. She complained feeling tired and lethargic for last 2 months. On examination, wt 108 kg, alopecia on the occipital scalp. Obese lady, CVS and respiratory system examination were normal. Her Short Synacthen test showed blunted response. She was immediately started on Hydrocortisone 10-5-5. Furhter bloods showed TSH-18, FT4-5.6, positive Anti TPO Ab, positive adrenal Ab, LFT-normal, FBC-normal. All the antibodies for coeliac disease, T1DM and pernicious anaemia were negative. She also had multlocular ovarian cyst- undergone laparoscopic surgery. She was also diagnosed with depression and recently started on Citalopram

Questions;

1. Is this Polyglandular Autoimmune syndrome Type 2.
2. How to follow up these cases

DOI: 10.1530/endoabs.62.WD13

WD14

When nature takes its course...

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Congenital Adrenal Hyperplasia is a group of autosomal recessive disorders characterised by enzyme defects in the steroidogenic pathways involved in the biosynthesis of cortisol, aldosterone and androgens. 21-hydroxylase deficiency accounts for more than 90% of cases.

Case history

41-yr-old female was referred to Endocrinology with a serum **testosterone of 14.3 nmol/l (0.20–2.86).** She was a full term baby born to non-consanguineous parents. At the age of 2 years she was admitted to a hospital being poorly and was treated with IV fluids'. Age of 7–8 years was started on Dexamethasone, Hydrocortisone and Fludrocortisone. She achieved menarche at the age of 17 years, had regular cycles, severe acne and hirsutism. Age of 30 years she stopped all tablets and did not attend her appointments. She gained weight, developed abdominal striae, hirsutism got worse and stopped her periods. On examination, BMI of 38.9 kg/m^2 with Male pattern hair loss, marked facial hirsutism, thick coarse skin, acne, acanthosis nigricans and Clitoromegal. Investigation: sr testosterone 14.3 nmol/l ((0.20–2.86), FSH: $<$0.8 IU/l (2–9), LH: $<$0.2 IU/l (2–9), 17-Hydroxyprogesterone: $>$152, Androstenedione 45 nmol/l (2–4) DHEA 4.1 umol/l (1.6–7.8) and Haemoglobin: 180 g/l (120–160). CT scan of the abdomen showed hypertrophy and nodules in both adrenals, 6 cm mass in the medial limb of the left adrenal which contained fat and calcification and a large fibroid uterus. On an Ultrasound the right ovary measured 30 $\times$ 25 $\times$ 20 mm and the left ovary measured 23 $\times$ 14 $\times$ 15 mm. A diagnosis of Classical Congenital Adrenal Hyperplasia, Probable virilising form was made. Treatment options were discussed with the patient and decided to have bilateral adrenalectomy. The histology showed bilateral florid adrenal hyperplasia with multiple myelolipomas and bilateral adrenal cortical tumours. Started on hydrocortisone and fludrocortisone. One month post operatively her sr testosterone was 0.8 with normal FSH and LH. Her 17 OHP was 4.3. She lost weight and restarted her periods.

Conclusion

The case describes a natural course of less severe forms of CAH in a noncompliant patient Management of congenital adrenal hyperplasia (CAH) involves suppression of the hypothalamic-pituitary-adrenal (HPA) axis using supraphysiological doses of exogenous glucocorticoids. This can pose a challenge, with Cushing's syndrome and poor compliance. Bilateral adrenalectomy, with subsequent replacement of glucocorticoids and mineralocorticoids at physiological doses, has been proposed as an alternative therapeutic strategy in carefully selected patients who have had unsatisfactory outcomes with conventional medical management.

Reference

Phyllis W. Speiser. Congenital Adrenal Hyperplasia. F1000Research 2015.

DOI: 10.1530/endoabs.62.WD14

WD15

Polyglandular Endocrine complications of checkpoint inhibitor therapy: the importance of continued vigilance and multidisciplinary management

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Case history

At 1 year follow-up post excision of invasive melanoma, a 63-year-old gentleman, with no other significant past medical history, was found to have CT evidence of metastatic disease. In the absence of a BRAF mutation, he was consented for combination immunotherapy with Ipilimumab (anti-CTLA4) and Nivolumab (anti-PD1). Monitoring bloods during cycle 2 of treatment revealed asymptomatic thyroiditis (TSH 0.03 miu/l, T4 35.5 pmol/l, T3 15.1 pmol/l), which did not require medication. However during cycle 3, the patient was admitted with polydipsia, polyuria and weight loss. Investigations revealed glucose 30.4 mmol/l, ketones 0.6 mmol/l, HbA1c 9.4% and weakly positive anti-GAD antibodies. He was diagnosed with new-onset type 1 diabetes and commenced on basal bolus insulin. Three days later, blood tests demonstrated development of primary hypothyroidism (TSH 10.51 miu/l, FT4 $<$5.2 pmol/l, FT3 $<$1.5 pmol/l, cortisol 641 nmol/l), hence levothyroxine therapy was commenced. Glycaemic control worsened however, with unexplained hypoglycaemia despite reduction in basal insulin. He was admitted one week later with fatigue, postural hypotension and collapse. He denied any headache or visual disturbances.

Investigations

Notwithstanding acute illness, cortisol was inappropriately low (44 mmol/l) with concurrent hyponatraemia (Na 122 mmol/l). Adrenal insufficiency was confirmed with a short synacthen test, which demonstrated an inadequate rise in cortisol from 35 mmol/l to 300 mmol/l. Pituitary profile showed TSH 21.09 miu/l, FT4 5.8 pmol/l, prolactin 106 mu/l, FSH 3.0 iu/l and LH 0.9 iu/l. MRI brain showed no radiological evidence of hypophysitis.

Management

Emergency treatment of acute adrenal insufficiency was commenced with 100 mg hydrocortisone IV followed by 50 mg hydrocortisone IV every 6 hours, and intravenous rehydration as per society guidelines. Recovery was rapid, and he was changed to oral hydrocortisone. Previously erratic glycaemic control improved considerably, with resolution of hypoglycaemia.

Discussion

Endocrine complications of checkpoint inhibitor therapy are well recognized, with adrenal insufficiency reported in 2.6% of patients, primary hypothyroidism in 15.0% (particularly associated with Nivolumab treatment) and type 1 diabetes in 0.4%. Hypophysitis causing ACTH and TSH deficiency is reported in up to 7.7% of cases, and is often unassociated with clinical or radiological features of

mass effect. Our patient experienced transient hyperthyroidism, then type 1 diabetes, subsequent primary hypothyroidism and finally adrenal insufficiency. The index of suspicion for concomitant endocrinopathies should be particularly high with checkpoint inhibitors, which are increasingly indicated for various malignancies. Biochemical monitoring protocols are crucial as clinical symptoms may occur late. Close collaboration between oncology and endocrinology teams is therefore essential when following up such patients, to facilitate early recognition and management of these complications.

DOI: 10.1530/endoabs.62.WD15

WD16

Congenital Adrenal Hyperplasia in the context of 46XX genotype leading to grade 5 virilisation

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This 31 year old patient was referred to the endocrinology department with a history of dizziness and fatigue. Past medical history identified that he had been diagnosed with congenital adrenal hyperplasia, presumed to be secondary to 21-hydroxylase deficiency, by 18 months of age whilst living abroad. He had been raised as a male but was found to have 46XX genotype with grade 5 virilisation. During childhood and early adolescence, he underwent multiple operations to remove Mullerian derivatives, uterus and ovaries and had bilateral testicular prostheses inserted. Glucocorticoid replacement was initiated but there was a long gap from adolescence to adulthood when the patient did not receive glucocorticoid replacement and did not experience symptoms of hypoadrenalism. There was also a family history of congenital adrenal hyperplasia. In clinic, he was hypotensive with a blood pressure of 100/70 mmHg and phenotypically there was evidence of grade 5 virilisation. Early morning cortisol was 80 nmol/l with no cortisol response on short synacthen test. 17-OHP was elevated at 542 nmol/l with ACTH 764.5 ng/l. Testosterone 4.9 nmol/l with adrenal androgens – DHEA 3.4 umol/l and Androstenedione >80 nmol/l. Renin was elevated at 4 nmol/l/hour. Glucocorticoid replacement was commenced with hydrocortisone before being converted to dexamethasone and then prednisolone. Mineralocorticoid replacement with fludrocortisone was commenced. Unfortunately the patient experienced adverse effects with multiple steroid preparations which included weight gain, rash and reduced libido likely due to glucocorticoid suppressing adrenal androgen production. This led to him stopping steroids on one occasion despite knowledge of the importance of taking steroids regularly and of the sick day rules which precipitated a hospital admission. In order to improve his acceptance of glucocorticoid therapy and his symptoms of sexual dysfunction, testosterone therapy is being considered. Ongoing management plan includes measurement of bone mineral density, referral to the Clinical Genetics Team and emphasis of the importance of regularly taking glucocorticoid and mineralocorticoid replacement to avoid adrenal crisis.

DOI: 10.1530/endoabs.62.WD16

Workshop E: Disorders of the gonads

WE1

Testosterone: Is it all about figures

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44 years old gentleman referred to endocrinology clinic complaining of reduced libido. Initial blood test showed borderline low testosterone levels measuring 8.4 nmol/l (10–37) on 2016. SHBG 28. He has a past medical history of type 2 diabetes diagnosed March 2015, fibromyalgia, bilateral carpal tunnel syndrome, spinal osteoarthritis and asthma. medication includes Amitriptyline 30 OD, Buprenorphine 15 µg patches weekly and inhalers together with metformin and sitagliptin. He is not hypertensive, no history of CVD, non-smoker and drinks alcohol only occasionally. His BMI is 34. He is not using recreational drugs and never used anabolic steroids. He was found to have low sperm count in the past and underwent with his partner two cycles of IVF that were unsuccessful. He subsequently fathered two daughters, with natural conception, of 11 and 13 years old. He sometimes gets early morning and nocturnal tumescence. He gets partial tumescence with sudden detumescence. Sometimes, he is able to orgasm and ejaculate. He describes his libido as very poor and it has been for ten years. He is in the same relationship for 20 years. He has constant stresses in his life with illness and family problems. Prostate size around 30 gm of benign smooth outline His penis is normal. His testicular size around 10 ml bilaterally. HbA1c on diagnosis 88 mmol/mol on diagnosis, now measuring only 49. FSH and LH are inappropriately normal for the levels of testosterone measuring 10 and 3.6 respectively. Pituitary MRI normal. His hypogonadism is deemed as secondary to his diabetes, obesity and painkillers. A trial of testosterone replacement with Testogel 50 mg daily was considered to see if he will benefit from it. 8 months later, He hasn't experienced an improvement in terms of his libido in any way. This was reiterated by his wife, who explained that intimate relations between the couple are rare. His testosterone came back as 6.7 nmol/l. Although he confirmed proper compliance and daily gel application. we agreed on Sustanon injection 250 mg 4 weekly. 6 months later, latest testosterone was 4.8. He wanted to try another form of injection. Started Nebido 1 g injection every 12 weeks. Sildenafil and Tadalafil, prescribed were also unhelpful. Referred to ED clinic. His last testosterone in Feb 2018 was 11.6 and in June came back as 25.4. The patient and his wife mentioned that there is no difference in terms of libido. Injections stopped for 6 months, testosterone 10.3.

DOI: 10.1530/endoabs.62.WE1

WE2

Unexplained anaemia in men: Remember to screen for hypogonadism

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Introduction
Hypogonadism is linked to anaemia, sarcopenia and osteoporosis in men. Whereas secondary hypogonadism (SH) is biochemically indistinguishable from nongonadal illness, primary hypogonadism (PH) can be easily diagnosable by the identification of raised gonadotropins.
Case Presentation
A 66-years old male with a background history of type 2 diabetes mellitus, arthritis, and hypertension was referred to the haematology services to investigate his anaemia. Other past medical history included osteoporosis which he is under the follow up of the bone clinic. He had no history of gastrointestinal bleeding, malignancy or kidney diseases. His regular medications included bisoprolol, candesartan, Alendronic acid, metformin and atorvastatin. He was sexually active and reported no concerns with regards to his sexual performance. His main complaint was tiredness. He was noted by his general practitioner to have abnormal full blood for the last year with haemoglobin of 119–127 g/l (reference range 130–180) and haematocrit of 0.35–0.37 l/l (reference range 0.4–0.5). Other aspects of blood component were otherwise normal. His serum folate was 4.2 ug/l (reference range 3.9–26.8), B12 402 pmol/l (reference range 145–569) and serum ferritin 105 ug/l (reference range 20–300 ug/l). After a referral and investigation by the haematology team, he was labelled as having 'unexplained anaemia'. Given his osteoporosis and anaemia, serum follicular stimulating hormone (FSH) was requested to screen for primary testicular failure. His FSH was raised at 31 U/l (reference range <12), with subsequent investigations showing raised serum luteinizing hormone (LH) at 15.8 U/l with low total Testosterone of 8.4 nmol/land low free calculated Testosterone at 161 pmol/l (reference range 215–760 nmol/l), confirming the unequivocal diagnosis of primary hypogonadism. He was started on testosterone replacement therapy with intramuscular testosterone undecanoate, at an initial frequency of 1 g every 12 weeks. 6 months later, there was remarkable improvement in his symptoms, so as his testosterone levels and full blood count.
Conclusion
PH is a common cause of anaemia among older men. Testosterone treatment has the potential to completely reverse anaemia, as well as improving bone density, muscle bulk and, if relevant, sexual function. Screening for PH should thus form part of anaemia work up by all Physicians, not just Endocrinologists.

DOI: 10.1530/endoabs.62.WE2

WE3

Erectile dysfunction

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This is a 46 year old man who was referred by GP for erectile dysfunction. He is a married with two daughters. His complaint started 1 year back with lethargy and tiredness. He is fit and well. He does not take any regular medication. He is shaving regularly. On examination, wt 80 kg. All the secondary sexual characteristics were present. No Galactorrohoea. Testes size was normal. His total testosterone level was low. Anterior pituitary hormone profile showed very low LH and FSH. All the other anterior pituitary hormone profile was normal. No complain of headache or visual disturbance. On MRI of pituitary, it showed pituitary macroadenoma and touching the optic chiasma. We have done the formal visual field testing. Bloods: TSH-2.4, Testosterone-0.5, Prolactin-359, FSH-1.4, LH-0.9.
Questions:
1. How to manage this case?
2. How should we follow up?

DOI: 10.1530/endoabs.62.WE3

WE4

Hypogonadotropic hypogonadism in a young woman undertaking intense exercise

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Background
Functional hypothalamic amenorrhoea (FHA) is a common cause of secondary amenorrhoea and is related to a combination of weight-loss, exercise and psychological stressors. These factors lead to suppression of pulsatile GnRH secretion. Diminished LH and FSH concentrations result in a hypoestrogenic state. We present an archetypal case of FHA that clearly demonstrates the '*hypothalamic set-point*' for the body composition of a young woman below which she has profound biochemical hypogonadotrophic hypogonadism and amenorrhoea.
Case
A 19 year old Caucasian woman was referred with a 6 month history of secondary amenorrhoea. She had normal pubertal development with menarche at 12 and thelarche at 13. She reported 'irregular periods' for several years with cycles between 28 and 47 days. Her current BMI was 17.6 with weight loss of 6–8 kg over the preceding 12 months. The patient reported an intense exercise regimen including 90 minutes cycling 5–6 days a week and 45 minutes swimming biweekly. Physical examination was unremarkable with development at tanner stage 5 and no clinical features of hyperandrogenism.
Investigations
FSH 4.1 IU/l, LH 0.4 IU/l, Oestradiol 29 pmol/l [98–571 pmol/l], Testosterone 0.7 nmol/l [0.2–2.9], prolactin 78 mIU/l [40–485], SHBG 159 nmol/l [30–100], TSH 0.51 mU/l [0.35–3.50] and FT4 13 pmol/l [8–21]. MRI pituitary showed no structural abnormality. A progesterone challenge was undertaken with Norethisterone 5 mg TDS for 5 days. The challenge was negative with no withdrawal bleeding.
Progress
The patient was advised to gain weight resulting in an improvement of her BMI to 20.4 over the following 12 months but without return of spontaneous menses. The patient opted to defer any form of oestrogen replacement despite the risk of skeletal fragility. Further weight gain over the next 5 months lead to an improved Oestradiol of 92 pmol/l. Achieving a BMI of 21 resulted in a regular 28 day cycle.

Conclusions
FHA is a diagnosis of exclusion; once structural pituitary lesions, systemic disease and other endocrinopathies have been excluded. FHA is known to be more prevalent amongst female athletes undertaking endurance sports. A detailed diet and exercise history is required. Balancing the risks from a prolonged hypoestrogenic state against attempts to restore menses naturally via intentional weight gain can be very challenging. Unfortunately, the patient was unable to maintain her weight gain. Her BMI has fallen back to 18 and she is amenorrheic again.

DOI: 10.1530/endoabs.62.WE4

WE5

An interesting case of male hypogonadism

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Introduction
We describe a case of a 29 year old man who was referred to endocrinology services with a 4 month history of erectile dysfunction, decreased libido and low testosterone. He denied symptoms suggestive of pituitary pathology. And he had no previous testicular infections or trauma. His past medical history included asthma, which was well controlled with b-agonist inhaler as required. He had normal development. He was a non smoker, abstinent from alcohol and a keen cyclist (cycling over 200 miles per week). He worked as a teacher. He was in a longterm relationship and he had never fathered children yet (by choice). They were planning for pregnancy with his partner in near future. On examination, weight was 77.4 kg, with a BMI of 22.9, normal secondary sexual characteristics and no other clinical features of hypogonadism. Visual fields were normal on confrontation.
Investigations and results
Pituitary profile: low morning testosterone confirmed on two separate samples (6 and 5), Inappropriately normal LH/FSH (1.7, 2.1 respectively), rest of pituitary profile was normal with a satisfactory morning cortisol level. Normal kidney and liver function. He also underwent MRI pituitary which was unremarkable and a bone densitometry scan; L1–L4 T score: −2, Hip T score: −1.2.
Conclusion and discussion
Based on the history and investigations above, a diagnosis of hypogonadotrophic hypogonadism (HH) was made. His symptoms coincided with a period of substantial physical activity (cycling over 200 miles per week) and he had lost approximately two stones in weight. Refraining from intense training and a period of monitoring was advised. A few months later, his testosterone level had increased and a sustained restoration of the gonadal axis with improvement of his symptoms were noted during his follow up appointments. However, a repeat DEXA scan after 1,5 years showed no improvement. L1–L4: T score: −2.2 (Z score −2.2) and hip T score −0.7 (Z score −0.6). He was offered treatment with bisphosphonates, after he sustained a medial condyle fracture. This case is an interesting demonstration of the transient phenomenon of low testosterone related to the acute stress of intense exercise training. Points for discussion: 1. Functional HH; 2. Treatment with testosterone and impact on fertility. 3. Impact on BMD.

DOI: 10.1530/endoabs.62.WE5

WE6

Hormone Replacement Therapy and fertility options in a patient with Premature Ovarian Insufficiency

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Case
A 20 year old female was referred for further evaluation of ovarian function. She has a history of beta thalassemia and bone marrow transplant in 2009 at age 11. Her menarche started in 2008 and she continued having regular periods until shortly after her bone marrow transplant. She was subsequently started on Loestrin oral contraceptive pill. Examination showed a height of 164 cm and weight of 57 kg. She had well developed secondary sexual characteristics. Her OCPs was stopped and hormonal panel was requested. Investigation included two sets of hormonal panel confirmed premature ovarian insufficiency with elevated LH 23 & 34 IU/l, elevated FSH 54 and 72 IU/l, low estradiol <70 pmol/l and AMH <0.2 pmol/l.
Management
With results confirming premature ovarian insufficiency, the patient was started on HRT with Elleste Duet 2 mg (contains Norethisterone Acetate). On follow up visit, she reports feeling unwell with anxiety and sleep disturbance for one to two weeks prior to having the withdrawal bleed and then symptoms will ease. Therefore HRT was changed to Femoston 2 mg (contains Dydrogesterone) which she tolerated well. Also, she was concerned regarding her future fertility options. She was informed that she had sustained damage to her ovaries following her treatment for beta thalassemia (probably as a result of the cytotoxic agents especially the alkylating agent Busulphan used in the conditioning regimen for her bone marrow transplantation). She was informed that egg donation is the only current available option in such cases.
Discussion points
- Types and forms of Hormone Replacement Therapy.
- Fertility preservation in patients prone to iatrogenic POI (e.g. Oncology, transplant)

DOI: 10.1530/endoabs.62.WE6

WE7

Challenging case of Gonadotropins treatment prior to microdissection testicular sperm extraction (mico-TESE) in patient with Klinefelter syndrome and history of thromboembolism

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Case
A 34 year old was reviewed in reproductive clinic for gonadotropins therapy prior to micro-TESE. He was diagnosed with Klinefelter syndrome in his 20s in another hospital. Testosterone replacement was initiated with Nebido injection. However, he developed polycythemia, DVT and PE in 2013 and therefore the testosterone replacement was stopped. He had thrombophilia screen that showed heterozygous prothrombin gene mutation. Thereafter, he received anticoagulation for few months and was maintained on testosterone gel replacement 50 mg three times a week. Examination showed height of 184 cm. No eunuchoid body habitus but sparse body hair. Testicular volume was 2 cm on each side. On gel, his blood results showed serum testosterone level 19.5 nmol/l with FSH level of 36.5 unit/l and LH level of 10.8 unit/l and Hct of 47%. With view of his increased risk of thromboembolism, we agreed on cautious introduction of gonadotropins and withdrawal of Testogel to optimise any sperm production prior to surgical sperm retrieval by the urologist. From mid-august 2018, he was started on Menopur 75 units and Gonasi 2500 units to be taken twice weekly subcutaneously each. Five weeks on to therapy, he developed DVT eight days after flight to Canada. He was reviewed few weeks after the event in the clinic (November 2018), when he was off gonadotropins for few weeks and was already on anticoagulation (Apixaban 5 mg twice daily). Understandably, he was having hypo-gonadal symptoms with low testosterone level of 2.7 nmole/l.
Management
Along with his anticoagulation, he was restarted again on Menopur 75 units twice weekly with Gonasi third vial (∼1500 IU twice a week). It was expected to have modest increase in testosterone level. Four weeks later, the testosterone level was still 2.8 nmol/l and therefore Gonasi increased to 2500 units twice daily plus continuing the Menopur 75 units twice a week. Six weeks later, his testosterone level was 4 nmol/l with Hct of 44.6%. At this point we agreed to increase his Menopure to 150 units twice weekly and keep the same dose of Gonasi in order to avoid increase risk of DVT. He was referred back to urologist for sperm retrieval with haematology consultation prior to the procedure. He is waiting to be seen.
Discussion Points:
- The increase risk of thromboembolism in patient with Klinefelter syndrome
- The challenge of spermatogenesis induction in patients with underlying risk of thromboembolism.
- The role of Gonadotropines therapy prior to micro-TESE.

DOI: 10.1530/endoabs.62.WE7

WE8

A case of primary testicular failure

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A 38-year-old gentleman was referred to the endocrine clinic after a male fertility test done as part of investigation for infertility showed the following:
Volume 4.4 ml
Total sperm number =6.16 Mill/ejac
Sperm concentration 1.4 Mill/ml
Progressive motility 10%

Nonprogressive motility 1%
Impotence 89%
55% sperm vitality
Previous semen analysis tests were also consistent with a diagnosis of oligospermia. The patient had been trying to conceive for four years with no success. He had normal erections, normal morning erections and libido. He denied headaches, visual disturbances, galactorrhoea or weight change. He had no change in shoe/ring/hat size and described a normal sense of smell. He denied use of opiate, steroids, recreational or other prescribed medications. There was no history of mumps in the past. He did not smoke. Testicular examination showed an atrophic left testicle and normal sized right testicle. He was at Tanner Stage V. Systemic examination was unremarkable. Visual fields were normal to confrontation. A hormone profile revealed the following:
FSH 13.5 U/l (0.7–11.1) ↑
LH 9.2 U/l (0.8–7.6) ↑
Testosterone 18.4 nmol/l (2.5–29.57)
Oestradiol 172 pmol/l (0–146)
Cortisol am 526 nmol/l (145–619)
TSH 2.199 (0.3–3.0 micIU/ml)
T4 12.33 (11–18 pmol/l)
GH <0.05 ug/l (0–3)
Other blood tests including complete blood count, liver profile, lipid profile, renal profile, random blood glucose, corrected serum calcium, iron profile and serum ferritin were within normal limits. He has been referred for genetic screening for chromosomal analysis, tests for Y microdeletion and cystic fibrosis screen. He is also booked for an US scan of the testes. Results are awaited. The patient was counselled regarding the possibility of cryopreservation in view of his impending primary testicular failure and oligospermia.

DOI: 10.1530/endoabs.62.WE8

WE9

Male hypogonadotrophic hypogonadism; fitting fertility with life

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A 33-year-old male with a background of idiopathic hypogonadotrophic hypogonadism was referred to the endocrine clinic to discuss fertility. He was originally diagnosed overseas when presented with delayed puberty in late teens. He had a normal pituitary MRI and since then he had been on testosterone replacement; other pituitary function was normal. He was not anosmic however no other information was available from diagnosis. When he attended the clinic the patient and his wife were keen to conceive. At the time he was on testosterone injection every 3 months. He reported normal sexual function and libido. On examination he was post pubertal and his testes were 3 ml each. Following discussion, he discontinued testosterone and started HCG 3000 units twice weekly. In subsequent clinical review semen analysis showed he remained azoospermic therefore FSH was added at a dose of 150 units 3 times a week. Gradually, over the following 2 years, sperm count improved with a range 0.5–1,000,000/ml. At the same time his wife was found to have normal ovulatory cycles as well as normal hysterosalpingography. Twenty eight months after starting FSH, while on the IVF waiting list, the couple conceived naturally and had a healthy baby born. Following the birth of the baby the patient discontinued FSH therapy however remained on HCG as he was keen to have another baby in the future. Three years later he restarted FSH. On this occasion his wife conceived naturally however she had a miscarriage. Sadly, soon after this, patient's wife passed away and the patient switched from HCG and FSH to testosterone replacement. Most recently the patient returned to the clinic because he had a new partner and was keen to be fertile again. At that stage his testosterone was stopped, and he started HCG therapy with a view to measure sperm count and consider adding FSH.
Discussion points
1. Initiation of FSH from first appointment, before/coincident with HCG?
2. Storage of sperm after 1st conception?
3. What's the optimal sperm count? These individuals might have high fertility with very low sperm counts.

DOI: 10.1530/endoabs.62.WE9

WE10

Endocrine manifestations of malnutrition secondary to restrictive eating in the context of anankastic behaviour

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A 45 year old man was referred to endocrinology with increasing weakness, lethargy, loss of libido and erectile dysfunction. Initial investigations showed hypogonadotrophic hypogonadism with testosterone 0.8 nmol/l (8.2–32.2), FSH <1 U/l, LH <1 U/l, SHBG 93 nmol/l and secondary hypothyroidism with TSH 1.65 mU/l, FT3 2.1 pmol/l FT4 9 pmol/l, prolactin 180 mU/l, IGF-1 12.5 nmol/l. Short synACTHen test showed normal adrenal response (692 to 1014 nmol/l) with a higher baseline cortisol than expected. He had ongoing weight loss 61.4 kg (BMI: 18.1 kg/m^2) from 67 kg (BMI: 19.8 kg/m^2) few months earlier. MRI scan of pituitary gland was normal. The Patient was commenced on Levothyroxine 150 mcg daily and Tostran 2% titrated up to 4 pumps. However, he continued to lose weight (51 kg, BMI:15 kg/m^2) and he was hospitalised for extensive investigations. During admission the ward staff noticed very restricted eating. Psychiatric review revealed unusual perfectionist personality with anankastic traits. He attributed a number of symptoms to different foods which he subsequently avoided. He received dietetic input and at discharge he had regained some body mass BMI 16 kg/m^2. Unfortunately, his weight dropped further down (BMI: 12.6 kg/m^2). Endocrine biochemistry was entirely in keeping with that seen in starvation and anorexia nervosa: with hypogonadotrophic hypogonadism (LH 1.0 U/l, FSH 6.5 U/l,) hypercortisolaemia (cortisol 843 nmol/l), low IGF-1 2.8 (13–35. Despite Levothyroxine 150 mcg daily thyroid function shown low FT3 conversion (<2.5 pmol/l), TSH 0.26 mU/l, FT4 14 pmol/l He underwent a percutaneous endoscopic gastrostomy for enteral feeding and his BMI has so far improved to 16.4 kg/m^2. Follow-up endocrinology investigations 2 months later shown improved gonadotrophins (FSH 14.2 U/l LH 3.5 U/l), testosterone 5.5 nmol/l (tostran has been discontinued 3 months prior). Thyroid function shown TSH 0.61 mU/l, FT3 improved but borderline low (3.4 pmol/l) and FT4 12 nmol/l. He continues to take levothyroxine 125 mcg with the plan to titrate this down and discontinue in the future.
Discussion
The Endocrine consequences of chronic malnutrition seen in eating disorders have been mostly reported in women with anorexia nervosa. Eating disorders rarely affect men, however both genders seem to suffer from many of the same endocrine complications [1] such as: hypercortisolaemia, hypogonadotrophic hypogonadism, secondary hypothyroidism, low IGF-1 secondary to chronic GH resistance seen in starvation. Hypothalamic down-regulation occurs as a protective mechanism aiming to reduce metabolic rate and conserve the resources [2].
References
[1] Miller, 'Endocrine Effects of Anorexia Nervosa.'
[2] Usdan, Khaodhiar, and Apovian, 'The Endocrinopathies of Anorexia Nervosa.'

DOI: 10.1530/endoabs.62.WE10

Workshop F: Disorders of the parathyroid glands, calcium metabolism and bone

WF1

Osteoporosis: Asymptomatic until fracture occurs

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74 year old female presented in ED with history of fall 2 weeks ago and worsening severe back pain, unable to weight bear. She has background history of hypertension, epilepsy and chronic back pain. She had distal radial fracture in 2016, and Dexa scan at that time showed osteopenia with T-score of −1.8, but she was not receiving conventional osteoporosis treatment (e.g., bisphosphonates), hormone replacement therapy, or using natural or synthetic steroids. Furthermore, she did not have a history of rheumatoid arthritis, Paget's disease, type 1 or type 2 diabetes, or primary hyperparathyroidism. On examanition she was haemodynamically stable. No focal neurology and tender over mid to lower back. No sphincter involvement. Bloods showed raised calcium level of 2.94 mmol/l, phosphate 0.65 mmol/l. Alkaline phosphatase was normal, Renal functions were normal, Vitamin D was low at 10.4 ng/ml. CT-scan spine was done which showed multiple recent osteoporotic fractures at T12, L1 and L5, and old fractures at L2, L3 and L4. Her Dexa scan was repeated which showed T-score of −3.1. Due to raised calcium her PTH levels were done which were raised to 10.6 pmol/l. She was started on analgesia, bisphosphonates and Vitamin D replacement and further plan was to investigate for primary hyperparathyroidism.

DOI: 10.1530/endoabs.62.WF1

WF2

A case of severe osteoporosis and multiple vertebral fractures with very good response to combined Teriparatide and hormone replacement therapy

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A 43 year old female experienced sudden sever back pain after lifting her baby's buggy in January 2014. In October 2013, she had an emergency caesarean section to deliver her baby. This was performed for a prolonged first stage of labour with foetal distress. She breast fed her baby for 16 weeks. Her baby was conceived in early 2013 on the first attempt using donor egg and sperm. Her husband was found to have azoospermia. They therefore approached a Fertility Clinic and started trying to have a baby when the patient herself was in her late 30's. By that stage, she was already experiencing irregular periods and occasional hot flashes. Her FSH was 23.1, AMH 0.07 and a trial of Clomiphene was unsuccessful. Her last menstrual period was in December 2012 and periods never returned after stopping breastfeeding. Menarche was at the age of 15. She was found to have multiple vertebral fractures on MRI spine. She had DEXA scan which revealed severe osteoporosis with T score −4.4 at lumbar vertebrae and T score −2.7 at hips. She was initially given oral bisphosphonate and Hormone Replacement Therapy (HRT) but after few months bisphosphonate was stopped and Teriparatide was started in August 2014, HRT was continued. Secondary causes of osteoporosis were ruled out. She also had Kyphoplasty done at levels T8, T10, T12, L1, L2, L4 and L5. She had 2 years of Teriparatide treatment. DEXA scan after treatment improved significantly and revealed T score −0.7 at L2-L4 and mean femoral −1.1. HRT was continued after stopping Teriparatide. She had repeat DEXA scan in January 2018 and T score −0.8 at L2-L4 and mean femora T score is also −0.8. She had repeat MRIs of spine and no new change was noted. This patient had very good response to Teriparatide and BMD remains stable on HRT after stopping Teriparatide.

DOI: 10.1530/endoabs.62.WF2

WF3

Benign Parathyroid Adenoma: Rare presentation of severe Primary Hyperparathyroidism, Hypercalcaemic crisis

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Primary hyperparathyroidism (P-HPT) is one of the most common of all endocrine disorders. 80 to 85% of cases are due to parathyroid adenomas while hyperplasia accounts for 10% to 15% and carcinoma less than 1%, of cases.[1] Its very rare for parathyroid adenoma to present with clinically severe hypercalcaemia or a 'parathyroid crisis'. There are some existing case reports.[2,3] We report a case of a 67 year old woman who presented with severe irritability and drowsiness. Her conscious level was so persistently reduced she required intensive care unit admission. Investigations showed a calcium of 5.98 mmol/l (2.20–26.60 mmol/l) with a PTH of level 214.1 pmol/l (1.6–6.9 pmol/l). She was also biochemically severe dehydrated deranged kidney functions, urea = 22.2 mmol/l.creatinine = 212 umol/l. Her only past medical history was mild hypercalcaemia. The working diagnosis was initially malignant parathyroid cancer after excluding other common causes of hypercalcaemia. She was managed in the intensive care unit by aggressive IV fluid resuscitation (4–8 litres / 24 hours). Pamidronate and oral Cinacalcet were used as adjuncts. She was discharged home after normalisation of her calcium to 2.12 mmol/l on Cinacalcet therapy with her further follow up with her scan and surgical excision. Imaging on NM SCAN Spect CT showed an avid 19 mm parathyroid nodule in the right lower position and she underwent surgical resection within a week of her initial presentation. Her PTH rapidly normalised post-operatively. Unfortunately, due to pre-operative vitamin D deficiency she developed mild post-operative hypocalcaemia. Histology showed an adenoma with no atypical features. She was subsequently discharged on calcium replacement and vitamin D. We present an unusual case of very severe primary hyperparathyroidism secondary to a parathyroid adenoma with the highest calcium this authors seen requiring critical care support for its early management.

References
1. DeLellis RA, Mazzaglia P, Mangray S. Primary hyperparathyroidism: a current perspective.
2. S. Tahim, J. Saunders, and P. Sinha. A Parathyroid Adenoma: Benign Disease Presenting with Hyperparathyroid Crisis.
3. Georges CG, Guthoff M, Wehrmann M, Teichmann R, Gröne E, Artunc F, Risler T, Friedrich B, Müssig K. Hypercalcaemic crisis and acute renal failure due to primary hyperparathyroidism.
4. Marienhagen K, Due J, Hanssen TA, Svartberg J. Surviving extreme hypercalcaemia–a case report and review of the literature.
5. Nishimura K, Nozawa M, Hara T, Sonoda T, Oka T. A case of primary hyperparathyroidism associated with marked hypercalcemic crisis.

DOI: 10.1530/endoabs.62.WF3

Workshop G: Disorders of appetite and weight

WG1

Assessment and management of obesity in Tier 3 services - a case study

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With over 650 million people obese in 2016 and 2.8 million people dying a year from being overweight or obese, the obesity epidemic is now linked to more deaths worldwide than being underweight. This high mortality rate and disease burden are potentially preventable if risk factors such as unhealthy diet and physical inactivity were eliminated. The classification of obesity is defined as a Body Mass Index (BMI) equal to or above 30 kg/m^2. Weight management services in the UK are divided into tiers. Tier 1 and 2 cover advice and lifestyle interventions in primary care; Tier 3 covers specialist weight management services; Tier 4 covers bariatric surgery. Referral to Tier 3 services is criteria led, accepting patients with a BMI of >35 in the presence of diabetes and/or significant comorbidities or BMI >40 without the presence of these conditions. A 58 year old man was seen in the Tier 3 services at the Norfolk and Norwich University Hospital, with a BMI of 39.1 kg/m^2. He wished to achieve a BMI of 35 g/m^2 to help with preoperative fitness for a troublesome hernia. He suffered hypertension, obstructive sleep apnoea, recurrent venous thromboembolism and hypogonadotrophic hypogonadism (normal LH/FSH, testosterone level <0.4 ng/dl). On exploring the patient's beliefs about weight gain, he felt this stemmed from physical inactivity since early adulthood, he did not suffer any psychological issues or binge eating behaviours. Examination indicated insulin resistance, there were no cushingoid features. An Intensive Weight Management Programme (IVMP) consisting of 3 phases each lasting 8 weeks was initiated. Throughout the programme, the patient was seen fortnightly. Phase 1 induced rapid and consistent weight loss using a low energy liquid diet of; 3–5 pints of semiskimmed milk, 2 pints of free fluid, fibre sachets and multivitamins daily. This provided 800–1200 kcals and 60–100 g of protein. Phase 2 stabilised weight with the reintroduction of a solid food in combination with pharmacotherapy. Phase 3 provides advice in the principles of behaviour change and an increase in activity to maintain the weight that has been lost. The IVMP was a success, on completion the patient's BMI decreased to 31.8 kg/m^2, his exercise tolerance increased and obstructive sleep apnoea improved dramatically. Additionally, his testosterone levels returned to normal. Obesity is a complex medical, psychosocial condition affecting all ages and income groups. There is a pressing need to prevent premature death and improve the quality of life of millions of people.

DOI: 10.1530/endoabs.62.WG1

WG2

Surgical management of diabetes

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Bariatric surgery has emerged as an effective tool for people with severe obesity and type 2 diabetes. A 38 years old lady with type 2 diabetes for 10 years and a BMI of 51 kg/m^2, underwent bariatric surgery (Roux-en-Y gastric bypass). Other past medical history includes hypertension and hyperlipidemia. She was diagnosed with gestational diabetes in her 1st pregnancy and type 2 diabetes in subsequent pregnancy. She has lifelong problems with her weight. Despite multiple diet clubs in the past and a number of courses for level 2 weight management services, she failed to achieve any significant weight loss. Her glycemic control has been poor with a HbA1c between 75 and 134 mmol/mol despite adherence to healthy diet. She was initially treated with metformin 1 gram bd, liraglutide 1.2 gram od and dapagliflozin 10 mg od. Liraglutide was initially successful with weight loss of about one stone however, her weight increased again. She has been on dapagliflozin, but she cannot tolerate taking it. Then, she was put on novomix 30 insulin 22 units am, 24 units pm. Finally, it came to the decision that bariatric surgery would be the best option for her case. Post-operatively, she has lost a significant amount of body weight (38% since her first appointment) and her glycemic control also showed a significant improvement. She has been off insulin and currently only on metformin 1 gram bd. Her most recent body weight was 96.3 kg and most recent HbA1c was 66 mmol/mmol.

DOI: 10.1530/endoabs.62.WG2

Workshop H: Miscellaneous endocrine and metabolic disorders

WH1

Secondary adrenal failure with profound hyponatraemia

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A 73-year-old gentleman known to suffer from hypothyroidism was admitted to hospital with severe symptomatic hyponatraemia of 112 mmol/l. He was acutely confused with a GCS of 12/15. He was found to be in urinary retention with 650 ml residual urine post catheterisation. Initially, his serum sodium concentration improved on catheterisation and fluid restriction. The syndrome of inappropriate ADH secretion in the context of urine retention was initially suspected on the bases of a hypo-osmolar hyponatraemia, a urine concentration of >100 mOsmol/kg and urine Na $>$ 40 mEq/l. His serum sodium started dropping again. A CT Trunk was performed which was normal. An MR Head was requested on account of persistent hyponatraemia. This revealed a large pituitary mass lesion measuring 18 $\times$ 17 $\times$ 18 mm (AP/COR/CC). This lesion filled the sella turcica and extended suprasellarly with mild superior displacement and impingement of the optic chiasm. The lesion was of intermediate - low signal intensity on T1-weighted image and intermediate signal intensity on T2 with another small 5 mm cystic lesion seen on the left. It enhanced moderately and homogeneously post contrast administration. On direct questioning, the patient denied any headaches or visual disturbances, lethargy, nausea or vomiting, poor appetite, weight loss or galactorrhoea. He complained of longstanding low libido, erectile dysfunction and lack of morning erections. Sampling of his pituitary profile revealed hypocortisolaemia, hypogonadotrophic hypogonadism and hyperprolactinaemia as seen below. He was already on adequate levothyroxine replacement therapy.
Pituitary Function Tests:
FSH: 1.3 U/l (0.7–11.1)
LH: 0.3 U/l (0.8–7.6)
TSH: 0.52 IU.ml (0.3–3)
Free T4: 13.46 pmol/l (11–18)
Prolactin: 508 mIU/l (45–375)
Growth Hormone: 0.19 ug/l (0–3)
Total testosterone: $<$0.69 nmol/l (4.47–29.5)
Cortisol am: 83 nmol/l (145–619)
Serum osmolality: 291 mOsmo/kg (282–300)
Urine osmolality: 728 mOsm/kg (50–1200)
IGF-1: 48 ng/ml (40–180)
Goldman's perimetry test was within normal limits. The patient was started on hydrocortisone 10 mg – 5 mg – 5 mg on account of hypocortisolaemia. He was educated re the importance of lifelong steroids, sick day rules and usage of the hydrocortisone emergency pack. His serum sodium improved and remained normal. This gentleman has been referred for consideration of trans sphenoidal surgery and shall be followed up at our endocrine clinic with a six-monthly pituitary function test, Goldman's perimetry and repeat MRI pituitary until his surgery is performed. Our case highlights a rarer presentation of a pituitary macroadenoma with hyponatraemia due to secondary adrenal insufficiency.

DOI: 10.1530/endoabs.62.WH1

WH2

SIADH in the context of pre eclampsia

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A 40 year old lady known to have type 1 diabetes on insulin pump therapy presented with hypertension at 33 weeks gestation. Treatment with labetalol 100 mg bd was initiated but she was admitted at 34 weeks due to lack of BP control. Sodium levels were 136 mmol/l (135–145 mmol/l) on admission. Labetalol was increased to 300 mg tds and she was discharged after 4 days with a sodium level of 129 mmol/l. She was readmitted at 35 weeks with pre-eclampsia as evidenced by severe headaches, persistent hypertension (186/92 mmHg), a high uric acid (400 umol/l), low platelet count (91×10^9/l) and proteinuria (1557.1 mg/24 hrs). Her sodium rapidly dropped to 125 mmol/l. Urine sodium was 38 mmol/l, urine osmolality: 267 mOsm/kg, serum osmolality: 269 mOsm/kg. The patient was euvolemic with normal thyroid and adrenal function. These results were consistent with SIADH. Labour was induced but an emergency caesarean section was performed in view of signs of foetal distress. The baby's sodium level was 127 mmol/l. The mother's fluid intake was restricted to 1.25 litres/day initially and then to 2 litres/ day. Within 48 hours of delivery, her sodium improved from 125 to 133 mmol/l. Proteinuria decreased to 759.9 mg/24 hrs and platelet count and uric acid normalised. Pre eclampsia is associated with reduced intravascular volume which may stimulate ADH release resulting in SIADH. Foetal sodium rapidly equilibrates with maternal sodium and this can cause foetal jaundice, tachypnoea and seizures if serum sodium is $<$130 mmol/l. Acute hyponatremia further increases the likelihood of seizures in pre eclampsia. Management includes fluid restriction and delivery in a timely manner.

DOI: 10.1530/endoabs.62.WH2

WH3

A case of treatment-resistant Hyponatraemia successfully treated with Fludrocortisone

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A 60-year-old lady with known Rheumatoid arthritis, Ulcerative colitis and hypothyroidism was admitted with a 10-day history of diarrhoea and vomiting in June 2017. Sodium on admission was 107. Sodium rapidly improved with intravenous (IV) saline. She had 3 further admissions in quick succession in July and August. She always had a quick response to IV saline, but sodium dropped once IV Saline was withdrawn. She was started on oral sodium replacement but this had no effect on her sodium. It was felt that she had hyponatremia secondary to dehydration but also possible saltwasting nephropathy secondary to Golimumab. SF had been started on Golimumab in January of 2017 and this seems to have been the beginning of her sodium problems. The cause of diarrhoea was extensively investigated by Gastro services and felt it was not related to her ulcerative colitis. She had a normal pituitary profile. By this time she had been in the hospital for 30 days.
Hypothesis
Given the persistent Hyponatraemia, we hypothesized that she had proximal as well as distal renal tubular damage and her aldosterone was not able to compensate for this loss of function. To prove this hypothesis we did a series of tests and calculations.
Urine 24 Protein Excretion 0.23 (Normal $<$0.15)
Serum Uric Acid 0.09 mmol/l (Normal 0.14–0.34)
Urate Excretion - 1.3 mmol/24H (1.2–5.9) - Inappropriately normal.
TTKG - 5.8 (A TTKG of less than 8 implies inadequate potassium excretion, which is usually secondary to aldosterone deficiency or unresponsiveness)
TMP/GFR- 1.008 (Normal 0.8–1.35 mmol/l)-Low levels suggest renal tubular phosphate wasting.
Aldosterone-780 pmol/l (90–700) Renin-0.9 nmol/l per hr (0.5–3.5)
Aldo/Renin Ratio 867 (Ratio $>$850 Conn's likely)
Beta 2 Microglobulin-Normal
Interpretation
These tests suggest this patient had damage to proximal as well as distal renal tubules. Furthermore, she had a high aldosterone level and a high Aldosterone/ Renin ratio of Conn's range. This again suggests there was an element of distal tubular dysfunction.
Treatment
She was started on fludrocortisone at a dose of 100 mcg OD and it was gradually increased to 300 mcg and this stabilized her sodium. In the next 24 to 48 hours sodium continued to improve without any intravenous normal saline. She was discharged with a serum sodium of 130 about a week after starting her on fludrocortisone. Her sodium continued to remain normal on fludrocortisone post discharge.

DOI: 10.1530/endoabs.62.WH3

WH4

Conn's Syndrome presented as resistant Hypertension in 33-year-old male

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Background
Hypertension affects 28.6% of adults in the United States. In most, hypertension is primary (essential or idiopathic), but a subgroup of approximately 15% has secondary hypertension. In young adults ($<$40 years old), the prevalence of secondary hypertension is approximately 30%. Endocrine disorders remain one of the leading causes of secondary hypertension. Primary aldosteronism (Conn's syndrome), Once thought to be a rare condition and not worth investigating in patients with hypertension unless hypokalemic, however, it's now considered the most common, specifically treatable, and potentially curable form of

hypertension, accounting for at least 5% to 10% of hypertensive patients, with most patients normokalemic.
Clinical Presentation
A 33-year-old male has presented with recurrent attacks of dizziness, muscle pain and fatigue every few months, which was treated conservatively in ER by IV Fluid. His PMH include uncontrolled hypertension diagnosed since 2015, he had visited many specialized centres for his condition. His current medications list includes; amlodipine 5 mg, valsartan 160 mg and hydrochlorothiazide 12.5 mg. On examination is BMI is 22 kg/m^2, he is anxious, his blood pressure is 150/100 mmHg, the abdomen is soft, no masses, there is no radio-femoral delay and no renal bruit can be detected.
Investigations
- S.Potassium: 2.5 mg/dl.
- Renin: 2.6 pg/ml, aldosterone: 373 pg/ml, and Aldosterone Renin Ratio (ARR) of 66.9 (normally <25).
- Echo: LVH
- CT of adrenal glands shows right adrenal mass 20 mm, 15 HU, which increases to 30 HU after contrast.

Treatment: the patient had been referred to surgery and the team decided to do laparoscopic unilateral adrenalectomy. The histopathology confirms the diagnosis.
Outcome
The operation normalized his aldosterone level (from 373 to 62 pg/ml), and with continuous follow-up, still the patient is normotensive without any hypertensive medications.
Conclusion and Take Home Messages
First: always think of secondary causes of hypertension in young patients especially if it's resistant to therapy, as hypertension may be the initial clinical presentation for at least 15 endocrine disorders. Second: don't depend on serum potassium as a screening test for primary hyperaldosteronism, and Third: Aldosterone Renin Ratio (ARR) remains the gold-standard test for screening of primary hyperaldosteronism.

DOI: 10.1530/endoabs.62.WH4

WH5

Use of Tolvaptan in the management of recurrent episodes of Hyponatremia due to SIADH secondary to Traumatic Brain Injury

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History
80 years old male was admitted in June 2016 with a head injury. His CT head showed small subarachnoid haemorrhage and shallow frontal subdural hematoma. He was managed conservatively as per advice from neurosurgical department and was discharged on 4th July. He was readmitted on 9th July suffering from confusion and found to have sodium of 114 which was 141 a week ago.
Investigation
Investigations carried out to find the cause of low Na showed serum osmolality of 232, urine osmolality of 479, urinary Na of 60 with normal cortisol and thyroid function test.
Management
He was put on fluid restriction to 750 mls, followed by sodium tablets but despite that Na remained low with range 109–116. During admission he had further falls and repeat CT head showed stable appearance of previous finding. Apart from confusion he never developed any other symptom of neurological deficit. Due to poor response to standard treatment and being symptomatic he was given one stat dose of 5 mg of Tolvaptan on 28th July which improved Na gradually to 125 by 2nd Aug with clinical improvement so he was discharged home with the advice to continue fluid restriction. During that admission his medications were reviewed as well. Unfortunately his Na levels subsequently dropped leading to re- admission with confusion on 10th Aug with Na of 118 which further dropped to 112 and again he failed to respond to strict fluid restriction when Tolvaptan dose (5 mg) was repeated on 18th Aug and caused safe improvement in Na to 119 on 19th Aug and to 123 by 23th Aug which was maintained with clinical improvement in symptoms. He was monitored in endocrine clinic thereafter, his Na levels oscillated with normal results in Oct 16 then reducing to 127 in Dec 16 and finally returning to normal in Jan 17.
Conclusion
This is an example of hyponatremia due to SIADH secondary to traumatic brain injury with recurrent episodes of hyponatremia, resistant to fluid restriction and sodium tablets. It is important to identify such patients and exclude other differentials like cerebral salt wasting. This case illustrates safe and effective use of Tolvapatan as a single small dose in the treatment of SIADH which can be done at the general ward level. It is interesting to see that sodium levels recovered and maintained after single dose Establishing the dose of Tolvaptan needs further discussion and experience.

DOI: 10.1530/endoabs.62.WH5

WH6

Hyponatraemia; a cause not to miss

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We report the case of a 65 year old lady who was admitted to A&E with neurological symptoms (slurred speech, ataxia, intermittent confusion) and she was found to have low sodium (116 mmol/l). She reported 2–3 week history of lethargy and lightheadedness. There was no history of shortness of breath, cough, haemoptysis, weight loss, night sweats, altered bowel habits or excessive fluid intake. Her past medical history included hip osteoarthritis and dyslipidaemia. She lived with her husband. She was independent, lifelong smoker (20 cig/day) and consumed no alcohol. Her regular medications included Pantoprazole, Celecoxib, Atovastatin and Cetirizine. Pantoprazole was discontinued on admission. On examination, she appeared euvolaemic. Gait was mildly ataxic, but no other focal neurology was noted. Cardiovascular, respiratory and GI systems were unremarkable. She was investigated initially with a CT-head to rule out stroke which revealed no evidence of acute pathology. The blood tests showed normal kidney and liver function, normal FBC and Glucose. To investigate further the hyponatraemia, paired serum/urine osmolalities and urine sodium as well as cortisol and TSH were requested. Serum Osm: 246, Urine Osm: 477, Ur Na: 62. Normal cortisol (521 nmol/l) and TSH (1.77 mu/l). The test was suggestive of SIADH. She was placed on fluid restriction 1 l and her Na increased to 120. However, failing to increase further, she was started on Demeclocycline 300 mg TDS. In view of the above diagnosis, a CT thorax-abdomen-pelvis was performed revealing a pathological right hilar and mediastinal lymphadenopathy. Subsequently, she underwent EBUS to obtain a definite diagnosis. During her inpatient stay, she developed a rash in her legs. This was thought to be a photosensitivity rash secondary to the recent initiation of Demeclocycline (The patient reported spending some time in the hospital yard with her family). The following days her blood tests revealed increasing inflammatory markers and therefore she was covered for possible cellulitis with antibiotics as per Trust guidelines. In the meanwhile, her sodium had improved, but she developed acute kidney injury stage 3. As a result, fluid restriction and demeclocycline were discontinued. US Kidneys was normal. EBUS guided FNA cytology revealed small cell lung cancer. She was referred to oncology services with sodium of 143 on discharge.
Conclusion
This is a case of ectopic ADH production secondary to small cell lung cancer. It highlights the diagnostic considerations in SIADH and side effects of treatment with Demeclocycline.

DOI: 10.1530/endoabs.62.WH6

WH7

A case of cocaine-induced acute symptomatic hyponatraemia

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A 34-year old lady with a history of Crohn's colitis and depression presented to the Emergency Department (ED) reporting an allergic reaction to azathioprine. She complained of mild headache, anxiety and nausea but denied wheeze, shortness of breath, tongue swelling or rash. Her medications were prednisolone, predfoam enemas, escitalopram, combined oral contraceptive pill (OCP) and azathioprine, commenced one month ago. She denied alcohol or recreational drug consumption. Bowel symptoms had been improving. Physical examination was unremarkable. A routine blood test earlier that day had shown normal sodium (139 mmol/l) but on repeat blood test in ED, only 8 hours later, her sodium was 121 mmol/l, with normal serum potassium and renal function. She became increasingly confused with mood changes and then had a seizure, terminated with lorazepam. Further repeat bloods showed another fall in sodium to 118 mmol/l with low serum osmolality (250 mOsm/Kg), lactic acidosis and raised white cell count post seizure. Thyroid function, bone profile and liver function tests were normal. She was commenced on hypertonic saline (European guideline protocol), IV hydrocortisone (history of chronic steroid use) and intravenous antibiotics for potential meningoencephalitis. Urine toxicology was positive for cocaine, urine osmolality was elevated at 430 mOsm/Kg and urinary sodium was 84 mmol/l,

consistent with SIADH (syndrome of inappropriate antidiuretic hormone). CT head demonstrated hyperattenuation in the pituitary gland, which raised the possibility of haemorrhage. Her sodium level increased to 127 mmol/l following boluses of hypertonic saline and she was kept on fluid restriction afterwards. Her conscious level remained labile even after the rise in sodium and it improved only after she was given intravenous levetiracetam. This raised the possibility of status epilepticus post cocaine use. 24 hours following her admission, her mental state had improved and sodium normalised. She also admitted that she had used cocaine. Pituitary profile was normal (normal IGF1, TSH, prolactin) and her LH and FSH were appropriately suppressed on OCP. She subsequently had an MRI pituitary, which showed no abnormality in the pituitary gland. There are very few reports of hyponatraemia related to the use of cocaine. Cocaine is an indirect sympathomimetic agent. It acts in the nervous system by blocking the presynaptic reuptake of serotonin and catecholamines, increasing their bioavailability at post-synaptic receptors, which can stimulate ADH release. Acute cocaine use can have a number of consequences and should be considered as a potential cause for acute, severe hyponatremia.

DOI: 10.1530/endoabs.62.WH7

WH8

More than just a co-incidence? Hyponatremia as the first manifestation of profound Hypothyroidism

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Background
Hyponatraemia is a frequent finding in medical inpatients, where a comprehensive evaluation is warranted to establish the underlying mechanism and guide further management. Whilst the role of confounding medications, syndrome of inappropriate anti-diuretic hormone (SIADH), adrenal insufficiency and polydipsia is well-established as causative factors in the development of hyponatremia, the link between hypothyroidism and hyponatremia is controversial in the medical literature and often described as merely 'an association 'rather than a direct causality.
Case Presentation
A 72- years old male was referred to the acute medical unit after a biochemical finding of hyponatraemia. Past medical history included chronic obstructive pulmonary disease (COPD), fibromyalgia, age-related macular degeneration and recent diagnosis of hypertension. He reported fatigue, muscle cramps, constipation, headaches and confusion over the last 6 weeks. His medications included amlodipine, Loratadine and citalopram. He was euvolemic on examination. His initial biochemical panel showed sodium of 125 mmol/l (NR 135–145), serum potassium of 4.2 mmol/l (NR 3.5–5.5), urea 4.0 mmol/l (NR 2.5–7.8), creatinine of 101 umol/l (NR 60–105). Citalopram was stopped and he was commenced on 1L fluid restriction. However, his biochemistry failed to improve after 3 days and an endocrinology referral was requested. Further investigations showed a 9.00 am cortisol of 307 nmol/l (NR of 172–497),thyroid stimulating hormone (TSH) of 85 mIU/l (NR 0.5–3 mIU/l), free Thyroxine (Free T4) of $<$3.0 pmol/l (NR 10–22) with undetectable Free T3 levels. His Thyroid peroxidase antibodies were raised at 83.6 kU/l (NR 0–34) confirming the diagnosis of primary autoimmune hypothyroidism. The patient was prescribed Levothyroxine at a starting dose of 50 mcg once daily and with further up titration of the dose, his symptoms and biochemistry normalised in 8 weeks' time.
Conclusion
Though perceived as an incidental association, our case demonstrates that hyponatremia could be the first presenting sign of severe hypothyroidism. Serum TSH measurement is a reliable and rapid tool to screen for unrecognized hypothyroidism in the context of hyponatraemia with the potential (subjective to optimisation of all other confounding factors), to achieve normalisation of serum sodium with Levothyroxine therapy.

DOI: 10.1530/endoabs.62.WH8

WH9

A challenging case of chronic hyponatraemia

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A 56-year-old male presented in 2017 with acute symptomatic hyponatraemia. He was admitted with a seizure and a plasma sodium of 112 mmol/l. His past medical history was notable for alcohol excess and smoking. The acute presentation was managed with 3% hypertonic saline infusion in ITU. Plasma osmolality was 240 mOsm/Kg, urine osmolality 327 mOsm/kg and sport urine sodium 28 mmol/l. CT TAP showed some oesophageal thickening only; endoscopy was normal. He made a good recovery from this episode and was discharged home with a normalised pNa. The patient was followed up in the outpatient clinic. Eight months after discharge, his pNa fell to 122 mmol/l. Repeat biochemistry testing confirmed SIAD; he was asymptomatic and managed as an outpatient with fluid restriction. He subsequently presented with acute appendicitis; CT abdomen showed an abscess but no evidence of malignancy. pNa remained chronically low ranging from 120 to 129 mmol/l. Eighteen months after his initial presentation his pNa dropped to 111 mmol/l; this was associated with generalised fatigue and weight loss. He was admitted for further investigation and management. Repeat CT TAP demonstrated a new 6$\times$4 cm lung tumour with widespread lymphadenopathy and a mass adjacent to the pancreatic head. Biopsy confirmed small cell lung cancer. He was commenced on palliative chemotherapy. He did not respond to fluid restriction and was commenced on Tolvaptan. pNa initially responded well to Tolvaptan incrementing over 10 days to 129 mmol/l. Urine osmolality fell in conjunction with initiation of treatment. He required admission to hospital following his 2nd and 3rd cycles of chemotherapy due to worsening hyponatraemia. His Tolvaptan was increased to maximum dose yet there was no sustained improvement in his plasma sodium. Repeat urine osmolality measurement demonstrated a loss of aquaretic effect with urine osmolality ranging from 490 to 590 mOsm/Kg whilst on maximum dose Tolvaptan. This case highlights two key points in the management of chronic hyponatraemia. Firstly the cause of SIAD should be re-evaluated if there is a change in clinical condition e.g. acute drop in plasma sodium or development of new symptoms. Repeat imaging should be considered in patients with risk factors for malignancy who have persistent SIAD but normal initial imaging. Secondly Tolvaptan resistance is an emerging clinical phenomenon in patients with SCLC on long term V2-receptor antagonists with only a few cases reports in the literature. It is thought to be secondary to rising AVP concentrations associated with disease progression.

DOI: 10.1530/endoabs.62.WH9

Additional Cases

CB1

Abstract Unavailable.

CB2

Persistent hyperthyroidism post-total thyroidectomy

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A 51-year-old lady known to suffer from Graves' disease with associated orbitopathy since the age of 29 years, presented to endocrine outpatient clinic in view of recurrent symptoms of hyperthyroidism. She complained of heat intolerance, lethargy, tremor and diarrhoea. Appetite was normal and her weight remained stable. She had no worsening of visual symptoms. She was on carbimazole 5 mg daily since a year before. She had multiple courses of carbimazole in the past with subsequent recurrence. On examination she was clinically euthyroid. She had exophthalmos, lid retraction and lid lag bilaterally. There was no diplopia and full range of eye movements. Neck examination showed a diffuse smooth goitre with no retrosternal extension or bruits. There was no cervical lymphadenopathy.

Thyroid function tests on presentation were as follows:
TSH 0.033 mIU/l (0.3–3) ↓
Free T4 (fT4) 36 pmol/l (11–18) ↑
Free T3 (fT3) 9.03 pmol/l (3.5–6.5) ↑

Carbimazole was increased to 20 mg. Thyroid function tests improved and she was referred for thyroidectomy once rendered euthyroid on treatment. Post-thyroidectomy, she became hyperthyroid again on even small doses of levothyroxine and thus the latter was stopped (Table 1). She remained hyperthyroid even off levothyroxine and she was investigated for residual thyroid tissue. An NM Thyroid Scan initially showed no evidence of thyroid tissue in the neck. Stroma ovarii was also ruled out as there was no significant tracer uptake in the abdomen and pelvis. The patient was restarted on carbimazole as she remained hyperthyroid. A whole body Iodine scan performed at the time the patient was subclinically hypothyroid on treatment (TSH 11.954 mIU/l; fT4 15.25 pmol/l), showed a relevant focus of increased tracer uptake in the neck, practically at the midline, suggestive for the presence of residual thyroid tissue. The patient was referred for surgical re-evaluation.

Table 1

	TSH (mIU/l)	fT4 (pmol/l)	fT3 (pmol/l)
Pre-surgery	2.9	15.7	5.1
6 weeks post-operatively	0.037 ↓	33.7 ↑	8.17 ↑
On levothyroxine 75 mcg daily	0.008 ↓	30.11 ↑	5.8 ↑
On levothyroxine 50 mcg daily	0.013 ↓	45.00 ↑	9.5 ↑
On levothyroxine 25 mcg daily	0.008 ↓	37.13 ↑	9.4 ↑
Off treatment	0.011 ↓	30.78 ↑	6.8 ↑

DOI: 10.1530/endoabs.62.CB2

CB3

Endocrinopathies post immune check point inhibitors

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Introduction
Immune adverse related events are commonly recognized complications of immune check point inhibitors. Here we identify multiple endocrinopathies occurring concurrently in the same patient. In addition to highlighting the common immune adverse effects seen in other cases.

Case 1
33F Refractory Hodgkins Lymphoma tried on several therapies. She was started on Nivolumab (PD-1) with remarkable response. She developed symptoms of Amenorrhea, galactorrhea, vaginal dryness and hot flushes, and was found to have hyperprolactinaemia and partial hypopituitarism. MRI pituitary: lesion in clivus with possible infiltration of pituitary gland. This was discussed in Skull MDT and was felt to be a chordoma/sarcoma, unrelated to underlying lymphoma. Prolactin 4806 mU/l FSH <0.3 LH <0.3 Oestradiol <18.4 pmol/l IGF-1 and Short synacthen test normal. She was started on continuous estradiol patches with medroxyprogesterone for her bone health and general well-being. Soon after, she was admitted with a sudden presentation of DKA (BM >33.1 Ketones: 6.4) and hyponatremia (Na: 117). Upon investigation was found to have a newly diagnosed diabetes (HbA1c: 107 mmol/mol, islet cell antibodies negative) and hypothyroidism (Anti-TPO Abs Positive, TSH: 153 T42.8 T3:0.7), commenced on insulin and levothyroxine. Final diagnoses: Type 1 Diabetes, Hypothyroidism, Hyperprolactinaemia and partial hypopituitarism (possibly related to tumour). She is currently under endocrinology follow up. It was discussed with her that these endocrinopathies are likely side effects of Nivolumab, however she opted to continue on it with continued medical management these side effects.
Case 2
88M Stage 4 squamous cell lung CA T4 N3 M1a. Started on palliative treatment with Pembrolizumab (PD-1). After 8 cycles he developed hypothyroidism (TSH: 90, T4: 90) and started on levothyroxine. Previous records show a background of subclinical hyperthyroidism. He is currently well maintained on the levothyroxine.
Case 3
75M Metastatic adenocarcinoma of the lung T3 N3 M1b. Started on palliative therapy with Pembrolizumab (PD-1). Background of subclinical hyperthyroidism (TSH 0.08 T4 14.8) 2010, developed hyperthyroidism (TSH 0.08 T4 26) 2018. Endocrinopathies are well recognised Immune related adverse effects with immunotherapy due to enhancement of immune system with these agents. However the presentation of multiple endocrinopathies as demonstrated above in case 1 is a rare occurrence. With further widespread use of immunotherapy we are yet to see further effects of these drugs. These cases highlight the importance of early monitoring for endocrine adverse events as well as the importance of involving endocrinologist early in their care to provide better outcomes.

DOI: 10.1530/endoabs.62.CB3

CB4

Propylthiouracil-induced ANCA-associated vasculitis and agranulocytosis in a patient with Graves' disease

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42-year-old female with relapsing Graves' disease treated with propylthiouracil (PTU) presented to the Emergency Department with a two-week history of fevers, night sweats, transient rash, arthralgia and fatigue. Five years previously she presented with Graves' disease, TSH <0.02 mIU/l, FT4 of 39.8 pmol/l (9–16 pmol/l) and TSH receptor antibody positive with a titre of 11.3 IU/l. Initially treated with carbimazole therapy but developed an urticarial rash, lower limb swelling and eosinophilia and was switched successfully to PTU. At the time of presentation, she had been taking PTU for 18 months. She had a family history of hypothyroidism in one sister, was a non-smoker, rarely took alcohol and was an office worker. On examination the patient had a low-grade pyrexia (37.6°C), mild diffusely enlarged non-tender goitre with no evidence of retrosternal extension or thyroid eye disease. Initial investigations revealed a neutrophil count of 0.36×10^9/l and white cell count of 1.57×10^9/l, haemoglobin and platelet counts were normal. Biochemistry showed normal renal, liver and thyroid function. Blood and urine cultures were repeatedly negative. Extended viral screen was also negative. Chest radiograph was normal. Urinalysis showed a small amount of blood with no proteinuria, no crystals, no casts. Serum was positive for ANCA antibodies with dual positivity for myeloperoxidase (MPO), 6.4 IU/ml (NR 0–3.4), and proteinase-3 (PR3), 42 IU/ml (NR 0–2), consistent with vasculitis. Antinuclear factor was positive. Rheumatoid factor and complement were normal. Antibodies to DNA, RNP, Smith, Ro and La were negative. There was no evidence of renal or pulmonary involvement of vasculitis.
Results & Treatment
PTU was stopped due to both the agranulocytosis and ANCA-associated vasculitis (AAV). She was treated with broad spectrum antibiotics and granulocyte colony-stimulating factor, resulting in resolution of neutropenia. PR3 and MPO titres reduced and her vasculitic symptoms resolved upon discontinuation of PTU. Management options of Graves' disease were discussed and the patient opted for radioactive iodine (RAI). Following two doses of RAI, she became hypothyroid and was commenced on levothyroxine.

Conclusions and points for discussion
Clinicians should be cognisant of the significant risk profile of PTU. AAV is a rare side effect of PTU however, PTU is the most commonly reported medication causing drug-induced AAV. PTU-induced AAV has a better prognosis and milder course than primary AAV provided PTU is stopped, which is evident in the case outlined above. With prompt discontinuation of PTU, the patient's symptoms resolved precluding the need for immunosuppressive therapy.

DOI: 10.1530/endoabs.62.CB4

CB5

The double edge sword steroid facilitated diagnosis of primary thyroid lymphoma

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Introduction
Primary thyroid lymphoma (PTL) is a rare cause of malignancy, accounting for $<5\%$ of thyroid malignancies and $< 2\%$ of extra-nodal lymphomas. Most thyroid lymphomas are non-Hodgkin's lymphomas of B-cell origin. Patients with Hashimoto's thyroiditis are at greater risk for developing PTL. We report a rare case of primary thyroid lymphoma in a patient presenting with a rapidly enlarging thyroid goitre highly suspicious of anaplastic thyroid carcinoma posing as a diagnostic histological challenge due underlying Hashimoto's thyroiditis which was unmasked after a short course of oral steroids.
Case report
A 51 years old female was referred by GP with increasing painless swelling over the right side of neck over a period of 3 weeks. She did not have any difficulty in swallowing or breathing. There was no history of any weight loss or night sweats. Her TSH was 9.57 mIU/l with a normal free T3, T4 and positive thyroid peroxidase antibody suggestive of subclinical hypothyroidism secondary to Hashimoto's thyroiditis. The scan showed a large mass on the right side of the thyroid gland measuring $4.8 \times 4.6 \times 3.7$ cm, encasing the common carotid artery with complete compression and thrombosis of the internal jugular vein. There were multiple lymph nodes on the right side of neck. Initial imaging was highly suspicious of anaplastic thyroid cancer which carries a poor prognosis. She was referred to our thyroid surgeon and had a fine needle aspiration which unexpectedly only showed inflammatory/reactive picture with no clear signs of malignancy. She was given oral steroids for 4 days, which decreased the size of the neck swelling followed by a core biopsy. The resultant histology showed clearance of the inflammatory picture whilst unraveling histological features of a high grade lymphoma. A diagnosis of B cell lymphoma was confirmed by the Haematologist. From a haematological perspective, giving steroids prior to diagnostic biopsy for suspected lymphoma is strongly discouraged as steroids can partially treat high-grade lymphomas, induce necrosis and render the biopsy uninterpretable.
Conclusion
This case highlights the unexpected paradoxical role of steroids in unmasking the histopathological diagnostic dilemma of PTL which carries a more favourable prognosis compared to anaplastic thyroid carcinoma whilst shrinking the mass.

DOI: 10.1530/endoabs.62.CB5

CB6

Resistant Grave's disease not amenable to Thionamides, Thyroidectomy and Radioactive iodine

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Grave's disease is an auto-immune condition associated with hyperthyroidism caused by TSH-receptor antibodies (TRAB) expressed by follicular cells of the thyroid gland. Grave's ophthalmopathy has been reported in 25% of the patients and is rarely associated with dermopathy and thyroid acropachy. Management is by anti-thyroid drugs, radioactive iodine ablation or surgery, either alone or in combination. We present a rare case of resistant Graves who has detectable antibodies and thyroid remnant after being treated with all the above. A 55 years old lady presented with typical symptoms of hyperthyroidism associated with weight loss, sweating, palpitations and weight loss. Examination revealed an anxious lady with obvious outstretched hand tremors including extra thyroid manifestations such as thyroid acropachy, pretibial myxoedema and orbitopathy. Biochemistry confirmed the presence of TRAB 226.7 u/l, a suppressed TSH 0.14 mU/l with elevated T4 levels. She was treated with carbimazole and referred to ophthalmology for her eye disease. Due to worsening eye disease and high TRAB titres, she underwent a subtotal thyroidectomy and later, after 7 years, a total thyroidectomy. This did not have any significant impact on her TRAB levels. Thyroid uptake scan in 2012 revealing uptake in the thyroid bed. She had radioactive iodine treatment in 2013 under cover of high dose steroids with aim to reduce the TRAB and improve her acropachy and eye disease. A repeat uptake scan in 2017 has shown remnant thyroid tissue in the right thyroid bed reflecting residual active thyroid disease. This was treated again with a further dose of RAI in 2018. She is currently still under regular follow up by the local endocrinology team. This is a rare case of resistant Graves with persistent active thyroid tissue despite surgical and radioactive ablation of thyroid.

DOI: 10.1530/endoabs.62.CB6

CB7

Autoimmune thyroiditis with fluctuating antibodies

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This is the case 32y old Asian lady, who first presented to her GP in October 2013 with weight loss, palpitations and fatigue and found to have overactive thyroid. She has not experienced any neck pain or systemic illness. She has some neck tenderness but not goitre or any extra-thyroidal manifestation of Graves' disease, hence the thyroid nucleotide scan was requested. His scan was consistent with thyroiditis. By January 2014 her thyroid function test normalized with TSH 1.96, T4 11.1 and T3 2.7. Later in May 2014, she presented to her GP with weight fain and her repeat TFTs showed TSH 6.72, FT4 was 14.8 and FT3 4.7, consistent with transient sub clinical hypothyroidism. By October 2014 her TFTs normalized again with TSH 1.5 and FT4 14.7 without any thyroid replacement. In October 2015, she had features of over active thyroid with TSH 1.5 and normalize by itself. She was prescribed propranolol during that period. Her TPO antibody was 216. In Feb 2016, her TFTs were normal with TSH 5.78 and FT4 12.1 and she was discharged from clinic. In Feb 2018, she started to feeling tired and weight loss and fatigued. Repeat TFTs showed TSH was 0.30, FT4 14.6. No treatment given. She has another TFTs in march 2018, showed TSH of 15.7 and TPO antibody was significantly raised to 1209 iu/l. Based on these result, she was started levothyroxine 25 mcg. There was no neck tenderness and goiter. Her TRAB was checked in May 2018 and it was <0.3 and TSH was 6.0. The last TFTs in September checked with TSH well within the normal limits of 2.3 and was on LT4 25 mcg once a day. The two main disorders that comprise autoimmune thyroid disease are Hashimoto thyroiditis and Graves' disease. The Hashimoto is the most common cause of hypothyroditis, whereas the Graves' is major cause of hyperthyroidism. Occasionally, a patient may present with features of one of these disorders at one time and features of other at another time. The usual sequence is hyperthyroidism followed by hypothyroidism, however, vice versa can be seen in these type of patients.

DOI: 10.1530/endoabs.62.CB7

CB8

Interpretation of bilateral petrosal sinus sampling in Cushing's disease

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Case
A 46-year-old woman was initially investigated for right sided intermittent headaches for one year. Her MRI head revealed a pituitary adenoma. She had no history of vomiting with the headache episodes and had no history of visual acuity or field defect. She had amenorrhoea for the past 10 months. Prior to this, she had regular periods following her menarche at the age of 12 years. She admitted to easy bruising but had no hirsutism or acne. She did not report any weight gain. Her past medical history is significant for type 2 diabetes diagnosed April 2017 and managed with metformin. The patient is a non-smoker and does not drink alcohol. On examination, she had a raised BMI with a weight of 77.9 kg and sitting BP of 132/93 mmHg. She had a round face and central adiposity. There were pale striae on her lower abdomen and she had acanthosis nigricans around her neck. There was no evidence of proximal myopathy.
Investigations revealed state of hypercortisolemia with failure to suppress morning cortisol in both overnight dexamethasone and low dose dexamethasone suppression tests, 136 and 138 nmol/l respectively. Also she was found to have three sets of elevated late night salivary cortisol. Cortisol Day curve demonstrates

no diurnal variation in endogenous cortisol production with cortisol levels range between 313 and 368 nmol/l between 9 am and 6 pm. Her midnight serum cortisol was elevated at 377 nmol/l. Dedicated Pituitary MRI showed a central and left-sided adenoma measuring 15 mm by 9 mm in maximal axial dimensions. There was suprasellar extension with distortion of the pituitary infundibulum to the right. The adenoma extended to the under surface of the optic chiasm and marginally elevated left sided optic chiasm without overt compression. Subsequent bilateral petrosal sinus sampling excluded ectopic ACTH with a basal IPS:P (central: peripheral) ratio > 2.0 and a CRH stimulated IPS: P ratio >3.0 (Table 1).

Treatment

The patient was started on Metyrapone to control hypercortisolemia till she had surgery. Also, she was initiated on anticoagulation with Tinzaparin.

Discussion Points:

-Investigation of Cushing's disease (Tests and Interpretation)

-Bilateral petrosal sinus sampling indication, interpretation and limitation

-Medical management of Cushing's disease and the importance of thromboembolism prophylaxis.

Table 1

Time (min)	Left IPS	Right IPS	Peripheral
	Plasma ACTH (ng/l)		
−5	1125	130	64
0	1309	118	62
2	2053	326	61
5		1003	81
10		613	153
	Plasma Cortisol (nmol/l)		
−5	491	480	484
0	489	490	463
2	501	500	477
5		489	471
10		565	509
	Plasma Prolactin (mU/l)		
−5	1722	243	182
0	1439	253	181
2	1827	419	183
5		571	187
10		664	221

DOI: 10.1530/endoabs.62.CB8

CB9

To treat or not to treat: Two interesting cases of Alemtuzamab related Thyroid disorder

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Alemtuzumab, a humanized anti-CD52 monoclonal antibody is effective in treating multiple sclerosis. However, it has been associated with thyroid disorder in up to 30–40% patients. While Graves' disease is the most common disorder (70%), thyroiditis has been reported up to 4.9% cases.

Case 1: 34 year old woman with the background of multiple sclerosis and autoimmune hypothyroidism (on levothyroxine 50 mcg OD) was given Alemtuzumab infusion in July 2017. As part of surveillance, her TFTs were checked regularly. She developed thyrotoxicosis in July (TSH <0.01, FT4 84) before her next Alemtuzumab infusion in August 2018. Her GP stopped levothyroxine and she was seen in the endocrine clinic urgently. She was found to be mildly thyrotoxic (Heart rate 100/min, no sweating or tremors). There were no features to suggest Graves' eye disease. Her repeat blood test showed TSH <0.01, FT3 10.1 and FT4 30. Her TPO antibodies were 148 (positive) and TSH receptor antibodies were 1.3 (positive). In view of improving biochemistry, anti-thyroid medications were not initiated. Subsequently, her ultrasound thyroid showed increased vascularity throughout normal size thyroid suggestive of thyroiditis and no nodules were identified. Her technetium scan showed reduced uptake on right suggestive of recovering thyroiditis.. She received Alemtuzumab infusion in August and her thyroid function tests were closely monitored which improved initially. However, she became thyrotoxic (TSH 0.01.FT3 6.7, FT4 19.2, TSH receptor antibodies 17.5) after 3–4 months. She was therefore, started on Carbimazole with the plan to monitor thyroid function test closely.

Case 2: 37 year old woman was admitted for autologous stem cell transplant for treatment of multiple sclerosis. She was previously treated with Alemtuzumab in February 2016 and October 2017. During admission, She was found to be clinically thyrotoxic and her thyroid function test showed TSH was 0.00, FT3 >46, FT4 47.9 and TSH receptor antibodies >30. However, as she was pancytopenic with neutrophils of 0, she was started on beta-blocker initially and Carbimazole was initiated once her neutrophilia resolved. She responded well to treatment and repeat TFTs showed TSH<0.01, FT3 10.6 and FT4 17.5 after 3 weeks. She is being closely monitored. We have presented two cases of Alemtuzumab-induced thyroid disorders with different clinical presentations and clinical courses. As these disorders can present unique challenges, it is extremely important to properly investigate and closely monitor such patients.

DOI: 10.1530/endoabs.62.CB9

CB10

Amiodarone induced thyroid dysfunction

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68 year old lady was on amiodarone for atrial fibrillation and poor left ventricular systolic function. She was feeling unwell, so she had some blood tests which showed elevated free T4 and suppressed TSH. She did not have a family history of thyroid disease. She did not have a goitre or eye signs. She did not have overt signs of thyrotoxicosis. She was admitted as her heart failure was not controlled and her diuretics were optimised. Her thyroid antibodieswere checked and was sent for a radioiodine uptake scan. The uptake was slightly reduced and thyroglobulin was normal. The vascularity was normal or slight increased. She was started on steroids with carbimazole. Amiodarone was stopped. Repeat thyroid function showed in 6 weeks a fall in free T4 and TSH started to improve. This case shows the difficulty to differentiate between AIT type 1 and 2. You may have to treat as both and decide later.

DOI: 10.1530/endoabs.62.CB10

CB11

Pretibial Myxoedema (Thyroid Dermopathy) – a forgotten textbook sign!

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A 46 years old gentleman was referred by his GP to cardiology with 3 weeks history of bilateral leg swelling and rash associated with breathlessness and palpitations. He has no other past medical history to note. He smokes 20 cigarettes a day and works as a manager in a window installation company. He was started on diuretics and further investigations were arranged by cardiology. His symptoms persisted with worsening of skin rash. He was reviewed by GP again 1 month later. He had persistent tachycardia, resting hand tremors, weight loss and worsening lumps on his shins. He was referred to the ambulatory clinic for worsening rash and his symptoms. He had a blood test done revealing hyperthyroidism and was eventually referred to Endocrinology. He was seen in the thyroid clinic in January. On examination, he had hand tremors and was tachycardic. He had mild proptosis, lid swelling and marked pretibial myxoedema bilaterally (picture attached) His blood test revealed biochemical hyperthyroidism. TSH was suppressed <0.01 mU/l with T4 and T3 values of 68.6 and 40.6 pmol/l. Thyroid peroxidase antibody and anti-TSH receptor antibody levels were elevated and were 133 IU/ml and 31.2 u/l respectively. He was started on high dose carbimazole 60 mg a day. He noticed an improvement in his thyrotoxic symptoms after starting treatment. He was advised to abstain from smoking in the context of Grave's orbitopathy and to maintain his compliance with his anti-thyroid medication. He was also referred to the ophthalmology department for further review. He is under regular follow up under the endocrinology team. Pretibial myxoedema is part of the triad of Graves' disease which includes ophthalmoplegia and thyroid acropachy. It accumulates in the anterior shin area due to glycosaminoglycan accumulation produced by fibroblasts through cytokines stimulation. Majority of patients have high anti-TSH receptor antibodies and some degree of ophthalmoplegia suggesting that antigen-specific T cells may be responsible for initiating the inflammatory response. Most cases of pretibial myxoedema are asymptomatic and are mostly of cosmetic concern. Topical corticosteroids under occlusive dressing may be helpful. This case

intends to highlight the rare occurrence of pretibial myxoedema and to raise awareness among general physicians and endocrinologists.

DOI: 10.1530/endoabs.62.CB11

CB12

Acromegaly… challenges and treatment aspects

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Case history

We report a 25-year-old man who presented to Neurology with two years history of a migrainous headache mainly at night. MRI head scan demonstrated large lobulated pituitary macroadenoma with significant suprasellar extension and anterior visual pathway compromise along with distortion of the basal forebrain, particularly on the right. Consequently, he was referred to the endocrinology team for further management. Upon initial assessment, he reported foot size enlargement, loss of libido and erectile dysfunction. He was found to have acral facial enlargement when compared with his previous photos and thyroid goitre. The visual assessment showed mild bitemporal hemianopia and reduced colour vision.

Result and treatment

His biochemical investigation revealed significantly raised GH 207 ug/l and IGF1 84.6 nmol/l (16.3–39.3). Borderline low LH 1.8 IU/l (1.7–8.6) and FSH 1.6 IU/l (1.5–12.4) along with very low Testosterone 2.3 nmol/l (7.6–31.4) consistent with hypogonadotropic hypogonadism with mild secondary hypothyroidism. The diagnosis of acromegaly was confirmed by the failure of GH suppression during OGTT with nadir level 215 mcg/l. He was commenced on Lanreotide 60 mg every 4 weeks preoperatively. Trans-sphenoidal resection of the macroadenoma was performed. Histology showed sparsely granulated GH adenoma with elevated Ki 67 of 8%. This adenoma subtype is classified as a special aggressive variant in the WHO classification of tumours of the pituitary gland (2017). Unfortunately, complete excision of the tumour was not possible given the substantial size at presentation. Lanreotide dose was increased to 90 mg/four weeks however, biochemical remission was not achieved with persistently high GH and IGF1. Postoperative MRI scan showed significant residual lesion with suprasellar extension and compression of the optic chiasm. His visual deficit resolved postoperatively. Subsequently, further debulking surgery was performed three months later through craniotomy and somatostatin analogue dose was increased to 120 mg/four weeks. Six months later, Growth hormone and IGF1 were still raised at 78 ug/l and 76 nmol/l respectively. Cabergoline was started at 0.5 mg/week and titrated up to 2.5 mg/week with no significant side effects. His active disease is very resistant to medical and surgical interventions. Eventually, the patient received external beam radiotherapy 50.4 Gy and has been considered for pegvisomant therapy.

Discussion

Our patient represents a very challenging acromegaly case. Despite having various medical therapies and surgical resections, his disease still very active as illustrated above. Growth hormone receptor antagonist has been considered while awaiting radiotherapy effect. Genetic testing results awaited.

DOI: 10.1530/endoabs.62.CB12

CB13

Unusual thyroid case… Flying away from the herd…!

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We report a 42-year-old female who was known to have autoimmune hypothyroidism for nearly 20 years with positive antiTPO antibodies. She was well controlled on levothyroxine including three antenatal periods when she required a slightly higher dose of 125 mcg daily. No significant past medical history and denies use of herbal/over the counter medications. In early 2017, the patient started to experience nonspecific symptoms of lethargy and tiredness. Her thyroid state was managed in the community. Initially, her tests showed suppressed TSH and raised FT4 (see table). Her replacement therapy was adjusted by GP and had to reduce her dose to 25 mcg on alternate days to maintain levels within the desired biochemical range until September 2017 when the GP decided to stop treatment and was referred to the specialised endocrine clinic given her persistent thyrotoxic state. At this stage, she became profoundly hypothyroid with TSH 97.8 mIU/l and >100 mIU/l in November 2017 and January 2018 respectively. Upon clinical review in the endocrine clinic and given her fluctuating thyroid status, a provisional diagnosis of thyroiditis was made and a small dose of levothyroxine was restarted. US thyroid scan revealed hypervascular gland suggestive of active inflammatory thyroiditis.

Case Resolution

Interestingly the patient reports no change in her symptoms during TSH fluctuation but clinically she had fine tremor which was consistent with thyrotoxicosis. Further investigations revealed elevated TRAB antibodies at 9.1 u/l and Thyroid 99m pertechnetate scan is consistent with Graves. Carbimazole has been started to control her symptoms.

Learning point

There are two distinct thyroid syndromes most commonly caused by autoimmune aetiology, Hashimoto's thyroiditis and Graves' disease. The latest is induced by TRAB antibodies. There are two types of these antibodies cause two different clinical conditions. The first stimulates the thyroid (TSAb) causes Graves' thyrotoxicosis and the second type blocks thyrotropin action (TBAb) occasionally responsible for hypothyroidism. There are few case reports of switching between TBAb and TSAb (or vice versa) with complete variation in clinical status. The process of changing antibodies action is not fully understood as yet. We believe this lady has been TRAB positive even she was hypothyroid but it was never checked. Extreme fluctuation of thyroid status with small variations in levothyroxine dose in previously well controlled compliant patients should alert physicians to the possibility of switching stimulatory and inhibitory antibodies status.

DOI: 10.1530/endoabs.62.CB13

CB14

A case of amiodarone-induced hypothyroidism

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A sixty-four-year old lady with a past medical history of total thyroidectomy for Graves' disease and atrial fibrillation on amiodarone was referred to the endocrine out-patients in view of hypothyroidism. Since starting amiodarone, the TSH was noted to be elevated at 75 mU/l and the free T4 was 18 pmol/l. The patient complained of non-specific lethargy and was administered levothyroxine 50 mcg daily. Despite this her TSH remained elevated at 147 mU/l with a free T4 of 17.3 pmol/l and a free T3 of 2 pmol/l. TSH interference was ruled and a pituitary profile was normal. In the time of 2 years, despite gradual augmentation of her levothyroxine dose, the TSH remained elevated. At this point it was suspected that amiodarone might be causing type 1 5' deiodinase enzyme inhibition leading to reduced peripheral conversion of T4 to T3. Hence the patient was commenced on a trial of liothyronine 12.5 mcg twice a day in addition to her levothyroxine. This eventually resulted in normalization of her thyroid function tests. Amiodarone induced hypothyroidism highlights the importance of life long thyroid function monitoring (free T3, free T4 and TSH) in patients on amiodarone. This case of amiodarone-induced hypothyroidism also reveals another possible indication for levothyroxine/liothyronine combination therapy.

DOI: 10.1530/endoabs.62.CB14

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