

# Endocrine Abstracts

March 2020 Volume 69  
ISSN 1479-6848 (online)

Society for Endocrinology  
National Clinical Cases 2020

*12 March 2020, Royal Society of Medicine, London*

 Society for  
Endocrinology



published by  
**bioscientifica**

Online version available at  
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## **Society for Endocrinology National Clinical Cases 2020**

Thursday 12 March 2020

Royal Society of Medicine, London

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# Oral Communications

## OC1

**Biochemical and clinical cure of primary aldosteronism by ultrasound-guided endoscopic radiofrequency ablation**

Emily Goodchild<sup>1,2</sup>, Xilin Wu<sup>1,2</sup>, Alexander Ney<sup>3</sup>, Giulia Argentesi<sup>1,2</sup>, Jackie Salisbury<sup>1</sup>, Samuel O'Toole<sup>1,2</sup>, Teng-teng Chung<sup>3</sup>, Heok Cheow<sup>4</sup>, William Drake<sup>2,1</sup>, Steve Pereira<sup>3</sup> & Morris Brown<sup>1,2</sup>  
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A 65-year-old Afro-Caribbean gentleman, with a >10-year history of hypertension, frequently recorded blood pressures of >160/80 mmHg. His serum electrolytes showed Na<sup>+</sup> 145 mmol/l and K<sup>+</sup> 3.2 mmol/l. MRI demonstrated 13 mm left medial-limb adrenal adenoma. His hypertension was uncontrolled on treatment with amlodipine 10 mg OD, spironolactone 50 mg OD, losartan 100 mg OD and doxazosin 16 mg OD. Although his quality of life was reduced, and he disliked the polypharmacy, he did not wish to undergo invasive investigations and surgery to pursue potential cure. The diagnosis of primary aldosteronism (PA) was confirmed off interfering medicines: aldosterone 661 pmol/l, renin activity <3.3 pmol/l per min, ARR >200 (PA likely if >60). <sup>11</sup>C-metomidate PET CT scan demonstrated a 15 mm left adrenal nodule with high uptake; SUV time of flight (TOF) 30.4, SUVmax ratio, left to right, 1.92 (normal <1.25). He was enrolled into FABULAS (Feasibility study of endoscopic radiofrequency Ablation, with Ultrasound guidance, as a non-surgical, adrenal sparing treatment for aldosterone-producing adenomas), a prospective safety and efficacy evaluation of 30 patients with unilateral left-sided aldosterone-producing adenomas (APA). Under ultrasound guidance, a StarMed catheter was passed, through a 19-gauge needle in the stomach wall, into the APA. During the procedure, undertaken under GA, blood pressure was monitored and biochemical assessments of adrenomedullary activation were made. There were no adverse events. 48 h after ablation, a study-protocol CT scan demonstrated regional fat stranding, consistent with intervention, and no evidence of complications. At six-months post-ablation the patient felt well and reported significant improvement in his quality of life. His blood pressure (average of 12 home readings over 3 days) had decreased, from 161/81 mmHg to 123/79 mmHg, off all antihypertensive medications. He was cured biochemically: Na<sup>+</sup> 140 mmol/l, K<sup>+</sup> 4.7 mmol/l, aldosterone 209 pmol/l, renin activity 13.3 pmol/l per min, ARR 17.2. Repeat <sup>11</sup>C-metomidate PET CT scan demonstrated minimal left adrenal nodule uptake; SUV TOF 4.6, SUVmax ratio, left to right, 1.04 (normal <1.25). This patient case illustrates how minimally invasive ablation of a left adrenal APA, delivered by an ultrasound-guided endoscopic route, can achieve biochemical and clinical cure in a patient unwilling to have adrenalectomy. Fewer than 1% of patients with PA are currently diagnosed and, of those proceeding to adrenalectomy, fewer than 50% are completely cured of hypertension. As the frequency of PA diagnosis increases, ablation has the potential to increase capacity for intervention, by minimising morbidity and time off work.

DOI: 10.1530/endoabs.69.OC1

## OC2

**Paraneoplastic hypoglycaemia secondary to IGF-2 secretion from a metastatic gastrointestinal stromal tumour**

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## Case history

Herein, we report the case of a 79-year-old male who presented acutely to A&E with recurrent episodes of symptomatic hypoglycaemia. A random glucose at presentation was low at 1.4 mmol/l and upon correction symptoms resolved.

While hospitalized, he continued having episodes of symptomatic hypoglycaemia, requiring treatment with intravenous dextrose and *per os* steroids. Once stable, he was discharged with advice.

## Investigations

A contrast-enhanced CT scan of his abdomen revealed liver/omental deposits and a biopsy with subsequent immunohistochemistry was positive for CD117 (*C-kit*), Dog1, and CD34 with focal expression of SMA – confirming the diagnosis of a metastatic gastrointestinal stromal tumour (GIST). Genetic testing for *c-kit* activating mutations was carried-out to predict his therapy response and guide anti-CD117 dose with Imatinib Mesylate revealing an exon 11 deletion. Non-islet cell tumour hypoglycaemia (NICTH) was suspected, with an IGF-2 (105.9 nmol/l) to IGF-1 (4.6 nmol/l) ratio of 23 supporting the diagnosis (UNL <10).

## Results and treatment

Following discussion at the upper gastrointestinal malignancy MDT, treatment with Imatinib Mesylate 400 mg daily was initiated and prednisolone was gradually weaned. Surveillance imaging at six months post-treatment initiation revealed partial response and there were no hypoglycaemic episodes for the next 21 months.

## Conclusions and points for discussion

The incidence of NICTH remains scarce, typically seen with metastatic or advanced mesenchymal tumours. This presents as recurrent hypoglycaemia mostly affecting elderly patients with advanced disease. Occasionally, NICTH can predate the diagnosis of the underlying malignancy. Most cases are caused by tumour cell production of IGF2. The expression of 'big' IGF2 has been reported – the result of high concentrations of pre-pro-IGF2 levels that are not properly glycosylated, resulting in high molecular weight IGF2. This has a significantly higher affinity to the insulin receptor, and lower affinity to its binding protein (IGFBP3), leading to increased bioavailability, enhanced peripheral glucose consumption and suppressed hepatic glucose production. GIST diagnosis is confirmed by immunohistochemical positive staining of *C-kit*. Mutational analysis in GIST is crucial for identifying less sensitive/resistant genotypes (*PDGFR-D842V*) to selective Imatinib Mesylate and allows dose adjustment for patients with rarer *C-kit* exon 9 deletions. Surgical removal of primary tumour remains most rapid/effective therapy for normalising glucose metabolism in most cases of NICTH when indicated. NICTH is a poorly recognised cause of hypoglycaemia and consequently may remain undiagnosed. This case highlights the importance of recognising NICTH as a potential cause of hypoglycaemia in cases of patients with advanced malignancy and adds to limited cases confirming GIST as source of abnormal secretion of IGF-2.

DOI: 10.1530/endoabs.69.OC2

## OC3

**A rare case of bilateral carotid body paragangliomas and associated Burkitt's lymphoma in patient with a germline SDHB mutation**

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## Section 1&amp;2: Case history and investigations

We report the case of a 52-year-old man with recurrent immunodeficiency-related Burkitt's lymphoma. 11 years following remission of his disease he presented with a firm lump in the parotid region. A biopsy showed histopathological evidence of a relapse. An <sup>18</sup>F FDG PET was undertaken to determine the extent of the disease and response to R-DHAX chemotherapy. Areas of high uptake were identified in both sides of the neck (*SUVmax* *R*=24.7, *L*=30.0). These were further characterised by an MRI which revealed mildly T2-hyperintense heterogeneous masses at both carotid bifurcations. It was unclear as to whether these masses were malignant lymphoid tissue or represented a new pathology, such as bilateral paragangliomas (PGLS). The patient had no symptoms of catecholamine excess and this was confirmed biochemically. Plasma normetadrenaline 612 pmol/l [*<*1000], Plasma metadrenaline <180 [*<*600], 3-MT <75.0 [*<*180]. Biopsy of these lesions was too high risk given their proximity to the carotid arteries. Therefore the diagnosis of bilateral PGL required confirmation radiologically as biochemical tests were negative and a biopsy was not feasible. When considering the nuclear imaging modality, we needed a test that would be specific for PGL and, as the tumours were bilateral, we had to consider the effect that a potential *SDHx* mutation would have on the sensitivity of the test (<sup>123</sup>I-MIBG has high false negatives rates in *SDHx* mutated PGL).

A Ga-68 DOTATATE was undertaken modality and showed intense tracer uptake (*SUVmax 101.9 R and 144.7 I*) in both neck masses.

#### Section 3: Results and treatment

The patient had no familial antecedents but given the confirmed radiological diagnosis of bilateral PGL, genetic testing was performed and identified a pathogenic *SDHB* variant c.379dupA p.(Ile127fs). The patient currently awaits a surgical opinion.

#### Section 4: Conclusions and points for discussion

An association of *SDHB* germline mutations with lymphoproliferative disorders has been proposed based on a limited number of case reports and it is intriguing that there is an overlap in the molecular drivers that predispose to both PGL and lymphoproliferative disorders. This is the first report of an *SDHB* carrier with Burkitt's lymphoma. A recent study (*N*=104) has shown Ga<sup>68</sup> DOTATATE has a sensitivity of 96% for PCC and PPGL. It is increasingly being considered a first line imaging modality for PGL / PCC based on its superior sensitivity to <sup>123</sup>I-MIBG and superior specificity to <sup>18</sup>F-FDG PET.

DOI: 10.1530/endoabs.69.OC3

## OC4

### Come out, come out, wherever you are.....

Bijal Patel, Anastasia Gontsarova, Nigel Mendoza, Clara Limback-Stanic, Niamh Martin, Emma Hatfield & Karim Meeran  
Charing Cross Hospital, London, UK

A 57-year-old woman was referred in 2012 following an incidental finding of a pituitary macroadenoma. It measured 17×9 mm and was confined to the sella. There was no clinical or biochemical evidence of pituitary dysfunction. In 2017, she was found to have proximal myopathy, plethoric facies and purple abdominal striae. She was also on medication for hypertension and type 2 diabetes. There was no history of sleep apnoea, fractures or use of exogenous steroids. An MRI showed tumour shrinkage and screening tests revealed ACTH dependent Cushing's syndrome: cortisol following overnight dexamethasone = 307 nmol/l (NR <50 nmol/l), 24-h UFC = 390 (NR 50 – 270 nmol/24 h), cortisol 48 h post low dose dexamethasone = 227, and baseline ACTH = 59 ng/l. She was subsequently referred to the Imperial Pituitary Multidisciplinary Service in 2019, and underwent inferior petrosal sinus sampling (IPSS) which excluded ectopic ACTH: basal central-to-peripheral ACTH ratio of >2:1 and a CRH stimulated ratio of >3:1. This confirmed Cushing's disease and she was commenced on metyrapone, and rivaroxaban (for DVT prophylaxis). A trans-sphenoidal pituitary hypophysectomy was performed on 6th of June 2019 and histology confirmed a corticotroph adenoma. Unfortunately, her day 5+9 post-operative cortisol levels (taken 24 h after the last dose of glucocorticoid) remained elevated and a pituitary MRI showed residual tissue. This prompted re-exploratory surgery. Despite this second procedure, her hypercortisolaemia persisted, and a day curve showed cortisol burden with loss of diurnal variation: cortisol 199 nmol/l (at 09:00), 324 nmol/l (at 12:00), 218 nmol/l (at 15:00) and 363 nmol/l (at 18:00). Interestingly, no pituitary lesion was detected on imaging or histology; and following discussion at the Pituitary MDT, bilateral adrenalectomy was proposed. Whilst awaiting adrenalectomy she reported significant weight reduction (around 15 kg) and a vast improvement in diabetic control. Her cortisol day curve (3 months following pituitary surgery) showed a lower cortisol burden: cortisol 187 nmol/l (at 09:00), 87 nmol/l (at 12:00), 51 nmol/l (at 15:00) and 144 nmol/l (at 18:00). In view of these results, her adrenalectomy has been cancelled, and the plan is for surveillance.

#### Discussion

1. Is she in remission? If she relapses, what treatment strategies are appropriate?
2. What surveillance should be offered?
3. Given the 1500 h cortisol of 51 nM, should she be started on steroid replacement?

DOI: 10.1530/endoabs.69.OC4

## OC5

### A Rare Adrenal Tumour Presenting as an Adrenal Incidentaloma

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St. Bartholomew's Hospital, London, UK

#### Case history

An 18-year old lady being investigated for anaemia, was incidentally found to have a 15 cm left adrenal mass. History taking revealed a 6-month history of

weight gain, fatigue, and hirsutism. Past medical history was positive for mental illness. There was no learning disability or history of epilepsy. Physical examination was unremarkable.

#### Investigations

Biochemical work-up for a functional adenoma revealed normal serum cortisol and circadian rhythm, normal plasma metanephrines and normal adrenal androgens. A CT scan of the abdomen showed a well-defined, vascular, left suprarenal mass, measuring 11 cm. The mass had heterogeneous enhancement, with areas of necrosis. There was no evidence of direct invasion and no lymphadenopathy. The lesion was not MIBG avid.

#### Results and treatment

The patient underwent open left adrenalectomy. Macroscopically, the lesion was well-circumscribed, within the adrenal gland, weighing 450 g. The surface was heterogeneous with solid and cystic areas. Microscopically, the tumour was encased in a thick fibrous capsule. There was no evidence of capsular invasion or invasion into the surrounding tissue. Diffuse sheets of epithelioid tumour cells were visible, with very distinct cell borders, abundant eosinophilic cytoplasm and variable amounts of cytoplasmic clearing. Prominent nuclear pleomorphism was appreciated, with evidence of multinucleation. There was no evidence of tumour necrosis and no mitotic figures. Immunohistochemical staining was negative for Chromogranin, Synaptophysin, S100, Calretinin and Inhibin. The tumour, stained positive for MelanA, HMB45 and SMA. Based on these findings, a diagnosis of a Perivascular Epithelioid Cell Tumour (PEComa) was made.

#### Conclusions and points for discussion

PEComas may occur at various visceral and soft tissue sites. Renal PEComas constitute the majority of cases. Very few adrenal PEComas have been reported in the literature. While most lesions follow a benign course, 33% of PEComas exhibit malignant behaviour. Lesions >4 cm carry a higher risk for fatal haemorrhage. Benign tumours can be managed conservatively. Surgery should be considered for indeterminate tumours, based on size and previous haemorrhage. Genetically, 27% of PEComas have been linked to the tuberous sclerosis genes TSC-1 and TSC-2. Gene identification has led to advances in the therapy of malignant PEComas, allowing us to target specific metabolic pathways. In particular, future studies are aimed at identifying a possible role for mTOR inhibitors in the treatment of this rare tumor. At 9 months post-surgery our patient remains disease-free. There were no features in the history or physical examination to suggest tuberous sclerosis, hence genetic testing was not performed in this instance.

DOI: 10.1530/endoabs.69.OC5

## OC6

### MGES: Monoclonal Gammopathy of Endocrine Significance?

Gowri Ratnayake<sup>1</sup>, David Church<sup>2</sup>, Robert Semple<sup>2</sup>, James Cavenagh<sup>1</sup> & William Drake<sup>1</sup>

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A 65 year-old male was evaluated at another hospital for frequent episodes of fainting preceded by sweating, palpitations fatigue and hunger over several years. There was no personal or family history of diabetes mellitus. Hypoglycaemia was confirmed on a supervised fast and, guided by some equivocal uptake on a dotatate scan, he underwent a distal pancreatectomy, but the symptoms persisted. He was referred to our centre. He reported relentless weight gain and a need to eat porridge immediately prior to bed, together with nocturnal calories in order to prevent symptoms. In addition a monoclonal paraproteinaemia (IgG kappa, 21 g/l) was noted, without target organ involvement (normal serum calcium, no lytic bone lesions, normal renal function). He developed symptomatic hypoglycaemia after 10 h of a supervised fast: venous blood glucose 2.0 mmol/l; insulin and C-peptide concentrations >1000 IU/l and 6512 pmol/l respectively. During a prolonged oGTT, early hyperglycaemia (12.5 mmol/l at 60 min) was followed by a nadir value of 2.9 mmol/l which was detected at 300 min, in association with marked hyperinsulinaemia (52 850 pmol/l). These features strongly suggested the presence of insulin-binding antibodies and further testing indicated that these were of low affinity and high capacity. The insulin antibody is IgG specific and further detailed testing is underway to determine if the anti-insulin antibodies are monoclonal. The vast majority of patients with clinical symptoms related to anti-insulin antibodies have been treated with insulin or are receiving drugs known to be associated with their formation. Our patient's case is intriguing; according to conventional practice, he does not merit plasma cell directed therapy, but the demonstration of monoclonality of the anti-insulin antibodies would be considered a clinical indication to offer therapy with bortezomib for a 'monoclonal gammopathy of endocrine significance'.

DOI: 10.1530/endoabs.69.OC6

**OC7****Management challenges in a patient with papillary thyroid carcinoma and resistance to thyroid hormone**Parag Yajnik, Hassan Kahal & Fleur Talbot  
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Resistance to thyroid hormone (THR) is a rare genetic condition affecting the nuclear thyroid hormone receptor, and inherited in a dominant negative pattern. It is often diagnosed in patients with discordant thyroid function. Patients have a 'pituitary resistance' to the elevated circulating levels of thyroid hormone, resulting in the failure of TSH suppression. While this consequent TSH drive has been associated with follicular thyroid cancer, it is thought that coexisting papillary thyroid cancers (PTC) occur at a similar rate to the general population and are not more common in this patient group. This results in marked challenges in intermediate and high risk PTC as the need for TSH suppression is challenging to achieve without unacceptable cardiovascular risk.

**Case history**

We present a 40 year old woman, diagnosed with resistance to thyroid hormone 16 years previously, following investigations for goitre and discordant thyroid function tests. She was confirmed to have a NM\_000461.4:c.1357C>T p.(Pro453Ser) heterozygous, missense THRB mutation. Baseline investigations were normal, with the exception of bone densitometry which confirmed osteopaenia.

**Investigations**

Serial ultrasounds were performed of her multinodular goitre. In June 2019 a single suspicious nodule was identified. Fine needle aspiration demonstrated a Thy 5 papillary thyroid carcinoma. She underwent total thyroidectomy in Italy and returned to the UK for post-operative care. Histology confirmed a 1.5 cm PTC with pT1bN0R0 resection. Dynamic risk stratification recommended the need for post-operative radioiodine ablation, low-normal TSH suppression and serial monitoring of thyroglobulin levels.

**Results and treatment**

Pre-operatively her thyroid function was: TSH 2.17 mIU/l (0.27–4.2), free T4 36.9 pmol/l (12–22) and free T3 9.3 pmol/l (3.1–6.8). Post-operatively she was started on 100 mcg and 125 mcg of levothyroxine on alternate days, resulting in: TSH 58.5 mIU/l, free T4 26.6 pmol/l. Her levothyroxine was incrementally increased in response to her thyroid function. She is presently on 200 mcg, resulting in: TSH 9.9 mIU/l, free T4 48.8 pmol/l. This is a challenging clinical situation, and future measures may include the use of beta blockers to limit her cardiovascular side effects. Radioiodine has not yet been administered due to patient reluctance; this is still being considered.

**Conclusion and points for discussion**

Supraphysiological doses of levothyroxine are likely to be needed to achieve TSH suppression in patients with THR after total thyroidectomy for thyroid cancer. Accurate dynamic risk stratification of PTC patients with THR is important to determine the TSH target following thyroidectomy. Managing these patients is challenging due to the associated cardiovascular risks.

DOI: 10.1530/endoabs.69.OC7

**OC8****Bones, Moans and Groans: A Calcium Conundrum**Harriet Esdaile, Katharine Lazarus, David Saliu, Giulia Sartori & Asjid Qureshi  
Northwick Park Hospital, London, UK**Case history**

A 51 year old gentleman presented to ED with severe right thigh pain, a 6 month history of weight loss, and 2 weeks of polyuria. He had no medical history and took no regular medications. He worked as a postman, was a non-smoker and non-drinker.

**Investigations**

Bloods showed adjusted calcium of 5.04 mmol/l, parathyroid hormone (PTH) 1.4 pmol/l, and alkaline phosphatase 438 IU/l. Vitamin D was reported one week later as 37 nmol/l. His haemoglobin was 155 g/l and platelets were  $46 \times 10^9/l$ . His creatinine was 214  $\mu\text{mol/l}$  (nil previous). His prostate specific antigen was 2333  $\mu\text{g/l}$ . A CT showed diffuse axial lytic skeletal changes and a bone marrow was consistent with metastatic carcinoma.

**Results and treatment**

Following 48 h of intravenous hydration and calcitonin, he had large volume haematemesis secondary to severe oesophageal ulceration. His calcium remained elevated at 4.74 mmol/l. He was transferred to ITU where he received 7 days of

haemofiltration and 2 doses of denosumab 60 mg. He was commenced on bicalutamide and goserelin for presumed prostate carcinoma. 3 days after stopping filtration and 8 days after his last dose of denosumab his calcium dropped to 1.49 mmol/l. His calcium was supplemented parentally and he was discharged with alfacalcidol 1 mcg, colecalciferol 1000 units OD and sandocal 2 tablets QDS. Despite good compliance, our patient was readmitted a week later with an adjusted calcium of 1.29 mmol/l, PTH of 42 pmol/l, and vitamin D of 41 nmol/l. He was treated again with parental calcium supplementation, IV magnesium, and given intramuscular ergocalciferol 50 000 units. He was discharged on 2.5 mcg alfacalcidol OD. Twice weekly bloods showed a normal calcium. 3 weeks later, he was readmitted with symptomatic hypercalcaemia (4.81 mmol/l), and an acute kidney injury (AKI). He required further haemofiltration, and a further dose of denosumab 60 mg, but subsequently became hypocalcaemic. He remains on alfacalcidol 0.25 mg, sandocal and colecalciferol 1000 units OD and most recent blood tests show a calcium of 2.30 mmol/l. His most recent PSA had dropped to 174  $\mu\text{g/l}$ .

**Conclusion**

We present a case of severe hypercalcaemia, with a number of management challenges. A bisphosphonate was contraindicated due to oesophageal ulceration and severe AKI, and therefore denosumab, a RANK Ligand inhibitor was used. With a long elimination half-life, denosumab can produce severe, prolonged hypocalcaemia requiring hospitalisation for aggressive IV calcium and vitamin D supplementation. Preventing this complication via careful baseline assessment, calcium and vitamin D coadministration, and monitoring, is crucial for patients.

DOI: 10.1530/endoabs.69.OC8

**OC9****Should SHBG be measured in every patient before diagnosing hypogonadotropic hypogonadism?**Maria Phylactou<sup>1</sup>, Ali Abbara<sup>1</sup>, Pei Chia Eng<sup>1</sup>, Sophie Clarke<sup>1</sup>, Chioma Izzi-Engbeaya<sup>1</sup>, Channa Jayasena<sup>1</sup>, Alexander Comminos<sup>1</sup>, Sasha Howard<sup>2</sup>, Tricia Tan<sup>1</sup> & Waljit Dhillon<sup>1</sup>  
<sup>1</sup>Imperial College London, London, UK; <sup>2</sup>Queen Mary, University of London, London, UK**Section 1: Case history**

A 19-year-old British-Asian man presented with a two-year history of gynaecomastia. He had no other symptoms of hypogonadism. He had an unremarkable past medical history, did not take any regular medications and denied the use of any illicit drugs. There was a family history of consanguinity, with his parents being first cousins. On examination, his BMI was 28  $\text{kg/m}^2$  and he had post-pubertal-sized testes (20 ml) with normal secondary sexual characteristics.

**Section 2: Investigations**

Hypogonadism was confirmed by two morning fasting total testosterone levels of 4.7 and 5.2 (RR 9.2–31.6 nmol/l). Haemoglobin was normal (152 g/l) and serum oestradiol was <100 pmol/l. He had inappropriately normal serum gonadotrophin levels: LH 1.2 (RR 1.2–7.8 iU/l), FSH 2.1 (RR 2.0–5.0 iU/l) consistent with hypogonadotropic hypogonadism. Other pituitary hormone levels and MRI pituitary were normal. In view of his unequivocal biochemical hypogonadism, he was started on testosterone replacement therapy. A DEXA scan following six years of testosterone replacement showed slightly low bone density for chronological age in the spine only (spine Z –2.1, hip Z –1.3). Seminal fluid analysis was normal on several occasions and he had fathered a child.

**Section 3: Results and treatment**

He was re-evaluated following 7 years of testosterone therapy. Both pituitary function tested with a 100 mcg GnRH test, and hypothalamic function tested with a kisspeptin-54 challenge test, were consistent with responses of healthy men. His sex hormone binding globulin (SHBG) was found to be consistently low at 6 (RR 15–55 nmol/l). His calculated free testosterone level by the Vermeulen equation was found to be borderline at 0.251 (RR >0.225 nmol/l). His father was also found to have a low fasting morning testosterone of 4.3 nmol/l and low SHBG of 4 nmol/l (father's BMI 24  $\text{kg/m}^2$ ), suggestive of a rare inherited SHBG mutation (analysis pending). Blood samples from the patient and his father have also been sent for direct measurement of salivary testosterone and free testosterone (results pending).

**Conclusion and points for discussion**

The interpretation of serum gonadotrophins relies on the initial determination that testosterone levels are consistent with hypogonadism. Endocrine Society guidance suggests that SHBG does not need to be measured unless the testosterone level is borderline, or conditions that could affect the SHBG level exist. This case highlights the potential for misdiagnosis of gonadal function even

in patients with very low (ie non-borderline) testosterone levels, if SHBG is not evaluated. Minimal end-organ pathology and/or kisspeptin challenge may provide a clue in these cases.

DOI: 10.1530/endoabs.69.OC9

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## OC10

### **Hiding in plain sight: A case of severe refractory primary hyperparathyroidism due to an intrathyroidal ectopic parathyroid adenoma**

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#### Section 1: Case history

A 30 year-old female patient with a background of symptomatic primary hyperparathyroidism diagnosed in 2008 and a history of two failed neck surgeries, was reviewed in clinic complaining of persistent symptoms of hypercalcaemia. Previous pre-operative neck imaging had failed to localise a parathyroid adenoma and the patient had undergone two neck explorations by an experienced ENT surgeon; one which removed thymic tissue and the other which removed a mildly hyperplastic right inferior parathyroid gland. The patient's mother had been diagnosed with PHPT, but genetic studies for hyperparathyroidism were all negative.

#### Section 2: Investigations

Biochemistry revealed elevated serum calcium of 3.05 mmol/l, and an elevated PTH of 18.02 pmol/l. 24 h urinary calcium was also elevated at 17.34 mmol/24 h. Additional localisation was arranged including an ultrasound of the neck, which did not identify an abnormal parathyroid but demonstrated a solitary left lower pole thyroid nodule. A subsequent 4D CT scan again showed a left thyroid nodule measuring 12×8 cm which demonstrated avid contrast enhancement and washout most in keeping with a parathyroid adenoma. No other abnormal parathyroid was identified. A Methionine PET-CT showed a focus of high tracer uptake in the same left-sided intra-thyroidal nodule.

#### Section 3: Results and treatment

As this patient had two previous failed neck surgeries, we were keen to ensure that the future surgery would be curative. An US-guided fine needle aspiration of the left sided intrathyroidal nodule was performed and samples reserved for cytology and parathyroid hormone measurement. Immunohistochemistry was positive for chromogranin A but negative for TTF-1, in keeping with parathyroid rather than thyroid tissue, and cytological appearances favoured parathyroid tissue. PTH measurement from the FNA sample was 726 pmol/l (levels > 10 pmol/l consistent with sampling from parathyroid tissue). The patient subsequently underwent a left hemi-thyroidectomy and pathology confirmed a left thyroid lobe containing an enlarged, well circumscribed, intrathyroidal parathyroid gland. Post-operatively serum PTH and calcium levels normalised.

#### Section 4: Conclusions and points for discussion

In this case, we present a patient who had refractory PHPT despite two previous neck operations. An intrathyroidal parathyroid adenoma was subsequently detected on 4D CT and Methionine PET CT and confirmed by a fine needle biopsy. In this case, the PTH level in the aspirate and the ratio between aspirate PTH and serum PTH (59 times) confirmed the suspicion of an intrathyroidal parathyroid adenoma. This case highlights the potential utility of fine needle aspiration in selected cases to confirm a diagnosis of a parathyroid adenoma.

DOI: 10.1530/endoabs.69.OC10

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# Poster Presentations

## P1

**Two contrasting cases of spontaneous severe hypoglycaemia secondary to anti-insulin antibodies (Insulin Autoimmune Syndrome / Hirata disease)**

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Insulin Autoimmune Syndrome (IAS)/Hirata disease is a very rare condition in which anti-insulin antibodies result in accumulation of high circulating concentrations of insulin in complexes. Hypoglycaemia in IAS occurs when insulin is released from the antibodies during fasting. We present two contrasting cases of Hirata disease. Both patients presented with symptomatic hypoglycaemia. Patient-A is a 52-year old obese Thai female, with acanthosis nigricans and a strong family history of T2DM. Patient-B is a 28 year-old normal-BMI Caucasian female. None of the patients received any regular medication or had history of autoimmunity. Whipple's triad was confirmed at 10 h supervised fast for patient-A. Nadir laboratory glucose was 1.8 mmol/l, coupled with hyperinsulinaemia and a high insulin-to-C-peptide ratio (insulin=9809 mIU, C-peptide=3690 pmol/l, insulin:C-peptide=18.5). Patient-B has ongoing issues with recurrent hypoglycaemia due to chronic persistence of high capacity insulin autoantibodies, developed hypoglycaemia at 4 h during a supervised fast, with hyperinsulinaemia and a high insulin-to-C-peptide ratio (plasma glucose=2.2 mmol/l, insulin=17 800 pmol/l, C-peptide=409 pmol/l, insulin:C-peptide-ratio=43.5). Hook-effect phenomena were excluded in both cases. Insulin was lower post-PEG precipitation, indicating that much of the measured insulin was complexed in macromolecular aggregates. Sulphonylurea screen was negative, imaging unremarkable, ANA and anti-dsDNA antibodies negative. Anti-insulin-receptor Abs were negative, whereas anti-insulin IgG antibodies were positive. Chromatography demonstrated insulin sequestration by anti-insulin antibodies, identifying monomeric and antibody-bound insulin. Pending diagnosis, a trial of diazoxide was ineffective in both cases. In light of positivity of anti-insulin IgG antibodies, prednisolone and mycophenolate mofetil (MMF) treatment were initiated in patient-A, and later euglycaemia maintained on MMF monotherapy. In patient-B dexamethasone and adjuvant MMF induced only partial response. Subsequent Rituximab-induced CD20 depletion and adjuvant steroid treatment strategy was adopted with partial efficacy. Patient-B later underwent plasmapheresis with adjuvant Rituximab therapy. We discuss the diagnostic challenges in IAS, the diverse phenotype and treatment responses in our two cases.

DOI: 10.1530/endoabs.69.P1

## P2

**Non-islet cell tumour hypoglycaemia in a patient with type 1 diabetes mellitus**

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## Case history

A 73-year-old gentleman was admitted for evaluation of recurrent hypoglycaemia. He has had type 1 diabetes mellitus for 60 years, which was well controlled on a basal-bolus regime with carbohydrate counting. He had frequent hypoglycaemic episodes for 5 months despite drastic reduction in insulin dosage. His insulin was completely stopped on admission. He did not develop ketosis and continued to have hypoglycaemia. He did not have end-organ complications from T1DM. Examination was unremarkable except for vitiligo.

## Investigations

His venous glucose dropped to <2 mmol/l. Endocrinologic investigations revealed high levels of insulin like growth factor-2(IGF-2), suppressed insulin like growth factor-1(IGF-1), elevated IGF-2 : IGF-1 ratio with low insulin/ C-peptide levels, which was consistent with non-islet cell tumour.

## Results and treatment

CT thorax abdomen and pelvis revealed a massive right-sided pleural-based mass, occupying most of the lower right hemithorax. Biopsy after excision showed a fibrous tumour with abundance of spindle-shaped cells. There was no mitotic activity. It was positive for CD34, CD99, and vimentin on immunohistochemistry. The patient was given dietary counselling. He had successful surgical resection of the large solitary benign tumour with complete resolution of hypoglycaemic episodes.

## Conclusions and points for discussion

This patient had recurrent hypoglycaemia due to a non-islet cell tumour (NICT). NICT is well described but we have not been able to find any reports of tumoural hypoglycaemia in a patient with established (>60 years) type 1 diabetes. Paraneoplastic phenomenon with spontaneous overproduction of IGF-2 can be seen in both mesenchymal and epithelial derived tumours such as fibromas, fibrosarcoma, gastrointestinal stromal tumours and hepatocellular tumours. Tumoural IGF-2 acted in a similar way to insulin, causing hypoglycaemia. Normally, IGF-2 binds to IGF-binding protein 3(IGFBP-3) and an acid-labile a-subunit forming a ternary complex. However, more than 60% of total IGF-2 in NICT is high-molecular weight ('big IGF-2') with low affinity to a-subunit, thus forming dimers. This smaller complex is easier to pass through capillary membrane and penetrate tissues, causing hypoglycaemia. Large quantities of big IGF-2 in NICT displace free IGF from IGFBP, increasing numbers of free IGF. Therefore, there is a direct relation between big IGF-2 and free total IGF-2 in NICT. The case was unique in that a patient with T1DM effectively became insulin-free. Surgery was still necessary because of the risks of recurrent hypoglycaemia. Hypoglycaemia resolved post-operatively and he resumed his basal-bolus insulin. He subsequently developed cognitive decline, which may be due in part to recurrent hypoglycaemia.

DOI: 10.1530/endoabs.69.P2

## P3

**Occult ectopic ACTH: controlling the disease to find the source, with unique sequelae**

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## Case history

A 43-year-old man was admitted to Intensive care with life-threatening pneumonia, along with acute hypertension and hypokalaemia. There were several Cushingoid clinical features, therefore ectopic ACTH syndrome was suspected. Investigations

The diagnosis of severe ACTH-dependent Cushing's syndrome was confirmed with unsuppressed cortisol after low dose dexamethasone (763 nmol/l with ACTH 131 ng/l, 24-h urinary cortisol levels (x2) of >6000 nmol/24 h, and no response to CRH. Axial imaging with CT and <sup>18</sup>F-DG-PET/CT failed to localise the source of ACTH, but there was marked adrenal hypertrophy. He was commenced on metyrapone.

## Results and treatment

When reviewed in Sheffield bilateral adrenalectomy was discussed due to the extreme severity of his disease and lack of source for ACTH being identified (including urgent Gallium-68 DOTA-TATE PET/CT), but after careful counselling he continued on medical therapy: metyrapone (titrated to total 5500 mg per day) with additional ketoconazole, however the later was not tolerated. Long-acting octreotide (Sandostin LAR 30 mg I.M. every 28 days) was added with the aim to reduce ACTH (and cortisol) levels: these reduced to normal. Replacement doses of hydrocortisone were given throughout in a 'block and replace' regime with serum day curve monitoring using LC-MS/MS for serum cortisol. The patient's clinical condition improved, greatly. After six months of medical treatment repeat CT revealed mediastinal and right hilar lymphadenopathy suspicious for malignancy. Biopsy, however, was consistent with sarcoidosis and serum ACE levels were elevated. The repeat CT also showed that the adrenal hypertrophy had now reduced. After a further six months of medically induced eucortisolaemia a repeat Gallium-68 DOTA-TATE PET/CT was performed which revealed uptake in a <1 cm nodule in right middle lobe (confirmed on dedicated CT) but with avid uptake in mediastinal lymph nodes. The patient underwent VATS right middle lobectomy and the histology confirmed a 14 mm ENETS grade 1 tumour (Ki67 <1%) and strong immunostaining for ACTH, and is currently in full remission. Lymph node histology was negative for tumour but positive for sarcoidosis, which is being monitored.

## Conclusions and points for discussion

- The urgent need for treatment of severe Cushing's, even if cause is unidentifiable, often in combination.
- SST2 receptor down-regulation due to severe Cushing's, but reversal with eucortisolaemia – may explain why SST2R-directed imaging fails to demonstrate the source of ectopic Cushing's.
- Although autoimmune conditions have been reported after Cushing's remission, sarcoidosis due to steroid withdrawal has never been reported before.

DOI: 10.1530/endoabs.69.P3

**P4****Applying a novel molecular imaging technique in a case of pseudo-pheochromocytoma**

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**Case history**

A 41 year old female was admitted following development of severe hypertension (226/146 mmHg), complicated by heart failure and acute kidney injury. She otherwise had no relevant past medical history. On clinical examination she was obese (BMI 51.94 kg/m<sup>2</sup>). As part of her cardiac investigations, she underwent a cardiac magnetic resonance imaging (MRI) which detected a 3 cm right sided adrenal nodule. An adrenal biochemical screen identified an elevated plasma normetadrenaline (1418 pmol/l, range <1000) with normal plasma metadrenaline (<180 pmol/l, range <600). This corresponded with high urinary normetadrenaline levels (6998 nmol/24 h, range 0–4900) and normal urinary metadrenaline level (535 nmol/24 h, range 0–2000). Her medications included Doxazosin and Ramipril, which can interfere with the metanephrine assay.

**Investigations**

A repeat fasting and supine plasma metanephrine sample demonstrated results consistent with previous investigations (plasma normetadrenaline 12 692 pmol/l, metadrenaline <180). The remainder of the adrenal biochemistry screen was reassuring.

**Results and treatment**

Further characterisation of the suspected adrenal lesion on a dedicated non-enhanced CT adrenals demonstrated bilateral hypodense adrenal lesions measuring 38 mm on the right and 24 mm on the left, consistent with benign adenomas (based on Hounsfield units of <10). Although the imaging was reassuring, rarely pheochromocytoma can have a density <10 HU<sup>(1)</sup>. In the light of the abnormal serum and urinary metanephrine results, additional investigations were considered. We were unable to stop antihypertensives that were potentially confounding the assay results due to the severity of her hypertension. Therefore, we employed a molecular imaging approach using [<sup>11</sup>C] Metomidate PET-CT (MTO-PET) to determine if the adenomas were of adrenocortical origin, therefore excluding a pheochromocytoma. MTO-PET reassuringly demonstrated tracer uptake by both adenomas. On further questioning, it was noted that the patient was experiencing daytime somnolence, heavy snoring with apnoeic episodes. Following diagnosis and treatment of obstructive sleep apnoea, she achieved normalisation in BP and an improvement in biventricular function on repeat cardiac echocardiogram.

**Conclusions**

The case highlights the limitations in the specificity of plasma and urinary metanephrine assays, and for the first time highlights the potential role of MTO-PET in excluding a pheochromocytoma by confirming that an adrenal lesion is of adrenocortical origin. This may provide reassurance in cases where there is discordance between biochemistry and radiological findings.

**Reference**

(1) Management of adrenal incidentalomas: European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors. Eur J Endocrinol 2016. PMID 27390021.

DOI: 10.1530/endoabs.69.P4

**P5****Isolated ACTH-deficiency following immune checkpoint inhibitors: diagnostic challenges demonstrated by a clinical case**

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**Case history**

A 53-year-old male with melanoma who had a previous surgical excision of his skin lesion in December 2018 was being treated with adjuvant pembrolizumab. In June 2019 his treatment changed to combination immune checkpoint inhibitor therapy (ICPi) with ipilimumab and nivolumab due to radiological recurrence.

**Investigations**

There were no pre-ICPi endocrine investigations available. In July 2019, thyroid function tests (TFTs) showed thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels of 0.2 mu/l (0.55–4.78) and 20.3 pmol/l (10–22) respectively leading to a diagnosis of ICPi-mediated thyroiditis. A mid-afternoon cortisol was measured as 352 nmol/l. In August 2019, TFTs showed primary hypothyroidism (TSH 49.93 mu/l; fT4 2.2 pmol/l). A random mid-afternoon cortisol was 140 nmol/l and consequently a short synacthen test (SST) was performed. This showed cortisol measurements of 331, 707 and 836 nmol/l at 0, 30 and 60 min (post-tetracosactide) respectively and a serum adrenocorticotrophic hormone (ACTH) of 30 ng/l (0–46) at baseline. The remainder of his pituitary function was normal. A subsequent CT scan of the thorax, abdomen and pelvis showed a reduction in tumour volume.

**Results and treatment**

The patient was started on levothyroxine replacement. In September 2019 he presented with weight-loss, dizziness, headaches and a reduction in appetite. A repeat SST showed cortisol values of 187, 556 and 706 nmol/l at 0, 30 and 60 min respectively. Due to the reduction in the baseline cortisol, the patient was advised to contact endocrinology if symptoms progressed. After 20 days, he complained of progressive fatigue and muscle aches; his 0900 h cortisol was undetectable with a corresponding ACTH of 27 ng/l. Hydrocortisone replacement therapy was commenced and led to symptom resolution. His pituitary magnetic resonance imaging (MRI) scan was normal.

**Conclusions and points for discussion**

1. Important to consider endocrine consequences of immunotherapy, including isolated ACTH-deficiency. It is not uncommon for multiple gland pathology (in this case thyroid and pituitary).
2. The SST may lack sensitivity in the early phases of ACTH deficiency, as in patients with recent pituitary surgery, considering it may reflect residual adrenal reserve.
3. An SST may have a role (depending on random/morning cortisol) in the diagnosis of ICPi-mediated ACTH deficiency (based on existing national guidelines). It is important though to recognise the need for re-assessment if clinical suspicion persists despite an initial satisfactory SST.
4. A normal MRI pituitary scan does not reliably rule out hypophysitis, especially when the manifestation is isolated ACTH-deficiency.

DOI: 10.1530/endoabs.69.P5

**P6****Once pituitary adenoma is not always an adenoma**

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**Section 1: Case history**

A 52 years old gentleman initially presented with visual field defect and headache due to a large multi-lobulated pituitary adenoma and underwent an endoscopic transphenoidal sub-total resection in March 2018. Histology revealed a non-functioning adenoma with mitotic index Ki-67 of 3%–5%. His visual field defects resolved post-operatively and he was monitored with serial imaging. A year later he suffered a collapse at his GP surgery and was found to have a new visual field defect. Repeat MRI scan demonstrated an increase in the size of the adenoma with a haemorrhage. At the time of his elective re-do surgery, he happened to mention to have been experiencing some leg pain and on examination a mild quadriceps weakness was noted which prompted an MRI lumbar spine.

**Section 2: Investigations**

The initial CT and MRI scans of the pituitary demonstrated an increase in tumour size, suggestive of apoplexy event in the residual pituitary adenoma. Visual fields testing revealed a new onset of incomplete bitemporal hemianopia. MR lumbar spine showed a bulky left renal mass and subsequent scans showed multiple metastases. Histology from his pituitary tissue from the repeat surgery demonstrated morphological and immunological features in keeping with a metastatic carcinoma.

**Section 3: Results and treatment**

He developed hypopituitarism following apoplexy and was commenced on hormone replacement therapy. He underwent a second endoscopic resection of the haemorrhagic suprasellar mass and the visual field defect resolved post-operatively. Due to patient's complex burden of disease, multi-specialties input had been gathered and he is currently being treated with palliative immunotherapy.

**Section 4: Conclusions and points for discussion**

This gentleman who was fit and healthy with no significant past medical history, presented with a convincing history suggestive of pituitary apoplexy with a background history of pituitary adenoma. He would not have undergone surgery if

he did not have a new visual field defect and the diagnosis of renal cell carcinoma would have been delayed. We present this case to highlight the importance of lateral thinking to consider malignancy and metastasis, especially with early recurrence and rapid increase in the size of adenoma.

DOI: 10.1530/endoabs.69.P6

## P7

### Synchronous pheochromocytoma crisis and acute anaphylaxis, precipitated by intra-articular Triamcinolone injection

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#### Section 1: Case history

A 66-year-old man, with a history of hypertension controlled on 3 anti-hypertensives and diet-controlled Type 2 Diabetes, presented to a community-based musculoskeletal clinic to have an intra-articular Triamcinolone injection for a frozen shoulder. 30 min after the injection, he developed dyspnoea, widespread urticaria and facial angioedema. He was initially treated for suspected anaphylaxis with adrenaline, antihistamine and Hydrocortisone at the GP surgery and repeated by paramedics before presenting to Yeovil District Hospital casualty. In view of refractory hypotension not resolving with IV fluids and I/M adrenaline, he was admitted to ICU for a noradrenaline infusion, with regular hydrocortisone and antihistamine. Blood pressure remained stable overnight, but he became pyrexial with moderate hyperlactataemia. Sixteen hours later, he became extremely agitated, with a paroxysmal surge in systolic blood pressure to 300 mm Hg and a sudden rise of lactate to 15.0 mmol/l, requiring intubation and ventilation.

#### Section 2: Investigations

Mast cell tryptase samples were sent off during the first 24 h. Abdominal CT undertaken to assess for sepsis, revealed a large left sided adrenal mass measuring 4.6 by 4.8 cm with central necrosis. Noradrenaline was discontinued, blood pressure normalised quickly and he was soon extubated. He had further investigations > 48 h after discontinuing the nor-adrenaline infusion, including plasma metanephrines. He was discharged on Doxazocin and Bisoprolol. Allergy clinic assessment and endocrine follow-up were arranged.

#### Section 3: Results and treatment

Mast cell tryptase levels were 9.6 µg/l at presentation to casualty, 10.9 µg/l at 4 h and 1.6 µg/l at 24 h (NR 2–14), consistent with a clinically relevant dynamic rise. Skin testing confirmed a positive response to Triamcinolone. Plasma normetanephrine 1134 pmol/l (NR 0–1180); plasma metanephrine 4839 pmol/l (0–510). MIBG scan: confirmed solitary left adrenal uptake. Further history revealed intermittent episodes of warmth, palpitations and sweating, for the preceding 10 years. He was fully blocked with phenoxybenzamine and Propranolol. The suspected pheochromocytoma was surgically removed and confirmed on histology. Post-operative plasma normetanephrine 525 pmol/l; metanephrines < 100 pmol/l.

#### Section 4: Conclusions and points for discussion

Our patient presented acutely with synchronous anaphylaxis and pheochromocytoma crisis following intra-articular steroid injection. Although each of these has been well described as separate adverse events following glucocorticoids, we are not aware of a synchronous presentation and this was challenging to diagnose. It is possible that the Triamcinolone precipitated both events, or the anaphylaxis precipitated the pheochromocytoma crisis.

DOI: 10.1530/endoabs.69.P7

## P8

### Management of Adipsic Cranial Diabetes Insipidus while evading methotrexate toxicity

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#### Introduction

We present a challenging case of central diabetes insipidus secondary to hypothalamic large B cell lymphoma. These are rare tumors accounting for less

than 1% of lymphomas. Conventional treatment involves the MATRIX regime (methotrexate, rituximab, thiotepa, cytarabine) chemotherapy, coupled with intensive intravenous fluid therapy to avoid methotrexate toxicity. The main challenges in the management of this case were maintaining fluid and electrolyte balance in a patient with nearly adipsic DI with ongoing chemotherapy.

#### Case history

49 year old female was admitted under hematology with diagnosis of hypothalamic lymphoma associated with panhypopituitarism and DI. Matrix chemotherapy involves intensive fluid therapy to induce diuresis and avoid methotrexate toxicity. Therefore desmopressin dose needed to be reduced or withheld to avoid subsequent fluid overload. Patient received 4 cycles of chemotherapy. During each cycle, patient received fluids at the rate of 250 ml/h for a period of 5 days. Ensuring normal sodium levels during these periods were extremely challenging. Alterations including 50 % reduction of the desmopressin dose while on fluids, brief omission of desmopressin, reduction of fluid infusion rate as well as alternate route of desmopressin administration were tried. Patient being adipsic followed by intercurrent diarrhoea added to the challenges. Despite intense monitoring, there were episodes of extremes of both hyper and hyponatremia (121–170 mmol/l) as well as significant fluid overload.

#### Conclusion

This case highlights importance of multidisciplinary management of patients on MATRIX chemotherapy with underlying pituitary dysfunction especially diabetes insipidus. Prompt speciality in reach with frequent monitoring of electrolytes and osmolalities, strict documentation of fluid balance chart and frequent adjustment of desmopressin doses with regular review is pivotal in management of such complex cases.

DOI: 10.1530/endoabs.69.P8

## P9

### Idiopathic spontaneous bilateral adrenal haemorrhage in pregnancy

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#### Section 1: Case history

Adrenal haemorrhage in pregnancy is rare but life threatening. We present the case of a 23-year-old woman who developed idiopathic spontaneous bilateral adrenal haemorrhages during pregnancy. The patient, without significant past medical history, presented at 35 weeks of gestation with right sided lower thoracic and abdominal pain which was thought to be musculoskeletal in nature; she was discharged home once the pain settled. She re-presented at 37 weeks with recurrent pain which was left-sided in association with breathlessness. Given concern for pulmonary thromboembolism she was anti-coagulated with enoxaparin but a V/Q scan the following day did not demonstrate pulmonary thromboembolism. However, owing to foetal distress an emergency caesarean section was performed at 37 +4 weeks and following this the patient became unwell. The patient was referred to the on-call medical team with suspected sepsis: she was hypotensive and blood tests revealed raised inflammatory markers and a low random cortisol level of 108 nmol/l. CT Abdomen demonstrated bilateral sub-acute adrenal haemorrhages and possible colitis. The patient was treated with IV Hydrocortisone and IV Antibiotics before making a recovery.

#### Section 2: Investigations and results

Adrenal insufficiency was confirmed during admission by ACTH stimulation test: basal cortisol was <30 nmol/l rising to 43 nmol/l at 30 min. There was no biochemical evidence of hormone excess. ACTH level as an inpatient was 9 mu/l (<20 mu/l) but increased above the reference range as an outpatient. In addition, her aldosterone level whilst an inpatient returned below the level of detection at <130 pmol/l and this did not improve. Repeat ACTH stimulation tests failed to show recovery. MRI adrenals had initially shown large adrenal glands bilaterally but these had become atrophied on repeat imaging at 6 months.

#### Section 3. Treatment

The patient remains well but continues on steroid replacement therapy.

#### Section 4: Conclusions and points for discussion

Bilateral adrenal haemorrhage in pregnancy is extremely rare. It is thought that adrenal cortex hyperplasia with hypertrophy during pregnancy predisposes the adrenal gland to venous congestion and therefore haemorrhage. The clinical history and the brief duration of anticoagulation lead us to believe that LMHW was not causative but that this was an idiopathic process. Adrenal haemorrhage should be considered as a potential diagnosis in a pregnant woman presenting with abdominal pain.

DOI: 10.1530/endoabs.69.P9

**P10****A rare case of thyrotoxicosis arising as a paraneoplastic syndrome of uterine choriocarcinoma**

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We describe a 40-year-old female who presented with fine tremors, weight loss, dyspnea and hemoptysis. On examination she appeared diaphoretic and tachycardic without goiter or thyroid eye disease. Thyroid function tests confirmed biochemical hyperthyroidism: [fT4 >100 pmol/l (NR: 12–22), TSH <0.005 mu/l (NR: 0.270–4.200)]. Chest X-ray showed numerous metastatic pulmonary nodules bilaterally. CT chest confirmed multiple large pulmonary metastases throughout both lung fields. Biochemical assays confirmed B-HCG level of 729 013 IU/l (N: <5 IU/l). Patient was admitted as a case of hyperthyroidism associated with elevated  $\beta$ -human chorionic gonadotropin (B-HCG) and diffuse lung metastases highly suggestive of metastatic disease. Hyperthyroidism was treated with Carbimazole and propranolol. CT scan of abdomen and pelvis showed the whole uterine body is being replaced by a mass increasing the size of the uterus to measure around 10×11×9 cm. Patient underwent hysterectomy, pathology report confirmed diagnosis of uterine choriocarcinoma. Chemotherapy (dactinomycin, etoposide) was initiated for uterine choriocarcinoma. After the second cycle of chemotherapy, the concentration of B-HCG dramatically decreased and the patient became euthyroid, allowing us to discontinue antithyroid medication. This case illustrates the rare occurrence of thyrotoxicosis secondary to uterine choriocarcinoma. The patient's hyperthyroidism was triggered by stimulation of the thyroid gland by high B-HCG levels, as shown by the marked improvement of the thyroid function after surgical resection of uterine choriocarcinoma and chemotherapy.

DOI: 10.1530/endoabs.69.P10

**P11****Autoimmune hypophysitis induced by Anti-PD-1 Monoclonal Antibody, Nivolumab and anticytotoxic T-lymphocyte antigen-4 (CTLA-4) agent, Ipilimumab, presenting by compressive symptoms and treated with intravenous methyl-prednisolone**

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We are presenting a 57 year old male victim of recurrent metastatic melanoma who was treated surgically in 2015 by wide local excision together with right axillary dissection for axillary nodal spread. He re-presented to dermatology clinic in December 2018 with skin lesion that was histologically proven to be a BRAF-mutant malignant melanoma. CT scans at that time showed spread to mediastinal and hilar nodes. Oncology team decided to commence Ipilimumab/ Nivolumab combination therapy for four cycles, three weeks apart, followed by two-weekly Nivolumab maintenance. After the fourth combination dose, he started to suffer from continuous deep-seated progressive headache along with severe fatigue particularly towards mid-day, cold intolerance and poor libido. He denied polyuria or any visual symptoms. Anterior pituitary profile confirmed hypopituitarism with a morning cortisol of 17 nmol/l, TSH of 0.05 mu/l and testosterone of 0.5 nmol/l. He was immediately started on hydrocortisone replacement 10-5-5 mg and levothyroxine 125 mcg daily. Regarding headaches, urgent MRI was done and showed generalised enlargement of the pituitary gland with a central domed component extending up out of the pituitary fossa which is distorting the underside of the chiasm which was bowed superiorly as a consequence. Thus, a three-day course of intravenous methylprednisolone acetate was commenced at a dose of 1 mg/kg per day on an ambulatory care setting along with an urgent visual field assessment that came back normal. The patient was then weaned down to prednisolone 40 mg daily and then was gradually weaned off over several weeks to 5 mg daily. MRI scan was repeated after 4 weeks of methylprednisolone doses and it showed complete resolution of the previous robust radiological findings. The patient reported marked clinical improvement as well. Now six months after the initial diagnosis, the patient is almost asymptomatic and in clinical remission in regards to the melanoma. However, he is still hypopituitary requiring regular replacement of Hydrocortisone 10-5-5 mgs, Levothyroxine 125 mcg per day and Nebido 1 g intramuscularly every twelve weeks. His most recent morning cortisol (24 h off-hydrocortisone) is 40 nmol/l with a normal thyroid profile and pre-Nebido testosterone level of 12 nmol/l.

**Conclusion**

Intravenous methyl-prednisolone might have helped to reduced inflammation and pituitary gland size in immunotherapy-induced hypophysitis but still failed to restore eu-pituitarism in this patient after 6 months.

For discussion

1. Role of intravenous methyl-prednisolone in immunotherapy-induced hypophysitis.
2. Role of routine MRI in these patients.

DOI: 10.1530/endoabs.69.P11

**P12****A case of non-islet cell tumour hypoglycaemia due to advanced hepatocellular carcinoma secondary to previously undiagnosed chronic HBV-infection**

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&amp; Itopa Fidelis Bedo

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**Case history**

A 30-year-old Ugandan male, now living in UK, presented to A&E with confusion and agitation. Capillary blood glucose was 0.9 mmol/l and he was commenced on intravenous Dextrose. During blood donor screening in Uganda, he was told that he had a blood-borne infection. He had gross hepatomegaly on examination. During admission, he experienced repeated episodes of hypoglycaemia despite increased dietary intake of carbohydrates and continuous infusions of 5%-10% Dextrose. He also required rescue treatment with 20% intravenous Dextrose.

**Investigations**

INR: 1.3 (0.8–1.2), bilirubin: 18  $\mu$ mol/l (0–21), ALP: 574 U/l (30–130), ALT: 71 U/l (<50). CT Chest/Abdomen/Pelvis: Gross hepatomegaly with innumerable low density lesions and associated intrahepatic duct dilation. Suspicious for cholangiocarcinoma with liver metastases. MRI Liver: Massive occupation of the liver by multiple confluent solid lesions. Differentials were epithelioid haemangioendothelioma, hepatocellular carcinoma, cholangiocarcinoma and metastases. HBsAg: Reactive, Anti-HBe IgG: Reactive, HBeAg: Negative, Anti-HBe IgG: Reactive, Anti-HBe IgM: Negative. Profile consistent with persistent HBV-infection. Alpha-fetoprotein >250 413.0 KU/l (<7.4). Ultrasound-Guided Liver Biopsy: Hepatocellular carcinoma of fibrolamellar type. Random cortisol: 402 nmol/l. During a hypoglycaemic episode, blood glucose: 2.4 mmol/l, insulin: 6 pmol/l (18–173), C-peptide: 528 pmol/l (370–1470), IGF binding protein-3: 3.6 mg/l (3.5–7.6), IGF-1: 6.6 nmol/l (10.0–32.5).

**Treatment**

Dexamethasone 2 mg BD was commenced and was up-titrated to 8 mg BD but to no avail. Glucagon infusion was started at 0.1 mg/hour and was up-titrated to 0.3 mg/h with no improvement. Recombinant Human Growth Hormone 3 mg subcutaneous OD was then commenced and was titrated to 6 mg OD and hypoglycaemia resolved. He was weaned off Dextrose and Glucagon infusions and was discharged on Growth Hormone injection. He was also started on Tenofovir for HBV-infection and chemotherapy was being considered by tertiary centre HCC team. However, he was readmitted 2 weeks later with worsening ascites, generalised oedema and acute kidney injury. Unfortunately he died after being palliated.

**Conclusion**

Non-islet cell tumour hypoglycaemia is a rare but serious complication of malignancy. The management strategy is multi-pronged and involves correction of hypoglycaemia and treatment of the underlying malignancy. If hypoglycaemia persists despite increasing caloric intake and intravenous dextrose, other adjunct therapy like glucocorticoids, glucagon infusion and growth hormone should be considered. In this case, hypoglycaemia was resistant to initial treatment and required all these measures sequentially to correct hypoglycaemia. Unfortunately the underlying tumour was at an advanced stage and the patient could not survive.

DOI: 10.1530/endoabs.69.P12

**P13****Etomidate for the management of acute psychosis due to Cushing's syndrome in a patient with a glucocorticoid-secreting adrenocortical carcinoma**Rachel Daly<sup>1</sup>, Sharifah Faradila Wan Muhamad Hatta<sup>2,3</sup>, Cyril Chacko<sup>4</sup> & Harit Buch<sup>2</sup><sup>1</sup>University of Birmingham, Birmingham, UK; <sup>2</sup>Department of Endocrinology and Diabetes, New Cross Hospital, Wolverhampton, UK;

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#### Section 1: Case history

A case of a 23-year-old lady with a known history of Perthes disease, pulmonary stenosis, bronchial asthma, primary hypothyroidism on levothyroxine and newly diagnosed hypertension on amlodipine, who presented to Accident and Emergency with symptoms of generalised lethargy, weakness of the upper and lower limbs, rapid onset of weight gain for 6 months, increasing abdominal girth and recurrent genital thrush.

#### Section 2: Investigations

On presentation, the patient was tachycardic (123 bpm), hypertensive (162/98 mmHG) and overweight (BMI 27.2 kg/m<sup>2</sup>). Further examination showed evidence of Cushingoid features (moon facies, central obesity, light purple abdominal striae of 1 cm in diameter and intra-scapular fat pad). Neurological examination revealed proximal myopathy and abdominal examination showed abdominal distension. Blood and urine investigations revealed elevated 24-h urinary cortisol (2182 nmol/24 h, N: 0–130), random cortisol of 800 nmol/l and ACTH level of <0.3 ng/l. The patient had hypokalaemia, an elevated DHEAS and androgen profile, with evidence of hypogonadism on pituitary hormone profile.

#### Section 3: Results and treatment

The patient was diagnosed with a large lobulated malignant adrenal carcinoma with direct involvement of the left renal vein and bilateral widespread metastatic lung lesions, after undergoing a computed tomography of thorax, abdomen and pelvis. On day three of her admission, she became acutely confused, agitated and verbally aggressive. She was intubated and ventilated in the Intensive Care Unit (ICU). Ketoconazole and etomidate were initiated at 400 mg three times daily and 42.86 mcg/kg per hour respectively. Her cortisol level was monitored 12-hourly and dexamethasone was initiated when cortisol dropped to 101 nmol/l. Upon initiation of etomidate, the haemoglobin gradually dropped, which investigation suggested was due to haemolysis and she was transfused. The dose of etomidate was gradually reduced and stopped on day four. She was later transferred to an endocrine tertiary centre where she underwent left adrenalectomy. Post-operatively, she was initiated on mitotane and her ketoconazole and dexamethasone were substituted to metyrapone and hydrocortisone.

#### Section 4: Conclusions and points for discussion

Our patient's hypercortisolism was managed successfully with intravenous etomidate. This patient may have had haemolysis, which has been suggested to be a side effect of the propylene glycol in the preparation of etomidate. Few previous case reports discuss etomidate's use for acute psychosis due to a glucocorticoid-secreting adrenal carcinoma. It is important to remember Cushing's Syndrome as a cause of acute psychosis and investigate further if suspected.

DOI: 10.1530/endoabs.69.P13

## P14

### Follow your endocrine instincts: a neurosarcoïd conundrum

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#### Case history

A 54-year-old man was admitted with a history of syncopal episodes. Orthostatic hypotension led to an endocrine referral and subsequent diagnosis of pan-anterior hypopituitarism but with no evidence of posterior pituitary involvement. Although an initial aetiological diagnosis remained elusive, further work-up (see below) led to a histology-confirmed diagnosis of ACE-negative neurosarcoïdosis. This diagnostic conundrum could have been contributed by a prior neurological diagnosis of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) which was later revoked to neurosarcoïdosis due to endocrine involvement. Following replacement with hormones, there was a remarkable improvement in the patient's quality of life.

#### Investigations

Pituitary profile: showed secondary adrenocortical deficiency (ACTH <5 ng/l, cortisol <25 nmol/l); gonadotrophin deficiency (both FSH & LH <1 u/l); somatotroph deficiency (paired IGF-1 <6 & GH -0.30 ug/l) and normal prolactin - 483 mIU/l. Posterior pituitary osmolality data was normal. MRI showed white matter, basal ganglia and brainstem hyperintensities but with normal pituitary morphology. We however felt that despite the lack of posterior pituitary dysfunction, the pituitary stalk appeared inappropriately thickened and

hence worthy of further investigations into an aetiological diagnosis – especially systemic infiltrative disorders. Vasculitis screen was negative and so was IgG4 and Aquaporin 4 antibody. ACE levels were thrice negative. CSF studies did not show oligoclonal bands. PET-CT scan demonstrated small volume FDG-avid mediastinal and hilar lymphadenopathy which on biopsy showed non-caseating granulomatous sarcoidosis. It would be worthwhile to mention that based on initial presentation of optic atrophy and slurred speech two years prior to this presentation, neurology had made a former diagnosis of 'Clinical CADASIL' but it was noted that genetics for the same were negative and so was skin biopsy.

#### Results and treatment

Following histological confirmation, neurology revisited their previous diagnosis and agreed to treat the patient as neurosarcoïdosis with azathioprine and prednisolone. This has led to significant improvement in his vision and motor-sensory disabilities. Furthermore, hormonal supplementation in the form of growth hormone, levothyroxine and testosterone has further improved the quality of life. He now has no use of crutches!

#### Conclusions and points for discussion

This complex presentation of pan-anterior hypopituitarism demonstrates that it is important to look for an aetiological diagnosis rather than simply treating deficiencies. Furthermore, neurological involvement in sarcoidosis including pituitary dysfunction occurs in only 5–10% of patients, needing a high degree of clinical suspicion and can be missed by simply relying on negative ACE levels.

DOI: 10.1530/endoabs.69.P14

## P15

### 'Tiger Woman Sign'; Hypercalcaemia Secondary to Atypical Isolated Sarcoid Myositis

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#### Section 1: Case history

A 57-year-old female shop assistant presented with a four week history of increasing thirst and lethargy. The patient also reported non-specific pain in her shoulders, ribs and hips. She was otherwise well with no past medical history. Systemic enquiry was unremarkable. On examination nothing abnormal was noted. Specifically there were no rashes, lymphadenopathy or hepatosplenomegaly. Joint examination was normal and there was no muscle tenderness or weakness.

#### Section 2: Investigations

Initial investigations revealed an elevated calcium (2.92 mmol/l) with an acute kidney injury (eGFR 38). The PTH was suppressed (0.7 pmol/l). Myeloma screen was negative. CXR was normal with no hilar lymphadenopathy, infiltrates or masses. The calcium levels increased further despite rehydration peaking at 3.24 mmol/l. A CT TAP was undertaken but no abnormal findings were identified. A PET scan was therefore performed to exclude an occult malignancy. No focal mass was noted but there was diffuse uptake in a number of muscle groups. Creatinine kinase levels were normal. The serum ACE was raised and 1,25 (OH) 2 Vitamin D levels were elevated. A muscle biopsy was performed showing non-caseating granulomas confirming a diagnosis of systemic sarcoid with primary muscle involvement.

#### Section 3: Results and treatment

Once a diagnosis of sarcoid was confirmed the patient was initiated on 40 mg OD prednisolone and subsequently 20 mg weekly methotrexate was added. The patient's serum calcium level quickly normalised following treatment and symptoms begun to resolve.

#### Section 4: Conclusions and points for discussion

This case describes a patient with significant hypercalcaemia due to acute atypical isolated sarcoid myositis. This case highlights an uncommon but well recognised clinical condition which is distinct from classical sarcoid. A recent case series found only 8 published cases of hypercalcaemia associated with acute isolated sarcoid myositis. In these cases, like ours, myositis was not initially suspected due to the non-specific symptoms and normal CK. All of the patients in this case series had a PET scan performed for malignancy screening incidentally revealing intense, diffuse fluorodeoxyglucose (FDG) uptake isolated to muscles. The PET scan in our case showed uptake which has previously been described as characteristic for sarcoid myositis and coined 'The tiger man sign'. Our case highlights an uncommon but well recognised cause of hypercalcaemia which is responsive to steroids and immunosuppressive medication. PET scanning seems to be of particular utility in the detection of this condition and may be useful in monitoring treatment response.

DOI: 10.1530/endoabs.69.P15

## P16

### **Feminising adrenal tumours (FAT): the most common rare tumours of the adrenal gland?**

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#### Case history

Adrenal masses are often a diagnostic challenge and can present with unusual symptoms. We describe a case of a 37-year-old male with a background of ulcerative colitis, who presented with bilateral gynecomastia in the breast clinic of, worsening over last one year. He had marked breast tenderness, a decline in his libido but no erectile dysfunction. There was no history of recreational drug use. Investigations

His serum biochemistry showed a persistently elevated oestradiol and with low testosterone and FSH. His prolactin day curve was within normal limits. Ultrasound testes and MRI pituitary were normal. Subsequently, a CT adrenal showed well defined, enhancing tumour arising from the left adrenal gland measuring 5 cm in the maximum axial dimension. PET-FDG confirmed hypermetabolic tumour on the left adrenal with no distant metastasis.

#### Results and treatment

Testosterone 2(6–27) nmol/Lit; FSH 0.20(1–9) IU/l; Oestradiol 331(0–116) pmol/l. A diagnosis of oestradiol secreting adrenal tumour was made, and the patient is listed for urgent surgery. Results of histology will be available after the surgery.

#### Conclusions and points for discussion

Adrenal masses are often a diagnostic challenge and can present with unusual symptoms such as gynecomastia.

- We will discuss rarer causes of gynecomastia including mutations in the *CYP19A1* gene (aromatase overactivity), feminising Sertoli cell tumours along with feminising adrenal tumours (FAT).
- We will review the current literature for FAT and describe its prevalence, clinical presentation, investigations, treatment options and prognosis.

DOI: 10.1530/endoabs.69.P16

## P17

### **An unusual Paraneoplastic Syndromes related to Neuroendocrine Tumours**

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A 70 year-old male with a long standing history of IgG kappa paraproteinemia presented with sudden onset of confusional state. His friend had noticed short term memory lapses, behavioural changes, increased aggression and agitation for the last 3 months. He had developed proximal muscle weakness and pain. He was admitted to the hospital. He had no history of alcohol abuse, smoking or illicit drug use. He was not on any medication. He was under haematology surveillance for his paraproteinemia. His renal and liver function tests were normal. CSF revealed normal glucose, and marginally elevated protein. His CT scan showed a 3 cm thickened and hyperenhancing segment of distal ileum with enhancing nodes in the ileocolic mesentery. There were focal areas of low attenuations within the liver. The MRI scan showed enhancing soft tissue in the terminal ileum. There were multiple lesions in the mesentery and in the liver. He had 2 liver biopsies and histology confirmed a well differentiated metastatic NET. His N-methyl D-aspartate receptor antibodies (NMDA) and voltage gated potassium channel-complex antibodies (VGKC) were negative. His MRI scan of the brain did not show any space occupying lesion. His gut peptides were normal apart from chromogranin B that was elevated. He was treated with somatostatin analogues and steroids. His confusion improved and he is now clinically stable.

#### Discussion

A diagnostic criteria proposed by Gutelkin is used in the diagnosis of paraneoplastic limbic encephalitis. These are:

1. a clinical picture of short-term memory, loss, seizures, or psychiatric symptoms suggesting involvement of the limbic system,
2. an interval of < 4 years between the onset of neurological symptoms and the cancer diagnosis,
3. exclusion of other cancer-related complications (metastasis, infection, metabolic and nutritional deficits, cerebrovascular disorder or side-effects of therapy) that may cause symptoms of limbic dysfunction,
4. one of the following: CSF with inflammatory changes (pleocytosis, oligoclonal IgG bands); or MRI showing unilateral or bilateral temporal lobe abnormalities; and EEG showing slow- or sharp-wave activity in one or both temporal lobes.

Employing the above mentioned criteria, paraneoplastic limbic encephalitis secondary to midgut NET was considered as a possible explanation for his confusion and behavioural changes. He fulfilled 4 of the above criteria. In conclusion Paraneoplastic limbic encephalitis is a rare presentation in neuroendocrine tumors. There are only few cases reported. The diagnosis requires high index of clinical suspicion for the effective patient management.

DOI: 10.1530/endoabs.69.P17

## P18

### **Don't miss the pus-an abscess of the pituitary**

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#### Section 1: Case history

A 69-year-old female with a past history of treated hypertension and Graves' disease presented to the emergency department with a two-day history of headaches, vomiting, confusion and difficulty swallowing following a recent holiday in Spain. She had clinical meningism and a diagnosis of meningitis was made.

#### Section 2: Investigations

After an initial CT scan of her head was reported as unremarkable, a lumbar puncture was performed. A CT scan of her head was repeated ten days later as she reported worsening headaches. The second CT scan was followed by a contrast enhanced MRI of her head as the scan revealed an abnormality in her pituitary fossa.

#### Section 3: Results and treatment

The MRI of the head confirmed a peripherally enhancing lesion in the pituitary extending to involve the hypothalamus, with surrounding oedema, consistent with a pituitary abscess. In retrospect, the previous two CT scans also showed the abnormalities. The lumbar puncture revealed turbid CSF with a total WBC of 2180, 80% of which were neutrophils, consistent with bacterial meningitis. PCR was negative for meningococcus and pneumococcus. CSF cultures were sterile. She was treated with intravenous ceftriaxone and underwent a transphenoidal drainage of pus from the pituitary fossa. She had transient diabetes insipidus but was otherwise eupituitary. The histology did not show evidence of Rathke's cleft cysts or craniopharyngiomas.

#### Section 4: Conclusions and points for discussion

Pituitary abscesses are very rare, with around 200 cases reported to the best of our knowledge. Often, they present sub-acutely with hypopituitarism and a mass lesion. They present with systemic signs and symptoms of infection in less than 20% of cases. Irreversible pan-hypopituitarism is common. Pituitary abscesses may occur in either an anatomically normal gland or in the context of Rathke's cleft tumours or craniopharyngiomas. The mechanisms of infection in the pituitary are believed to be haematogenous seeding or rarely contiguous spread from sphenoiditis. Our patient had a number of unusual features including acute presentation with meningism, systemic features of infection and transient diabetes insipidus. She has done well, being eupituitary on followup with no long-term sequelae after five years. A pituitary abscess is a differential diagnosis of a pituitary lesion, often associated with pan hypopituitarism. It can be misdiagnosed as an adenoma as it infrequently presents with features of infection. A correct diagnosis will result in appropriate antibiotic treatment, drainage and prognostication with regards to endocrine sequelae.

DOI: 10.1530/endoabs.69.P18

## P19

### **Hypoglycaemia associated with high grade transformation of a previously non-functioning pancreatic neuroendocrine tumour (pNET)**

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Naureen Starling<sup>2</sup> & Daniel Morganstein<sup>1,2</sup>

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#### Section 1: Case history

75 year old female diagnosed with Grade 1 pNET (Ki-67 index 70%) in 2018. Treated with subtotal pancreatectomy but 8 months post-surgery a follow up scan

showed new liver metastases, at which point she was commenced on lanreotide. 3 months later she presented with an 8 week history of episodic weakness, sweating and confusion consistent with hypoglycaemia. These episodes initially improved with eating but had become more severe and unresponsive to carbohydrates prior to admission.

#### Section 2: Investigations

Capillary glucose was undetectable in the Emergency Department. She was admitted for further investigations and underwent a supervised fast with plasma insulin, glucose and C-peptide measurements.

#### Section 3: Results and treatment

24 h fast confirmed hypoglycaemia with glucose 2.2 mmol/l, C-peptide 1117 pmol/l, total insulin 26.6 mU/l, consistent with endogenous insulin secretion. Urinary sulphonylurea screens were negative. She was given dietary advice and oral prednisolone was commenced with some improvement in symptoms, but early morning hypoglycaemia persisted. CT showed progression of liver metastases, but no other sites of disease. She therefore underwent re-biopsy of a liver lesion at the same time as hepatic arterial embolization. Biopsy confirmed high grade transformation to grade 3 pNET/carcinoma, with mitotic index >90%, positive CD56, chromogranin and synaptophysin and negative stain for insulin. This resulted in resolution of hypoglycaemia and she has now commenced chemotherapy with Carboplatin and Etoposide.

#### Section 4: Conclusions and points for discussion

Non-functioning pancreatic NETs rarely acquire hormone secretion. In this case there was evidence of endogenous insulin secretion only several months after liver metastases developed, in the context of high grade transformation. Notably there were no symptoms suggestive of hypoglycaemia at the time of the original presentation with a pancreatic primary NET. We hypothesise that the transformation to a high grade neuroendocrine tumour was associated with dysregulated hormone secretion. Although the liver biopsy did not stain for insulin the brisk improvement in hypoglycaemia following hepatic artery embolization suggests the liver metastases were the source of the hyperinsulinaemia.

DOI: 10.1530/endoabs.69.P19

## P20

### Hypercalcemia and electric storm in patient with primary hyperparathyroidism

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#### Case history

A 65 year-old Caucasian gentleman was admitted with out-of-hospital VF arrest at work place. ROSC was achieved after shock by paramedics but developed multiple in-hospital arrests requiring (>100 shocks in 24 h) with incessant polymorphic ventricular tachycardia which was resistant to anti-arrhythmic therapy including drugs and pacing. Investigations revealed hypercalcemia and newly diagnosed high PTH with no change in mild LV dysfunction from previous myocardial infarction. He finally got stabilised with intubation and ventilation along with hypercalcemia management.

#### Investigations

Admission bloods revealed mild hypokalemia of 3.3 mmol/l, adjusted calcium was significantly high at 3.18 mmol/l and PTH of 376 ng/l. ECG did not show any evidence of Brugada syndrome or short QT interval. Echo did not show any change from previous one done 2 years back following MI in terms of functional status and valvular function.

#### Results and treatment

Hypercalcemia was treated with IV fluids and zoledronate infusion followed by cinacalcet. Though hemofiltration was considered with persistent arrhythmia, calcium level and arrhythmias eventually settled. Patient became hemodynamically stable and calcium level dropped to 2.8 prior to discharge. TFT, metanephrines and calcitonin were normal.

USS neck: multiple nodules in the left thyroid lobe with retrosternal extension. Sestamibi scan showed left thyroid lobe nodule with peripheral calcification but no separate parathyroid adenoma. Intrathyroid parathyroid adenoma was suggested as a possibility. CT CAP was unremarkable except for 2 sub-

centimetre lung nodule at lung base. Patient had left hemi-thyroidectomy with a significant drop in intra-operative parathyroid measurement confirming the diagnosis. Histology confirmed intra-thyroidal parathyroid adenoma with incidental finding of minimally invasive follicular carcinoma of Hurthle cell type. Patient awaits completion right hemithyroidectomy.

#### Conclusions and points for discussion

Hypercalcemia with short QT interval is known to cause ventricular arrhythmia but it could occur even in patients with normal QT interval. PTH per se could be arrhythmogenic, triggering ventricular arrhythmia at lower calcium levels. Ectopic parathyroid adenoma can be found as intrathyroidal nodule and is a rare cause of primary hyperparathyroidism. Intrathyroidal parathyroid adenoma can be associated with thyroid malignancy.

This case raises few questions

- What is the pathophysiology of ventricular arrhythmia in hyperparathyroid patients with normal QT interval?
- How can we risk stratify the hyperparathyroidism patients at risk of ventricular arrhythmia?
- What are the optimal treatment options in hypercalcemia-induced electric storm?
- What are the appropriate investigations for identification of the thyroid malignancy associated with intrathyroidal parathyroid adenoma?

DOI: 10.1530/endoabs.69.P20

## P21

### Functional heterogeneity of pancreatic neuroendocrine tumours in multiple endocrine neoplasia type 1 (MEN-1)

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We present a 24 year old gentleman with Multiple endocrine neoplasia type 1 with a truncating mutation in the Menin gene arising *de novo*. He has a past medical history of optic atrophy, pituitary macroprolactinoma in 2007 with ommaya reservoir *in situ*, hyperparathyroidism with subsequent parathyroidectomy (3 glands removal) and spinal osteoporosis. He had a laparoscopic pancreatic nodule enucleation for pancreatic tumours (×2 in tail of pancreas) in 2017 with his histology stained positive for glucagonoma with Ki67 index of 3.2% and elevated glucagon levels at 206 pmol/l (0–50) though he was asymptomatic. He is on pituitary hormone replacement – hydrocortisone, cabergoline, levothyroxine and nebido injection. He recently presented with 1–2-month history of increasing lethargy, confusion, persistent hunger, sweatiness and shakes. His libre showed persistently low blood sugars ranging between 2–3 mmols. His investigations showed – HbA1c 22 mmol/mol, C-peptide 2012 pmol/l, insulin 14.7 mu/l, glucose 1.5 mmol/l, IGF-1 10.2 nmol/l, SHBG 108 nmol/l, PTH 11.2 pmol/l, testosterone 10.3 nmol/l, corrected calcium 2.57 mmol/l, chromogranin A 43 pmol/l (0–60). His MRI of the pituitary gland showed a large cystic pituitary mass with small enhancing solid components measuring 25.4×27.7×27 mm with normal appearance of the craniocervical junction. His repeat CT chest abdomen and pelvis showed A 5 mm hypervascular nodule in the distal pancreatic body, a 2 mm hypervascular focus in the inferior pancreatic head and also enlarged node in the region of gastrocolic vessels suggestive of neuroendocrine tumours. He was commenced on diazoxide 100 mg three times a day. He was discussed in our neuroendocrine MDT meeting and subsequently undergone a distal pancreatectomy, splenectomy and cholecystectomy due to gallstones.

#### Conclusion

Multiple endocrine neoplasia type 1 (MEN1) is a complex inherited condition, presenting with hyperparathyroidism, pituitary tumours and pancreatic endocrine tumours. Pancreatic endocrine tumour releases excessive hormones such as gastrin, somatostatin, insulin, glucagon and vasoactive intestinal polypeptide or may be silent (Non-functioning NET). MEN-1 is known to be associated with pancreatic tumours heterogeneity in size and grade. The metachronous functional heterogeneity is less common. This case serves to further enhance awareness among endocrinologist of such possibilities and need for ongoing functional and radiological surveillance.

DOI: 10.1530/endoabs.69.P21



**P22****A Grave cause of hypercalcaemia in hypoparathyroidism**

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## Section 1: Case history

A 58 year old lady presented to the Emergency Department with a two week history of general lethargy, weight loss, increased thirst and polyuria as well as muscle cramps in her legs. Aside from sinus tachycardia, her observations and physical examination were unremarkable on admission. She had a background of hypertension on Indapamide as well as idiopathic hypoparathyroidism on Alfacalcidol. The latter had been diagnosed nine years prior following admission with difficulty in speaking due to jaw stiffness as well as facial weakness and hand numbness in the context of marked hypocalcaemia. Three years later, she developed hypercalcaemia related to a diagnosis of Graves' thyrotoxicosis for which she completed 18 months of Carbimazole therapy to good biochemical and clinical effect.

## Section 2: Investigations

Her biochemical profile on this admission revealed a marked hypercalcaemia and hyperthyroidism; adjusted Calcium 3.35 (2.20–2.60), Phosphate 1.65 (0.80–1.50), free T4 level 51.5 (9.0–23.0), free T3 level >30.7 (2.5–5.7) and Thyroid Stimulating Hormone (TSH) <0.01 (0.30–4.20). Her Parathyroid Hormone level was suppressed at <0.3 (1.6–7.2), she had a very low Vitamin D level of 14.3 (70–150) and a raised TSH receptor antibody level of 1.1 (<0.4). There was an increased uptake function of 5.58% (normal <3.5%) of the thyroid gland on imaging with Technitium in keeping with mildly active Graves' thyrotoxicosis. A DEXA scan revealed normal bone density of the hips and lumbar spine.

## Section 3: Results and treatment

The patient was recommenced on Carbimazole which was uptitrated to 40 mg and Propranolol was introduced for palpitations. She received intravenous fluid rehydration as an inpatient whilst her Indapamide was held. She improved clinically and her bloods were closely monitored as an outpatient; the Calcium level normalised as her thyroid function improved on Carbimazole treatment and her Alfacalcidol was eventually reinstated. She proceeded to have definitive treatment of her thyroid with radioiodine therapy.

## Section 4: Conclusion and points for discussion

A mildly raised Calcium level can be found in the hyperthyroid state due to increased bone metabolism. However, this lady interestingly presented with recurrent and severe Graves' thyrotoxicosis that manifested with hypercalcaemic crisis on both occasions. The hypercalcaemia persisted even when off Alfacalcidol for her concurrent idiopathic hypoparathyroidism which had initially presented with a marked hypocalcaemia. This case shows a remarkable biochemical pattern over the course of nine years where the patient's calcium status significantly shifts with her thyroid state, despite an underlying hypoparathyroidism.

DOI: 10.1530/endoabs.69.P22

effusion. Pulmonary oedema, not present on admission, required intensive offloading and bilateral drainage.

## Investigations

Weekly Thyroid Function Tests. Serial troponin and ECHOs.

## MDT team

ITU, Endocrinology and Cardiology

## Results and treatment

Liothyronine 10 µg IV BD was initiated. Levothyroxine was started at Day 3 at 25 µg NG and increased by increments of 25 µg every 7 days until 150 µg. Hydrocortisone, initiated at 100 mg QDS was weaned. Cortisol levels showed no adrenal insufficiency.

## Thyroid function tests

Week 0: TSH >100 mIU/l; T4 0.7 pmol/l  
Week 1: TSH 28.15 mIU/l; T4 0.6 pmol/l  
Week 2: TSH 10.78 mIU/l; T4 2.8 pmol/l  
Week 3: TSH 16.48 mIU/l; T4 3.4 pmol/l  
Week 4: TSH 39.55 mIU/l; T4 8.1 pmol/l  
Week 5: TSH 55.84 mIU/l; T4 12.4 pmol/l  
Week 6: TSH 11.43 mIU/l; T4 16.5 pmol/l

## Conclusion and points for discussion

True myxoedema crisis is rare. Therefore, there are limited studies to guide on the optimum rate of thyroid function correction. Rapid thyroid replacement risks precipitating myocardial infarction, particularly in those with poor cardiac baseline. This case highlights the importance of establishing a cardiac baseline (i.e., an admission ECHO) to plan for a slower correction and early involvement of the cardiology team. Myxoedema coma continues to have poor prognosis, which is worsened further in those that experience cardiac complications. Avoiding these events through a better understanding of optimum correction rates will improve outcomes in this subsection of patients.

DOI: 10.1530/endoabs.69.P23

**P24****Dopamine agonists (DA) therapy down-titration may prevent CSF leakage in cases of structurally responsive macroprolactinomas**

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## Case history

A 20-year-old male presented with a one-year history of reduced libido, headache and slowly progressive blindness. His symptoms (particularly the visual deterioration) had a great impact on his daily life, leading to dismissal from work. Examination showed decreased visual acuity (12/6 bilaterally), reduced colour vision and a dense bitemporal visual field loss. Testes measured 15 ml bilaterally. He had no clinical stigmata of acromegaly, nor Cushing's disease. Other systems' examination was unremarkable.

## Investigations

Routine laboratory investigations (full blood count, kidney, liver and bone functions) were unremarkable. Baseline pituitary function test showed a significantly raised serum prolactin level of 57 000 [reference range: 50–500 mU/l]. Ancillary lab tests excluded the presence of macroprolactin in the sample. The rest of the pituitary blood tests were within the normal range. Pituitary MRI showed a large sellar mass invading a significant portion of the skull base, extending superiorly to compress the optic chiasm and laterally to invade both cavernous sinuses.

## Results and treatment

Based on the imaging and the biochemistry data, a diagnosis of large macroprolactinoma was made and the patient was started on a titrated dose of cabergoline therapy (initial dose: 250 µg twice weekly). He tolerated the treatment very well with no side effects despite gradual dose escalation to 1 g thrice weekly. After six months of treatment, his vision had dramatically improved and his serum prolactin decreased to 4500 mU/l. This was associated with a rapid reduction in tumour size to more than 50% of the initial measurement. A skull base computed tomography (CT) scan showed areas of bony defects that were occupied by tumour tissue. A decision was made to reduce the cabergoline dose to avoid the possibility of cerebrospinal fluid (CSF) leakage due to skull defects.

**P23****Myxoedema crisis: The importance of establishing cardiac baseline at admission to guide optimum thyroid function correction rate**

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## Case history

A 65 year old unresponsive female, admitted as a stroke call, was found to have myxoedema crisis with admission TSH level of >100 mIU/l and T4 of 0.7 pmol/l. She was known hypothyroid with poor medication compliance. ITU admission for intubation and ventilation, CVVH (renal filtration) and vasopressors was required. Total length of ITU stay was 62 days, prolonged by cardiac complications during correction. There was no known cardiac history. On Day 7 of admission, X had increasing noradrenaline requirements alongside new ST depression and troponin rise. Cardiology diagnosed type two MI. Aspirin, clopidogrel and a beta-blocker were commenced. On Day 34 of admission there was further deterioration. X required return to DuoPAP having been on BiPAP for 5 days. Serial troponins showed a substantial rise reaching 1066. X received 4 stents in angiography on Day 44 of admission. The first ECHO carried out was Day 5 of admission, which showed moderate mitral regurgitation. This deteriorated during admission to severe MR with new RWMA and a pericardial

## Conclusions

In macroprolactinomas that are structurally very sensitive to DA therapy, careful down-titration of the DA dose is crucial to avoid CSF leaks. CT scanning is informative in the assessment of skull base integrity and may inform decision making regarding DA dose adjustment.

## Points for discussion

- DA dose titration/adjustments based on imaging data in prolactinomas
- CT skull base interpretation and recognising potential areas of CSF leakage

DOI: 10.1530/endoabs.69.P24

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## P25

### GCM2 variant – A rare genetic cause of Familial Isolated Hyperparathyroidism

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#### Section 1: Case history

A 46-year-old woman was referred to the Endocrinology clinic for evaluation of persistently elevated parathyroid hormone levels despite correction of previous vitamin D deficiency. She had a history of calcific tendinitis of the left shoulder and iris pigment dispersion syndrome. Notably, her mother had undergone two parathyroid surgeries for primary hyperparathyroidism with removal of three parathyroid glands, revealing multiple parathyroid adenomas and an incidentally detected papillary thyroid carcinoma. The mother had three sisters, one of whom had also been diagnosed with primary hyperparathyroidism; another (deceased) sister had had osteoporosis. Genetic screening in the mother had identified a heterozygous single nucleotide polymorphism of GCM2 gene at c. 1181A>C p. (Tyr394Ser). In view of the strong family history, the patient went on to have further investigations as follows:

#### Section 2: Investigations

Corrected serum calcium: 2.32 (reference range, 2.20–2.60) mmol/l

Parathyroid hormone: 11.2 (2.0–9.3) pmol/l

Vitamin D: 53.6 (50.0–125.0) nmol/l

Kidney and thyroid function: normal

DEXA bone densitometry scan: normal

Renal ultrasound scan: normal; no calculi.

Ultrasound scan of neck: 5 mm paratracheal nodule inferior to the left thyroid gland which may represent a parathyroid adenoma.

SESTAMIBI scan: no focus to suggest parathyroid adenoma.

#### Section 3: Results and treatment

*Genetic analysis in our patient confirmed heterozygous* single nucleotide polymorphism of GCM2 gene at c. 1181A>C p. (Tyr394Ser) identical to her mother. In light of the familial GCM2 variant, she was advised that she runs the risk of developing symptomatic hyperparathyroidism in the future. Since there was no target end organ damage, she opted for wait and watch monitoring. Vitamin D replacement was increased to target a serum level >75 nmol/l.

#### Section 4: Conclusions and points for discussion

- GCM2 single nucleotide variant is a less well-known genetic cause of Familial Isolated Hyperparathyroidism (FIHP).
- GCM2 stands for Glial Cell Missing Transcription Factor-2. It is a gene that encodes a transcription factor required for parathyroid development, located on chromosome 6p24.2.
- Inactivating mutations of GCM2 result in hypoparathyroidism whereas gain-of-function mutations are associated with hyperparathyroidism.
- Persons with FIHP and GCM2 variants present as adults with mild hypercalcemia and multiple parathyroid tumours, as in this patient's mother. The long-term prognosis and best practice clinical management remains unknown.

DOI: 10.1530/endoabs.69.P25

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## P26

### An unusual cause of primary amenorrhoea

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## Case history

The patient was a 17-year old lady who was referred to us by her primary care provider for hyperprolactinaemia and primary amenorrhoea. She was of short stature (0.4th centile for height and minus 2 centile spaces of the mid-parental height) and in the 9th–25th centile range for weight. There was no history of galactorrhoea. Her breast development was Tanner stage 3–4, and pubic hair 2–3, with no axillary hair. There was no evidence of any intellectual impairment. There was a family history of hypothyroidism in her maternal aunt and grandfather.

## Investigations

FT4 <3 pmol/l, TSH >100 mU/l, Prolactin 2069 mIU/l (Monomeric Prolactin 1635 mIU/l), LH < 1 IU/l, FSH 4.5 IU/l, Oestradiol <98 pmol/l, SHBG 57 nmol/l, IGF-1 23.8 nmol/l, AM Cortisol 436 nmol/l and positive coeliac screen. The calculated bone age was 13.2 years. MRI pituitary and the ultrasound of her uterus and ovaries were normal.

## Results and treatment

After initiation of thyroid hormone replacement, serum TSH and prolactin levels fell progressively into the normal range. Along with these changes, the patient noted a return of normal menstrual function.

## Conclusion and points for discussion

Hyperprolactinemia is a common cause of secondary amenorrhoea, but an uncommon cause of primary amenorrhoea. The presentation is similar to hypothalamic amenorrhoea except for the additional finding of galactorrhoea in some patients. The combination of amenorrhoea and hyperprolactinemia in a young woman usually suggests a prolactin-secreting adenoma of the anterior pituitary gland. Primary thyroid failure may also be associated with hyperprolactinemia, galactorrhea and suprasellar enlargement of the pituitary (pseudoprolactinoma).

DOI: 10.1530/endoabs.69.P26

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## P27

### The normalisation of a serum testosterone using GnRH analogue therapy in a case of a single testosterone-secreting adrenal adenoma confirmed on adrenal vein sampling

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## Case History

A 53 year old woman presented with a 12-month history of progressive hirsutism and deepening of her voice. Her symptoms coincided with the onset of the menopause. On clinical examination she had evidence of virilisation with muscle hypertrophy.

## Investigations

Biochemical tests revealed a serum testosterone (serT) of 30 nmol/l, a DHEA-Sulphate of 1.5 umol/l (1.0–12.0), an androstenedione of 3.2 nmol/l (0.0–6.0), a post-overnight dexamethasone suppression test cortisol of <50 nmol/l (and corresponding serT of 40 nmol/l), aldosterone: renin ratio of 159. Urinary metabolites were normal apart from slight elevation in androgen metabolites, androsterone-5 beta 1880 ug/24 h (260–1270) and aetiocholanolone of 2260 ug/24 h (270–1390). An abdominopelvic CT scan showed a 2.4 cm right adrenal mass and this was corroborated on an adrenal MRI scan. Due to the presence of the adrenal adenoma we performed adrenal vein sampling (AVS) with ovarian and peripheral venous samples (without ACTH-stimulation) in order to exclude a testosterone-secreting adrenal adenoma.

## Results and treatment

AVS measurements of testosterone using Liquid Chromatography with tandem mass spectrometry showed testosterone values of 3803, 30, 20.1 and 29.9 nmol/l for the right adrenal vein (RAV), left adrenal vein (LAV), inferior vena-cava (IVC) and left ovarian vein (LOV) respectively. Attempted cannulation of the right ovarian vein was unsuccessful. Serum cortisol measurements in the RAV,

LAV and IVC were 824, 24 033 and 216 nmol/l, respectively which provided selectivity indices of 4 for the RAV and 111 for the LAV, both which confirmed adequate cannulation. This was further confirmed by marked differences in metanephrine levels between the RAV (20 897 pmol/l), LAV (23 459 pmol/l) and IVC (99 pmol/l). Following AVS GnRH analogue therapy, Goserelin, was introduced to assess for a response in testosterone with gonadotrophin suppression after which there were weekly measurements of testosterone and gonadotrophins. Four weeks following treatment with Goserelin there was suppression of her gonadotrophins and improvement in the serT to 1.3 nmol/l.

Conclusions and points for discussion

Our results suggest a single testosterone-secreting right adrenal adenoma that responded to gonadotrophin suppression.

Points for discussion are

1. Reviewing the AVS results with the response to GnRH analogue therapy what are the possible mechanism for this; could there be an HCG or other gonadotrophin-responsive receptor expression on the adrenal nodule?
2. What further investigations would be indicated?
3. Is there sufficient evidence to proceed with a right-sided adrenalectomy?

DOI: 10.1530/endoabs.69.P27

## P28

### A case of macroTSH masquerading as subclinical hypothyroidism

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Case history

A 47 year old male presented to his GP with non-specific symptoms of fatigue and weight gain. Thyroid function tests revealed elevated TSH (28.4 mU/l) with normal Free T4 (14.3 pmol/l). Anti-TPO antibodies were undetectable. A presumptive diagnosis of subclinical hypothyroidism was made and he was commenced on Levothyroxine which was titrated over 9 months to 150 mcg/d given a persistently elevated TSH. The patient was unable to tolerate this dose due to the development of sweating, palpitations, heat intolerance and insomnia. His dose was then reduced to 125 mcg/d and he was referred to his local Endocrinology service.

Investigations

On examination he appeared clinically euthyroid with no goitre and no eye signs. Repeat thyroid function demonstrated Free T4 26.9 pmol/l and TSH 11.67 mU/l. SHBG was elevated at 88 nmol/l. Alpha-subunit was normal at 0.2 U/l. The clinical impression was of iatrogenic thyrotoxicosis with possible underlying thyroid hormone resistance, TSHoma or assay interference. Levothyroxine was discontinued and the patient re-evaluated after 6 weeks.

Results and treatment

The patient's free T4 normalised on cessation of Levothyroxine (13.2 pmol/l) however TSH remained elevated (20.26 mU/l). There was a normal response to TRH testing. T3 suppression testing demonstrated appropriate Free T4 suppression but a persistently high TSH of 12.08 mU/l. THRβ sequencing was normal. Given the persistence of TSH elevation despite various concentrations of thyroid hormone, the suspicion was of MacroTSH or heterophilic antibody interference. TSH measurement by alternative assays revealed discrepant results; 12.21 mU/l (Roche Cobas) and 1.7 (Abbott Architect). PEG extraction of TSH yielded a recovery 15.7%. Sephadex gel filtration chromatography was performed and confirmed the presence of high molecular weight TSH variant alongside normal TSH. Displacement of this high molecular weight variant was seen on acidification in keeping with IgG bound macroTSH. The patient remained well to follow up in the absence of any treatment.

Conclusions and points for discussion

MacroTSH is a rare phenomenon that presents as a spuriously elevated TSH and which may mimic subclinical hypothyroidism. Careful history and examination should alert the clinician to thyroid function tests that are discordant with the clinical picture. Non-specific symptoms should not be automatically ascribed to abnormal thyroid function. Recognition of macroTSH avoids misdiagnosis and prevents inappropriate treatment.

DOI: 10.1530/endoabs.69.P28

## P29

### Calcium sensing receptor mutation causing familial hypocalcaemic hypercalcaemia

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Case history

A 16 month old boy was referred to Community Paediatrics with developmental delay. Bloods taken as part of a developmental delay screen, revealed a raised calcium, with an inappropriately normal parathyroid hormone (PTH) and a normal vitamin D. There was no family history of hypercalcaemia. Blood tests in the boy's mother and grandmother also showed hypercalcaemia.

Investigations

Calcium was raised at 3.46 mmol/l. A urinary calcium creatinine ratio was low at 0.0045. A renal ultrasound showed no evidence of renal calcinosis. This was similarly the case in his mother and grandmother. Genetic testing showed a heterozygous Calcium Sensing Receptor (CaSR) mutation, c.554G>A p.(Arg185Gln), confirming the diagnosis of Familial Hypocalcaemic Hypercalcaemia (FHH) in all 3 relatives. Interestingly, the severity of hypercalcaemia increased down the generations, with the boy having a higher calcium level than his mother and grandmother, respectively.

Results and treatment

FHH is typically a benign condition, with no specific treatment required. Patients with FHH typically have an excellent prognosis. It is important to differentiate from primary hyperparathyroidism, the latter of which may require surgery.

Conclusions and points for discussion

FHH is rare, with a prevalence of 1 in 78 000<sup>1</sup>. Patients are not at increased risk of renal calculi or osteoporosis. The main differential is the much more common condition, primary hyperparathyroidism. There are several subtypes of FHH. The most common, occurring in approximately 65% of cases<sup>2</sup>, FHH type 1, is due to a mutation in the CaSR gene, located on chromosome 3. This is responsible for making CaSR protein, which monitors and regulates blood calcium levels, and is found predominantly in the parathyroid glands and kidneys. CaSR mutations results in reduced sensitivity of the parathyroid gland to high calcium levels, resulting in hypercalcaemia as well as ongoing raised PTH levels. Patients with FHH typically have an excellent prognosis. FHH is not generally associated with developmental delay, the exception to this being FHH type 3. In this case, another microduplication was found, known to be associated with developmental delay.

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DOI: 10.1530/endoabs.69.P29

## P30

### ADHD and Addison's: similar in name, similar in nature?

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Section 1: Case history

An 18 year old young man with a background of several years' ADHD (Attention Deficit Hyperactivity Disorder) and moderate learning disability presented generally unwell, with recent weight loss, abdominal pain, vomiting and poor oral intake in May 2019. He had been unsettled for some time with his mother convinced that his current condition warranted further investigation. When blood tests were done, severe hyponatraemia and hyperkalaemia were found and urgent referral made to the hospital. His past medical history was of preterm labour at 27 weeks, developmental delay, delayed speech and language development, coordination difficulty and cholesteatoma. He was on Methylphenidate 10 mg BD and Medikinet XL 40 mg OD, under follow up at the Paediatric clinic for his ADHD. His weight and height changed from 24 kg, 132 cm in 2010 to 40 kg, 160 cm in 2015 and 56 kg, 182 cm in March, 2019. On admission, his weight was 52 kg, examination revealed hyperpigmentation with pulse 103 and BP 94/65 mmHg.

Section 2: Investigations

On admission various blood tests were performed including a random cortisol, assessment of osmolality; later a short synacthen test (SST) and test for adrenal antibodies were organised.

Section 3: Results and treatment

The results on admission showed Sodium 122, K 6.4, Urea 19.4, Creatinine 154, Calcium 2.49, Albumin 43, Serum osmolality of 279 mmol/Kg (275–295), Urine osmolality 784 mmol/Kg and Random Cortisol of 271 nmol/l. The SST confirmed adrenal failure; Cortisol level 0 min 324, 30 min 336 and 60 min 342. Renin was 85 mU/l (5.4–60). TFTs (thyroid function tests); TSH 1.86, T4 17.6, TTG 0.8 u/ml (0–6.9), and 17OH Progesterone 1.9 nmol/l (0–5) were within range. The adrenal cortex autoantibodies result was positive. He was treated with Hydrocortisone 50 mg IV TDS and Fludrocortisone 100 mcg OM. Clinical and biochemical improvement took place, with electrolytes back to normal after 5 days of treatment. He is now on replacement oral Hydrocortisone 20 mg/24 h and Fludrocortisone 100 mcg and is under the Adult Endocrinology clinic.

Section 4: Conclusions and points for discussion

ADHD can present with a variety of symptoms and there is some evidence of HPA-axis dysregulation with associated variability in cortisol dynamics. Current guidelines for evaluating patients with ADHD do not suggest extensive or regular endocrine screening, which may lead to delays in diagnosis. In those treated for ADHD, altered behaviour and/or a change in physical development may warrant careful elucidation, especially for Addison's disease.

DOI: 10.1530/endoabs.69.P30

**P31**

**A rare case of carotico-cavernous sinus fistula associated with pituitary enlargement**

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Introduction

Hyperprolactinaemia, amenorrhoea with ophthalmoplegia and radiological abnormalities in suprasellar region usually suggest a pituitary tumour. We present a case of carotico-cavernous sinus fistula causing pituitary engorgement (CCF) mimicking pituitary tumour.

Case history

45 year old female with background history of long term amenorrhea, migraine admitted under Neurology with worsening headache, nausea, vomiting and blurred vision. There was no associated pyrexia, rash or diarrhoea. Other background history included PTSD, obesity, chronic fatigue syndrome, depression, hypothyroidism and fibromyalgia. She was on regular pericyazine, citalopram, levothyroxine, pregablin. Physical examination revealed bilateral chemosis, right eye proptosis with diplopia on right horizontal gaze consistent with right sixth nerve palsy.

Investigations

All initial investigations, including autoimmune screen for rheumatoid arthritis, SLE, were normal. MRI brain suggested a potential CCF and also a possibility of a suprasellar lesion. At this point endocrine input was sorted, hormonal testing indicated a moderately raised prolactin of 1906 mU/l, low TSH 0.15 (0.35–3.50 mU/l) with T4 of 16 (8 – 21 pmol/l), LH 1.8 IU/l, FSH 3.5 IU/l, oestradiol 147 pmol/l, IGF1 14.8 (7.6–28.5 nmol/l), 0600 h cortisol 302 nmol/l. She subsequently had a dedicated MRI pituitary which was reported having a pituitary tumour with suprasellar extension. Her case was further discussed in radiology MDT and it was concluded that appearance was more in keeping with pituitary engorgement secondary to low cerebral pressure. This was confirmed on CT angiogram which showed CCF. She underwent bilateral cavernous sinus embolization with 35% precipitating hydrophobic injectable liquid and recovered slowly with a period of rehabilitation. Her prolactinaemia was likely from combination of stress and pericyazine therapy. Repeat MRI was not carried out to see whether engorgement was resolved due to potential radiology interference of metal coils used in the embolization. Subsequent pituitary function tests were normal. Her menstrual period also returned spontaneously.

Conclusion

CCF is an abnormal communication between the cavernous sinus and the carotid arterial system. CCF may result in enlargement of the interconnecting components of the cavernous sinus around the pituitary fossa. Radiologically this can mimic pituitary enlargement/tumour thereby proving to be potential diagnostic pitfall. Careful history, clinical examination and multi-disciplinary approach are essential for correct diagnosis and management.

DOI: 10.1530/endoabs.69.P31

**P32**

**An illustrative case highlighting the risk of nephrocalcinosis with 1-alfacalcidol in chronic hypoparathyroidism**

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Case history

Twenty-one year-old female with Di-George syndrome, genetically confirmed at the age of 6 years, was on 1-alfacalcidol for chronic hypoparathyroidism. Her initial presentation was with Seizures in childhood. She has been seizure free with treatment of hypocalcaemia. Her serum calcium levels have been fluctuating with intermittent hypercalcaemia over the years.

Investigations

Initial results on 1.5 mcg of 1-alfacalcidol OD:

Corrected serum calcium 2.33 mmol/l

Serum phosphate 1.05 mmol/l

Renal functions >60 ml/min per m<sup>2</sup>

24-h urinary calcium 10.91 mmol/24 h

Renal USS – Evidence of nephrocalcinosis

Follow up results on 1-alfacalcidol 0.75 mcg and 0.5 mcg alternate days with Indapamide MR 1.5 mg OD:

Corrected serum calcium 2.26 mmol/l

Serum phosphate 1.42 mmol/l

Renal functions >60 ml/min/m<sup>2</sup>

24-h urinary calcium 2.91 mmol/24 h

Results and treatment

Her 1-alfacalcidol dose was reduced to keep serum calcium levels towards lower end of normal; however, despite these measures she remained hypercalcaemic and the renal ultrasound showed evidence of nephrocalcinosis. After initial reluctance, her mother agreed for 1-alfacalcidol dose reduction with close monitoring. She was commenced on Indapamide and her 1-alfacalcidol dose was reduced further. Now she remains normocalcaemic at 2.26 mmol/l without hypercalcaemia. Gradually we have managed to reduce her 1-alfacalcidol dose from 1.5 mcg once daily down to 0.5 mcg and 0.75 mcg on alternate days. We are considering further dose reduction. Patient remains well and seizure free.

Conclusions and points for discussion

In chronic hypoparathyroid patients 24-h urine calcium is not routinely checked in clinical practice. Renal complications (hypercalcaemia 38%, intrarenal calcification 31% and reduction in eGFR 41%) are common in this group. Compared to age matched controls CKD stage 3 or higher is 2–17 fold higher in hypoparathyroid patients. This is due to lack of PTH induced renal tubular calcium reabsorption. Guidelines recommend keeping serum calcium towards the lower end of the reference range (while avoiding symptoms of hypocalcaemia) in order to minimise hypercalcaemia and associated complications. 24-h urine calcium should be monitored along with rest of the biochemical monitoring. In those with hypercalcaemia, renal stone or reduced eGFR; ultrasound kidneys should be arranged. Thiazide diuretic is shown to reduce urinary calcium excretion and it can be used successfully as demonstrated in this case.

DOI: 10.1530/endoabs.69.P32

**P33**

**Gynaecomastia as a paraneoplastic syndrome secondary to hCG secreting lung cancer**

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Case history

73-year-old male was seen in breast clinic for right breast lump which was noted 6 weeks back with no nipple discharge. Mammogram and ultrasound confirmed bilateral gynaecomastia more on right side. Referred to endocrine clinic with abnormal hormone profile. He is a retired builder. He was a heavy smoker for 50 years and has stopped smoking 1 year back. He drinks socially and has never used illicit drugs. His only past medical history was GORD for which he takes lansoprazole. Clinical and ultrasound examination of testes were normal.

Investigations

FSH 0.3 IU/l, LH <0.3 IU/l, 17 beta oestradiol 416 pmol/l, testosterone 29.7 nmol/l, TSH 1.6 mU/l, beta-HCG 69.8 IU/l, Alpha-fetoprotein 1.5 kU/l.

Whole-body CT showed 5.7×6.4 cm malignant appearing mass in left lung lower lobe with mediastinal lymphadenopathy and nodular lesion in right adrenal gland suspicious for metastases. Radiological staging T4 N2 M1c.

#### Results and treatment

He was seen in respiratory clinic as priority. His performance status is 1 and his spirometry is normal with only moderate diffusion defect. Flexible bronchoscopic biopsy and bronchial washings with immunohistochemical stains favoured diagnosis of squamous cell carcinoma. He had another rigid bronchoscopic biopsy and is awaiting its results.

#### Conclusions and discussion

Gynaecomastia results from oestrogen to androgen imbalance. Gonadal and extragonadal tumours can present with gynaecomastia. Gonadal tumours causing gynaecomastia could originate from sertoli cells, granulosa cells, Leydig cells or germ cells. Sertoli cell tumours and granulosa cell tumours produce excess of oestrogen whereas Leydig cell tumours produce oestrogen and testosterone. Gonadal germ cell tumours (both seminomatous and non-seminomatous type) produce hCG. The non-seminomatous tumours (embryonal carcinoma, yolk sac carcinoma, choriocarcinoma and teratoma) produce AFP in addition to hCG. Extra-gonadal germ cell tumours that ectopically express hCG can be lung, stomach, head/neck, ovary, leiomyosarcoma, renal-cell and hepato-cellular cancers (20–40% of all common epithelial cancers). The increased hCG acts as LH analogue to stimulate Leydig cells to produce more of oestrogen and less testosterone leading to gynaecomastia. Though paraneoplastic syndromes are common in lung cancer (10%), gynaecomastia occurs as a paraneoplastic syndrome only in 2.4% cases. Though hCG expression occurs in 12–14% of small cell lung cancers, it is exceedingly rare in non-small cell lung cancers (NSCLC). Among NSCLC types, adenocarcinomas express hCG more frequently than squamous cell carcinomas. Prognosis for hCG producing tumours are poor as they are generally aggressive and chemo resistant.

DOI: 10.1530/endoabs.69.P33

### P34

#### Radio-iodine treatment for thyrotoxicosis in unsuspected pregnancy

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Our endocrinology department had been looking after a patient with Graves' disease since 2007. At this time, she was 17 years old (TSH <0.03 mIU/l, T4 62.6 pmol/l). Carbimazole was prescribed but she was non-compliant with medications and clinic appointments. Her background history included DiGeorge Syndrome (22q11 deletion) manifesting with a bicuspid aortic valve, primary hypoparathyroidism and chronic constipation. She was seen in October 2011 and carbimazole increased to 60 mg OD (TSH <0.03 mIU/l, T4 = 54 pmol/l). In November 2011, Carbimazole was switched to Propylthiouracil temporarily due to neutropenia. She was again lost to follow up. In March 2017, now aged 27, she was still thyrotoxic and having discussed alternative options, opted for radio-iodine therapy. Both the referring endocrinologist and the Oncologist delivering the treatment explained that she must not conceive for 6 months and she signed a consent form. She appeared to understand this and radio-iodine treatment was given on 10/03/2017. A few weeks after treatment she discovered she was pregnant (LMP = 21/02/2017). An MDT meeting including the patient, endocrinology and oncology was held to explain the possible risks to the foetus/child. Advice from the nuclear medicine department was as follows: for a dose of 26 mSv, the increased risk of inducing a childhood cancer is estimated to be 1 in 500. This is in the context of the natural incidence of all childhood cancers in England and Wales of 0.2%, or 1 in 500. In addition, the natural incidence of genetic diseases for all babies born is 1%–3% and the overall risk of natural congenital abnormalities is 5%–6%. The patient initially decided to terminate the pregnancy, but subsequently changed her mind. She had an uncomplicated pregnancy and gave birth to a healthy baby. She was seen in clinic in January 2019 when her son was 14 months old. He was healthy and following his milestones. Her Thyroid Function Tests are now normal off treatment; TSH = 2 mIU/l, T4 = 13.8 pmol/l.

#### Discussion

DiGeorge syndrome can be associated with moderate intellectual disability and problems in social emotional functioning. This case highlights the importance of appropriate communication of the risks of radio iodine therapy when such concerns exist. It also raises the questions of pregnancy testing prior to radio-iodine administration, and the appropriate evaluation required in a child born to a mother exposed to radio-iodine therapy.

DOI: 10.1530/endoabs.69.P34

### P35

#### 'I have type 2, my brother has type 1, I can't hear you doctor! Metformin give me diarrhoea'

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#### Case history

A 41-year-old lady referred to diabetes clinic due to chronic diarrhoea on Metformin and for consideration of any injectable treatment. HbA1c was 41 and BMI is 35. In 2007, OGTT during pregnancy showed fasting glucose of 4.1 mmol/l and 2 h glucose of 7.8 mmol/l. In 2013 her fasting glucose was 7.5 and HbA1c was elevated at 53 mmol/mol. Since July 2013 she has been diagnosed as type 2 DM and started on Metformin. In October 2013 HbA1c fell to 49. Over the succeeding years her HbA1c has never been greater than 41 mmol/l. She has a very strong family history of diabetes. Mother was diagnosed with diabetes in her early 30s and she had deafness. Her brother has been diagnosed with type 1 diabetes and he has deafness in both ears. Maternal grandmother and her brothers were also diagnosed with type 1 diabetes. Our patient is also suffering from deafness in her left ear.

#### Investigations

Diagnosis of maternally inherited diabetes and deafness (MIDD) is considered in our patient. Diabetes related antibodies (Anti GAD Antibodies, IA2 Antibodies and Znt8 Antibodies) were requested. A genetic test is requested for possible diagnosis of MIDD.

#### Results and treatment

All diabetes related antibodies came back negative. The pathogenic mitochondrial DNA (mtDNA) variant NC\_012920.1:m.3243A>G was detected in patient's urinary epithelial cell DNA sample (Royal Devon and Exeter NHS Foundation Trust, UK). The m.3243A>G mitochondrial variant is associated with MIDD (maternally inherited diabetes and deafness) and MELAS (mitochondrial encephalopathy, lactic acidosis and stroke-like episodes). The patient is correctly diagnosed with MIDD. Given her HbA1c of 41, diarrhoea and diagnosis of MIDD, metformin was stopped. She is appropriately screened for other associated conditions.

#### Discussion

- To identify patients with MIDD is challenging but important as therapy is different from individuals with type 1 and type 2 DM. Our patient and her brother were wrongly diagnosed as type 2 DM and type 1 DM respectively in this case. A very strong family history of DM and deafness should prompt an investigation for MIDD.
- It should be noted that Metformin, the most commonly used first-line medication for type 2 DM, may actually be harmful because of the increased risk of lactic acidosis in these individuals.
- There are many reported clinical manifestations of m.3243A>G mutation. Individuals who are correctly diagnosed will be screened for those manifestations.
- Genetic testing can be offered to maternal relatives and offspring.

DOI: 10.1530/endoabs.69.P35

### P36

#### Somatostatin analogue therapy in a patient with von Hippel-Lindau Disease and multiple pancreatic neuroendocrine tumours

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#### Case report

Von Hippel-Lindau Disease (VHL) is an autosomal-dominant disease with almost complete penetrance, characterized by the development of several types of neoplasia. Non-functioning pancreatic neuroendocrine tumours (pNETs) are part of the syndrome in up to 16% of the patients. A 36 year old female with a known diagnosis of VHL (Mutation exon 3) was under surveillance. She had previous surgeries twice for haemangioblastomas, and an adrenalectomy for pheochromocytoma with a stormy postoperative course.

#### Investigations

During her surveillance imaging, the MRI scan showed a mass in the tail of pancreas and a possible lesion within the pancreatic head. These lesions were not

consistent with either simple pancreatic cysts or serous cystadenomas and most likely represented neuroendocrine tumours. All the lesions were avid on Gallium DOTA-TATE imaging, confirming somatostatin receptor expression.

#### Treatment

She did not want to have surgery because of the recent adrenalectomy, a young child to look after and high risk of pancreatic insufficiency. She underwent a trial of primary somatostatin analogue (SSAs) therapy (lanreotide, Somatuline Autogel 90 mg monthly) which was well tolerated. After 6 months of treatment, reimagining demonstrated that all the pNETs were stable with no further progression.

#### Discussion

An important management consideration in VHL patients is their young age and potential of multifocal disease. The disease has slow progression but the malignant potential of this subgroup of pNETs is poorly characterised. Generally surgical intervention is done when the lesion exceeds 3 cm in the pancreatic body and 2 cm in the head, has doubling time <500 days or there is evidence of the regional disease. These criteria are based on limited retrospective data and have not been validated. Repeated pancreatic surgical intervention in such cases risks progressive parenchymal loss resulting in pancreatic insufficiency. Nearly 80% of non-functioning NETs express somatostatin receptors, making them a suitable target for therapy with somatostatin analogues. SSAs are now established treatment for advanced non-functioning enteropancreatic NETs. These drugs have shown to increase progression free survival. Evidence of the efficacy of SSAs in the context of pNETs in VHL is lacking. We report the use of SSA therapy for multiple pNETs in a patient with VHL and it has shown short-term radiological response. This requires confirmation in other patients and long-term response assessment. It raises the possibility of SSA use as an early strategy to delay the need for surgical intervention in VHL-related pNETs, thereby deferring, the associated risks of pancreatic insufficiency.

DOI: 10.1530/endoabs.69.P36

### P37

#### **Liquorice: a sweet root with a sour aftertaste: A case of pseudoaldosteronism, cardiomyopathy and an upper gastrointestinal bleed**

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#### Case history

73-year-old woman recently commenced on oral diuretics for peripheral oedema was admitted with severe hypokalaemia and refractory hypertension. Conn's syndrome was initially considered but admission of regular liquorice consumption made a diagnosis of hypokalaemic hypertension (pseudoaldosteronism) secondary to liquorice over-indulgence more likely. She went on to develop cardiomyopathy and had haematemesis from a bleeding duodenal ulcer (DU). Endocrine tests as an outpatient excluded Conn's syndrome.

#### Investigations

Following intravenous replacement for hypokalaemia (K+ 2.1) and hypomagnesaemia (Mg<sup>2+</sup> 0.50) on admission, Ms X became hyperkalaemic (K+ 6.1). An electrocardiogram (ECG) showed new widespread T-wave inversion and serial raised troponins (122, 101, 90). She developed fast AF and an echocardiogram showed reduced left ventricular (LV) function and regional akinesis which had spontaneously improved on a subsequent echocardiogram, consistent with Takutsu cardiomyopathy (TC). Ms X had an episode of coffee ground vomiting. Bloods showed haemoglobin had dropped to 6.7 and urea had risen to 30.2 (Glasgow-Blatchford score 14). Urgent oesophagogastroduodenoscopy (OGD) showed a DU with adherent clot over it; a repeat 5 days later showed no active bleeding. Endocrine tests as an outpatient excluded Conn's syndrome (aldosterone 131, renin 35.7).

#### Results and treatment

Ms X was provisionally treated as a NSTEMI with dual antiplatelets (aspirin & clopidogrel) given her raised troponins and ischaemic ECG at the time of her rebound hyperkalaemia. A repeat ECG showed fast AF, treated with bisoprolol and anticoagulation (apixaban). Antiplatelets were discontinued after TC confirmed on echocardiography due to their inefficacy in TC. Following her episode of haematemesis, Ms X was transfused and culprit blood-thinning medications were withheld. OGD showed DU with adherent clot. She was commenced on high-dose intravenous omeprazole before switching to oral. Anticoagulation was not reinstated given Ms X's excessive alcohol intake and high re-bleeding risk.

#### Conclusions and points for discussion

Liquorice-induced pseudoaldosteronism with cardiac muscle failure resembling dilated cardiomyopathy has been previously reported. The pattern of spontaneous improvement in LV function over time described was mirrored by Ms X but it is difficult to determine whether her TC reflected the cumulative effect of chronic liquorice use or was secondary to its withdrawal. The liquorice herb (*Glycyrrhiza glabra*) confers gastroprotective effects and has been used as an anti-ulcer drug. The withdrawal of liquorice from Ms X may have precipitated the development of a DU. However, bleeding from it was likely potentiated by concurrent use of antiplatelets/anticoagulants without acid suppression.

DOI: 10.1530/endoabs.69.P37

### P38

#### **Requirement of staged interventions in a complex case of Acromegaly and Obstructive Sleep Apnoea**

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#### Section 1: Case history

We present the case of a 35-year-old gentleman referred by his GP to Endocrinology clinic for loss of libido and testosterone deficiency. His co-morbidities included obesity (BMI 59 kg/m<sup>2</sup>), hypertension and obstructive sleep apnoea (OSA) requiring overnight continuous positive airways pressure (CPAP) therapy. Routine pituitary profile showed luteinising hormone 4.8 IU/l (1–8), testosterone 7.1 nmol/l (8–25), prolactin 232 mU/l (86–324) and, unexpectedly, insulin-like growth factor 1 (IGF-1) 123 nmol/l (13–50 age-adjusted). Subsequently, growth hormone secretion failed to suppress on 75 g oral glucose tolerance test, confirming acromegaly. Further focussed history revealed the patient had suffered headaches, palmar sweats, joint pains and increasing shoe size for about 2 years.

#### Section 2: Investigations

CT and MRI pituitary were inconclusive. Owing to anticipated anaesthetic risk, a long-acting somatostatin analogue (Lanreotide) was started. His symptoms improved but he continued to gain weight (BMI 62 kg/m<sup>2</sup>) and to suffer severe headaches. Serum IGF-1 had only reduced to 75 nmol/l, so further treatment was felt to be necessary.

#### Section 3: Results and treatment

The pituitary multidisciplinary team identified a possible neurosurgical target on the left of the pituitary but the patient's BMI was felt to be a serious contraindication. Furthermore, his CPAP requirement with full face mask presented a challenge for nasal packing after transsphenoidal surgery, with risks including pneumocephalus. The patient was referred instead for bariatric surgery to improve risk factors prior to neurosurgery. Sleeve gastrectomy led to 30 kg weight loss and he no longer required CPAP. 9 months later, at BMI 46 kg/m<sup>2</sup>, he underwent transsphenoidal resection of an 8 × 10 × 3 mm pituitary somatotroph adenoma and made an excellent post-operative recovery.

#### Section 4: Conclusions and points for discussion

This is a unique case of acromegaly complicated by OSA requiring MDT input and staged interventions i.e. medical therapy and bariatric surgery prior to neurosurgery. In the future, there is scope for further bariatric surgery.

DOI: 10.1530/endoabs.69.P38

### P39

#### **Primary hyperparathyroidism in pregnancy: Uncommon manifestation of significant weight loss**

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#### Section 1&2: Case history and investigations

Primary hyperparathyroidism is a rare condition in pregnancy. The occurrence rate is about 1 % and up to 80 % of the patients are asymptomatic. Clinical

symptoms are nonspecific. However, severe maternal, foetal and neonatal complications including neonatal death have been reported in literature. 27 years old Asian lady presented to Emergency Department with abdominal pain in July 2019. She was found to have raised calcium at level of 2.8 mmol/l (2.20– 2.60) with a phosphate level of 0.64 mmol/l (0.81–1.45). Adequate hydration was advised with a referral to endocrine outpatient clinic. She was next seen in obstetric clinic three months later with significant weight loss and persistent hyperemesis. She was 13 weeks pregnant at that time and also complained of abdominal discomfort. Her biochemical markers revealed raised calcium of 3.13 mmol/l with phosphate of 0.71 mmol/l. Her PTH was elevated 16.4 pmol/l (1.6–6.9), vitamin D 29 nmol/l and 24 h urine calcium creatinine ratio was 0.039. Parathyroid ultrasound showed right sided parathyroid adenoma. MRI neck as a confirmatory imaging further confirmed 4×6×20 mm right sided adenoma. Her renal and thyroid functions were normal.

#### Section 3: Results and treatment

Despite of adequate hydration her serum calcium remained persistently raised above 3.00 mmol/l therefore she underwent parathyroid surgery during the second trimester at 22 weeks. Her calcium levels completely normalised post operatively 2.24 mmol/l with normalising PTH 0.4 pmol/l. Histology confirmed benign parathyroid adenoma. There have been no operative, maternal or foetal complications. She is currently 30 weeks into pregnancy and will be followed up next in the endocrine clinic for MEN genetic testing.

#### Section 4: Conclusion

Symptoms of primary hyperparathyroidism can often occur in normal pregnancy which can lead to diagnostic challenges. Severe maternal complications like hypercalcaemic crisis, pre-eclampsia, nephrolithiasis, pancreatitis, hyperemesis gravidarum might be the first manifestation of primary hyperparathyroidism and its prevalence can be as high as 67% in untreated cases. Weight loss is a rare first manifestation and reported only in few cases in literature so far.

DOI: 10.1530/endoabs.69.P39

## P40

### The great masquerader-Phaeochromocytoma presenting as ST elevation Acute Coronary Syndrome

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#### Case history

A 75-year-old lady presented with sudden central chest discomfort to Emergency Department. The chest pain was preceded by palpitations. She had a background of Hypertension. She was non-smoker and otherwise fit and well. She mentioned receiving a steroid injection one day ago for joint pain. Her B.P on presentation was 226/106. Her physical examination was otherwise normal.

#### Investigations

Her ECG on admission revealed atrial tachycardia and ST depression in anterior chest leads. She was admitted under cardiology team who started her on beta blockade for atrial tachycardia. CT aortogram was organised to rule out aortic dissection. Aortic dissection and large pulmonary embolism were ruled out by CT but an incidental complex cystic abnormality was seen behind the stomach which was deemed unrelated to her condition at the time. Her lab Troponin levels were 270 (on admission), 1877 (5 h), 2462 (7 h post admission). Her Echo revealed severely reduced Ejection fraction 35% and inferolateral hypokinesia. Her chest pain continued and she then developed new ST elevation 3 h post admission. At this point, she was started on ACS treatment and taken to cath lab for PCI. On angiography, no blockade amenable to PCI was found so no procedure could be performed. Patient then developed severe pulmonary edema post PCI and needed CPAP. Cardiology team considered phaeochromocytoma as cause of patient's symptoms (in view of cystic mass found on CT) and endocrinology review was sought.

#### Results and treatment

CT abdomen and 3 collections for urinary catecholamine metabolites levels were performed on endocrinology advice.

CT abdomen revealed 5 cm part-solid, part-cystic mass.

Urinary Levels were as below:

– Urinary metadrenalines 34.61

– Nor-metadrenalines 33.15

– 3 methoxy tyramine urinary: 3.15

Based on above results, she was diagnosed with Phaeochromocytoma.

Patient was referred to tertiary endocrine surgical centre for surgery. She underwent removal of a left adrenal phaeochromocytoma 3 months later. Her

PASS score was 6/20, indicating borderline phaeochromocytoma with potential for recurrence. Her genetic analysis did not reveal any phaeochromocytoma/paraganglioma susceptibility gene.

#### Conclusion and points for discussion

This was a challenging case as initial presentation matched acute coronary syndrome and beta blockade was started which likely led to pulmonary edema and worsening of symptoms. It should be borne in mind that Phaeochromocytoma can present as acute coronary syndrome and should be considered among differentials in unexplained acute coronary syndrome. The possibility of recent intra-articular steroids injection in precipitating phaeochromocytoma crisis should be considered.

DOI: 10.1530/endoabs.69.P40

## P41

### Metastatic phaeochromocytoma and catecholamine-induced cardiomyopathy

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#### Case history

A previously asymptomatic 58-year-old gentleman presented following an out-of-hospital cardiac arrest, precipitated by multiple, bilateral pulmonary emboli.

#### Investigations

In the course of investigation, a 35 mm, MIBG-negative, right adrenal lesion was discovered. Functional adrenal tests revealed significantly elevated normetanephrine and 3-methoxytyramine levels. Severe hypertension and type 2 diabetes were concurrently diagnosed.

#### Results and treatment

Histology confirmed a phaeochromocytoma and a marked improvement in normetanephrine levels, glycaemic control and blood pressure followed surgical resection. Four months later, biochemical tests revealed disease recurrence. Echocardiography showed moderate LV systolic dysfunction and high pulmonary artery systolic pressures, but there were no signs of fluid overload. Liver, perineal and rib metastases subsequently developed, and cardiac function continued to deteriorate, precipitating admission with acute, decompensated heart failure. Cardiac MRI showed a dilated LV with severe systolic dysfunction, LVEF of 19% and RV systolic dysfunction. MRI appearances were typical of myocardial fibrosis. Alpha-blockade was commenced and titrated against decreasing diuretic requirement and anti-failure medications. This allowed commencement of Temozolomide and external beam radiotherapy. As shown in the table below,

Table 1

Date	Normetanephrine (<1180 pmol/l)	3-Methoxytyramine (<180 pmol/l)	Clinical Event
09.07.19	13 138.0	314.9	LVEF 33%
03.07.19	13 506.0	232.6	
27.02.19	16 836.0	327.2	
22.02.19	18 840.0	116.3	
19.10.18			External Beam Radiotherapy Completed
10.10.18			Completed Temozolomide X 6
04.05.18			Commenced Temozolomide
10.02.18	115 697.2		LVEF 19%
Alpha-blockade commenced			
17.05.17	18 345.0		
20.03.16	3367.6		Liver metastases
25.07.15	726.3		
17.08.14	418.3		13 weeks post-operatively
03.07.14	13 461.0		Diagnosis

commencement of alpha-blockade and subsequent chemotherapy and radiotherapy translated into an improvement in cardiac status. There was a fall in LV size and LVEF improved to 33%. A significant fall in RV size and normalisation of RV systolic function from 28 to 56% was also observed. These changes accompanied a reduction in late gadolinium enhancement and resolution of pleural effusions (Table 1).

Conclusions and points for discussion

The potential reversibility of cardiac remodeling in catecholamine-induced cardiomyopathy (CIM) highlights the importance of a prompt diagnosis. CIM is characteristically associated with a poor prognosis, caused by excessive adrenergic stimulation resulting in vasoconstriction, vasospasm, myocardial ischemia and necrosis. This case highlights the physiological benefit of alpha-blockade, in addition to lowering the catecholamine burden. We have demonstrated that alpha-blockade is important in normalising cardiac physiology, irrespective of whether this is given alone or in conjunction with systemic oncological treatment. This case also demonstrates the prognostic benefit of chemotherapy and radiotherapy even when complete biochemical normalisation of catecholamines is not attained.

DOI: 10.1530/endoabs.69.P41

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## P42

### Urinary retention causing severe hyponatremia, an association often missed

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#### History

A 54 years old gentleman was admitted to the hospital after being found unconscious at home by his wife with a tongue bite and urinary incontinence. He had perineal approach biopsy 2 days ago for prostate cancer. Since biopsy, he had poor urine output with clots and dribbling. He also gave 2 days history of constipation. Wife was a doctor and mentioned that she palpated a distended bladder the night before. On examination, he was haemodynamically stable although he did have a palpable and tender bladder. He was confused and lethargic but no focal neurological deficit.

#### Investigations and treatment

His sodium on admission was 100 mmol/l on arterial blood gas and 109 mmol/l on the lab result. Serum osmolality at that point was 233 mOsmol/kg. He was given 250 ml of 1.8% hypertonic saline over 20 min but sodium remained 100 mmol/l on repeat blood gas and 109 mmol/l on the lab report. He was catheterized and drained 1.5 l of urine. His sodium came up to 113 mmol/l over the next 5 h. He was then given maintenance 0.9% normal saline 50 ml/h. His sodium steadily increased to 122 mmol/l over 10 h and then to 126 mmol/l in 21 h.

#### Results

Admission bloods showed urea 6.8 mmol/l, creatinine 158 µmol/l, eGFR 40. Repeat bloods post catheterization at 2 h improved to urea 5.6 mmol/l, creatinine 106 µmol/l, eGFR 63 in keeping with resolved obstructive uropathy. Paired serum and urine osmolalities and urine sodium were not sent until 10 h after admission. Patient had already received treatment with hypertonic saline and drained 1500 ml of urine. Results showed serum osmolality 253 mOsmol/kg, urine osmolality 229 mOsmol/kg, urinary sodium <10 mmol/l, normal cortisol and thyroid function tests. CT head was also reported normal.

#### Conclusion and points for discussion

Urinary retention is one of the unrecognized causes of hyponatremia. The mechanism is mainly due to stretching the bladder wall causing activation of

sympathetic nervous system and inappropriate release of ADH hormone. In our case, the patient initially did not respond to hypertonic saline but sodium went up quickly after bladder catheterization. Fortunately, rapid sodium rise did not cause him any complications. Treating physicians should be aware of this association and the quick sodium rise following catheterization and be ready to do interventions as appropriate.

DOI: 10.1530/endoabs.69.P42

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## P43

### Case report: Dramatic improvement in severely constricted visual fields within days of bromocriptine treatment in a patient with giant prolactinoma

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#### Section 1: Case history

A 38 year old man with no significant past medical history presented to the emergency department with a sudden onset, severe frontal headache. He had been experiencing peripheral visual disturbance for six days prior to this. Routine observations including blood pressure were normal on arrival. Neurological examination of the upper and lower limbs revealed no abnormalities. Bedside visual field test demonstrated significant loss of peripheral vision bilaterally. There were no other cranial nerve abnormalities on examination.

#### Section 2: Investigations

A CT scan of the head done in the emergency department did not show any acute haemorrhage but demonstrated a heterogenous soft tissue density within the pituitary fossa extending to the suprasellar region measuring 1.6×3.8×1.3 cm. Subsequent MRI of the head confirmed the presence of a large pituitary tumour extending superiorly compressing the optic chiasm and laterally into cavernous sinuses encasing both internal carotid arteries. The appearances were in-keeping with a locally aggressive pituitary macroadenoma. Laboratory tests showed a prolactin level of 185 537 mIU/l (0–350), confirming the diagnosis of macroprolactinoma. Assessment of visual fields showed severe bilateral deficits with constricted peripheral vision.

#### Section 3: Results and treatment

In view of severely constricted visual fields secondary to a large prolactinoma, the options were either to start dopamine agonist therapy to shrink the prolactinoma or to consider pituitary surgery to decompress the optic chiasm. The risk of CSF leak with rapid shrinkage in prolactinomas with medical treatment was also carefully considered. After a multidisciplinary approach involving neurosurgery, endocrinology and ophthalmology teams, the patient was started on bromocriptine at an initial dose of 2.5 mg daily. He experienced a rapid improvement in his visual symptoms within a week of starting bromocriptine. Repeat visual field testing demonstrated significant improvement in his vision. He was discharged home with an urgent follow up in the joint endocrinology-neurosurgery clinic.

#### Section 4: Conclusions and points for discussion

Giant prolactinomas are rare, making up 2–3% of all prolactin producing tumours. They are more common in men than in women. First line treatment is medical management with dopamine agonist therapy. This treatment can induce rapid resolution of neuro-ophthalmological symptoms within days of initiating treatment, as demonstrated in our patient within a week. Prior to initiation of medical treatment, the risk of CSF leak with rapid shrinkage in aggressive prolactinomas needs to be considered although it is rare.

DOI: 10.1530/endoabs.69.P43



**P44****Lymphocytic Hypophysitis and Pituitary Adenoma – The diagnostic conundrum and how differentiating between the two masquerading entities forms a pivotal role in management**Ashutosh Kapoor<sup>1</sup>, Ambar Basu<sup>1,2</sup> & Aye Aye Thant<sup>1</sup><sup>1</sup>Royal Bolton Hospital, Bolton NHS Foundation Trust, Bolton, UK;<sup>2</sup>University of Bolton, Bolton, UK**Introduction**

Lymphocytic Hypophysitis (LH) is an autoimmune endocrinopathy characterised by extensive infiltration of the anterior pituitary gland with chronic inflammatory cells, thus causing pituitary expansion and a variable degree of hypopituitarism closely mimicking the features noted in pituitary adenoma and seen most frequently in women. The aetiology has a general preponderance of occurring at the end of gestation or during the early postpartum period.

**Case history and investigations**

We report a case of a 49 year female, with a background of Hypertension (HTN), Asthma and Gastric Reflux, who presented to our Endocrine Clinic with a 4 to 5-year history of lethargy, headaches, menstrual irregularities and gradual weight gain accompanied with intermittent visual blurring.

Blood Pressure 178/108 mm Hg.

Bloods-TSH-3.26 mu/l (0.2–5.0), Free T4 – 8.1 pmol/l (10–24), T3 – 1.3 nmol/l (1.3–3.1) FSH – 0.88 u/l, LH – <0.50 u/l, Serum Oestradiol – 17 Beta – 28 pmol/l, Prolactin – 882 mu/l (150–812)

Coeliac Screen – Negative

Renal functions, Electrolytes- Historically Normal

On the basis of the Biochemical results and clinical symptoms, a baseline Visual field assessment from Ophthalmology and MRI were requested. Visual assessment conducted by ophthalmology revealed bilateral visual acuity to be 6/9, with no remarkable findings or changes in the Optic Discs. MRI reported as findings consistent with Lymphocytic Hypophysitis with the differential diagnosis of Pituitary Adenoma being less likely based on MRI criteria.

**Results and treatment**

Taking into account the findings, this case was brought forth and discussed in our Endocrine MDT with joint input from the Radiology, Surgical and Endocrine teams. The likely diagnosis of Lymphocytic Hypophysitis was confirmed. A Short Synacthen test is being organised for the patient, depending on the results of which, Hormone replacement (Steroid replacement first) +/- implementation of immunosuppressive therapy would be given careful consideration.

**Conclusion and points for discussion**

Lymphocytic Hypophysitis displays a close association to pregnancy, approximately 70% of cases in women presenting during pregnancy or postpartum, which makes this case extremely unique in nature. Understanding and differentiating the Radiological manifestations of Lymphocytic Hypophysitis (LH) and Pituitary Adenoma on the basis of MRI criteria is of paramount importance, since the management plans vary based on the underlying aetiology. This case brings to the forefront that LH is not isolated solely to the pregnant or peri-partum population and the importance of MRI criteria used to differentiate between LH and Pituitary Adenoma. Due to the complexity in diagnosis and differentiation, discussion in a MDT setting is highly recommended.

DOI: 10.1530/endoabs.69.P44

**P45****Chronic urticaria as a rare presentation of primary hyperparathyroidism**

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James Clark &amp; Sunil Zachariah

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**Case history**

We present a 44 year old female with persistent severe burning itchy rash over the face, scalp and upper body for ten months. She was reviewed in multiple dermatology clinics and a diagnosis of chronic urticaria was made. Despite various treatments including antihistamines and steroids, symptoms persisted affecting her quality of life significantly.

**Investigations and diagnosis**

Routine blood investigations revealed mild persistent elevated calcium up to 2.75 mmol/l (NR: 2.15–2.55) and she was referred to the Endocrine clinic. Further investigations showed inappropriately normal parathyroid hormone level of

5.6 pmol/l (NR: 1.6–6.9). 24 h urinary calcium was elevated 8.05 mmol/24 h (NR: 2.5–7.5). Serum electrophoresis, ACE, LDH and immunoglobulins were within normal limits. Sestamibi scan was negative for parathyroid adenoma. US parathyroids revealed right inferior parathyroid adenoma. She underwent parathyroidectomy followed by immediate resolution of symptoms. Histology confirmed parathyroid adenoma. She continued to remain symptom free when reviewed in clinic six weeks later.

**Conclusion and points for discussion**

Primary hyperparathyroidism is a rare cause of chronic refractory urticaria. Literature review shows less than six reported cases so far. Antibodies to calcium sensing receptor genes might be postulated in some cases. IgE receptor antibodies may also play a role, although there is no clear evidence linking these autoimmune mechanisms or autoantibodies to primary hyperparathyroidism. In conclusion, it is worth checking serum calcium and parathyroid hormone levels as part of work-up for refractory urticaria.

DOI: 10.1530/endoabs.69.P45

**P46****Diabetic neuropathic cachexia**

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**Case**

55 year old male presented with severe sharp and burning pain at anterior aspect of both legs (radiating from groin to feet), worse at night, unable to keep bed sheets lying on legs due to pain (allodynia). Patient reported weight loss of 3 stones in last 1 year including a recent 1 stone weight loss in 2 months. Patient is a type II DM for the last 3 years. He was intolerant to Metformin and is on Gliclazide 160 mg BD. Alcohol intake around 40 units per week. Initial investigations revealed poorly controlled diabetes with ketonuria and glycosuria and HbA1c 116 and Hyponatremia Na 126. Patient was started on basal bolus insulin, dietician review and optimization of Insulin and adequate pain control. After initial presentation, patient had several readmissions with symptoms of significant postural drop, ongoing weight loss leading to cachexia and ultimately bed bound along with significant hyponatremia

**Investigations**

Cortisol = 215(1048 h)

Short Synacthen Test 00 min = 102

60 min = 550

CTCAP: Bilateral lower paratracheal and right hilar lymph nodes of unclear significance.

Neurology review: Lumbar puncture and immunological tests: No evidence of paraneoplastic syndrome.

Nerve conduction studies: Sensory motor polyneuropathy->axonal type.

Lumbosacral MRI-> Normal

PET scan->FDG avid lymph nodes

EBUS guided lymph nodes biopsy->negative

Further PET scan->reduction in size of lymph nodes

Further interval CT scan->resolution of the lymph nodes

Autonomic tests at NHNNà Normal

**Results and treatment**

Patient HbA1c improved to 68 mmol/mol with insulin and diet optimization.

Marked improvement in symptoms over next 7–8 months.

Weight slowly came up by 4 stones.

Postural symptoms resolved. Urinary catheter removed.

Sharp leg pains completely settled.

Has some difficulty in getting up from sitting but mobile with no support.

**Conclusion and point of discussion****Learning points:**

- A case of dramatic deterioration in a diabetic patient with severe weight loss and neuropathy à eventual spontaneous and marked recovery
- Clinical picture fits with the rare syndrome of 'Diabetic neuropathic cachexia'
- Typically Men with T2 DM in 6th/7th decade life
- Severe rapid symptoms, Anorexia, marked weight loss, Bilateral painful neuropathy often with allodynia, Emotional disturbance, autonomic dysfunction
- Spontaneous recovery over months
- Retinopathy and nephropathy are usually absent
- Pathophysiological basis remains unknown
- Having knowledge of this syndrome, we can optimistically predict recovery.

Question for discussion:

- How far should we have investigated for weight loss? Was PET scan appropriate?
- Do we agree with the final diagnosis? OR is there an alternative more appropriate diagnosis

DOI: 10.1530/endoabs.69.P46

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### P47

#### Fact or fiction? A discussion on the subject of Hashimoto's Encephalopathy and presentation of a case study

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#### Case history

A 35-year-old female presented to a district general hospital with convulsive status epilepticus. In the two weeks preceding the seizure, she complained of migrainous-type headaches, transient aphasia and ataxia. Her general practitioner organised a confusion screen, revealing hypothyroidism and commenced levothyroxine 50 µg. She had no other medical history and denied illicit drug use or alcohol-excess. Examination revealed mild pyrexia (38.2°C), clonus and brisk reflexes. Following termination of seizures, the patient was intubated.

#### Investigations

Admission bloods and arterial gases found no abnormality other than raised c-reactive protein (35.1 mg/l). Chest X-ray, CT head and MRI head/neck were reported normal. Lumbar puncture found normal opening pressure, clear fluid and high-normal protein on analysis with negative viral polymerase-chain-reaction studies. Further bloods on day two revealed hypothyroidism (thyroid stimulating hormone 13.2 mU/l, free-thyroxine 13.8 pmol/l), low vitamin-B12 (129.0 ng/l) and low folate (3.0 µg/l). Complement and auto-antibody screen found anti-thyroid peroxidase levels of 1130.0 IU/l.

#### Treatment

Prior to cerebro-spinal fluid (CSF) analysis, the patient received 24 h of intravenous aciclovir. On ITU, her condition rapidly improved and she was extubated just 40 h post-intubation. A diagnosis of Hashimoto's Encephalopathy (HE) was suspected by neurologists and levothyroxine was increased to 100 µg. Following extubation, intravenous co-amoxiclav was commenced for aspiration pneumonia and hydroxocobalamin was administered. On day three, she was remarkably well and discharged home.

#### Conclusions

Brain *et al.* [1] first described HE in 1966 following a case of neuropsychiatric impairment in a middle-aged man with Hashimoto's thyroiditis. Since then, there have been over 100 published case studies [2]; although pathophysiology of the condition is still poorly understood. HE is a rare diagnosis, predominantly affecting middle-aged women with a sub-acute onset over weeks [3]. A 2011 systematic review of reported cases found seizures (60%), myoclonus (65%), transient aphasia (80%) and ataxia (65%) were the most common presentations of the disease [2]. The diagnosis is one of exclusion in addition to some key diagnostic features including high titres of anti-thyroid antibodies in serum/CSF, encephalopathy and rapid response to steroids [4]. However, spontaneous recovery has been reported in over ten cases [2]. We explore the controversies surrounding a diagnosis of HE, draw parallels and review differences in our case study compared to the current literature and discuss key learning points.

DOI: 10.1530/endoabs.69.P47

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### P48

#### Metabolic bone disease as presentation for primary hyperparathyroidism

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#### Case history

A 74-year old gentleman was referred from Urology clinic for hypercalcemia after being treated for left vesico-ureteric calculus causing mild hydronephrosis. Past medical history included asthma, eczema and hypertension. He had been taking calcium supplements for 5 years, but stopped 2 months prior to clinic. He was asymptomatic and quite well with no recent fracture.

#### Investigations

Adjusted Ca ranged from 2.62 to 2.78 mmol/l, PTH from 2.6 to 9.5 pmol/l, ALP from 250 to 394 u/l. LFTs including GGT were normal. Vitamin D was depleted at 40 nmol/l. 24 h urinary Ca was high at 15.7 mmol/d. Serum electrophoresis & urine Bence Jones protein were negative. PSA was normal at 3.9 mcg/l. ALP isoenzymes were raised for bone isoenzymes. Radionuclide bone whole body scan showed superscan result. ALP was consistently getting higher and these results with the bone scan were concerning for malignancy.

#### Results and treatment

He was proceeded to bone marrow biopsy, which showed increased osteoclastic activity & suggestive of hyperparathyroidism or ectopic hormone production. Next step was CT(TAP) to exclude malignancy and it only showed inflammatory changes in lingular nodes, but nil other significant findings. Serum ACE level was normal. PTHrP level was undetectable. Sestamibi scan did not localise parathyroid adenoma. USG (neck) showed no abnormalities. DEXA showed osteoporosis. Bone histopathology report was suggestive of hyperparathyroidism. ALP was elevated to 1747 u/l at this point. Bone turnover markers were significantly raised (P1NP 3489 µg/l & CTX 2.17 H µg/l). He was treated with zoledronic infusion and improved markedly after 3 lots of treatment. All investigations point towards metabolic bone disease with increased bone turn over and high urinary calcium probably primary hyperparathyroidism. MDT decision was to proceed with neck exploration. Biopsy confirmed parathyroid adenoma. Bone turnover markers improved significantly and have normalised after surgery (P1NP 53 µg/l, CTX 0.49 H µg/l). Post-surgery ALP 80 u/l, adjusted Ca 2.46 mmol/l and PTH 3.7 pmol/l. He is waiting for a repeat radionuclide scan.

#### Conclusions and discussion points

This case demonstrates that primary hyperparathyroidism can present with the form of metabolic bone disease despite fairly normal calcium and PTH levels with negative localisation scans. Differentials to be considered for 'superscan' include metabolic bone disease, disseminated malignancy & haematological disorder. MDT approach is vital in managing such cases. This patient has a remission after surgery even with negative sestamibi scan.

DOI: 10.1530/endoabs.69.P48

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### P49

#### Amiodarone induced thyrotoxicosis presenting as significant heart failure

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#### Case presentation

A 66 year old male presented to the clinical physiology department for a routine ECHO. He was found to be hemodynamically unstable with fast Atrial fibrillation and was referred to ED for immediate management. He was subsequently admitted in CCU under Cardiology. He presented with a 3 month history of shortness of breath, palpitations, persistent tremors, unintentional weight loss and generalised fatigue. No previous thyroid problems. He had a longstanding history of dilated cardiomyopathy and uncontrolled atrial fibrillation and was awaiting ablation. He had underwent 3 unsuccessful cardioversions previously. He was on Amiodarone which was stopped 8 months ago. His LVEF on admission to CCU was < 20%. On examination, he had a small firm goitre, fine tremors and mild ankle oedema.

#### Investigations

Serum TSH – 0.01 µU/l [0.3–4.2]

Serum free T3 – 25.4 pmol/l [3.1 – 6.8]

Serum free T4 – >100 pmol/l [12 – 22]

Thyroid stimulating Immunoglobulins and Thyroid Peroxidase Antibodies – negative

#### Ultrasound thyroid

The thyroid gland appeared diffusely enlarged and hypoechoic in keeping with chronic thyroiditis. Tiny colloid cyst in the right lobe of the thyroid. No solid nodules identified

#### Treatment

While the patient was in CCU, an endocrine referral was sought. He was started on Carbimazole 60 mg OD and PTU 100 mg TDS. As it was unclear if this was Amiodarone induced type 1 or 2 thyrotoxicosis, the case was discussed with tertiary care centre and it was decided to start Dexamethasone 0.5 mg BD with a subsequent thyroidectomy when thyroid levels settled. In the following weeks the patient was reviewed in the endocrine clinic and had a marked improvement in his symptoms and TFT's. Furthermore, the LVEF significantly improved to >40%. The Dexamethasone and Carbimazole were gradually tapered and stopped

completely. An outpatient cardioversion is planned by cardiologists. Due to his marked improvement it was decided not to proceed with thyroidectomy.

Conclusion and points for discussion

AIT is a condition which when diagnosed correctly responds rapidly to treatment. Despite this it still presents as a challenge to clinicians for proper diagnosis and differentiation between type 1 and type 2 AIT. Thionamides represent the first-line treatment for type 1 AIT. Type 2 AIT is best treated by oral glucocorticoids. The response very much depends on the thyroid volume and the severity of thyrotoxicosis. Mixed/indefinite forms may require a combination of thionamides, potassium perchlorate, and steroids.

DOI: 10.1530/endoabs.69.P49

## P50

### Pregnancy against the odds

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A 17-year-old young lady presented with tiredness, weight loss, palpitations, hot flushes and irregular menstruation in April 2016 and her initial TFTs showed TSH <0.03 mU/l with a fT4 of 48.2 pmol/l. She was treated with carbimazole 40 mg daily and further investigation confirmed she had Graves' disease as TSH receptor antibodies (2.10 U/l), TPO antibodies (>1300 IU/ml), thyroid ultrasound scan demonstrated mildly enlarged and thyroiditis. She had only six periods between October 2015 and September 2016 and was having hot flushes and night sweats despite her Graves' disease improving biochemically. Therefore, sex hormones were screened to rule out premature ovarian failure. LH raised at 72.8 U/l, FSH raised at 129.7 U/l, with Oestradiol <90 pmol/l, SHBG 89 nmol/l and negative ovarian antibody. She was diagnosed as likely autoimmune ovarian insufficiency with a low egg count. She would have only a 5% to 15% chance of getting pregnant. Ultrasound scan of the pelvis done for abdominal discomfort showed small quiescent ovaries and normal uterus. HRT (Femoston 2/10) was commenced. Her Graves' disease went into remission (TSH 0.73 mU/l, fT4 16.9 pmol/l, fT3 5 pmol/l) after 12 months and carbimazole was stopped in March 2017. Unfortunately, her Graves' disease relapsed in July 2017 (fT4 65 pmol, TSH < 0.03 mU/l, fT3 >30.8 pmol/l) and carbimazole 40 mg re-commenced. Secondary treatment such as radioiodine and surgery were discussed but she was not very keen those options as she was concerned, they would affect her fertility. In November 2017, Carbimazole was increased to 60 mg as her fT4 was 50 pmol/l, TSH <0.03 mU/l. When this did not produce an improvement, she was switched to Propylthiouracil 400 mg. In January 2018, as her thyrotoxicosis improved, PTU was reduced to 150 mg BD with TSH < 0.03 mU/l, fT4 11.5 pmol/l. In April 2018, she was well from a thyroid point of view and gradually reducing PTU doses to 100 mg AM and 50 mg PM. An ultrasound pelvis scan was organized to investigate lower abdominal pain during that visit and it revealed a 5 weeks gestation pregnancy. She delivered a baby uneventfully and her Graves' disease was stable during pregnancy.

Discussion

Treatment with HRT for premature ovarian failure and good control of her Graves' disease with PTU, provided the correct environment for a much longed-for pregnancy against the odds.

DOI: 10.1530/endoabs.69.P50

## P51

### Incidental diagnosis of Bilateral Adrenal Myelolipomas in a patient with Congenital Adrenal Hyperplasia results in enhanced adherence to treatment, with limited evidence to guide management

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Introduction

Adrenal myelolipomas are rare benign tumours consisting of fat and haematopoietic elements. We present an adult male patient with congenital

adrenal hyperplasia (CAH) with an incidental diagnosis of bilateral adrenal myelolipomas, resulting in an improvement in adherence to treatment, but uncertainty regarding his future management.

Case history

53 year old man with known CAH was referred into the endocrine clinic, historically requiring large doses of fludrocortisone and hydrocortisone. Following an admission with adrenal crisis and acute kidney injury, an abnormal renal tract ultrasound scan (USS) result (Jan 2018) prompted a follow-up CT scan (Mar 2018). This showed incidental findings of bilateral adrenal myelolipomas, 3.6 cm (right) and 9–10 cm (left). It was decided to monitor the myelolipomas annually using ultrasound imaging rather than CT, as the larger tumour could be visualised by USS and this would limit radiation exposure. Compliance with his prescribed medication was encouraged, in the hope that this might reduce the risk of the myelolipomas getting bigger.

Investigation results

The results summarised in the Table (1) evidence enhanced adherence to treatment following the abnormal USS and CT imaging results (January and March 2018). However, his most recent USS (December 2019) suggests a slight increase in the size of the myelolipoma on the left to 12 cm.

**Table 1** Evidence of enhanced adherence to treatment following the abnormal USS and CT imaging results (January and March 2018).

Date	Renin (mcg)	Potassium	Fludrocortisone dose	Hydrocortisone dose (mg)
May 2017	3340	4.9	200 increased to 300	20 plus 10
April 2018	445	4.0	300	20 plus 10
Oct 2018	53	3.1	Reduced to 200	Reduced to 15 plus 5
Nov 2019	36.6	3.3	Reduced to 100	15 plus 5

(Reference ranges: Renin: Erect 5.4–60 mU/l, Supine 5.4–30 mU/l; Potassium: 3.5–5.1 mmol/l)

Conclusion and points for discussion

The diagnosis of adrenal myelolipomas in this case was based on the characteristic imaging appearance in the context of adult CAH. Since the diagnosis, our patient's compliance with his medication has improved, but despite this there is evidence of slow growth of the myelolipoma with time. The evidence base to guide the management of adrenal myelolipomas is limited and based on case reports and opinion. Usually adrenal myelolipomas can be followed without surgical excision. There are no reports of malignant change. However there are reports of spontaneous rupture and haemorrhage, and the risks may increase with the size of the tumour.

DOI: 10.1530/endoabs.69.P51

## P52

### Hypercalcemia of advanced chronic liver disease: a forgotten clinical entity!

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Case history

A 67 year-old male was referred from GP to Endocrine clinic due to incidental high Calcium level in a routine bone profile. Adjusted Serum Calcium was 2.69 mmol/l. In Endocrine clinic, a detailed history was taken. The patient denied all symptoms of hypercalcemia.

Past medical history

Alcohol-related cirrhosis (complicated with Varices banded by OGD), Diverticular disease, Type 2 diabetes mellitus, Hypertension, Hyperlipidemia.

Alcohol history: one to two bottles of wine per day for five years

Family history: no family history of known hypercalcaemia

Medications: Hydrochlorothiazide-Metformin.

On examination: BMI 36. BP 170/80. No lymphadenopathy. Heart/chest normal. Mild Hepatomegaly. Tinge Jaundice.

#### Investigations

The aim of investigations was:

1. Confirm Hypercalcaemia (Adjusted to Albumin)
2. Determine the mechanism (PTH dependent or independent)
3. Seek underlying illness/cause (CXR, FBC, ESR, liver and kidney functions, electrolytes, TFT, myeloma screen, Vitamin D, serum cortisol, CT chest/abdomen/pelvic, ACE level)
4. To Determine end-organ damage (24 h urine calcium, urine creatinine, renal US)

#### Results and treatment

Adjusted Calcium: 2.69 mmol/l – PTH: <1 – Phosphate: 0.83 – Alkaline Phosphatase: 82 – Calcium/I (urine): 7.4 mmol/l – Fractional excretion of Calcium: 0.016 mol/mol – Creatinine/I (urine): 12.4 mmol/l  
Gamma GT: 234 – ALT 200 – Bilirubin 70  
Serum Mg: 0.50 mmol/l

• And ALL the following tests were within normal range:

1. Kidney function Tests-Sodium and Potassium
2. FBC– ESR
3. Immunoglobulin assay
4. Urinary Metanephrines
5. Autoimmune screen
6. Vitamin D 1.25 and 25Oh Vitamin D
7. Thyroid function and cortisol
8. Tumor markers
9. HBA1C
10. Insulin Like G.FI
11. Vitamin A

CT Chest–Abdomen–pelvis: No Malignancy-cirrhosis- Portal hypertension

Gastroscopy: Esophageal Varices

Skeletal Survey: Normal

The first impression was this hypercalcaemia is likely related to thiazide diuretics. Hydrochlorothiazide stopped then adjusted calcium level repeated afterwards and was higher (2.71 mmol/l). Despite extensive evaluation, no cause for hypercalcaemia was identified. **This was a PTH-independent hypercalcaemia** with normal vitamin D metabolites. He was ambulatory. He had not used vitamin A supplementation, lithium or antacids. He was managed with fluids and cut off alcohol drink and no specific medication was given for hypercalcaemia. His ionized Calcium levels returned back to normal limits.

Conclusions and points for discussion

Hypercalcaemia with CLD is a diagnosis of exclusion. Hypercalcaemia is more reported with CLD with hepatic neoplasm but less reported in absence of neoplasm. 2 points for discussion:

- 1) Mechanism of Hypercalcaemia in CLD
- 2) Relation between the etiology of CLD and Hypercalcaemia (e.g., Alcoholic, NASH, Viral hepatitis, Neoplasm)

DOI: 10.1530/endoabs.69.P52

#### P53

##### **Hyperparathyroidism and severe vitamin D deficiency: a bone breaking combination**

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#### Case history

A 43-year-old Syrian woman presented with severe right thigh pain following a fall from standing height. Progressive hip and back pain in the preceding 18 months resulted in her mobilizing with crutches. Past medical history included a reported bony tumour resected from her wrist three years earlier, clavicle fracture and previous renal calculi. She took no regular medications.

#### Investigations

Pelvic radiograph showed a right proximal femoral shaft fracture, with appearances of a surrounding lytic lesion. CT body demonstrated a 10 cm pelvic soft tissue mass centered around the right ileum extending towards the acetabulum, soft tissue deposits in the pubic rami bilaterally and left iliac crest, and sclerotic and lytic areas in the sternum. Serum adjusted calcium was elevated 2.74 mmol/l (2.15–2.5), and rose to a peak of 3.0 mmol/l during her admission. The working diagnosis was malignancy with pathological fracture. PTH was unexpectedly elevated 88.4 pmol/l (1.6–6.9), 25-hydroxyvitamin D <8 nmol/l (50–120), creatinine 37 mmol/l (45–90) and eGFR>60 ml/min/1.73 m<sup>2</sup>. Histology from a CT guided biopsy of the iliac lesion showed a benign primary bone

lesion with presence of osteoclast-like giant cells, suggestive of osteitis fibrosa cystica (Brown's tumour). Parathyroid ultrasound and MIBI scan confirmed a left inferior parathyroid adenoma. The diagnosis of primary hyperparathyroidism with secondary osteitis fibrosa cystica was made.

#### Results and treatment

She underwent fixation of the fracture under the orthopaedic team, followed by a left inferior parathyroidectomy. Intraoperatively, PTH fell from 36.4 pmol/l to 4.5 pmol/l and histology revealed an enlarged parathyroid (4×1.5×1 cm) with no atypia. Pre-operatively she was hydrated and given vitamin D replacement. She developed hypocalcaemia (adjusted calcium 2.10 mmol/l) six days post-operatively, at which point started oral calcium replacement. She underwent rehabilitation and was subsequently discharged with a normal calcium.

#### Conclusions and points for discussion

This case demonstrates the consequences of unregulated osteoclast activity secondary to untreated hyperparathyroidism. The considerably elevated PTH was likely attributable to both primary hyperparathyroidism due to parathyroid adenoma, and secondary hyperparathyroidism due to longstanding vitamin D deficiency. Early diagnosis and treatment of hyperparathyroidism can prevent the development of osteitis fibrosa cystica and subsequent fractures, which carry morbidity and mortality consequences and an opportunity was likely missed several years earlier in this case. Furthermore, adequate vitamin D replacement pre-operatively is essential to prevent hungry bone syndrome post-operatively, particularly in patients with extensive bony involvement. Finally, although the operative and histological findings were not suggestive of a parathyroid carcinoma, ongoing careful clinical follow up is paramount.

DOI: 10.1530/endoabs.69.P53

#### P54

##### **Seeing beyond a diagnosis of familial short stature**

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#### Case history

A fifteen year old female was seen in general paediatric clinic after multiple GP attendances based upon persistent maternal concerns for short stature (height below 0.4th centile). She was otherwise healthy, had achieved menarche at age 14, and had no dysmorphic features. She had been reviewed by endocrinology age ten and discharged with a diagnosis of familial short stature. Her mother's height was on the 0.4th centile and her father's on the 75th, resulting in a target range of 9th–91st centiles. Both of her siblings, females aged six and 11 years, were following the second centile for height.

#### Investigations

Karyotype and array comparative genomic hybridization demonstrated a female karyotype with unbalanced derivative chromosome X from an apparent translocation between the short arm of the X chromosome (Xp) and the short arm of chromosome 3. This abnormality results in loss of the SHOX gene and is consistent with variant Turner syndrome. The patient's mother and siblings had identical translocations. Her father's genetic analysis was normal. All three children had normal renal ultrasounds and echocardiograms as part of Turner syndrome surveillance.

#### Results and treatment

The patient and her family expressed disappointment that the diagnosis was missed by the endocrinology team, and that as a result the window of opportunity for growth hormone had been lost. Her younger sisters were started on growth hormone at age six and 11 years with gain of one height centile at six month follow up. After multiple miscarriages thought to be related to the translocation, the parents are considering pre-implantation genetic diagnosis for future pregnancies.

#### Conclusions and points for discussion

Parents with genetic disorders causing short stature can pass these disorders to their children, which in this case led to an erroneous diagnosis of familial short stature. Variant Turner syndrome, unlike classical Turner syndrome, can be associated with normal fertility. The clinical consequences of missed diagnosis include missing the window of treatment with growth hormone, effects on fertility (male fetuses carrying the translocation are non-viable), and implications for diagnosis and screening of other family members. It is crucial to consider an underlying genetic diagnosis at an early stage, particularly if one parent has marked short stature themselves.

DOI: 10.1530/endoabs.69.P54

**P55****'A Case Report on Eruptive Xanthoma as the First Presentation of Undiagnosed Diabetes Mellitus'**

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**Case history**

A 33 year old gentleman presented with a 4 month history of an evolving rash. This initially appeared on the extensor surfaces of the knees bilaterally and progressed to involve both arms and the trunk. This rash was not associated with fever, pain, pruritis or any other symptoms. These lesions were diffuse erythematous crops of yellow papules visible over the knees, arms and trunk. The patient was initially diagnosed with folliculitis and treated with oral flucloxacillin with no clinical improvement observed. This necessitated the need to find an alternative explanation for this presentation.

**Investigations**

On admission, the patient was noted to have a blood pressure of 146/102 mmHg and weight of 84 kg. Venous sampling demonstrated a marked hypertriglyceridemia, hypercholesterolaemia and hyperglycaemia. His triglyceride level was 45.4 mmol/l and total cholesterol 14.1 mmol/l. His HbA1c was 106 mmol/mol with random glucose above 11.1 mmol/l. His renal, liver and thyroid function were normal.

**Results and treatment**

The description of this rash combined with marked hypertriglyceridemia was suggestive of eruptive xanthomas. These are benign skin lesions presenting as sudden eruptions of grouped, red-yellow papules over the arms, legs and trunk.<sup>1</sup> These lesions can be painful and pruritic, or asymptomatic as in our case. Effective treatment of these lesions requires management of the underlying systemic condition or primary hyperlipidaemia, whereby the lesions typically resolve within weeks to months.<sup>1</sup> In our case, eruptive xanthomas were the only symptom of undiagnosed diabetes mellitus and clinically improved three months after diet, lipid and glycaemic control.

**Conclusions and points for discussion**

This case highlights the importance of first recognising eruptive xanthomas as a cutaneous manifestation of hypertriglyceridemia. This needs to be followed by a work up for the aetiology of hypertriglyceridemia. Whilst hypertriglyceridemia can be attributed to primary hyperlipidaemia, it can alternatively be linked to metabolic diseases such as diabetes mellitus, hypothyroidism, nephrotic syndrome or be drug induced.<sup>2</sup> Finally, whatever is the determined underlying aetiology needs to be treated. In our case, eruptive xanthomas acted as the sole presentation of diabetes mellitus. Identifying the aetiology allowed for management of the underlying condition, whereby the lesions resolved within months.<sup>2</sup> Such prompt recognition and treatment is essential to prevent potentially life-threatening complications such as acute pancreatitis and coronary artery disease. To conclude, this case emphasises the need to recognise eruptive xanthomas, identify the aetiology of hypertriglyceridemia and treat the underlying cause.

DOI: 10.1530/endoabs.69.P55

**P56****A tale of two siblings; the importance of urine calcium creatinine clearance ratio**

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**Case history**

29 year old lady presented to A&E with UTI. She had a history of emotionally unstable personality disorder and was an elective inpatient in a psychiatric hospital at the time of her presentation. Blood tests done on admission showed that she was hypercalcaemic. She was treated for UTI and referred to endocrinology. Biochemistry tests were in keeping with familial hypocalciuric hypercalcaemia (FHH). It transpired that her father and sister also had hypercalcaemia and both had parathyroidectomies done in different hospitals. We have not been able to obtain information about her father but her sister remains hypercalcaemic after parathyroidectomy. Investigations for her sister are currently on-going.

**Investigations**

Blood tests for calcium, phosphate, PTH, creatinine, vitamin D, TSH, 24 h urine collection for calcium and creatinine.

**Results and treatment**

Adjusted calcium was 2.97 mmol/l with previous calcium readings as high as 3.02 mmol/l.

PTH 83 ng/l (15 – 65), Vitamin D 62, Phosphate 0.67 mmol/l. TSH 1.4. Serum creatinine 60 umol/l, Urine Creatinine 5.8 mmol/l, Urine Calcium 1.1 mmol/l, Urine Calcium creatinine clearance ratio (UCCCR) was 0.0038.

**Genetic test**

Heterozygous for AP2S1 mutation.

**Conclusions and points for discussion**

FHH is a rare, lifelong condition. In FHH 3 (due to mutation of AP2S1) cohort blood calcium levels are much higher. It is important to distinguish FHH from Primary hyperparathyroidism (PHPT). As PTH and serum calcium may be elevated in both conditions urine calcium creatinine clearance ratio must be done to distinguish these two conditions. UCCCR > 0.02 excludes FHH. Failure to diagnose FHH can lead to unnecessary parathyroidectomy.

DOI: 10.1530/endoabs.69.P56

**P57****Severe symptomatic hyponatremia with SIADH picture due to influenza A**

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**Case history**

A previous healthy 69 year-old female was brought into the ED by her worried husband after he noticed worsening confusion. She developed seizures post arrival to the ED and was admitted under ITU for further care. Retrospective history from the husband indicated she had started feeling unwell around Christmas with a feeling of malaise. She self-medicated with amoxicillin which she had access to as a nurse practitioner. Over the next 2 days she developed headaches, nausea, vomiting, diarrhoea and became increasingly confused prompting her attendance to the ED.

**Investigations**

Her sodium came back as 111; her hyponatremia workup showed low serum osmolality 230, high urine osmolality 549 and high urine sodium 88. Her blood count was normal and CRP slightly elevated at 9. TSH and cortisol levels were normal. Her CXR showed increased in her broncho-vascular markings specially on the left side, but with no clear infiltrates or consolidation. CT brain with contrast and CT chest, abdomen and pelvis with contrast was reported as showing no significant abnormalities. A Flu swab came back positive for influenza A. Legionella and mycoplasma work up was negative.

**Treatment**

Despite the patient's symptoms of vomiting and diarrhoea, she did not objectively seem hypovolemic and she had a normal urea to creatinine ratio. The patient was given 2.7% of 150 ml normal saline due to her symptomatic presentation; she was initially given IV phenytoin for her seizures as the cause was still uncertain and started on oseltamivir. She remained stable while intubated in the ITU with no further seizures and was extubated when her sodium normalized after 3 days to 130.

**Conclusion and discussion**

This case illustrates that influenza A can cause SIADH with severe hyponatremia, as all other causes were excluded. The incidence and prevalence of this is unknown which calls for further studies. There is no data available on the severity of hyponatremia caused by INFLUENZA A per se. After reviewing the literature, this is the first case reported in the UK. There have been 3 previous case reports worldwide highlighting influenza A to be the cause of severe hyponatraemia. This case highlights that it may be more common than previously thought and should be screened for on admission, particularly in patients with prodromal symptoms consistent with a viral illness.

DOI: 10.1530/endoabs.69.P57

**P58****Unexplained hypercortisolaemia in a patient without a Cushing's phenotype: potential for cortisol receptor mutation?**

Christopher Horne

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**Section 1**

A 57 year old gentleman was referred to the endocrinology clinic with hyponatraemia. His past medical history included hip dislocation and Peyronie's

disease. He was very anxious. He did not smoke or drink alcohol, and he was taking Ibuprofen, paracetamol and amitriptyline 75 mg ON. He had raised urinary sodium and was diagnosed with SIADH. As part of a routine workup he was found to have a raised morning cortisol. The patient had a BMI of 21 and had no abdominal striae or evidence of bruising. He was normotensive, had a normal HbA1c and a normal DEXA scan. His hyponatraemia improved with fluid restriction and no obvious cause was found for his SIADH.

#### Section 2: Results

MRI head: normal

0900 h Cortisol: 704–927 nmol/l (119–619 nmol/l)

Midnight Salivary cortisol: 6.7 nmol/l, 2.7 nmol/l

24 h urine collection for cortisol: 390 nmol/24 h

Cortisol binding globulin: 44.3 mg/l (27.1–52.3 mg/l)

Low Dose DST: Cortisol 627 (Time 0) 201 (48 h), ACTH 41 (time 0) 31 (48 h) (Immediately followed by) High Dose DST: Cortisol 17 (48 h) ACTH <5 (48 h) Dexamethasone Suppression Test 2 g 6 hourly for 48 h then CRH test:

Time:	Pre Dex,	15 min pre CRH,	0, 5, 10, 15, 20, 30, 60, 90, 120 (minutes)
Cortisol:	602	439	379, 407, 376, 380, 400, 383, 314, 257, 194
ACTH:			20, 23, 29, 23, 22, 18, 19, 18, 18

#### Section 3: Results and treatment

The result of the dexamethasone-CRH test pointed towards pseudocushings but he clinically he had no signs of Cushings. He was referred to a tertiary centre who diagnosed glucocorticoid receptor defect, CRD which can cause increased anxiety.

#### Section 4

Cortisol receptor deficiency is a rare disorder, first described by G Chrousos, which is either inherited or sporadic. It has been attributed to various different receptor loci meaning that the clinical spectrum of CRD can be broad. In this case, there appears to be no negative clinical consequences due to the chronically raised cortisol. However, in other patients high levels of circulating glucocorticoid can cause considerable consequences such as mineralocorticoid excess, female androgenisation and infertility. This opens up the possibility of treatment modalities such as low dose dexamethasone. Therefore, understanding and interpretation of hypercortisolaemia without phenotypic translation, and awareness of CRD, could lead improved diagnosis and management of potential complications.

DOI: 10.1530/endoabs.69.P58

## P59

### Massive asymptomatic creatine kinase elevation (MACKE) as a result of aripiprazole and quetiapine use

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#### Case history

20 year old male with Asperger's and OCD was admitted as a psychiatric inpatient and started on aripiprazole and subsequently quetiapine. His symptoms were well controlled, however his creatine kinase rose significantly over the subsequent 3 months. He had no symptoms of neuroleptic malignant syndrome and despite other parameters being investigated, no other causes were found. For this reason, advice from endocrinologists was sought for advice on management of a case of massive asymptomatic creatine kinase elevation (MACKE).

#### Investigations

Creatine kinase rose from a 2530 u/l baseline while on aripiprazole, to 6293 u/l upon changing to quetiapine. His GFR and U&Es were consistently stable with no symptoms of neuroleptic malignant syndrome. His TSH was mildly elevated, however even after normalising with treatment, his creatine kinase remained elevated.

#### Results and treatment

Discussions were had with the Psychiatry and Endocrinology consultants. It was decided to cautiously continue the antipsychotics in order to manage his debilitating mental health symptoms. His U&Es and symptoms such as muscle rigidity and high temps were monitored for. The patient was initially on low-dose sertraline, which was stopped when the high creatine kinase was noted. After a dose reduction of quetiapine, his creatine kinase dropped to 2393 u/l. It was decided that this range was acceptable and he could continue on the treatment regime with regular monitoring.

#### Points for discussion

This appears to be a case of massive asymptomatic creatine kinase elevation (MACKE), which is rarely documented with use of aripiprazole and quetiapine. This patient's situation was difficult to manage and there was very little literature available for case comparison. Despite TFT normalisation and cessation of sertraline, elevated creatine kinase persisted. It is important to make medical professionals aware of cases such as this, so those treating similar patients can see how other teams have managed such conditions.

DOI: 10.1530/endoabs.69.P59

## P60

### Recurrent hypoglycaemia – beyond Whipples Triad

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#### Case history

A 61-year-old gentleman first presented to A&E following a collapse at work. After missing lunch, he became combative towards his colleagues and was found to be hypoglycaemic with capillary blood glucose of 2.5 mmol/l. Symptoms rapidly improved after oral glucose intake. The patient reported similar episodes in the past, usually occurring before meals and mainly if missing or delaying a meal. The patient did not have any past medical history of note, did not have diabetes and not taking any regular medications.

#### Investigations

Physical examination revealed a healthy male with BMI 28. Liver and renal functions as well as thyroid profile were normal, HbA1c 41 mmol/mol, 0900 h cortisol level at 401 nmol/l. Drug-induced hypoglycaemia and sulfonylurea use was excluded. During a fasting test the patient's blood glucose dropped to 2.0 mmol/l at 4 h. Insulin was 10 800 pmol/l, C-peptide 671 pmol/l, discrepant for such a high insulin concentration. Because of this, the insulin concentration was measured using PEG precipitation – total insulin was 2930 pmol/l, PEG precipitated insulin 202 pmol/l, and the presence of anti-insulin antibodies was confirmed. Exogenous insulin administration was excluded by the use of two different insulin assay platforms. The patient underwent CT pancreas which revealed a possible 0.5 cm pancreatic lesion which was not demonstrated on MRCP, and determined to be vascular in nature.

#### Results and treatment

A diagnosis of Insulin Autoimmune Syndrome was made. He was advised to eat regularly and to stick to a low GI diet. Within 8 months follow up, he did not develop further hypoglycaemic episodes and his weight remained stable. He was not found to have other autoimmune conditions and remains under follow up.

#### Conclusions and points for discussion

The presence of anti-insulin antibodies is a very rare cause of hypoglycaemia. Anti-insulin antibodies delay insulin clearance, increasing receptor mediated insulin signalling. Recovery of plasma immunoreactive insulin after PEG precipitation of the plasma showed lower insulin concentration and confirmed the presence of anti-insulin antibodies. Insulin Autoimmune Syndrome may be related to use of exogenous insulin or associated with human leukocyte antigen DRB1\*0406, more common in people of Japanese heritage. It has also been described in multiple myeloma. First-line treatment should be dietary management and patients need advice on emergency hypoglycaemia treatment. Acarbose may be of use, and in severe cases, treatment with corticosteroids or rituximab might be necessary. Although rare, the presence of anti-insulin antibodies should be considered in patients with recurrent hypoglycaemic episodes and inappropriately high insulin levels.

DOI: 10.1530/endoabs.69.P60

**P61****A case of pulmonary neuroendocrine tumours secreting ACTH and GHRH**Yun-Ni Lee<sup>1</sup>, Riyah Jiwan<sup>1</sup>, Anju Sahdev<sup>1</sup>, Daniel Berney<sup>1</sup>,Henrietta Wilson<sup>1</sup>, Scott Akker<sup>1</sup> & Zoe Davies<sup>2</sup><sup>1</sup>St Bartholomew's Hospital, London, UK; <sup>2</sup>Whipps Cross Hospital, London, UK**Section 1: Case history**

A sixty-three-year-old Caucasian male presented with a six-week history of lethargy, emotional lability, polydipsia, polyuria, increased appetite and weight gain. He also reported changes in his facial features and widening of the gaps between his teeth. He has a background of hypertension, obstructive sleep apnoea and benign prostatic hyperplasia. On examination, the patient appeared plethoric, had coarsened facial features, mild prognathism and evidence of easy bruising.

**Section 2: Investigations**

Initial investigations revealed hypokalaemia of 2.4 mmol/l, HbA1c of 54 mmol/mol and a chest X-ray which showed a rounded lesion near the right heart border. Baseline morning cortisol was 664 nmol/l and an overnight 1 mg dexamethasone suppression test failed to suppress cortisol at 625 nmol/l. ACTH was 49 ng/l. IGF-1 was 287 mcg/l. Growth hormone day curve measured as follows: 1.8 mcg/l (08:30), 2.15 mcg/l (11:00), 2.85 mcg/l (13:00), 2.19 mcg/l (17:00), 1.34 mcg/l (19:00). Growth hormone releasing hormone levels of 248 ng/l (0–59 ng/l). CT thorax showed a 54 mm solid, highly vascular lesion at the right cardiophrenic angle with several right lower lobe nodules and a solitary 11 mm middle mediastinal node. The large 54 mm lesion was also FDG and Gallium-68 DOTATATE avid, indicating somatostatin receptor positivity. CT adrenals revealed bilateral adrenal hyperplasia and MRI pituitary was unremarkable.

**Section 3: Results and treatment**

Clinical presentation and investigations suggested ectopic ACTH/GHRH production likely from the right lung nodule. He was initially managed with an etomidate infusion followed by metyrapone. A trial of octreotide did not show any improvement in his cortisol day curve. He was discharged with metyrapone 500 mg, 750 mg and 750 mg. The patient proceeded to surgical management and underwent a right middle lobe and right lower lobe wedge resection with mediastinal lymph node dissection. Post operatively, cortisol level was 305 nmol/l and ACTH was 10 ng/l, and he was started empirically on hydrocortisone 10 mg, 5 mg, 5 mg. Pathology from surgical resection revealed a 55 mm typical carcinoid tumour with a Ki-67 of 1–2% and a 9 mm typical carcinoid tumour with a Ki-67 of 30%. The lymph nodes were negative for metastases. Immunohistochemistry for ACTH was negative in both tumours. There were multiple foci of neuroendocrine hyperplasia in the background lung which raises the possibility of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH).

**Section 4: Conclusions and points for discussion**

Diagnosis is GHRH & ACTH secreting pulmonary neuroendocrine tumour and DIPNECH.

**Points for discussion**

- Management of DIPNECH
- Negative staining for ACTH on histology
- Follow up management

DOI: 10.1530/endoabs.69.P61

hyperinsulinaemic hypoglycaemia was confirmed following an overnight fast, and subsequently managed by diet prior to definitive surgery. Pre-operative work up with Octreotide scan demonstrated avid tracer uptake in the pancreatic lesion as well as a focal area of uptake in the left breast.

**Section 3: Results and treatment**

Further investigation and subsequent mastectomy confirmed ductal carcinoma *in situ* pT2 (23 mm) grade 1, N0 (ER positive; HER2 negative). Following this, she underwent a successful pancreatectomy and splenectomy. Patchy insulin staining was seen on the pNET with no lymph node spread.

**Section 4: Conclusions and points for discussion**

MEN1's association with breast cancer is unclear. Previously, 12 cases of breast cancer were reported in a cohort of 190 MEN1 females (Dreijerink *et al.* 2014). This cohort had early-onset breast cancer diagnosed at a young median age of 48 years, in line with our patient's history. In our patient, loss of heterozygosity (LOH) at the MEN1 locus was seen in the breast tissue and pNET specimen, in keeping with a 'two-hit' hypothesis of oncogenesis, a suggestive but non-definitive clue for causation. However, only 3/9 cases showed loss of heterozygosity (LOH) in the Dutch cohort. Of note, somatic truncating *BRCA2* and *TP53* mutations were also identified in the breast tumour but the variant allele frequency of < 10% for both mutations suggesting that these mutations were sub-clonal rather than the primary genetic driver. This case highlights the need for further studies to determine the potential role of MEN1 in breast cancer development and to guide surveillance strategies.

**Reference**

Dreijerink, Koen M.A., Pierre Goudet, John R. Burgess, Gerlof D. Valk, and International Breast Cancer in MEN1 Study Group. 2014. 'Breast-Cancer Predisposition in Multiple Endocrine Neoplasia Type 1.' *New England Journal of Medicine* 371 (6). <https://doi.org/10.1056/NEJMc1406028>.

DOI: 10.1530/endoabs.69.P62

**P63****Coexistence of Refetoff syndrome and papillary thyroid carcinoma**

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A 30 year-old Caucasian male presented for a routine check-up. He was known to have abnormal thyroid function tests since the age of 23 years of unclear nature/aetiology. He reported occasional palpitations and anxiety. There were no other symptoms on systems' review. He did not take regular medication, was an ex-smoker and consumed alcohol socially. His mother had hypothyroidism and his maternal aunt's thyroid nodules. He was euthyroid. A palpable isthmus nodule ~1.5 cm was noted. He had no lymphadenopathy or other findings of note on examination. Free-T4 was 31 pmol/l (NR: 12–22 pmol/l), free-T3 8.4 pmol/l (NR: 3.1–6.8 pmol/l), TSH 1.96 mU/l (0.3–4.2 mU/l).

Thyroid hormone assay interference was excluded.

Pituitary MRI showed a 3 mm right-sided lesion.

The rest of the pituitary profile was normal.

TSH alpha-subunit was normal 0.15 U/l (NR < 0.4 U/l).

Genetic analysis for congenital hypothyroidism and thyroid hormone resistance (TRH) sequencing panel with copy number variants (CNV) detection showed heterozygous status for the *THRB* gene for a variant designated c.1286G>A, predicted to result in the amino acid substitution p.Arg429Gln. He was negative for CNV within the genomic regions encompassing the genes of this panel. US thyroid revealed a 1.5 cm midline U4 isthmus nodule with no evidence of extracapsular spread/infiltration. In the left lobe a nonspecific 3 mm nodule was also noted along with the 2 cm colloid cyst. FNA showed features of papillary thyroid carcinoma for the isthmus nodule. For the left lobe small nodule, the findings were compatible with Thy2. Genomic PCR analysis revealed BRAFV600E mutation at high-mutant allele frequency, but no other high-risk mutations, such as *TERT* or *TP53*. He was diagnosed with Refetoff syndrome (thyroid hormone resistance syndrome), coexistent papillary thyroid carcinoma and pituitary incidentaloma. He underwent total thyroidectomy. Histology showed 1.3 cm papillary thyroid carcinoma in contact with the capsule with no apparent capsular invasion, R0 resection, 0/6 lymph nodes free of neoplasia. Our case offers the opportunity to discuss the challenges in the diagnosis and management of THR. Moreover, coexistence of THR and differentiated thyroid carcinoma is very rare with only a few cases reported. Differentiated thyroid carcinoma in the context of THR is a distinctive model of thyroid cancer, where follow-up likely occurs in the setting of non-suppressed/constantly elevated TSH. We discuss the pitfalls resulting from failure to inhibit TSH secretion, we review the relevant literature and discuss the thresholds for RAI administration

**P62****Breast Cancer in MEN1: Coincidence or association?**Seong Keat Cheah<sup>1</sup>, Bisambar Chad<sup>1</sup>, Deborah Pitfield<sup>1</sup>, Olivier Giger<sup>1</sup>,Rogier ten Hoopen<sup>1</sup>, Jose Ezequiel Martin<sup>1</sup>, Soo-Mi Park<sup>1</sup>,Craig Parkinson<sup>2</sup>, Benjamin Challis<sup>1</sup> & Ruth Casey<sup>1</sup><sup>1</sup>Cambridge University Hospital Foundation Trust, Cambridge, UK; <sup>2</sup>East Suffolk and North Essex NHS Foundation Trust, Ipswich, UK**Section 1: Case history**

A 38 year old female was identified as carrying a heterozygous pathogenic *MEN1* variant (c.13404delG) through predictive testing, following a diagnosis of familial hyperparathyroidism.

**Section 2: Investigations**

Routine screening for hyperparathyroidism and pituitary disease was negative. However, a CT thorax–abdomen–pelvis revealed a 41 mm pancreatic tail mass. Biopsy via endoscopic ultrasound confirmed a well-differentiated (grade 1) pancreatic neuroendocrine tumour (pNET) with MIB1 < 1%. Biochemically,

post-thyroidectomy in a clinical area lacking consensus for the standardized management of such cases.

DOI: 10.1530/endoabs.69.P63

## P64

### So Close, Yet so Fahr!

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A 58 year old male diagnosed with 'Parkinson's Disease' in 2016 following symptoms of Parkinsonism and a DaTscan, was admitted with seizures. He was given Benzodiazepines in the A&E which helped control the seizures. A CT scan of his head revealed Bilateral Basal Ganglia calcification. This was the first time he had seizures, but he did complain of having on and off facial twitching and muscle spasms. There was no history of trauma to the head, fevers, or change in consciousness levels. He said that in 2014, before any of the symptoms of PD developed he had seen his GP who noted that he had low Vitamin D and Calcium levels, and had replaced his Vitamin D. He was then lost to follow up. He had no other significant Past or Family History. He did not smoke, and was a teetotaler. Examination revealed, the presence of an Expressionless face, Chvostek's sign, increased general tone, and reduced mobility.

Investigations

• Labs:

1. FBC: NAD
2. Renal Profile: Na: 144 mmol/l, K: 4.4 mmol/l, Cl: 104 mmol/l, Creat: 78 umol/l, eGFR>90 ml/min
3. Bone Profile: Protein: 68 g/l, Albumin: 40 g/l, ALP: 89 u/l, C.Ca: 1.32 mmol/l, Phosphate: 1.85 mmol/l
4. Vitamin D: 18 nmol/l, Magnesium: 0.84 mmol/l
5. Parathormone: 4.5 ng/l

• Imaging:

1. CT head (02/12/2019): Bilateral basal ganglia calcification.
2. DaTscan: (2018): Reduced uptake of Dopamine in Basal ganglia.

The patient was treated with IV calcium gluconate till Corrected Calcium levels reached 1.9 mmol/l. He was started on Vitamin D correction with colecalciferol 40 000 IU/weekly for 7 weeks, Alfacalcidol 1 mcg/day, and calcium carbonate. He was discharged, and followed up in our clinic a couple of weeks later. Unfortunately there was no improvement in neurological symptoms as yet. His bloods revealed a normalisation of his Vitamin D levels to 65 nmol/l, while his Corrected Calcium continued to be 1.9 mmol/l. We have planned a referral for genetic testing, and are awaiting his consent for it.

Conclusions

Fahr's Syndrome is a rare, genetically dominant, inherited neurological disorder associated with Hypoparathyroidism and abnormal deposits of calcium in areas of the brain that control movement, like the basal ganglia and the cerebral cortex. Patients with Fahr's syndrome often present with deterioration of motor function, seizures, headache, dementia, dysarthria, rigidity/spasticity, tremors, mask-like face and shuffling gait. Fahr's Syndrome should remain a differential in patients with features of parkinsonism and hypocalcaemia.

Points for discussion

- Neurological features of Fahr's syndrome, may or may not improvement with calcium replacement.
- Could this gentleman's fate be any different if the condition was picked earlier?

DOI: 10.1530/endoabs.69.P64

## P65

### Fluctuating adrenal hyperplasia

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Adrenal lesions are commonly detected incidentally during cross-sectional imaging examinations, and the majority are benign adrenal adenomas. A 52 year old gentleman with a history of hypertension and paroxysmal atrial fibrillation

was referred to our service following a fall in which he fractured several ribs. Subsequent abdominal CT revealed an incidental finding of bilateral adrenal masses, reported as approximately 5 cm and 4 cm on the right and left side respectively with a density on the unenhanced scan. On further questioning he reported problems with fatigue and weight gain. Endocrine tests to assess adrenal functionality were negative. Three months later, repeated adrenal CT showed his adrenal lesions had significantly decreased in size without any treatment. The right adrenal gland measuring 4.5×2.8×2.7 cm (previously 5×4.2×4.1 cm) and the left adrenal gland measuring 3.7×3.5×3.4 cm (5.6×5.2×4.6 cm). Soon afterwards, he presented to the Emergency Department with fatigue, weakness and dizziness on standing. He was pancytopenic and short adrenocorticotrophic hormone stimulation test revealed adrenal insufficiency. He was commenced on hydrocortisone (20 mg + 10 mg + 10 mg daily) and fludrocortisone (50 mcg). His case was reviewed in the Adrenal multi-disciplinary meeting. Histology from a subsequent adrenal biopsy showed diffuse large B cell lymphoma with a Ki-67 of approximately 80%. The patient was administered R-CODOX-M (rituximab-cyclophosphamide, doxorubicin, vincristine and Methotrexate) chemotherapy. He was re-evaluated on completion of his chemotherapy cycles (2 cycles) with a non-contrast CT scan revealed complete resolution of the previously detected bilateral adrenal masses. It is important to get a histological diagnosis from indeterminate adrenal lesions to ensure adequate treatment, as diagnoses of adrenal lymphoma are <1% of the Primary extranodal non-Hodgkin lymphomas cases. The case exhibited unusual presentation of fluctuating bilateral adrenal lymphoma with an excellent response to the chemotherapy, as shown by complete resolution in the sizes of both adrenal glands. This case complements the few other reported cases in the literature regarding diffuse large B cell lymphoma with adrenal insufficiency that showed a complete response to chemotherapy. He has now reduced his dose of hydrocortisone (15 mg + 10 mg+5 mg). Can adrenal function recover after treating adrenal lymphoma?

DOI: 10.1530/endoabs.69.P65

## P66

### A case of sellar paraganglioma; rarest of the rare

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Introduction

Paragangliomas are neuroendocrine tumours, usually found from the base of the skull to pelvis. They are extremely rare in the sellar and parasellar region which normally lacks paraganglion cells. We report a rare case of an incidental sellar paraganglioma.

Case

A 66 years old female had progressive retinopathy and maculopathy of unclear cause since 2011. Lung nodules were seen on CT performed to exclude paraneoplastic retinopathy. 18F-FDG PET/CTscan showed normal lungs but a high uptake (SUV<sub>max</sub> 78.3) in the pituitary. MRI pituitary showed a new lesion (not visible on MRI brain done 5 years before). Serial MRI scans over 10 months showed growth from 8×4×5 mm to 11×8×7 mm with no impingement of the chiasm (or field defect) or cavernous sinus invasion. Pituitary function tests were normal except partial diabetes insipidus on formal water deprivation test. Although she was asymptomatic, increasing size, uncertain diagnosis and PET avidity led to an uncomplicated transsphenoidal pituitary resection. There was appearance of a complete resection on post-surgery MRI scan. Biopsy showed a low-grade parenchyma tumour of the pituitary gland with overall morphology and immunophenotype suggestive of a paraganglioma with low MIB-1 immunoreactivity (<1%). Plasma metanephrines, MRI Neck, Thorax, Abdomen, and Pelvis were normal and analysis of the FH, MAX, RET, SDHA, SDHB, SDHC, SDHD, SDHAF2, TMEM127 and VHL genes did not detect a pathogenic variant.

Discussion

Incidence of focal 18F-FDG uptake in the pituitary gland is reported between 0.07 and 0.8% and follow up investigations with MRI and histology showed that nearly half were non-functioning pituitary adenoma, followed by Langerhans cell histiocytosis, hypophysitis and, metastasis. 18F-FDG avidity of paragangliomas has been reported to show higher SUV avidity for malignant than benign lesions and for extra-adrenal paragangliomas. The avidity of the tumour in our case was high and therefore careful radiological follow up is warranted. Sellar or parasellar paraganglioma is extremely rare and only numbered cases are reported. Most of the sellar paragangliomas presented as pituitary masses on MRI or CT scan causing local invasion and the size and invasiveness has made them difficult to resect completely. Diagnosis is made based on characteristic histology features (zellballen pattern) and immunopositivity for synaptophysin and S-100 protein as



none of the reported cases presented with features of catecholamine excess or radiological features to distinguish it from pituitary macroadenoma. This case was unusual as it presented as a growing microadenoma with high 18F-FDG-PET avidity. Rarer causes of PET avidity should be considered when assessing these lesions.

DOI: 10.1530/endoabs.69.P66

## P67

### Complete recovery following osmotic demyelinating syndrome in a patient with craniopharyngioma

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#### Introduction

Hyponatremia in patients with pituitary tumours are common due to many reasons including secondary hypoadrenalism and secondary hypothyroidism. When these causes are treated with the background of hyponatremia, serum sodium should be regularly monitored as it could get corrected too rapidly leading to ODS.

#### Case report

34 Year old patient presented to a tertiary care hospital with headache. His MRI brain revealed a large suprasellar lesion suggestive of a craniopharyngioma. He was discharged with outpatient endocrinology referral. Several weeks later, before his endocrinology review, he presented with nausea, vomiting and postural symptoms. His blood results showed serum Na of 108 mmol/l. He was managed in the acute medical ward with 3% saline followed by normal saline. Although his sodium improved to 148 mmol/l, his symptoms persisted. He was referred to the endocrine team. Adrenal crises was suspected and he was commenced on intravenous hydrocortisone and intra venous 0.9% saline. Biochemistry revealed panhypopituitarism (0900 h cortisol 81 nmol/l, TSH 1.7 mIU/l, FT4-4.65 pmol/l). His symptoms improved rapidly. Day 3 after hydrocortisone commencement he developed slurring of speech, spastic quadriparesis with upgoing plantars. Retrospectively, His blood results showed rise of Na (day 1-134, day 3-141) with associated polyuria unmasking diabetes insipidus. With the given clinical background, the diagnosis of osmotic demyelinating syndrome (ODS) was made. We aimed at reducing the Na level to 126 mmol/l based on 18 mmol correction in 48 h. He was managed with 5% dextrose and subcutaneous vasopressin. His Na results were as follows: day 3 evening-137, day 4-135, 129, 128, day 5-119, day 6-126, day 7-126 130, day 8-133. He gradually improved from his ODS from day 4. He completely recovered from the illness by day 8. He underwent transcranial surgery and had an uneventful recovery except for a side 3rd nerve palsy. His histology revealed craniopharyngioma.

#### Conclusion

Thus, when hyponatremia and hormonal deficiency is corrected in pituitary base tumours, Na should be carefully monitored to prevent a rapid correction and should use desmopressin if needed. If ODS develops we should bring the Na down based on the calculation with the help of hypotonic fluids and desmopressin.

DOI: 10.1530/endoabs.69.P67

## P68

### Refractory cyclical cushing's – clinical challenges

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#### Case history

Cyclical Cushing's is a very rare disease with rhythmic fluctuations in cortisol production with or without phenotypic features. It is a very challenging entity to

diagnose. The low index of clinical suspicion is key for timely diagnosis and prevention of long-term complications. A 66 years old male presented with intermittent, episodic bilateral leg swelling and reversible weight gain of ~6 kg following these episodes. Background history entailed femoral patella replacement and atrial tachycardia. Examinations reveal bilateral leg swelling and pitting edema up to the mid-shin level. There was no evidence of proximal myopathy or easy bruising. Routine biochemistry and baseline investigations including BNP, urine PCR/ACR/VEGF and echocardiography were normal. BP was 142/87 mmHg. The possibility of cyclical Cushing's syndrome was considered. He had a normal previous urine free cortisol by GP, all biochemistry repeated while being symptomatic.

#### Investigations

ONDST: post-test cortisol 92 nmol/l, ACTH 61.1 ng/l (reference range 0-46 ng/l).

LDDST: post-test cortisol of 123 nmol/l.

24 h UFC: 4129 nmol/24 h.

Volumetric MRI pituitary: 2 mm right-sided pituitary lesion.

FDG PET: normal FDG-avidity.

IPSS: Baseline ACTH central to peripheral ratio of 5.05. Left inferior petrosal sinus 327 ng/l, peripheral 64.7 ng/l, left to right ratio of 3.17 at baseline suggesting left lateralization. There was minimal response to CRH.

#### Treatment

Following MDT discussion, he underwent trans-sphenoidal hypophysectomy. His postoperative 0900 h cortisol was ~600-800 nmol/l. Post-redo completion trans-sphenoidal hypophysectomy at day-7 cortisol levels were 290 nmol/l. Histology did not show any evidence of ACTH secreting adenoma. He developed postoperative hypopituitarism including DI, hypothyroidism and hypogonadism. He was commenced on replacement including Nebido 1 g every 12 weeks, Levothyroxine 75 mcg, Desmopressin 100/100/300 mcg. His Cushing's remained active. He was commenced on the block and replace regimen with Metyrapone and prednisolone, metyrapone titrated on the basis of metyrapone-hydrocortisone day curve data. Adjuvant cabergoline was poorly tolerated. He received radiotherapy 45 Gy in 25 fractions for 28 days, using a 6-MV X-ray technique. Repeat imaging showed no evidence of recurrence. 11-C methionine PET imaging has been requested to consider the possibility of targeted therapy. Also discussed consideration of adrenalectomy if radiotherapy proves unsuccessful

#### Discussion points

Our case presents the opportunity to discuss the challenges in the diagnosis and treatment of cyclical Cushing's, new emerging therapies for Cushing's disease, pros and cons of adrenalectomy versus radiotherapy, and the role of methionine 11-C methionine PET imaging in the detection of ACTH-secreting tumors in ACTH-dependent Cushing's syndrome with facilitation of targeted therapy.

DOI: 10.1530/endoabs.69.P68

## P69

### Isolated Langerhans cell histiocytosis in hypothalamic-pituitary region

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#### Case history

We present a rare case of Langerhans cell histiocytosis (LCH) of pituitary stalk and hypothalamus in a 40 year old lady. She presented with 9 weeks history of a sudden onset of polyuria and polydipsia. She had extreme thirst even during night which led to significant nocturia and tiredness. She denied headache, blurring of vision, galactorrhoea or menstrual irregularity. She had no significant past medical history and was not on any medications. Physical examination was unremarkable.

#### Investigations and management

Basal pituitary profile was unremarkable. Short synacthen test, ESR, CRP, ACE and AFP were unremarkable. Water deprivation test was suggestive of central diabetes insipidus. Symptoms of DI responded very well to nasal desmopressin. Urgent MRI brain showed thickening of pituitary stalk. Biopsy was not needed at this stage. MRI after 6 months showed improvement in size of pituitary stalk swelling but prolactin level increased to 3600. Cabergoline 250 mcg twice a week was started. CT thorax, abdomen and pelvis were unremarkable. MRI whole spine showed multiple thoracic vertebral fractures and DEXA scan confirmed osteopenia. She was urgently reviewed with sudden onset headache and reduced visual acuity. MRI scan showed a sudden increase in the size of pituitary lesion which was now extending up into the third ventricle and hypothalamus and

encasing the optic chiasm. Radiological differential included sarcoidosis atypical craniopharyngioma and pituitaryoma. Pituitary profile showed panhypopituitarism therefore she was started on hydrocortisone and thyroxine. Autoimmune, Inflammatory, myeloma and lymphoma screening were negative. Biopsy of lesion was performed. Histology showed non necrotizing granulomatous chronic inflammation of suprasellar lesion. Differential diagnosis mainly included Rosai-Dorfman Disease and Langerhans' cell Histiocytosis. Final histological report confirmed the diagnosis of LCH. She developed hydrocephalous post biopsy and required VP shunt. Urgent radiotherapy was started to control the disease progression. Repeat MRI after completion of radiotherapy showed significant reduction in size of lesion. Three years following radiotherapy she remains stable with no evidence of local or systemic disease progression, although she remains hypopituitary and has significant hypothalamic symptoms.

#### Conclusion

Langerhans' cell histiocytosis, localised in the hypothalamic-pituitary region is very rare, especially in adults. Diabetes insipidus is considered to be a hallmark of this condition. The gold standard for diagnosis of LCH is positive histology and immunohistochemistry evidence. Limited literature data show that low-dose irradiation ( $\leq 22$  Gy) is usually the first-line treatment and adequate in most cases of isolated LCH of Hypothalamic Pituitary region.

DOI: 10.1530/endoabs.69.P69

## P70

### **Insulinoma diagnosed in a patient with learning disability with presentation of seizure being treated as epilepsy for two years**

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#### Case history

49 year old female with learning disabilities who was being treated as epilepsy for 2 years and attended the GP surgery for routine bloods. Patient had a seizure like activity and fell onto both knees. X ray which showed a distal femur fracture which was undisplaced and was extra-articular and patellar fracture. Patient was found to be hypoglycaemic on the ward and she was treated with 10% dextrose infusions. She underwent Left knee exploration and repair of medial retinaculum of quadriceps tendon and excision of patellar fragment. Post operatively, she was again found to be hypoglycaemic and had treatment with dextrose infusion. Due to persistent hypoglycaemic episodes, she was transferred to the endocrinology ward. She was found to have a C peptide of greater than 1100. Insulin antibodies were negative, cortisol  $>350$ , TSH = 1.8. Her sulfonlylurea screen was negative. Patient was started on diazoxide to help control blood sugar and this was found to be effective eventually.

#### Investigations

Patient underwent a CT AP which didn't showed any pancreatic lesion, she had endoscopic ultrasound which found a small lesion on the tail of the pancreas measuring  $13 \times 9$  mm hypochoic well defined lesion, which has good Doppler signals indicating high vascularity, suggesting a possibility of a NET. Biopsies were taken. Histopathology showed clusters of ovoid epithelial cells having bland nuclei resembling those of neuroendocrine cells that stain with synaptophysin and chromogranin in addition to Ber EP4, consistent with well-differentiated neuroendocrine tumour, Immunohistochemistry findings were positive for BerEP4 and Synaptophysin, chromogranin – smaller cells, it was negative for CA19.9, CD56.

#### Results and treatment

The morphology and IHC findings are consistent with a neuroendocrine tumour, case was discussed with regional tertiary care centre in NET MDT and the lesion was surgically excised with enucleation of the mass resulting in complete resolution of symptoms and came off anti-epileptic medications.

#### Conclusions and points for discussion

Insulinoma is a rare neuroendocrine tumour and can occur at any age with nonspecific sign and symptoms. While evaluating a patient with presentation of seizure, toxic and metabolic causes should always be considered as they are potentially curable, and may be fatal if left untreated. This case report highlights the need for careful assessment of all seizures and monitoring of blood sugars as this was a challenging case due to learning disabilities. A multidisciplinary approach and timely and effective collaboration of medical, surgical, radiological and histopathology teams for best patient outcome.

DOI: 10.1530/endoabs.69.P70

## P71

### **Metastatic clear cell renal carcinoma with initial presentation of thyroid mass**

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#### Case history

A 70 year old man presented with a six month history of sore throat and dysphagia. His past medical history included Type 2 diabetes and dysarthria due to tracheomalacia following tracheostomy at the age of 40 when he was involved in a road traffic collision. Initially he was diagnosed with gastroesophageal reflux, but symptoms did not settle with proton pump inhibitor medication. He as therefore referred to the ENT team for further evaluation.

#### Investigations

Fibreoptic assessment (rigid oesophagoscopy and tracheal bronchoscopy) by ENT team showed significant tracheal stenosis from external compression with normal pharynx and larynx structures. He underwent a thyroid CT scan which revealed a large goitre with severe retrosternal extension with anterior and posterior compression of the trachea. His thyroid function test was normal. He underwent left hemithyroidectomy. Histology revealed metastatic clear cell renal carcinoma (CCRC) grades 2–3. Staging CT scan of the chest, abdomen and pelvis identified a 5 cm right kidney upper lobe mass with paraaortic lymph node enlargement with lung and adrenal metastatic lesions, making it a T3aN1 renal cell carcinoma.

#### Results and treatment

The patient underwent right sided laparoscopic nephrectomy and total thyroidectomy. He also received tyrosine kinase inhibitor therapy for systemic treatment. Unfortunately his disease progressed, with increase in size of lung and lymph node metastasis and new pancreatic deposits.

#### Conclusions and points for discussion

CCRC is the most common subtype of renal cell carcinoma – up to 75% of cases. Metastatic malignancy in the thyroid gland from any primary cancer is rare (2–3% of thyroid malignancies) despite its good blood supply, and the commonest primary cancer that metastasizes to the thyroid is renal cell cancer (25–50% of thyroid metastasis).

Most thyroid metastases occur several years after treatment of primary cancer – on average 9 years. It is unusual for thyroid metastasis to be the first presentation on (despite of our case).

Thyroid imaging is not useful in differentiating between primary and secondary thyroid malignancies and CT imaging is not usually undertaken unless there are compressive symptoms.

FNAC is a good tool to establish definitive diagnosis but occasionally it is difficult distinguish metastasis from primary tumors of thyroid.

If FNAC is inconclusive, immunohistochemistry can help in the differential diagnosis. Thyroid metastasis should be considered in patients.

DOI: 10.1530/endoabs.69.P71

## P72

### **Parathyroid adenoma in a young man <35 years old**

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#### Section 1: Case history

23 Year old Caribbean gentleman attended A&E with several month history of non-specific headaches, changes in memory/mood and joint pains. Since the age of 5 he had been medically treated for renal stones. He had a past medical history of sickle cell trait and was not on any regular medications. There was no significant family history apart from sickle cell disease. He had initial bloods which showed serum adjusted calcium level 3.7 mmol/l and PTH 208 pmol/l. He was immediately treated with IV 0.9% saline. On review the next day he was started on IV pamidronate and had a full endocrine screen.

#### Section 2: Investigations

Initial blood results showed: PTH level 208 pmol/l, adjusted calcium level 3.7 mmol/l, phosphate level 0.56 mmol/l and a vitamin d level 35 nmol/l. Normal range TFTs, cortisol, GH, IGF1 and serum glucose. Normal renal profile. 24 h urine calcium collection showed a low creatinine level 3.20, calcium level in urine 2.83 making a calcium : creatinine ratio 0.9. US parathyroid was

normal. NM parathyroid scan SPECT showed focal uptake in the lower left pole of the parathyroid gland likely a parathyroid adenoma. US renal showed early changes in bilateral medullary nephrocalcinosis. DEXA bone scan was normal. CT chest abdomen and pelvis showed no significant findings. ECG changes showed left ventricular hypertrophy. Echocardiogram showed normal function.

#### Section 3: Results and treatment

Patient has been attending regularly for bone profile, vitamin d, PTH and renal review. He has been on fortnightly pamidronate infusions and has noticed a dramatic change in his memory, mood and non-specific bone pains. He continues to maintain oral hydration drinking 2–3 l water per day. He awaits for his genetic markers and parathyroidectomy.

#### Section 4: Conclusions and points for discussion

Most parathyroid adenomas as seen in middle aged women >55 years old. This is an interesting case of a young gentleman who presents with early onset renal stone disease since the age of 5. He has since suffered with school work and exams due to high calcium levels and this has impacted his education. This case highlights the importance of excluding genetic parathyroid adenomas. Currently at Guys and St Thomas Hospital we screen for 8 genes which are linked to >10% of inherited parathyroid adenomas in the <35 year old age category. All of these genes are autosomal dominant.

DOI: 10.1530/endoabs.69.P72

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