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Society for Endocrinology: Endocrine Update 2018

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National Clinical Cases

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Society for Endocrinology

NATIONAL CLINICAL CASES

National Clinical Cases

Oral Communications

OC1

Testosterone secreting clear cell ovarian tumor in a patient with Von Hippel Lindau (VHL) disease

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The *VHL* gene is a tumor suppressor gene located on chromosome 3p25.3. Mutations in this gene prevent production of the VHL protein and as a result, cells grow and divide uncontrollably to form the tumors and cysts. Germline *VHL* gene mutations predispose to a variety of tumors, most commonly retinal and cerebellar haemangioblastomas, renal cell carcinoma and phaeochromocytoma. Papillary cystadenomas of the epididdymis are seen in 10–26% of men are rarely in broad ligament of the uterus. Mutations in the *VHL* gene are inherited in an autosomal dominant pattern. A 26 years old female with a known mutation in *VHL* gene was under surveillance in genetic endocrine clinic. In the last 5 years she had undergone three surgeries for cerebellar haemangiblastomas. She had retinal angiomas and a cervical haemangioblastoma at C2/3. She was known to have a cyst in the right ovary measuring 4.9 cm. This had not changed in size in 4 years and her tumor markers were negative. She presented with 6 month history of feeling tired, amenorrhea and deepening of voice. Her pelvic ultrasound scan showed an increase in the size of right ovarian cyst. It measured 6.8 cm with a lobulated appearance. She had LH of 1.1 IU/l (1–9), FSH 2.3 IU/l (1–10) and testosterone of 22.1 nmol/l (0.5–2). She had a diagnostic laparoscopy and the right ovarian cyst was removed. Her periods started after 11 months of amenorrhea. Her postoperative testosterone was 1.5 nmol/l. Histology of the ovarian cyst showed it to be a clear cell carcinoma. In view of *VHL* mutation this was thought to be a metastasis from a renal cell carcinoma. This patient had no evidence of Renal cell carcinoma. The most likely diagnosis was testosterone producing clear cell carcinoma of the ovary. The ovarian cyst was documented on the ultrasound scan 4 years ago and was non functioning before changing to a testosterone secreting tumor. Over-expression of hypoxia inducible HIF 1a has been reported in clear cell carcinoma of the ovary. Did the character of the ovarian tumor change because of inducible proteins secondary to over-expression of HIF-1a? To our knowledge this is the first case of testosterone secreting clear cell ovarian tumor in association with VHL.

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OC2

Episodic primary aldosteronism associated with a novel gain-of-function mutation in a cell adhesion molecule

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Case history
A 46-year-old headmaster with a 10-year history of hypertension presented with a BP of 164/116 mmHg on four antihypertensive drugs. He had occasional headaches, chest 'aches', and described one syncopal episode after an 'exhausting rowing session'. A low plasma renin (routinely measured in our resistant hypertensives) and 26/20 mmHg fall in BP on changing hydrochlorothiazide to amiloride, led to investigations for primary aldosteronism (PA).
Investigations
Plasma electrolytes were normal. Initial plasma renin (10 mU/l) and aldosterone (537 pmol/l) were also below Endocrine Society thresholds for investigating PA. However values fluctuated between diagnostic (aldosterone 647 pmol/l, renin 5.0 mU/l) and completely normal (aldosterone 147 pmol/l, renin 11.0 mU/l) despite withdrawal of interfering medications. A 13 mm right adrenal nodule (HU4) was observed on CT. Initial adrenal vein sampling showed no increase in aldosterone or cortisol secretion compared to IVC from the contra-lateral (left) adrenal, but repeat during ACTH infusion showed a lateralisation index $>7{:}1$ (right:left).
Results and treatment
He successfully underwent a right adrenalectomy. H&E plus immunohistochemistry showed a zona glomerulosa-type macroadenoma, and adjacent microadenoma (cluster) with compact cells staining densely for CYP11B2, but only patchy weak staining for CYP11B1. At 3 years post surgery he remains normotensive off treatment, but complained of weight loss, muscle fasciculation, cramps and fatigue. Plasma aldosterone (150 pmol/l) and renin (0.4 nmol/l per hr) were normal. A random cortisol was 115 nmol/l, but a repeat pre-and post-synacthen showed values of 225 nmol/l (baseline), 463 nmol/l (30 min) and 640 nmol/l (60 min). On DNA sequencing the adenoma was negative for all known somatic mutations. Whole exome sequencing revealed a novel Valine-to-Aspartate mutation in the transmembrane domain of a cell adhesion molecule, whose transfection into H295R adrenocortical cells caused 10–20 fold increase in aldosterone synthesis and secretion.
Points for discussion
The significance of the new mutation was supported by the discovery of a similar patient in Munich, and studies point to the importance of cell-cell contact for regulation of normal zona glomerulosa function. The combination of variable aldosterone secretion by our patient, and experimental evidence of diurnal fluctuations, suggest that this mutation may cause episodic PA, and therefore be commonly missed. Borderline adrenal insufficiency many years post-adrenalectomy, *not* due to CYP11B1-expression (cortisol-cosecretion) by the adenoma, may be under-recognised. It is consistent with previously described genetic variants in the promoter of CYP11B1, which are compensated (and masked) by over-production of ACTH, but only while both adrenals are intact.

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OC3

Hyperprolactinaemia resistant to dopamine agonist due to an ectopic source of prolactin arising from a Uterine Tumour Resembling Ovarian Sex Cord Tumours (UTROCST)

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Introduction
Moderate hyperprolactinaemia occurring in a patient with a normal pituitary MRI, assuming macroprolactin and stress are excluded, is generally considered to be due to a lesion below the level of detection of the MRI scanner. Most patients with mild-moderate hyperprolactinaemia and a normal MRI respond to dopamine agonist therapy. We describe a patient who had prolactin elevation typical of a prolactin-secreting macroadenoma, but with a normal MRI, and in whom the prolactin rose further with dopamine agonist treatment.
Case
A 46 year-old female presented with 12 months history of secondary amenorrhoea without galactorrhoea. Prolactin was 4746 mIU/l without macroprolactin complexes, LH & FSH were low and oestradiol was undetectable. She had normal visual fields and no other clinical or biochemical features of pituitary dysfunction. She was not on regular medication. Pituitary MRI was normal with no focal lesion. She was started on cabergoline 250 mcg twice weekly which was subsequently increased to 500 mcg twice weekly. Repeat serum prolactin 5 months and 8 months later showed a progressive rise to 6649 mIU/l and 9653 mIU/l respectively, and rose to 11,611 mIU/l. Compliance with medication was confirmed. Repeat pituitary MRI scan was normal. An alternative source of prolactin was considered and further clinical assessment revealed a palpable pelvic mass. Pelvic CT showed an 11 cm uterine mass which raised the possibility of an ectopic prolactin source. She underwent surgical resection. Histological examination showed a benign Uterine Tumour Resembling Ovarian Sex Cord Tumours (UTROSCT). Immunohistochemistry was negative for prolactin, however, serum prolactin postoperatively was 59 mIU/L and her menstrual cycle returned to normal.
Discussion
The notable features of this case were (1) the high prolactin suggestive of a macroadenoma with a normal MRI scan (2) a paradoxical rise in the serum prolactin after initiation of dopamine agonist therapy. Out of eight previous reports of ectopic extra-cranial prolactin secretion in the published literature, there are three ovarian germ cell tumours (two teratomas, one dermoid) which had microscopic pituitary elements. UTROSCTs are very rare uterine neoplasms with the most literature review citing 77 cases. UTROSCTs have not been associated with hyperprolactinaemia prior to this report. However, two other cases have been reported with uterine tumours (one "fibroid" and one "mesenchymal tumour") which share characteristics with this case. Hyperprolactinaemia due to extra-cranial ectopic prolactin production is very rare. Where suspected, the majority of ectopic prolactin-secreting tumours have been located in the ovaries and uterus.

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OC4

Management of massive (up to 550 mm) bilateral adrenal masses in a non-adherent patient with 21-hydroxylase deficiency congenital adrenal hyperplasia:complex risk benefit analysis

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Case history
We report a 38 year-old Caucasian woman with classical salt wasting congenital adrenal hyperplasia (CAH) who increasingly omitted medication in adolescence and eventually spent over 10 years without any adrenal replacement therapy or adrenal crises and became lost to follow up. When seen, she complained of increasing abdominal girth, fatigue, hirsutism, had type 2 diabetes, had never had a romantic/sexual relationship and was amenorrhoeic. Examination revealed abdominal distension by a massive palpable mass.
Investigations
Initial blood tests showed random serum Cortisol 149 nmol/l (200–600), Renin (plasma) 751.0 mU/l (2–30), plasma ACTH 333.0 ng/l (0–40), 17-OH-progesterone $>$726 nmol/l and serum total Testosterone 6.4 nmol/l. CT showed massive bilateral adrenal tumours which grew substantially during 3 years follow up during which ACTH and 17-OHP were appropriately suppressed. Displacement and distortion of abdominal viscera were noted.
Results and treatment
Massive bilateral adrenal enlargement, secondary to chronic ACTH stimulation due to non-adherence with adrenal replacement therapy was diagnosed. A long process of re-engagement with the patient took place until it was felt that the risk of further non-adherence was lower than the risks of leaving such massive adrenal glands *in situ*. The surgical strategy was to remove the larger left adrenal gland and if straightforward, to proceed to the contralateral side. Bilateral surgery was performed. The left adrenal weighed 11,405 g and measured 550 $\times$ 310 $\times$ 230 mm. The smaller right adrenal measured 170 $\times$ 145 $\times$ 180 mm. Histology confirmed florid hyperplasia with myelolipomatous metaplasia, consistent with untreated CAH.
Conclusions and points for discussion
Bilateral adrenalectomy is a therapeutic option in CAH particularly where the GC dose required for acceptable androgen suppression causes unwanted effects. Here, bilateral adrenalectomy had the potential to create new complete adrenal insufficiency in a patient whose risk of adrenal crisis might well be augmented by established treatment non-adherence. However, this risk had to be weighed against the additional risk of such massive bilateral adrenal enlargement (including haemorrhage, torsion, rupture, infarction, neoplasia and displacement of other viscera and possible diabetogenic effects of the intra-abdominal fat) particularly as it was clear that the masses continued to grow even after appropriate treatment and apparent adherence for a total of 3 years. Although it seems likely that the process of adrenal enlargement was initially ACTH-dependent, it is clear that progressive adrenal expansion eventually became independent of ACTH.

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OC5

Stalk and infudibular thickening – A diagnostic conundrum

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Case history
Fifty-eight years old gentleman referred to endocrinology with erectile dysfunction and decreased libido for 1 year. He denied headache or visual disturbance. His past medical history include ulcerative colitis (1998), mild asthma, anterior scleritis (2003), previous DVT (1994), Episode of steroid induced psychosis in past. He is on levothyroxine, sulfasalazine, calcium /vitamin D and long term prednisolone 4 mg (9 years). Examination reveal testicular volume of 16ml bilaterally, penile length of 7.5 cm, normal visual field on confrontation.
Investigations
His initial testosterone was 0.5, FSH 2.9, LH 0.8, Prolactin 283, IGF-1 9.3, FT4 7.2 TSH 6.26 9am cortisol 108. MRI pituitary in 2012 reveal infundibular swelling in continuity with thickened pituitary stalk.
Results and treatment
His dose of thyroxine was increased and commenced on testosterone replacement. Reported history of polyuria lasted for 1 year, 3 years ago. His repeat imaging in April 2014 showed stable appearance. In February 2016, Pituitary size increased in size, referred to tertiary centre for consideration of biopsy. Whole body MRI reveal infundibular and pituitary enlargement. ESR, CRP, ACE levels, BHCG were all normal Anti ds DNA, Ro, La, Scl, Sm/RNP negative, pANCA positive, normal visual fields. His Repeat testosterone on testosterone replacement became 16.0 and FT4 normalized to 21.3 after increment in dose of thyroxine. PET Scan December 2016 showed low grade FDG activity in the pituitary with low grade avidity in right cervical, mediastinal and right paratracheal lymphadenopathy. Right cervical lymph node biopsy showed marginal zone lymphoma. He was reviewed by haematology, whether or not pituitary abnormality is caused by low grade lymphoma, which would necessitate treatment, otherwise wait and watch. He underwent pituitary biopsy which reported IgG4 related disease. He has been referred to rheumatology for consideration of steroids $+/-$ rituximab.
Conclusions and points of discussion
Diagnosis was Plasmocytic Hypophysitis secondary to IgG4-RD associated with hypopituitarism and marginal zone lymphoma. Prevalence of IgG4-related hypophysitis has been underestimated. It is increasingly recognized immune-mediated condition, most often occurring in middle-aged/older men. In a report of 170 patients with hypopituitarism, of whom 23 had hypophysitis, seven were diagnosed with IgG4-related hypophysitis giving a prevalence of 30 and 4 percent of hypophysitis and all hypopituitarism cases, respectively. Several types of lymphoma have been reported in patients with IgG4-RD, both in Japan and in North America. Discuss treatment options of this condition.

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OC6

Management of T3-toxicosis in pregnancy

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Case history: Pre pregnancy
A 31-year-old female with no family history of thyroid disease presented with clinical hyperthyroidism and large goitre with bruit. Graves' Disease was confirmed: TSH $<$0.01 (0.35–5.0 mU/l), free T4 53.4 (9.0–21.0 pmol/l), TSH Receptor Antibodies (TRAB) $>$40 (0–1.9 U/l), TPO 32.2 ($<$6 U/ml). She started on carbimazole (CBZ: 20 mg BD) and propranolol. She then switched to propylthiouracil (PTU: 150 mg BD) at 2 months due to desire for future pregnancy. US thyroid showed a $>$5 cm, hyper-vascular lobulated goitre.
First trimester
Booked to obstetric/endocrine clinic at 7–8 weeks' gestation, four months after original presentation**.** Booking bloods: T4 (fT4 7.1 pmol/l), Total T3 $>$ 12.3 nmol/l, TSH $<$0.01 mU/l). Due to low T4 in very early pregnancy, PTU and propranolol were continued but T4 considered, then eventually added, to maintain the mothers T4.
Second trimester
Mother continued anti-thyroid medication (PTU then CBZ) with supressed TSH, raised T3 and clinically improved but ongoing signs of thyrotoxicosis. Foetal thyroid scanning was commenced at 18 weeks. Foetal goitre ($>$95th centile) was seen from 21/40 with radiological evidence of thyrotoxicosis (central vascularization on Doppler) but normal foetal heart rate. Cordocentesis was offered but declined. In conjunction with obstetrics, CBZ was increased. Foetal goitre increased, therefore cordocentesis and foetal MRI were undertaken at 27/40. MRI confirmed a foetal goitre (right lobe 1.4 cm$\times$1.2 cm, left lobe 1.4 cm$\times$1.1 cm) with minor airway flattening. Cordocentesis suggested foetal hypothyroidism: TSH 36.45, fT4 9.8, total T3 0.3. Maternal CBZ was down-titrated to 5 mg with reduction in foetal goitre from 31/40; thyroid circumference $<$50th centile by 37/40. Foetal growth scans were normal throughout.
Delivery and postnatal
Maternal biochemistry at 39/40: TSH $<$0.01 mU/l, fT4 15.0 pmol/l, total T3 3.2 nmol/l, TRABs 3.7 U/l. Baby was delivered by uncomplicated SVD. Neonatal biochemistry was nominally euthyroid at birth but showed neonatal thyrotoxicosis at 5 days (TSH 0.31 mU/l, fT4 40.1 pmol/l, total T3 2.7 nmol/l, TRAB 6.1 U/l).
Conclusions and points for discussion
We describe a rare case of resistant T3 toxicosis in pregnancy. A number of discussion points include 1. Pre-pregnancy planning in women with Graves' Disease, 2. Consideration of need for T4 supplementation when levels are low in T3 toxicosis in pregnancy, 3. Foetal monitoring with role of fetal ultrasound (for size and signs of hypo- and hyperthyroidism) and cordocentesis, 4. Neonatal thyrotoxicosis.

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OC7

Prolonged response to radiolabeled Yttrium^{90} DOTATATE in a patient with metastatic insulinoma – 5 years follow up

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Case history
We have previously presented the case of a 31 year lady presenting with a seizure following exercise with a blood sugar of 1.4 mmol/l on a background of an 8 month history of episodic slurred speech, blurred vision and hunger relieved by eating in 2011.
Investigations
Investigations confirmed an insulinoma and imaging, including Ga^{68} DOTATATE PET CT identified a lesion in the tail of the pancreas with multiple liver metastases. MEN1 testing did not reveal any mutation.
Results and treatment
She was treated with PRRT receiving 4 cycles of radiolabeled Y^{90} DOTATATE therapy between August and November 2011. This resulted in a complete resolution of symptomatic hypoglycaemia. We now present 5 year follow up data.
Conclusions and points for discussion
She remains free of hypoglycaemia. Although she has suffered episodes of anxiety, capillary blood glucose monitoring has always remained normal. She has had annual MRI scans of the liver and pancreas which have shown stable changes. In 2017 she had a 5 year follow up Ga^{68} DOTATATE PET CT scan the showed no somatostatin receptor avid lesions. The remaining stable lesions seen in the liver could represent scar tissue. She continues to have clinical follow up. This case illustrates that PRRT can result in long lasting remission of hypoglycaemia even in metastatic insulinoma as 5 years after treatment, and 4 years since this case was last presented, the patient has remained symptom and somatostatic receptor avid lesion free.

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OC8

Recurrent severe hypoglycaemic episodes in the context of insulin receptor antibodies

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We present a 32-year-old woman with recurrent hypoglycaemic episodes and a history of juvenile onset SLE. Over months, she experienced severe hypoglycaemic episodes with unconsciousness, occuring mainly in the early morning resulting in several hospital admissions. The patient had to take precautions like eating snacks between meals and before going to bed, and even setting an alarm clock to eat a bowl of porridge at 0200 h. She was of normal weight, did not present with any hyperpigmentation or acanthosis nigricans and did not have a history of diabetes mellitus. The known juvenile onset SLE had been difficult to control over the years with recurrent flares. Current treatment included prednisolone, hydroxychloroquine and azathioprine. A fasting blood test revealed a blood glucose of 1.8 mmol/l with borderline insulin level of 2.3 mIU/l and undetectable C-peptide, making an insulinoma unlikely. NEFA and 3-hydroxybutyrate were inappropriately low, suggestive of hyperinsulinaemia or action via the insulin receptor. Drug-induced hypoglycaemia and sulfonylurea abuse was excluded, the ongoing prednisolone treatment contradicted an underlying hypocortisolism. Insulin antibodies were found to be negative on two separate samples. A random insulin study was performed, showing hyperinsulinaemia (3,504 pmol/l), elevated C-peptide (3,240 pmol/l) and raised adiponectin concentration (27.1 µg/ml), consistent with an insulin receptor dysfunction. In fact, insulin receptor antibodies were found to be weakly positive, giving diagnosis a type B insulin resistance syndrome. In view of another flare of her SLE and the newly diagnosed type B insulin resistance, our patient was commenced on Rituximab which helped control her hypoglycaemia. After two doses, she did not have any more hypoglycaemic episodes. Type B insulin resistance with insulin receptor antibodies is a very rare condition, commonly associated with other autoimmune diseases. The history of SLE in our patient, severe fasting hypoglycaemia, hyperinsulinaemia and raised adiponectin concentration were suggestive of the underlying insulin receptor dysfunction. The most common symptom of type B insulin resistance is hyperglycaemia with extremely high insulin need while some patients seem to suffer both from hyper- and hypoglycaemic episodes, possibly due to fluctuating antibody titers. Our patient presented purely with hypoglycaemic episodes. Treatment for this condition is not yet standardised, and the production of autoantibodies may even remit spontaneously. Different therapeutic approaches in the past achieved very mixed outcomes, and although our patient showed a great improvement on Rituximab, the duration of remission and possible long term treatment remains unknown.

DOI: 10.1530/endoabs.55.OC8

OC9

Appearances can deceive - a rare presentation of paraganglioma

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Case
A 36-year-old gentleman presented with two month history of severe headaches, vomiting, polyuria and polydipsia. He reported profound episodic sweating especially on exertion and gradual weight loss. He was hypertensive (220/110 mmHg) at presentation. He had no palpitations, anxiety, dizziness, flushing or pallor. He had no diarrhoea or abdominal pain. His only family history was of Type 2 diabetes mellitus.
Investigation
Biochemical investigations showed glucose (23 mmol/l), ketones (3.3 mmol/l), and mild acidosis (pH 7.32). A diagnosis of DKA was made and treatment initiated. At this point investigations for secondary hypertension demonstrated elevated urinary and plasma Normetanephrine 4786 pmol/l (120–1180). He had a normal response to overnight dexamethasone suppression test. A diagnosis of a phaeochromocytoma/paraganglioma was biochemically suspected and a CT-abdomen showed a 6 cm left retroperitoneal necrotic lesion and NM-MIBG (123) scan was consistent with a MIBG-avid left adrenal lesion.
Treatment
A laparoscopic left adrenalectomy was performed following adequate alpha and beta blockade. Histopathology demonstrated a paraganglioma (positive for chromogranin and synaptophysin, and negative for inhibin and melan-A) with a PASS score of 11/20. Genetic testing confirmed an heterozygous mutation for C.689G > A,p(Arg 230His) of *SDHB gene*. Unfortunately on follow up scan a new Rib deposit was identified as well as a carotid body tumour. From a diabetes perspective he was started on insulin, but interestingly, when he was started on alpha and beta blockade, his glycaemic control improved: he stopped his prandial insulin and remained on a low dose of basal insulin. At presentation, his fasting C-peptide (89 pmol/l) was low with a glucose of 7.2 mmol/l supported a diagnosis of type 1 diabetes mellitus. However his anti-GAD, anti-IA2 and anti-islet cell antibodies were negative and his HbA1c was 11%. Four months after the removal of his tumour he developed hypoglycaemia and his insulin injections were stopped. His HbA1c normalised as well as his C-peptide suggesting that the initial DKA was as a result of excess catecholamines. Glycaemic indices have started to rise again now when a new likely metastatic deposit has been identified.
Conclusion
Diabetic ketoacidosis as first presentation of a paraganglioma is extremely rare. This case demonstrates the importance of evaluation of secondary causes of hypertension in young patients even in the setting of DKA. In our case, it led to early identification of a tumour with malignant propensity and possible marker for follow up.

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OC10

An unexpected VIP

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Case history
A 69-year-old Caucasian male presented with persistent abdominal pain and was found to have a large right adrenal mass on CT. Interestingly his family history

revealed that his daughter had been treated for Cushing's disease. He was normotensive and denied classical symptoms of catecholamine excess. He had exertional dyspnoea in keeping with COPD. Subsequent tests were consistent with a secretory phaeochromocytoma and urine normetadrenaline 85,671 nmol/day (<4,400 nmol/day), metadrenaline 39,110 nmol/day (<2,00 nmol/day) and 3-methoxytyramine 3,154 nmol/day (<2,500 nmol/day). He was commenced on alpha- and beta-blockade. Whilst on holiday, prior to surgery, he collapsed with abdominal pain and developed severe watery diarrhoea.

Investigations

Blood tests on admission to A/E revealed acute renal failure with profound hypokalaemia. Stool samples tested negative for bacterial and parasitic infections but the life-threatening high volume diarrhoea continued, requiring large volumes of fluid resuscitation. A repeat CT abdomen was in keeping with new central necrosis.

Results and treatment

The patient was transferred, due to the difficult to manage severe diarrhoea and for consideration of an octreotide infusion. After 10 days and significant weight loss, the diarrhoea started to abate and five weeks later he underwent an open right adrenalectomy with an uneventful recovery period. Results received post-operatively revealed that his fasting gut peptides on transfer showed vasoactive intestinal peptide (VIP) levels of 300 pmol/l (<30). Subsequent post-operative fasting VIP levels were undetectable. Histology confirmed a phaeochromocytoma with a Ki-67 of up to 20% and SDHB immunohistochemistry was normally expressed.

Points for discussion

We present a rare complication, which we attribute to the partial infarction of a large secretory phaeochromocytoma. We will discuss the propensity of large phaeochromocytomas to undergo infarction or bleeding, which in turn can lead to a crisis. In this case the alpha and beta- blockade partially protected the patient from the catecholamine surge but the unexpected release of VIP was life threatening in itself. The timing of surgery for phaeochromocytomas remains a difficult clinical balance weighing up the benefits of a period of blockade versus the potential risks of having a 'blocked' phaeochromocytoma in situ. The fact that many phaeochromocytomas make other peptides adds to the uncertainty and we will discuss the peptides that can contribute to these management difficulties.

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Poster Presentations

P01

A case of primary aldosteronism and Hashimoto's thyroiditis – complicated relationship or pure coincidence?

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Aldosterone is a steroidal hormone that specifically binds to the mineralocorticoid receptor (MR). Production and secretion of aldosterone is triggered by changes in blood pressure (BP). Primary aldosteronism (PA) is an important cause of secondary hypertension. The effects of aldosterone have been described in renal and vascular tissue but recent studies have shown that MR is also expressed in non- epithelial cells such as those of the immune system. A 29-year-old Afro-Carribbean man was referred to clinic with treatment-resistant stage 2 hypertension and an elevated renin-aldosterone ratio. He was initially seen in cardiology clinic for palpitations, atypical chest pain and a BP 185/123 mmHg. Indapamide 2.5 mg daily was initiated. He had no history of headaches, dizziness, nausea or vomiting. Hypertension screen demonstrated an elevated aldosterone renin ratio (ARR) >1850. There were no features to suggest Cushing's or acromegaly and no evidence of goitre although the patient complained of recent weight gain and symptoms suggestive of hypothyroidism. Thyroid function tests (TFTs) performed at his initial visit were consistent with primary thyroid disease (free thyroxine 9 pmol/l, thyroid stimulating hormone 27.52 Miu/l) necessitating treatment with levothyroxine 50 mcg twice daily. His BP control remained suboptimal and Doxazosin 2 mg twice daily was added. The patient was reviewed in 4 months at which point his BP had improved to 139/77 mmHg. A saline infusion test was suggestive of primary disease (baseline aldosterone 750 pmol/l with a 4 h aldosterone suppression result of 430 pmol/l). Magnetic resonance imaging of the adrenal glands showed no evidence of adrenal adenoma. Adrenal venous sampling indicated bilateral secretion of aldosterone. Repeat TFT's on levothyroxine showed adequate replacement (TSH 5.37 Miu/l, free T3 5.6 pmol/l, free thyroxine 9.7 pmol/l) and very high titres of thyroid peroxidase antibodies 1579 u/Ml. The patient was started on Spironolactone 50 mg daily. Autoimmune diseases are more common in women with a more Th2- predominant immune response, whereas a Th1 response and inflammation is usually more severe in men. Chronic thyroiditis is classified as a Th1 disorder. There has been evidence to suggest that mineralocorticoids have been strongly associated with the modulation of various cells of the immune system. This is the first reported case of PA in a man exacerbating the course of autoimmune thyroid disease. For patients presenting with PA, it would be wise to consider the possibility of coexistent autoimmune disease.

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P02

Abstract withdrawn.

P03

Non-functional duodenal neuroendocrine carcinoma- a rare cause of diabetes mellitus

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Case history
We present a 40 year old female admitted with hyperglycaemia, polyuria, polydipsia and weight loss of 6 kg over a 1 month period. She had no night sweats or change in bowel habit. There was no personal or family history of malignancy or diabetes mellitus. She denied any alcohol, cigarette or illicit drug use. She took no prescription or OTC medication. On examination, she was jaundiced with pale mucous membranes. The rest of systemic examination was normal. Capillary glucose was 23.1 mmol/l.
Investigations
FBC, LFT, U and E, HbA1c, Urinary ACR, blood film, fasting gut hormone profile, CT- chest, abdomen and pelvis, duodenoscopy and biopsy, MRI liver, Octreotide scan, Endoscopic Ultrasound and biopsy, Screen for MEN 1 syndrome.
Results and treatment
Hb- 64, Wcc- 8.4, platelet count- 346, lab glucose - 21.8 mmol/l, T -bili 48, Alp 687, Ast - 96, Alt - 117, Urea- 2.5, Cr- 52, Na- 136, k - 4.6, Hba1c –79 mmol/mol, Blood film- iron deficiency anaemia, Urinary ACR- 5.4, Pituitary profile, Calcium and PTH normal. Fasting gut hormones: Vip- 4 (<30 pmol/l), pancreatic polypeptide- 12 (<3000 pmol/l), gastrin −8 (< 40 pmol/l), glucagon- 14 (0 to 50 pmol/l), Somatostatin- 174(0 to 150 pmol/l). Chromogranin A- 78 (0 to 60 pmol/l), chromogranin B −49 (0 to 150 pmol/l). Duodenoscopy and biopsy- flat velvet like lesion in anterior wall of 2ndpart of duodenum around ampulla. Biopsy – tubovillous adenoma with low grade dyplasia. CT chest, abdomen, pelvis - significant dilatation of intra and extra hepatic biliary tree including pancreatic duct. Periampullary 30 mm mass lesion projecting into lumen of duodenum. Enlarged nodes around superior mesenteric artery. Confirmed on MRI liver. EUS and biopsy- Mass in medial wall duodenum. Suspicious node over SMA. Fine needle biopsy of duodenal wall and lymph node in keeping with grade 1, well differentiated neuroendocrine tumour. NM octreotide whole body scan and Spect CT- no uptake. Treatment-BD mixed insulin, transfused to Hb>8 g/dl. WHIPPLES PANCREATICO-DUODENECTOMY: R0 pT3 pN1 well differentiated neuroendocrine carcinoma arising in duodenum; Grade G1 (Ki 67: 0.5%); Venous invasion present; Involvement of 4 of 17 lymph nodes.
Conclusions and points for discussion
Duodenal NET with main pancreatic duct obstruction can present with hyperglycaemia and cause diabetes. This is in the absence of gluconeogenic hormones such as somatostatin and glucagon. There was complete resolution of diabetes post Whipple's procedure and patient is now off insulin. Her last HBA1C was 31 mmol/mol.

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P04

Case report – severe metabolic acidosis secondary to starvation ketoacidosis

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During starvation, ketone bodies acetoacetate and 3-D-hydroxybutyrate are freely soluble energy substrates made by the liver. Their major role is to supply an alternative glucose substrate for the brain under conditions of medium- and long-term energy restriction. The most common cause of pathological ketoacidosis is poorly controlled type 1 diabetic mellitus triggering uncontrolled hyperglycaemia. Other common causes are alcoholic ketoacidosis and fasting ketosis. In non-diabetic patients developing significant metabolic acidosis, important differentials include salicylate poisoning, methanol or ethylene glycol poisoning, elevated serum lactate levels, uremic acidosis or malnutrition with extremely poor oral intake. Clinically, fasting is rarely a suspected cause of significant metabolic acidosis. A 46-year-old patient with a 20-year history of multiple sclerosis presented to the emergency department for the second time in a 72-hour period with intractable vomiting. Regular medications were sertraline and topiramate. She had a Glasgow coma score 14, respiratory rate 28 breaths per minute, heart rate 90 beats per minute, blood pressure 110/65 mmHg. The patient was clinically dehydrated and exhibited Kussmaul breathing. Initial venous blood gas (VBG) showed a metabolic acidosis pH 7.005, pCO2 3.55 kpa, lactate 0.96, HCO3 7.5 mmol/l (22 – 26), base excess −23.6 m Default (−2 to +2), blood glucose 5 mmol/l, blood ketones 4.8 mmol/l (<0.6 mmol/l). Admission bloods ruled out paracetamol and salicylate poisoning, uraemia (urea 3.4 mmol/l), acute renal failure (normal urea: creatinine ratio and eGFR >90 ml/min per 1.73 m^2) and tumour lysis syndrome – serum uric acid 205 micromol/l (155–357). The patient had a high anion gap metabolic acidosis 17.6 mEq/l. She was started on a fixed rate insulin infusion (FRII) as per diabetic ketoacidosis (DKA) protocol and intravenous sodium bicarbonate 1.26%. Repeat VBG showed a worsening metabolic acidosis pH 6.97, base excess −26.6 mEq/l, bicarbonate 4.3 mmol/l. She was admitted to the high dependency unit. Her ketosis resolved after 24 hours on FRII and IV sodium bicarbonate. Starvation ketoacidosis is a rare but important differential diagnosis for metabolic acidosis.This case is unique on account of severity of ketoacidosis in a young, relative healthy patient. An exaggerated response to fasting has been described in pregnant patients, the elderly and young infants. There are currently no set guidelines for treatment of this patient subgroup but use of FRII in conjunction with IV sodium bicarbonate has proven to be successful in reversing the metabolic acidosis.

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P05

Curious case of hypercalcemia in pregnancy

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Hypercalcaemia during pregnancy is unusual and primary hyperparathyroidism is the commonest cause: we present a more unusual case.

Case history

29-year woman, 34 weeks pregnant, was admitted with hypertension and oedema. She had gestational diabetes managed with diet alone. Initial calcium level was normal; it gradually increased in the next few days though this was not noted. She was diagnosed with preeclampsia and treated with steroids for foetal lung maturation. Calcium level normalized after steroids but on the day of delivery was 2.74. She had an induced vaginal delivery at 35 weeks. 6 days later she was readmitted due to high blood pressure. Calcium on admission was 3.09. This was treated with iv fluids and then, when calcium rose to 3.19, a dose of pamidronate. She felt well and her only symptom was constipation. Examination was normal except for a flow murmur. Calcium fell into the normal range 2 weeks after pamidronate and remained normal subsequently. She was on 400 units of Vitamin D supplements as per RCOG guidelines, during pregnancy.

Investigations

PTH was 12 (15–60) and 25-OH vitamin D was 115.8 reflecting supplementation. Serum ACE was normal A PTHrP was undetectable, however this was taken 21 days after delivery. A low dose CT scan of chest Abdo-pelvis was done to rule out occult malignancy: this was normal except focal thickening of the gall bladder wall which ultrasound suggested was adenomyomatosis.

Results and treatment

Calcium remained normal during puerperium after treatment with a single dose of pamidronate.

Conclusions and points for discussion

A diagnosis of humoral hypercalcaemia of pregnancy was made in this case based on the acute rise in late pregnancy, suppressed PTH, and no malignant cause found. We feel vitamin D toxicity is less likely as she was not on high dose of Vitamin D supplementation. Vitamin D binding protein levels increases during pregnancy showing elevated levels of 25(OH)Cholecalciferol. Placental PTHrP production is thought to drive this unusual condition: unfortunately, we could not test PTHrP during the puerperium. Recurrence risk for this condition is not known and we have recommended monitoring of calcium levels in her next pregnancy.

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P06

Abstract withdrawn.

P07

A rare case of Buprenorphine patch induced central adrenal insufficiency

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Case history

A 39-year-old lady first presented to our endocrine outpatient clinic in September 2014 when blood tests at her GP surgery showed serum cortisol of 65 nmol/l. She had been having chronic back pain which is treated with Buprenorphine patches for many years. A Short Synacthen test (SST) showed an inadequate response. A low ACTH suggest secondary adrenal insufficiency. Other pituitary function tests and MRI of the pituitary were normal. After staying off buprenorphine patch for 3 months, a repeated SST showed an improved baseline cortisol with an adequate response to SST. The patient's back pain recurred and she resorted to buprenorphine patches again which then precipitated another episode of secondary adrenal insufficiency. She was treated with steroids and low dose Fentanyl patch. Repeat SST after stopping buprenorphine patch showed an adequate cortisol response. She remained well when she was last seen in September 2017.

Investigations, results and treatment

September 2014
Na + 140 mmol/l
K 4.3 mmol/l
T4 10.6 pmol/l
TSH 5.99 mIU/l
Serum cortisol of 65 nmol/l
SST: baseline corticol: 11 nmol/l; cortisol at 30 mins: 139 nmol/l; 60 mins: 183 nmol/l
Paired ACTH: 10 nmol/l

TREATMENT (September 2014): Stop buprenorphine patch and steroid replacement.

March 2015
SST: baseline cortisol: 123 nmol/l; 30 minutes: 438 nmol/l.
September 2015 (after restarting buprenorphine patch)
9 am baseline cortisol: 35 nmol/l.

Treatment(September 2015): Stop buprenorphine patch and steroid replacement.

Post stopping buprenorphine in Sept 2015:
SST: baseline cortisol of 226 nmol/l; 484 nmol/l at 30 minutes; 548 nmol/l at 60 minutes.

Conclusions and points for discussion

Opioid is a commonly prescribed medication for chronic pain. Long-term opioid medications have been shown to impair the hypothalamic-pituitary-adrenal (HPA) axis. There are only a few reported cases of secondary adrenal insufficiency (AI) from chronic opioid exposure. This is the first clinical case of secondary AI caused by chronic buprenorphine patch use. Buprenorphine is a partial agonist at mu opioid receptor. It has a long half-life of 24–60 hours. It is mainly used to treat opiates addiction and moderate chronic pain. Our case report showed that stopping long-acting opioid improved the function of HPA axis in a patient diagnosed with secondary AI. The recurrence of AI on drug rechallenge support buprenorphine patch as the cause of the event. Symptoms suggestive of AI in a patient on chronic opioid should instigate investigation of the HPA axis. There are no treatment guidelines currently.

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P08

Abstract withdrawn.

P09

Interesting unfolding of a case of refractory hypoglycaemia

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Case history

A frail 79 years old lady with dementia presented with frequent falls since 2 years ago. Neurologist's assessment had attributed her fainting episodes to migraine. She later was found to have biochemically evident recurrent hypoglycaemia requiring multiple admissions and eventually continuous glucose infusion to maintain euglycemia.

Investigations

The severe spontaneous hypoglycaemia in this non-diabetic lady prompted investigations. TFT and Short Synacthen Test excluded thyroid dysfunction and hypoadrenalism. The anterior pituitary profile was normal. During the event of hypoglycaemia (blood glucose 1.57 mmol/l), inappropriate elevation of C-peptide 4210 pmol/l (174–960 pmol/l) and proinsulin > 200 (0–7 pmol/l) was noted, along with a suppressed Insulin at 12 pmol/l(0–180). However, a contrasted CT revealed a normal pancreas. Unexpectedly, a heterogeneously enhancing mass (6.6 cm) was identified at the lower pole of the left kidney consistent with renal cell carcinoma. Concomitantly there were extensive peripherally enhancing heterogeneous mass lesions in the liver, the largest measuring at 12 cm. IGF-II:IGF-I ratio during

hypoglycaemia was less than 10, which was inconsistent with non-islet cell tumour induced hypoglycaemia (NICTH).
Results and treatment
In view of multiple comorbidities, a palliative approach was taken. The post-mortem confirmed a clear cell renal carcinoma of the left kidney. Unexpectedly, the liver metastases has morphology and immunoprofile consistent with proinsulin secreting neuroendocrine tumour. The immunostaining showed focal strong insulin immunoreactivity, as well as widespread CD56, synaptophysin, and chromogranin A, with negative staining for RCC.
Conclusions and points for discussion
Proinsulinomas are rare and can be missed if plasma proinsulin concentration is not measured along with insulin. Proinsulin cross-reacts variably with c-peptide and insulin assays; the effect is assay dependent. In this case the discrepancy between the insulin and c-peptide concentrations was too great to be accounted for by the faster clearance of insulin, raising the suspicion of assay interference. The Diasorin liaison C-peptide assay used here has been shown to be 100% cross reactive with proinsulin based on spiking studies with a pro-insulin reference preparation. While reported cases of proinsulinoma are typically pancreatic in origin, this case has radiologically unremarkable pancreas despite concomitant renal and liver lesions. The unexpected radiological findings raised doubts if the hypoglycaemia was caused by the high malignancy load or NICTH. These were then confirmed to be completely separate entities immunohistochemically: Proinsulinoma of the liver, with a renal cell carcinoma. In view of proinsulinoma's rarity, no conclusive association had been drawn between the two to our knowledge.

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P10

Multiple bone tumours in primary hyperparathyroidism – not so brown after all

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Case history
A 28 year-old male of British origin was referred with a one-year history of a left-sided chest mass and an abnormal chest X-ray. He was otherwise fit and well, had a past medical history of vitiligo and had no relevant family history. His physical examination revealed some hypopigmented spots on his skin, several tattoos across his back and a firm mass on his left upper chest, which was mildly tender on palpation. He had no other palpable masses.
Investigations
Laboratory investigation revealed hypercalcaemia (adjusted serum calcium 2.63 mmol/l), an elevated parathyroid hormone (PTH 8.0 pmol/l), elevated bone markers (alkaline phosphatase 479 U/l, N-terminal propeptide of type 1 collagen 616 mcg/l) and a low vitamin D (9.1 nmol/l). Cross sectional imaging with computed tomography and whole body magnetic resonance imaging (MRI) showed multiple heterogenous tumorous areas involving the left superior pubic ramus, left acetabulum, left iliac bone, right clavicle as well as ribs bilaterally. The largest of these lesions was centred in the left 3rd rib and corresponded to the patient's palpable mass. Biopsy of this larger mass showed morphological features consistent with a brown tumour of hyperparathyroidism. Parathyroid scintigraphy revealed a hot spot that was thought to represent a parathyroid adenoma.
Results and treatment
The diagnosis of brown tumour of hyperparathyroidism secondary to a parathyroid adenoma was made and the patient underwent a targeted parathyroidectomy with histological confirmation of an adenoma. His post-operative bloods showed normal adjusted calcium and PTH levels, but worsening bone markers. MRI repeated serially to 3 years after the operation showed the bone lesions were increasing in size, instead of regressing, as might have been expected of a brown tumour. The initial biopsy was subsequently reviewed and found to show fibrous dysplasia with diffuse aneurismal bone cyst-like change. Genetic testing confirmed the diagnosis of polyostotic fibrous dysplasia. The patient has been managed conservatively and remains pauci-symptomatic.
Conclusions and points for discussion
We present a case of polyostotic fibrous dysplasia associated with primary hyperparathyroidism, which is the least frequent endocrinopathy in fibrous dysplasia. Whether hyperparathyroidism was a result of the genetic changes present in fibrous dysplasia or whether it was a mere coincidence for them to present in the same patient remains uncertain. The role of bisphosphonates in the management of these patients is controversial although we have concern over the proximity of this expanding bone lesion to the heart.

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P11

A challenging case of rapidly enlarging thyroid mass

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A 60 year old Caucasian woman presented with a three month history of rapidly enlarging neck swelling and hoarseness of voice. Her past medical history included Hypothyroidism. Her neck ultrasound scans showed 3.5 cm left thyroid nodule with bilateral lymphadenopathy (U5). The Fine needle aspiration (FNA) revealed densely grouped variable sized irregular epithelial cells with nuclear atypia and spindle shaped fragments with focal areas of lymphocytic thyroiditis. The differential diagnoses included poorly differentiated thyroid cancer or a metastatic head and neck tumor. Second ultrasound scan a week later showed a marked enlargement of the mass involving the entire left lobe of thyroid extending into adjacent soft tissues and encroaching towards right side. Second FNA showed widespread lymphocytes with thick fibrous bands and infiltrates of B and T cells, suspicion of a lymphoproliferative disorder. She developed stridor and bilateral vocal cord palsy and had an urgent tracheostomy with biopsy of the neck mass. Histology showed dense fibrous tissue extending into surrounding skeletal muscles and adipose tissue with lymphocytic infiltrate and chronic inflammatory features. The lymphocytes were composed of mixed T and B cell population with plasma cells and few epithelial cells. A diagnosis of Riedel's thyroiditis was made and the patient was started on high dose steroids. She reported a transient improvement, however the mass started to grow rapidly,prompting emergency admission. A trial of Tamoxifen was given with no benefit. CT neck revealed a marked progression of the mass compressing airways, vocal cords and left internal jugular vein, extending to the level of left oropharynx. The patient had emergency tracheostomy. Rituximab was given with some benefit. On repeat core biopsy, histology revealed atypical lymphocytes diffusely positive for CD20, CD79a, CD10, Bcl-6 and Oct-2. Ki-67 proliferation index was over 95%. This confirmed the diagnosis of large diffuse B cell lymphoma. Patient was referred for chemotherapy. This case highlights the challenges in diagnosis of Riedel's thyroiditis and differentiating Riedel's thyroiditis from lymphoma due to overlapping histological features and limitations of medical treatment available for Riedel's thyroiditis.

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P12

Idiopathic FSH deficiency

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Case history
A 24-year-old previously healthy male presented to his GP with unilateral "gynaecomastia", prompting investigations which showed a low FSH of 0.7 (1–12 IU/l). He had normal libido, erectile function, and a normal sense of smell. He had no children. He was subsequently investigated for persistent dysuria but imaging and cystoscopy were entirely normal. He was a non-smoker who took little alcohol and worked as an insurance agent. His past medical history and family history were unremarkable. Clinical examination revealed a normally androgenized male with no gynaecomastia and normal facial, axillary and pubic hair. His testes were normal in volume and consistency.
Investigations
Unstimulated pituitary hormone tests – (a) FSH – 0.7, 0.8, 0.8 (1–12 IU/l); LH – 1.3, 3.8, 3.3 (1–9 IU/l); (b) 9 am testosterone – 13, 21, 19 (9.7–38.2 nmol/l); (c) prolactin 176, 201 (53–360 mU/l); (d) free T4 14.8 pmol/l, TSH 1.82 mU/l; (e) random cortisol 393 nmol/l; (f) oestradiol 87 (<160 pmol/l); IGF1 – 32.
Semen analysis –
(a) volume 4.3 (>1.4 ml), pH 8.3 (>7.1); (b) sperm concentration 2 (>14.9 million/ml), total sperm/ejaculate 8.6 (38.9 million).
Gonadotrophin releasing hormone test –
Time after GnRH (minutes)

minutes	FSH	LH
15	1.3	4.1
30	1.3	4.1
45	1.5	13.5
60	1.7	11.1

Other tests – (a) plasma inhibin B – 180 pg/l (>80); (b) plasma HCG – <5;
Pituitary MRI scan – normal pituitary
FSH beta gene mutation analysis – none identified.

Results and treatment
The above results indicate that this man had isolated FSH deficiency probably of pituitary origin. This lack of FSH has led to poor spermatogenesis and reduction in sperm numbers both absolute and per ejaculate. However, this isolated FSH deficiency does not appear to be due to either a structural hypothalamo-pituitary defect or due to a FSH beta gene mutation.
Conclusion and Points for Discussion
We have presented a man with probable isolated pituitary FSH deficiency. However, the following matters need to be addressed – (a) would gonadotrophin releasing hormone "priming" have increased the FSH response to GnRH?; (b) should clomiphene citrate be given prior to GnRH testing?; (c) is there a need for testicular biopsy?

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P13

Exacerbation of hypercalcemia caused by lithium in a patient with familial hypocalciuric hypercalcemia due to a calcium sensing receptor mutation

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Case history
A 52 year-old lady was seen for further assessment of primary hyperparathyroidism (PHPT). She complained of intermittent symptoms of bloating but was otherwise asymptomatic. She was menopausal on hormone replacement therapy (HRT) and had started lithium for bipolar disorder 4 years ago. She had no known history of nephrolithiasis and no history of fractures. Her past medical history included Hodgkin's lymphoma treated with chemotherapy 14 years ago, bipolar disorder and alcohol related fatty liver disease. Her medications were HRT (consisting of estradiol gel and micronized progesterone), lithium, citalopram and vitamin D. She did not have any known family history of calcium disorders. Biochemistry confirmed PHPT. Calcium to creatinine clearance ratio was low, as often observed with the use of lithium. Going through her past medical records, she had a biochemical picture of PHPT for at least 5 years, however, serum calcium levels 5 years ago were only borderline. Calcium to creatinine clearance ratio was low even before the initiation of lithium. Her GP was not able to provide any calcium measurements dated more than 5 years ago.
Investigations
Biochemical results: Pre-lithium: Adjusted calcium 2.6 mmol/l (2.2–2.6), Phosphate 0.84 mmol/l (0.8–1.5), ALP 68 IU/l (30–130), PTH 7.2 pmol/l (1.1–6.8), eGFR $>$ 90 ml/min/1.73 m^2, 25OHD 58 nmol/l, calcium to creatinine clearance ratio 0.004. Post-lithium: Adjusted calcium 2.92 mmol/l, Phosphate 0.83 mmol/l, ALP 109 IU/l, PTH 9.5 pmol/l, eGFR 76 ml/min/1.73 m^2, 25OHD 99.8 nmol/l, calcium to creatinine clearance ratio 0.009, serum lithium 0.76 mmol/l (0.4–1.0). Kidney ultrasound: No evidence of nephrolithiasis. DXA scan: Lumbar spine T-score: -0.6 (stable over 3 years), femoral neck T-score: -1.8 (9% bone loss over 3 years), total hip T-score: -1 (3.9% bone loss over 3 years). Sequencing of the Calcium Sensing Receptor (CaSR) gene: heterozygosity for c.164C$>$T p.(Pro55Leu).
Results and treatment
A diagnosis of familial hypocalciuric hypercalcemia (FHH) was made. Lithium was considered to be the reason for the rise in the calcium levels. Currently the patient is under conservative regular follow-up.
Conclusions and points for discussion
This is the first reported case of the effects of lithium in a patient with FHH. This case illustrates that lithium can alter the CaSR set point even in the mutated protein. FHH is considered a benign condition but the long-term effects of this dual effect on the CaSR are unknown.

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P14

Low ACTH and cortisol production following adrenalectomy for primary aldosteronism

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Case history
A 74-year-old gentleman with primary aldosteronism (PA) was referred for the 'MATCH' study – a prospective comparison of 11C-metomidate PET CT with adrenal vein sampling. He took no exogenous steroids.
Investigations
Na 147 mmol/l, K 3.7 mmol/l, aldosterone 496 pmol/l, renin activity <0.17 nmol/l per h, random cortisol 247 nmol/l and concomitant ACTH 9.3 ng/l. Two overnight dexamethasone suppression tests recorded values of 61 and 24 nmol/l (<50). CT showed a 1.5 cm nodule on the left and a smaller nodule on the right. Adrenal vein sampling (table) showed apparent non-cannulation of the right adrenal vein. Metomidate-PET CT scan demonstrated high left adrenal adenoma uptake, with a diagnostic ratio L:R of 2.43 (<1.25).

	Right	Left	IVC
Aldosterone (pmol/l)	2,256	59,100	5,650
Cortisol (nmol/l)	1,836	4,552	1,739
Aldosterone/cortisol ratio	1.2	12.9	3.2
Selectivity index (>3)	1.0	2.6	
Lateralisation index	1	**10.6**	

Results and treatment
Following left adrenalectomy, he was discharged on amlodipine 10 mg and hydrocortisone 10 mg. Histopathology confirmed a 9$\times$9 mm adrenal 'nodularity' with a mixture of cells resembling either zona glomerulosa (ZG) or zona fasciculata (ZF). Eight weeks later, he reported severe tiredness. The 0900 cortisol was 69 nmol/l, ACTH 4 ng/l. His short synACTHen values were 41, 207 and 271 nmol/l. His symptoms resolved on steroid replacement. CT of his pituitary was normal. Post-operative blood pressure is 136/68 mmHg, renin 1.3 nmol/l per h and aldosterone 80 pmol/l.
Conclusions and points for discussion
Sustained post-operative adrenal insufficiency is, unusually, associated with isolated ACTH insufficiency. His small adenoma, with mixed ZG- and ZF-like cells, does not fit the picture of contralateral adrenal suppression by a large ZF-like adrenal adenoma co-secreting cortisol and aldosterone. A positive PET CT in MATCH permits adrenalectomy despite apparent failure of adrenal vein cannulation; in thee of nine patients to date, we have observed post-operative adrenal suppression. Suppressed cortisol production in the contralateral gland, from autonomous production by the adenoma, could result in a diminished selectivity index and misinterpreted as failure to cannulate the right adrenal vein. Under-expression of CYP11B1 (11 $\hat{I}^2$-hydroxylase), due to variants in its gene promoter, is a common feature of PA (MacKenzie et al 2017). We postulate that adrenal insufficiency is an under-recognised consequence of removing half of the adrenal mass; and that administering dexamethasone at induction of general anaesthesia may convert sub-clinical to overt insufficiency by suppressing the pituitary at the critical moment of adaptation to adrenalectomy.

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P15

A surgical treatment for cardiomyopathy

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Case history
A 59 year old Afro-Carribbean male with a 25 year history of cardiac enlargement and hypertension, on multiple anti-hypertensives, presented with increasing

breathlessness and several years of markedly reduced exercise tolerance. He was intolerant of spironolactone and eplerenone. His past medical history included hypertension, obstructive sleep apnoea, Steven-Johnson syndrome secondary to allopurinol, thyrotoxicosis treated with radio-active iodine, monoclonal gammopathy, pernicious anaemia, glaucoma, carpal tunnel syndrome and previous tuberculosis exposure. He was initially referred to a cardiologist for assessment for poorly controlled hypertension and heart failure.
Investigations
His echocardiogram revealed severe concentric LVH with a normal LV ejection fraction and a large pericardial effusion. His coronary arteries were unobstructed. A presumptive diagnosis was made of cardiac amyloidosis although subsequent investigations, including a rectal biopsy, were not supportive of this. Endomyocardial biopsy revealed only myocardial hypertrophy and focal fibrosis with no evidence of lymphocytic, granulomatous or amyloid infiltration. His cardiac MRI demonstrated a very unusual pattern of LVH. The patient continued to suffer from ongoing worsening of breathlessness and was treated with pericardial drainage, followed by formation of pericardial window. He was then referred to endocrinology from his local hospital for a right sided adrenal nodule and hyperaldosteronism. Four years previously, hypokalaemic hypertension with aldosterone 8,200 pmol/l (100–800) and renin 0.2 pmol/ml per h (0.5–3.1) had been noted. Primary aldosteronism was re-confirmed (serum aldosterone $>$4,271 pmol/l, renin $<$0.17 nmol/h per l); an adrenal CT demonstrated bilateral adrenal nodules, 3 cm on the right and 2 cm on the left. Adrenal venous sampling was not possible as his interfering medications could not be weaned without cardiac decompensation. Subsequent 11-C Metomidate scan demonstrated bilateral uptake but with an obvious dominant very hot nodule to the right.
Results and treatment
The patient underwent a right laparoscopic adrenalectomy without complication. Three months post-operatively, the patient's symptoms significantly improved with exercise capacity transforming from 5 to 10 metres to unlimited. His blood pressure and potassium normalised with a marked reduction in anti-hypertensive agents. His post-operative aldosterone normalised to 280 pmol/l with renin 0.80 nmol/h per l. More surprisingly there appeared to be significant LVH regression on his echocardiogram.
Conclusions and points for discussion
This case demonstrates the profound effect severe primary hyperaldosteronism has on myocardial function and the challenges faced with the diagnosis of lateralising disease justifying unilateral adrenalectomy. It also highlights the potential reversibility of myocardial inflammation and fibrosis when the aldosterone burden is reduced.

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P16

A case of low serum cortisol secondary to inhaled fluticasone use in a retroviral-positive patient on a protease inhibitor

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Case history
A 45-year-old male was referred to Endocrinology from the Infectious Diseases clinic for investigation of possible adrenal insufficiency. The patient had multiple co-morbidities including asthma, hepatitis B and HIV. The patient's GP had introduced a fluticasone inhaler to control the symptoms of his asthma, however when the patient was seen in Infectious Diseases clinic as an interaction with his protease inhibitor (atazanavir) was suspected. A random cortisol test was performed, showing a cortisol of less than 20, thus the patient's fluticasone inhaler was stopped and he was referred to Endocrinology. His history and examination showed no symptoms nor signs of adrenal insufficiency.
Investigations
A short synacthen test and subsequent long synacthen test were requested when the patient had discontinued use of the fluticasone inhaler for 1 week. Thyroid function tests were normal. HIV and hepatitis B viral loads were both undetectable.
Results and treatment
SST result: 0 min cortisol 158, 30 min cortisol 289, 60 min cortisol 315. LST result: 0 min cortisol 348, 60 min cortisol 501, 240 min cortisol 584, 360 min cortisol 600, 480 min cortisol 645, 1,440 min cortisol 543 and 2,880 min cortisol 393, ACTH level 49.2. The patient was reassured that although his SST was suboptimal, his subsequent LST result was completely satisfactory. It was explained he had temporary adrenal insufficiency with the combination therapy, which had resolved over time after withdrawal of the fluticasone inhaler.
Conclusion and points for discussion
Interactions between protease inhibitors and inhaled or intranasal corticosteroids are well documented in the literature. The drug-drug interaction is secondary to the inhibition of hepatic cytochrome P450 3A4 isozyme by protease inhibitors, which is partly responsible for the metabolism of steroids. This case concerns concurrent use of a protease inhibitor and inhaled corticosteroid, leading to low cortisol levels with temporary adrenal suppression. Such interactions have become a common source of referral to endocrinology. Could this interaction be minimised by the use of an alternative steroid inhaler such as beclometasone, or the use of an alternative anti-retroviral medication?

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P17

Hypercalcaemia in a body builder

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Case history
A 53-year-old obsessive body builder, presented with severe constipation. He had used growth hormone, anabolic steroids and testosterone at variable doses for over 20 years. He had a protein intake of over 400 g/day over an extended period. He denied osmotic symptoms, joint or muscle pains, and excessive tiredness. Previously, he had benign prostatic hyperplasia and renal stone disease but was not on any prescription medication and took no over the counter 'supplements'. He was a non-smoker and consumed no alcohol. There was no significant family history and his children were well.
Investigations
The following investigations were done at admission – i) corrected calcium – 3.66 (ref range), phosphate – 1.39 (0.80–1.50 mmol/l); ii) PTH – 2 (1.6–7.2 pmol/l); iii) urea 21.9 (ref range); iv) creatinine 319 (ref range) and eGFR 18; v) creatine kinase – 7,952 (ref range); vi) urine dipstick – protein 4+, glucose 4+, red cells 2+; vii) serum protein electrophoresis – normal pattern; viii) vitamin D – 46 (30 – 50 nmol/l), ix) vitamin A – 4.65 (1.10–2.60 µmol/l); x) CT of thorax, abdomen and pelvis – no abnormalities; xi) anti Jo-1, Ro-52+ve; xii) MRI of muscles – appearances suggestive of 'inflammation' and myositis with occasional calcification; xiii) normal thyroid function tests and a random glucose of 7.8 mmol/l; xiv) isotope renogram and GFR after rehydration – 68 ml/min; xv) muscle biopsy done – results awaited.
Results and treatment
A diagnosis of possible non-PTH mediated hypercalcaemia with acute kidney injury was diagnosed. He was rapidly rehydrated with normalization in serum calcium, his creatinine levelled to 180 µmol/l and creatine kinase to around 4,000 U/l. We believe the hypercalcaemia was caused by rhabdomyolysis induced by inflammatory myositis, excessive exercise (non-traumatic exertional rhabdomyolysis) and possible ingestion of myotoxins (hitherto unsubstantiated).
Conclusions and points for discussion
This subject presented with a possible rare cause for hypercalcaemia – rhabdomyolysis induced by a combination of factors in this obsessive body builder. Rhabdomyolysis produces hypercalcaemia by several mechanisms and is thought to be present in about 9% of these subjects. Points for discussion – i) the importance of isotope renography in subjects with high muscle mass and 'impaired' renal function; ii) why was PTH not completely suppressed despite significantly high serum calcium levels – is there coexistent primary hyperparathyroidism?; iii) could raised vitamin A levels play a role?

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P18

Type 1 diabetes presenting with unilateral left foot drop

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Case history
A 26-year-old lady presented with a two-week history of weakness associated with pins and needles affecting the lateral calf and dorsomedial aspect of her left

foot. The patient denied any trauma or symptoms including weight loss. She had no drug allergies and was taking no regular medications. She had a vegan diet supplemented with multivitamins. Her past medical and family history was unremarkable. On examination, she had a narrow-based high-steppage-gait. Lower limb exam revealed normal tone and full power except for left ankle dorsiflexion (MRC Grade 4/5) and left hallux dorsiflexion (MRC Grade 3/5). Inversion and eversion were normal. Reflexes were present with reinforcement and symmetrical with downgoing plantars. Sensation was intact and Romberg's sign was negative. Examination of all other systems was normal.

Investigations

A CT brain scan demonstrated no abnormalities. Initial laboratory investigations revealed a venous glucose level of 49.9 mmol/l, blood ketones of 2.2 mmol/l (normal <0.6 mmol/l), normal pH and $HCO3^-$. Her HbA1c was 142 mmol/mol (15.1%). The remainder of her work-up including full blood count, renal, thyroid and liver function, cortisol, vitamin B12 and folate levels was unremarkable.

Results and treatment

Anti-islet cells and anti-GAD antibodies were positive, confirming Type 1 diabetes mellitus (T1DM). She was treated with intravenous insulin, fluids and potassium replacement. She was discharged on a basal-bolus insulin regimen. Her foot drop resolved within three weeks with no recurrence at 12 months follow-up.

Conclusions and points for discussion

Symptoms of hyperglycaemia represent the most common presentation in patients with newly diagnosed T1DM. Some subjects may present with vague complaints such as weight loss and fatigue. Cases of T1DM presenting with neurological manifestations including cerebral infarction, extrapontine myelinosis and ataxia have been described in the paediatric population but they are extremely rare in adults. Hyperglycaemia-induced hemiballismus in adults with type 2 diabetes has been previously reported. Here we describe for the first time a new onset T1DM presenting with right foot drop and no symptoms attributable to hyperglycaemia. In our case no history of weight loss or osmotic symptoms was elicited and the identification of hyperglycaemia, thought to be responsible for the peroneal nerve conduction block, was merely incidental. Our case confirms that new onset diabetes can be associated with neurologic manifestations and reiterates the importance of including diabetes mellitus in the differential diagnosis of an otherwise healthy patient presenting with peripheral neuropathy.

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P19

A case of multi-systemic sarcoidosis in a male patient presented with long-standing erectile dysfunction and loss of libido due to hypothalamic involvement

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Case history

A male patient presented to the Endocrine clinic age 64, with an 18-year history of erectile dysfunction. He was treated under Urology with phosphodiesterase inhibitors and Nebido injections for hypogonadism. Notably the cause of hypogonadism had not been established. The patient was concurrently reviewed by Oral Medicine due to a 2.5-year history of xerostomia, and Dermatology for a non-healing, erythematous, pruritic lesion on his right lower leg and several white/pink polycyclic patches over the left upper arm. The patient had also been receiving levothyroxine for 10 years for presumed primary hypothyroidism.

Investigations

When under Urology, morning serum testosterone was found reduced at 4.9 nmol/l (reference range 8.0–30.0). Gonadotrophins and SHBG were not tested at that time. Following endocrine review, and whilst on Nebido, investigations for hypogonadism were as expected (testosterone 8 nmol/l; LH$<$ 0.3 IU/l; FSH$<$0.3 IU/l; SHBG 42 nmol/l). The anterior pituitary hormone profile revealed low IGF-1 (3.9 nmol/l; reference range 10.1–28.4), low morning cortisol (129 nmol/l), normal prolactin, TSH <0.05 mIU/l and free T4 of 13.6 pmol/l (on Levothyroxine). The patient was commenced on Hydrocortisone and a subsequent Glucagon stimulation test confirmed GH and ACTH deficiencies (peak GH 0.1 mcg/l; peak cortisol 202 nmol/l). A water deprivation test showed no evidence of diabetes insipidus. During investigations for xerostomia, a raised ACE was found on two occasions. Biopsy of the upper arm cutaneous lesions showed multiple non-caseating granulomas in the dermis consistent with sarcoidosis. A contrast pituitary MRI scan showed an ill-defined, small volume, soft tissue enhancement in the hypothalamic region, in keeping with neurosarcoid. No pituitary lesions were identified. Serum and urinary calcium were normal. Additional imaging revealed lung and salivary glands involvement.

Results and treatment

The patient was commenced on Prednisolone 60 mg daily, reduced gradually to 7.5 mg daily maintenance dose. Significant symptomatic relief, resolution of cutaneous lesions and normalisation of ACE levels were noted. Repeat imaging of the hypothalamic/pituitary region is due in April 2018, to assess for regression of neurosarcoidosis and determine whether further steroid therapy is required as monotherapy or combined with second-line immunosuppressant agents.

Conclusions and points for discussion

Hypothalamic/pituitary sarcoidosis is a rare manifestation of sarcoidosis and usually presents with symptoms of hypogonadotrophic hypogonadism or diabetes insipidus. Endocrine symptoms may precede other multi-systemic symptoms and therefore sarcoidosis should be considered when investigating patients for hypothalamic/pituitary dysfunction, so that appropriate treatment can be commenced early.

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P20

TSH-receptor-blocking antibody (TBAb) positive hypothyroidism presenting with myopathy

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Case history

A 37-year-old female presented to her GP with myalgia, lethargy and weight gain. Of note she was 24 months post-partum and had not experienced thyroid problems in either of her two pregnancies. On examination she was overweight with marked myxoedema and proximal myopathy.

Investigations

Serum TSH was greatly elevated at 206 mIU/l and free T4 was undetectable at <3.20 pmol/l. T3 was 2.8 pmol/l. She was referred urgently to the medical team for assessment in A&E where further blood tests demonstrated a raised creatinine at 90 umol/l with an eGFR 61 ml/min and a raised creatinine kinase (CK) at 1018 IU/l. Lipid profile was in keeping with an overt hypothyroidism. Total cholesterol was raised 6.13 mmol/l with normal triglycerides at 1.22 mmol/l, total cholesterol to HDL radio was raised at 5.24, LDL cholesterol was raised at 4.41 mmol/l and non-LDL cholesterol was raised at 5.0 mmol/l. ALT was raised at 63 IU/l. Her ECG was abnormal with a low voltage and flattened T waves with a rate of 75 bpm. An echocardiogram showed a slightly hypokinetic basal inferior wall.

Results and treatment

Thyroid ultrasound showed a hypotrophic thyroid gland with irregular contours with appearances suggestive of thyroiditis sequelae. There was no hypervascularity in doppler mode evidencing no acute thyroiditis. Interestingly, thyroid peroxidase antibodies were negative. TSH receptor antibodies, however, were greatly elevated at $>$ 30.0 u/ml. She was commenced on levothyroxine 125 mcg once daily and within one week of treatment had already noticed an improvement in her energy levels. She will be closely monitored, particularly as literature suggests that there is a risk of transition to hyperthyroidism following treatment with levothyroxine. She will also be screened for other concomitant autoimmune conditions such myasthenia gravis.

Conclusions and discussion

It is rare for autoantibodies to bind to, but not activate, the TSH receptor thereby blocking the action of TSH causing hypothyroidism. TSH receptor blocking antibodies, when present, are generally found to be of a higher titer than TSH receptor stimulating antibodies, as in this case the titer was >30 u/ml. The case also illustrates the importance of checking thyroid function when investigating myalgia. Polymyositis-like syndrome in hypothyroidism is a rare condition characterised by proximal muscle weakness and elevated muscle enzymes. Symptoms usually improve with thyroxine treatment.

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P21

A catastrophic case of adrenal insufficiency

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Case history
A 50 year old female presented with diarrhoea, facial rash and hyponatraemia. In addition, she described a 3 week history of headaches, malaise, intermittent joint pain and swelling. On examination, the patient was noted to have a malar rash and over the subsequent 2–3 days began to develop necrotic patches on both ears. She had no evidence of cutaneous pigmentation. She took no regular medication, other than dabigatran. Past medical history of note included extensive pulmonary embolism and proximal DVT 8 months prior to admission. She had also presented with a facial rash one week prior to admission, following a change in medication from warfarin to rivaroxaban. This had been attributed to a drug reaction and the patient had been changed on to dabigatran at this time.
Investigations
Bloods on admission: Hb 111; Platelets 113; CRP 118; Prothrombin time 16.1, activated partial thromboplastin time 72. Further results: random cortisol 17; ACTH 683 (in-keeping with primary adrenal insufficiency). Negative results: ANCA, HIV PCR, anti dsDNA, C3 and C4. Significant positive results: anticardiolipin IgG (124.6 [normal range <20]); antibeta-2-glycoprotein-1 IgG (528.7 [normal range <20]) – highly suggestive of Primary Antiphosopholipid Syndrome (APS).
Results and treatment
Following discussion with the haematology and rheumatology department at Royal Hallamshire Hospital, Sheffield the patient was commenced on IV methylprednisolone, IV immunoglobulin and warfarin loading (with bridging enoxaparin). However, she was found in cardiac arrest the following morning and resuscitation attempts were unsuccessful. Post-mortem examination was consistent with rapidly advancing APS causing widespread vasculitis and intravascular thrombosis, resulting in vascular occlusion and infarction of multiple organs including the skin, heart, lungs, kidneys, adrenals and small bowel.
Conclusions and points for discussion
Catastrophic antiphospholipid syndrome (CAPS) is the most severe form of APS and represents $<1\%$ of APS cases. Diagnosis requires vascular thrombosis in ≥ 3 organs/tissues; development of symptoms simultaneously or in <1 week; evidence of small vessel thrombosis and laboratory confirmation of APS. Due to its rarity, the majority of data regarding management comes from retrospective analysis of the CAPS registry. The current consensus is combination therapy with anticoagulation, IV immunoglobulin or plasma exchange, corticosteroids and rituximab. Mortality remains high despite optimum treatment.

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P22

Lactotroph hyperplasia in pregnancy: An unique case of pregnancy-induced progression

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Case history & Management
A 36-year old lady of Lithuanian descent first presented in 2011 with secondary infertility due to hyperprolactinaemia of 1554 ($N=0$–500). Her MRI was normal and was started on Cabergoline which was stopped 5 months later when she became pregnant. She delivered normally but was thereafter lost to follow-up. She was referred back in 2014 with galactorrhoea and hyperprolactinaemia (6856) and MRI this time showed a 0.7 mm microprolactinoma. Cabergoline was restarted and 6 months later was stopped again when she became pregnant for the third time. Following this successful pregnancy, she returned to Lithuania and was lost to follow-up. In 2016, she resurfaced as an emergency at 34 weeks of pregnancy with headaches, bitemporal visual field loss and reduced foetal growth. Prolactin level was 119,965 and MRI showed a 3.1×3.2 cm macroprolactinoma with some apoplexy. Fortunately, she delivered soon after and neurosurgical intervention was not required. Except prematurity, baby remained unaffected. Since 2016, she remains on Cabergoline with undetectable (<40) prolactin levels, visual fields have recovered fully and serial MRI surveillance demonstrating gradual reduction of tumour mass.
Conclusions and points for discussion
This unique case demonstrates in a step-wise manner, the stimulatory effects of pregnancy on pituitary lactrotrophs. Our subject's history suggests that every pregnancy led to a sequentlal increase in her lactrotroph cell mass as characterised by initiall a normal MRI and progressing to a microprolactinoma and culminating in a symptomatic macroprolactinoma. Current guidelines suggest that for hyperprolactinaemic patients with normal MRI or microprolactinoma, there is no utility of either biochemical, radiological or visual field surveillance during pregnancy. While this is applicable for the majority of such cases, this case example suggests that endocrinologists should still exercise caution and arrange for follow-up surveillance in such patients following completion of pregnancy. If future pregnancies are aspired, then it is important to have pre-pregnancy counselling to discuss potential risks including macroadenomatous transformation, growth retardation and consequences of pituitary insufficiency.

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P23

Abstract withdrawn.

P24

Amiodarone-induced thyroiditis in a patient with a history of VT cardiac arrests

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Case History
A 71-year old male, who had been on amiodarone therapy for many years, was receiving Levothyroxine therapy due to amiodarone-induced hypothyroidism. He was subsequently found to have thyrotoxicosis, which remained after levothyroxine discontinuation. He had type 2 diabetes and ischaemic cardiomyopathy and had an implanted cardiac defibrillator due to multiple VT arrests. Amiodarone therapy had contributed to stabilisation of his cardiac arrhythmias and had continued beyond his diagnosis of amiodarone-induced hypothyroidism for that reason.
Investigations
The patient complained of 10 kg unintentional weight loss and agitation and examination revealed a regular heart rate of 58 bpm, blood pressure 127/73 mmHg, euvolaemia and resting tremor. Neck examination was unremarkable. Thyroid function confirmed thyrotoxicosis with TSH <0.01 milliunit/l, FT4 31.8 pmol/l, FT3 5.9 pmol/l. TSH receptor and TPO antibodies were negative. HbA1c was 50 mmol/l. An urgent technetium uptake scan showed type 2 amiodarone-induced thyroiditis, with absent gland uptake.
Results and treatment
After consultation with the Cardiologist, amiodarone was discontinued and bisoprolol was uptitrated. He was commenced on prednisolone 40mg daily for one month, along with Gliclazide for glycaemic control, and repeat blood tests showed marked improvement (TSH 0.17 milliunit/l, FT3 3.2 pmol/l, FT4 15.7 pmol/l). Thereafter he was successfully weaned off the prednisolone and the Gliclazide within a total period of less than 3 months. At the end of that period his thyroid function has normalised, HbAc1c has remained stable at 43 mmol/mol and he is being monitored for the development of hypothyroidism once again. A short synachthen test was also performed to ensure his adrenal axis has not been affected and that was normal. He has not had any cardiac complications since stopping the amiodarone.
Conclusion and points for discussion
Amiodarone is a potent antiarrhythmic drug that is used to treat arrhythmias, but can precipitate thyroid dysfunction due to its iodine-rich chemical structure and long half-life. It remains unclear whether amiodarone should be continued after diagnosis of thyrotoxicosis. There have been instances of amiodarone-induced coronary vasospasm and ischaemic ventricular fibrillation related to hyperthyroidism and some studies have shown that continuation of amiodarone delays restoration of euthyroid status, and increases risk of recurrence. Risk of recurrence has been documented in the literature as being as high as 10%. However, in other cases euthyroid states are still achieved with continuation of amiodarone and treatment with steroids.

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P25

Detectable testosterone despite androgen deprivation therapy in prostate cancer: hunting for the source

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Background
Androgen-deprivation therapy (ADT) is commonly used in the management of advanced prostate cancer. ADT can be achieved through bilateral orchidectomy, by administration of GnRH receptor agonists, or by using by the newer GnRH receptor antagonist Degarelix. The classical desired biochemical goal is to achieve a serum testosterone of <1.7 nmol/l.
Case Presentation
A man with metastatic prostate cancer on androgen deprivation therapy and serum total testosterone above the therapeutic goal (3.7 nmol/l), was referred to the Endocrine clinic. He had a previous medical history of hyperprolactinaemia and hypogonadism diagnosed 17 years prior to his presentation. In the past he had been treated with Caberogline followed by testosterone replacement therapy with parenteral testosterone undecanoate. Previous MRI head scanning was normal. The last testosterone undecanoate injection was 13 months prior to his referral to the Endocrine clinic. Androgen deprivation consisted initially of Goserelin for four months, followed by Leuprorelin acetate for three months and subsequently Degarelix for another three months. During the time of treatment with the GnRH agonists (Goserelin followed by Leuprorelin) and the GnRH antagonist Degarelix, serum testosterone had shown little variation and was always above the therapeutic threshold. He was additionally on the androgen receptor inhibitor Enzalutamide, PSA was declining and the disease was clinically stable. Investigations showed a raised extracted testosterone with MS/LC-MS, undetectable gonadotropins, normoprolactinaemia and no rise in other serum androgens. Urine steroid biochemistry showed low androgen metabolites making an adrenal source for the measured testosterone unlikely, and measured testosterone did not change following a low dose dexamethasone suppression test. Review of available cross-sectional imaging showed unilateral adrenal nodularity that was unchanged in repeated scanning. In the subsequent months, total testosterone started to decline with a lowest achieved level of 1.8 nmol/l.
Discussion
Evidence suggests that a testosterone level below the classical therapeutic target in advanced prostate cancer is associated with improved outcomes and lower progression toward castration-resistant prostate cancer. In this context serum testosterone is together with PSA an important biochemical target. Because of its mechanism of action, the GnRH antagonist Degarelix prevents testosterone microsurges that have been observed immediately following GnRH agonists administration, with potential clinical implications. We speculate that the persistently detectable testosterone levels here are likely to arise from insufficient response to treatment with GnRH agonists, with eventual decline on prolonged treatment with Degarelix. A less likely explanation is the presence of residual testosterone undecanoate depot.

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P26

Normotensive hypokalemic primary aldosteronism: How is this Possible?

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Case history
A 40-year-old woman presented with long-standing hypokalemia fluctuating between 2.3 and 2.5 mmol/l. She had episodes of right-sided weakness and was seen by Neurologists without a clear diagnosis. She had no other past medical history. Physical examination was unremarkable. Her blood pressure (BP) was 116/63.
Investigations
Plasma aldosterone was 1363 pmol/l. Plasma renin activity was 0.18 ng/ml/h. Aldosterone-renin ratio (ARR) was 7570 (normal $<$ 550). There was inappropriate kaliuresis (173.2 mmol in 24 h). Her natriuresis was 315 mmol in 24 h. 24-hour ambulatory BP was 129/79. Her magnesium was normal at 0.88. MRI abdomen showed a 2-cm mass in the left adrenal gland. Adrenal vein sampling demonstrated lateralization to the left with an aldosterone-cortisol ratio of 36.49 in the left adrenal, 0.78 in the right adrenal, and 6.21 in the common femoral vein.
Results and treatment
She underwent a left laparoscopic adrenalectomy. Pathology revealed a $1.9\times 1.5\times 1.5$ cm adrenocortical adenoma. Post-operatively, her BP was 110/70. Her ARR normalized and her potassium normalized.
Conclusions and points for discussion
38 cases of normotensive primary aldosteronism (PA) have been reported since 1972. The majority of cases are in females (28/38) from Europe (15/38) and Japan (15/38). 31 cases of were detected due to hypokalemia. There are numerous proposed mechanisms of normotensive PA. It is thought that these individuals were detected at an early stage of the disease. However, data from PA registries suggest that the development of hypokalemia is a late development in PA. As most patients are female, estrogen and progesterone may counteract the effects of hyperaldosteronism. However, it is still common to see hypertensive PA in pre-menopausal women and in pregnancy. Partial resistance to aldosterone is an unlikely explanation as the patient had severe hypokalemia and a suppressed renin despite a normal BP. Normotensive PA has occurred patients with Gitelman's syndrome; however, this patient's magnesium was normal and her hypokalemia resolved preoperatively. Perhaps this patient's normal BP and salt-wasting was due to the natriuretic peptide system. Sodium and water retention from excess aldosterone leads to release of atrial natriuretic peptide (ANP). ANP induces systemic vasodilation. Furthermore, ANP increases glomerular filtration rate through vasodilation, promoting natriuresis and diuresis. Although there is no prospective data demonstrating long-term benefits in the diagnosis and treatment of normotensive PA, this case illustrates that PA is not confined to patients with hypertension.

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P27

A case of Idiopathic Infantile Hypercalcaemia (IIH) persisting into adulthood, caused by compound heterozygous mutations of 1,25-dihydroxyvitamin D_2 24-hydroxylase (*CYP24A1*)

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Case history
Idiopathic Infantile Hypercalcaemia (IIH) classically presents in the first year of life, usually resolves by 1 year of age and is due to mutations in 1,25-dihydroxyvitamin D_2 24-hydroxylase (*CYP24A1*) or, rarely, sodium-phosphate cotransporter-2A (*SLC34A1*). We report a case of IIH in a Caucasian female, who was born to non-consanguineous parents, with hypercalcaemia, hypercalciuria and associated complications persisting into adulthood. The proband was investigated for delayed developmental milestones and constipation at 7 months old and was found to be hypercalcaemic. Other causes of hypercalcaemia were excluded and she was diagnosed with IIH. Nephrocalcinosis was noted at diagnosis and progressed to a symptomatic renal stone aged 12 years. A DEXA scan following a wrist and heel fracture revealed osteoporosis (SDS -3.2 lumbar spine, -2.15 hip).
Investigations
At diagnosis, biochemistry showed an elevated serum calcium of 3.91 mmol/l (normal range (NR) 2.12–2.62), normal phosphate of 1.27 mmol/l (NR 0.80–1.45), elevated magnesium of 1.25 mmol/l (NR 0.75–1.05), normal $25(OH)D_3$ of 38.0 μg/ml (NR 7–50), elevated $1,25(OH)_2D_3$ of 127 pg/ml (NR 20–50) and suppressed PTH concentration of <0.7 pmol/l (NR 1.0–6.1). Her parents were normocalcaemic. In addition, on treatment her plasma calcium concentrations were typically at high-normal limits, and her urinary calcium: creatinine ratios are high and between 0.44 and 1.14 (hypercalciuria defined as >0.20).
Results and treatment
DNA sequence analysis of *CYP24A1* revealed compound heterozygous missense mutations comprising Trp134Arg and Leu409Ser, which were inherited from her mother and father, respectively. She was treated with a low calcium and low vitamin D diet that reduced her serum calcium levels, but required pamidronate to normalise her bone mineral density, and had renal stents for nephrolithiasis.
Conclusions and points for discussion
We report a case of IIH in a Caucasian child of non-consanguineous parents, caused by compound heterozygous mutations of *CYP24A1*. IIH may have a wide spectrum of penetrance and may persist into adulthood and cause renal stone

disease and osteoporosis, such that long-term surveillance is recommended. Serum calcium concentrations may be maintained through long-term regulation of dietary calcium and vitamin D. The reported incidence of IIH is ~2 per 100 000 live births in the UK. However, some individuals with IIH may be asymptomatic unless unmasked by supplemental vitamin D treatment, suggesting that the true incidence is higher.

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P28

Eponymous mischief: A syndrome within a syndrome

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Case history
A 32 year old male diagnosed with McCune-Albright syndrome aged 18, presented with a painful left knee and difficulty in walking, limiting his usual activities. He was diagnosed with Acromegaly (IGF-1 451 ng/ml, mean GH 2.71 ug/L) aged 26 years and had multiple sites of fibrous dysplasia, causing bone pain. On examination he had tall stature and features of acromegaly with normal visual fields and palpable masses behind his left knee and upper thigh.
Investigations
ALP 657 u/l, ALT 42 u/l, bilirubin 31 umol/l, cCa 2.3 mmol/l, PO_4 0.77 mmol/l, vitamin D 69 nmol/l, FT4 15.5 pmol/l, TSH 1.95 mu/l, IGF-1 365 mcg/l (82.5–240.4 mcg/l), mean GH 2.078 ug/l, serum procollagen type 1 amino terminal peptide (P1NP) 1158 ug/L (ref range 20–76), FGF23 160 RU/mL (ref range <100). MRI head demonstrated a normal size pituitary gland, without an obvious focal lesion, but with extensive fibrous dysplasia of the skull vault and facial bones. A whole body bone can confirmed diffuse intense tracer uptake throughout the skeleton, which showed stability in fibrous dysplasia from a scan 3 years previously. MRI demonstrated polyostotic fibrous dysplasia and multiple lobulated intramuscular soft tissue masses, with heterogeneous enhancement, the largest of which measured $6\times9\times10$ cm.
Treatment
Pituitary surgery was relatively contraindicated due to the extensive facial and skull bone disease making access difficult. He was therefore treated with monthly Sandostatin injections, but was not very compliant with this treatment, due to gastrointestinal side effects. He received bisphosphate infusions for his bone disease.
Discussion
McCune-Albright syndrome is a rare condition that remains difficult to diagnose and manage, due to the multiple endocrine and bone complications. There is a rare association between McCune Albright syndrome and multiple myxomas known as Mazabraud syndrome. The first case was described in 1967, but very few cases have been reported in the literature. It is more common in women and tends to affect the larger lower limb muscle groups. Its occurrence in men is extremely rare, and myxomas tend to occur before the onset of fibrous dysplasia. There is an association between Mazabraud syndrome and an increased risk of sarcoma in the underlying bone, although the myxomas themselves do not seem to have an inherent malignancy risk. Use of new biochemical tests confirmed poor compliance with medications and high bone turnover. We will discuss the difficulties and management options posed by this case.

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P29

Rapid severe relapse of autoimmune hyperthyroidism following 15 years low dose carbimazole treatment

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Case history
A 74 year old female was treated for hyperthyroidism of uncertain aetiology by her general practitioner. Carbimazole had been continued for 15 years - current dose 5 mg daily. Following referral to endocrine outpatients, consideration was given to stopping carbimazole as this treatment was possibly no longer required, although a small risk of relapse was accepted. Prior to stopping carbimazole, Free T4 - 10.5 pmol/l (7.5–21.1), TSH - 0.61 mU/l (0.35–4.7), TRAB <1.0 (negative). Twenty days following cessation of carbimazole the patient was admitted to hospital acutely unwell. She was breathless, mildly confused with anorexia and weight loss.
Investigations
She was in fast atrial fibrillation, had a positive TTU, microcytic anaemia: Hb - 77 g/l, MCV - 73 fL, WCC - 6.79×10^9/L, Ferritin – 40 ng/ml, CRP - 32, MSU no growth. Free T4 - 103 pmol/l (7.5–21.1), TSH <0.01mU/l (0.35–4.7), TRAB - 43.9 (>1.8 is positive). Thyroid isotope scan showed increased diffuse uptake.
Results and treatment
Treated for possible urine tract infection. Commenced on a beta-blocker and carbimazole 40 mg daily for autoimmune hyperthyroidism. Subsequent investigation of anaemia was unremarkable.
Conclusion and discussion
It is presumed that the initial hyperthyroid episode 15 years earlier was autoimmune. Long-term treatment with low dose carbimazole without ever having a trial period of withdrawal was inappropriate. The rapid and severe nature of the relapse of autoimmune hyperthyroidism after such long standing treatment with low dose carbimazole is exceedingly unusual. There is limited evidence that carbimazole has an immune modulating effect, perhaps seen with high doses. It is possible that low dose carbimazole was keeping the underlying autoimmune process in remission, given the dramatic change in TRAB. An alternative hypothesis is that an intercurrent urine infection triggered an immune response that also provoked the formation of TRAB. Hyperthyroidism can also be associated with a microcytic anaemia through disruption of iron metabolism. The patient has now been rendered euthyroid with carbimazole and sinus rhythm restored. Radioiodine treatment is planned.

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P30

Critical illness, adrenal insufficiency and steroid therapy

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A 71-year-old man was diagnosed with poorly differentiated T4N0M0 gastric adenocarcinoma. He received neoadjuvant chemotherapy, followed by elective subtotal gastrectomy. Mean arterial pressure was maintained above 70 mmHg throughout the 5-hour operation. On post-operative day 3, the patient became confused, pyrexial, hypotensive with new-onset atrial fibrillation. CT head was unremarkable and CT chest/abdomen/pelvis (CAP) showed bilateral pleural effusions with normal adrenal glands. He was treated for chest sepsis with IV antibiotics with improvement. On post-operative day 5, a repeat CT CAP, which was done to rule out gastric leak from the surgery site, due to worsening sepsis, showed new, bilateral adrenal haemorrhages. The patient had no history of tuberculosis or recent travel outside the UK.
Investigations
Adrenal function was interrogated with a short synacthen test (SST).
Results and treatment
Baseline serum cortisol was 474 nmol/l with an ACTH of 28.6 ng/l. The SST showed serum cortisol increment to 524 nmol/l and 599 nmol/l at 30 and 60 minutes respectively. Albumin at the time was 24 g/l (NR 35–50) and total protein 49 g/l (NR 60–80). The patient subsequently became severely septic with persistent hypotension, despite on-going antibiotic and fluid therapy, and was started on 100 mg intravenous hydrocortisone qds. His repeat SST whilst still on ITU 6 weeks later shows baseline cortisol 1416 nmol/l, cortisol 1333 nmol/l at 30 minutes and 1259 nmol/l at 60 minutes, in the context of albumin of 16 g/l. A repeat CT shows reabsorption of the previous haemorrhages and has revealed bilateral adrenal adenomas.
Conclusions and discussion
At first glance, the baseline serum cortisol was within normal reported range. However, that is for tests performed under 'normal' circumstances, ie not in critical illness. On the other hand, serum total cortisol levels in the presence of hypoproteinaemia, which may be present in critical illness, can be highly variable and the reported incidence of 'adrenal insufficiency' in sepsis and septic shock is between 30 and 70%. Furthermore, there is evidence for treating patients with septic shock and adrenal insufficiency with stress doses of steroids. The actual cortisol increment in this patient after administration of synachthen was suboptimal, both by 'normal' reported values (requires increment $>=150$ nmol/l) but also in the context of critical illness (requires increment $>=250$ nmol/l). The finding of adrenal haemorrhages further contributed to the decision for steroid therapy. Free cortisol index calculations can further assist in decisions towards steroid therapy.

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P31

Hyperprolactinaemia, Cushing's syndrome and Adrenal Insufficiency - diagnostic and management challenges with multiple co-morbidities and polypharmacy

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Case history
A 51 year old lady was referred to Endocrinology with low plasma cortisol, hyperprolactinaemia and galactorrhoea. Extensive past medical history included primary hypothyroidism, B12 deficiency, diaphragmatic paralysis requiring NIV, recurrent aspergillomas, sino-atrial node disease with PPM, immunodeficiency, inflammatory arthropathy and autoimmune pancreatic insufficiency. She took numerous medications:- Itraconazole 100 mg daily, Levothyroxine 75 µg daily, Creon 10 mg tds, Risendronate 35 mg, Carbocisteine 750 mg 2 tds, Hydroxychloroquine 200 mg daily, Domperidone 10 mg tds, Lansoprazole 30 mg daily, Uniphyllin 200 mg bd, intermittent IVIG infusions and Prednisolone 7.5 mg daily. She was Cushingoid, normotensive with no postural hypotension, had expressible galactorrhoea and normal visual fields to confrontation.
Investigations
Serum electrolytes were normal. Prolactin was markedly elevated at 4585 mu/l (normal range 100–500). Short synacthen test showed undetectable ACTH and cortisol of <20 nmol/l at baseline, 60 nmol/l at 30 minutes and 74 nmol/l at 60 minutes. Basal pituitary function was otherwise normal. CT pituitary, performed due to MRI incompatible PPM, was normal with no macroadenoma or haemorrhage.
Results and treatment
Exogenous Cushing's Syndrome with adrenal suppression secondary to interaction between Itrazconazole and chronic corticosteroids and hyperprolactinaemia secondary to interaction between Itraconazole and Domperidone were diagnosed. Prolactin rapidly normalised on stopping domperidone. Attempts to wean glucocorticoid treatment, to improve Cushing's and promote adrenal recovery, were hampered by flares of arthritis. Follow-up short synacthen test demonstrated persistent hypoadrenalism. She developed an episode of florid Cushing's syndrome with proximal myopathy following administration of intra-articular steroid for joint pain by her rheumatologist. With glucocorticoid weaning (total hydrocortisone 20 mg daily) she developed postural hypotension. Electrolytes remained normal but aldosterone was undetectable (<60 pmol/l). This could represent primary adrenal insufficiency (on a background of autoimmunity) or adrenal atrophy with loss of mineralocorticoid, becoming symptomatic on switch from prednisolone to hydrocortisone and dose weaning. Plasma renin was not interpretable as she was taking Propranolol. Adrenal antibodies were negative. Fludrocortisone was introduced, but very small doses required as higher doses caused hypertension.
Conclusions and points for discussion
This case illustrates endocrine presentations of drug interactions. Itraconazole inhibits microsomal enzymes including CYP3A4, resulting in delayed metabolism of drugs including domperidone and steroids. In our patient this caused galactorrhoea, hyperprolactinaemia and symptomatic Cushing's syndrome. We are developing patient alert cards to warn of such interactions. Itraconazole may also inhibit enzymes of steroidogenesis. Polypharmacy and co-morbidity can cause difficulties in diagnosis and management. MRI pituitary was contraindicated due to pacemaker and renin was uninterpretable due to propranolol.

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P32

Clinical and biochemical acromegaly associated with a functioning pituitary FSHoma

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Case history
A previously healthy 39 year-old male presented to his optometrist with visual disturbance. Visual field perimetry confirmed bitemporal hemianopia, prompting referral to endocrinology. On questioning, he reported an increase in hand and shoe size, but no headache or diaphoresis. Examination revealed classical acromegaloid features including prognathism, spatulate hands and prominent orbital margins, as well as marked bilateral macro-orchidism.
Investigations
Clinical investigations included conventional biochemical evaluation of anterior pituitary function, MRI pituitary and testicular ultrasound.
Results and treatment
Biochemical findings were in keeping with acromegaly, with IGF1 64.4 nmol/l (9.5–45.0), basal GH 1.5 mcg/l and GH nadir of 1.2 mcg/l after a 75 g oral glucose challenge. FSH was elevated (107 U/l (1.0–10.1)) with normal LH (1.2 U/l (1.5–6.3)) and testosterone (9.3 nmol/l (8.0–29.0)). Anterior pituitary function was otherwise intact. MRI demonstrated a large pituitary macroadenoma with suprasellar expansion, displacing the chiasm and extending into the left cavernous sinus. Ultrasound revealed testicular volumes of 46 and 50 ml on the left and right respectively, without features of neoplasia. Transsphenoidal resection of the pituitary lesion resulted in normalisation of visual fields and partial reduction in testicular volumes. Postoperatively, IGF1 remained elevated (55 nmol/l), however the GH nadir improved to 0.48 mcg/l after oral glucose challenge. FSH reduced to 26.3 U/l. Testosterone, FT_4 and cortisol were all below the normal range, so hormone replacement was commenced. MRI showed an intrasellar remnant with minimal suprasellar extension, no longer impacting on the optic chiasm. Histological analysis of the excised lesion confirmed a pituitary adenoma with predominant FSH staining, sparse LH staining, but no staining for GH. The possibility of coexistent ectopic GH or GHRH secretion was considered, however CT chest, abdomen and pelvis did not reveal an ectopic source, and no circulating GHRH was detectable by immunoassay. Serial follow up confirmed persistent mild elevation in IGF1 (1.1-1.4x ULN), GH nadir >0.6 mcg/l, and FSH between 30–40 U/l. MRI showed a slowly enlarging remnant in the pituitary fossa. Treatment with a somatostatin analogue was commenced, however there was no improvement in IGF1 or GH levels after 6 months. Repeat surgery is therefore planned.
Conclusions and points for discussion
This case (a) represents a functioning gonadotrophinoma in a male; (b) demonstrates clinical and biochemical evidence of GH excess without a somatotroph adenoma or hyperplasia, and without evidence for ectopic secretion; and (c) was refractory to somatostatin analogue therapy. Two further, similar cases have since been identified.

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P33

A case of vitamin D-dependent rickets type 2A (VDDR2A), caused by compound-heterozygous mutations in the vitamin D receptor (*VDR*)

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Case history
Vitamin D-dependent rickets type 2 (VDDR2) is an autosomal recessive condition caused by resistance to $1,25(OH)_2D_3$, either through vitamin D receptor (*VDR*) mutations (type A) or abnormal expression of interfering proteins (type B), resulting in hypocalcaemia despite elevated plasma $1,25(OH)_2D_3$ and parathyroid hormone concentrations. We report a proband, born to Caucasian non-consanguineous parents, who presented with rickets and alopecia aged 2 years. Investigations 20 years ago revealed abnormalities of plasma biochemistry that were consistent with VDDR2. A *VDR* mutation was not detected, although cellular studies identified an impaired *VDR* function. She was treated with high doses of oral calcium and alfacalcidol which ameliorated her rickets, and ultimately attained a normal height.
Investigations
Biochemistry at diagnosis showed a low adjusted calcium of 2.03 mmol/l (NR 2.25–2.55), low phosphate of 0.78 mmol/l (NR 1.29–1.79), elevated alkaline phosphatase of 1101 U/l (NR <300), elevated parathyroid hormone of 1283 ng/l (NR <660), normal $25(OH)D_3$ of 20 nmol/l and high $1,25(OH)_2D_3$ of 466–650 pmol/l (NR 48–156).
Results and treatment
Next generation sequencing was undertaken to expedite simultaneous analysis of the *VDR* and other possible genes involved in the aetiology of VDDR2B. This revealed compound heterozygous variants c.800C$>$A and c.1171C$>$T in *VDR*. These predict p.Ala267Asp and p.Arg391Cys alterations at evolutionarily conserved residues and were inherited from the father and mother, respectively. Although neither variant was observed in Genome Aggregation Database, the p.Arg391Cys variant has been previously reported in a patient with VDDR2A.

Conclusions and points for discussion
We report a Caucasian female, who was born to non-consanguineous parents, with VDDR2A caused by compound heterozygous mutations of *VDR*. Of the reported kindreds with VDDR2A ($n=53$), the majority with a known pedigree are the offspring of related, or likely to be related, parents (95%) and have homozygous mutations (92%). The prevalence is highest in Middle Eastern and South American populations (32 and 16% respectively), and only 11 and 14% occur in the North African and Caucasian populations, respectively. However, VDDR2A is less likely to be due to homozygous mutations in the Caucasian population (67% vs 92%), possibly reflecting the lower reported rate of consanguinity (17% vs 95%). In summary, this case illustrates the clinical utility of scientific advances in sequencing techniques and the increased likelihood of the occurrence of compound heterozygous mutations giving rise to VDDR2A in the Caucasian population.

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P34

Hyperkalaemia in Conn's syndrome masking hyporeninaemic hypoaldosteronism

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Background
Primary hyperaldosteronism (PHA) typically manifests as resistant hypertension, hypokalaemia and metabolic alkalosis. We present a case of PHA who subsequently exposed type 4 renal tubular acidosis (RTA) after surgical intervention.
Case history
A 62 year old man underwent investigation for chronic resistant hypertension, which had failed to respond to titration of three antihypertensive agents including Perindopril, Amlodipine and Doxazosin. His medical history consisted of type 2 diabetes, microalbuminuria, dyslipidaemia and stage 3a chronic kidney disease (CKD). Average blood pressure recordings were typically 190/100 mm per Hg on both arms, and fundoscopy revealed hypertensive retinopathy.
Investigations
Laboratory findings showed hypokalaemia (potassium 3.4 mEq/l), alkalosis (bicarbonate 33 mmol/l) and mild hypernatraemia (sodium 147 mmol/l). CT imaging of the adrenal glands demonstrated a 17 mm left adrenal adenoma. Adrenal vein sampling lateralized aldosterone secretion, with an aldosterone: cortisol (ACR) being 53 times higher from the left adrenal gland.
Results and management
Unilateral laparoscopic adrenalectomy proceeded uneventfully. The patient was readmitted post-operatively to the High Dependency Unit (HDU) due to severe hyperkalaemia (8.0 mmol/l), this was initially attributed to an acute kidney injury (AoCKD) where the eGFR deteriorated from a pre-operative value of 45 ml/min-1 to 17 ml/min-1. This was in the context of peri-operative hypotension and ACE inhibitor therapy. The eGFR subsequently rallied to 25 ml/min-1. Post-operative renin concentration (11 mUl/l) and aldosterone concentration (<70 pmol/l) proved hyporeninaemic hypoaldosteronism (type 4 RTA). The patient was treated with sodium bicarbonate and a low potassium diet. The patient has declined fludrocortisone against medical advice.
Conclusions and points for discussion
Type 4 RTA (hyporeninaemic hypoaldosteronism) has a close relationship to diabetic patients with interstitial disease especially diabetic nephropathy [1], and mild to moderate CKD, as seen in this patient with poorly controlled type 2 diabetes (Hba1c 65) and stage 3a CKD (baseline eGFR 49). In this case, surgical removal of the source of aldosterone unmasked an underlying type 4 RTA.
Reference:
[1] Andre Gustavo P Sousa, Joae Victor de Sousa Cabral, William Batah El-Feghaly, Luisa Silva de Sousa and Adriana Bezerra Nunes.
Hyporeninemic hypoaldosteronism and diabetes mellitus: Pathophysiology assumptions, clinical aspects and implications for management.

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P35

A case of cyclical Cushing's syndrome

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Case history
We present a 76-year-old woman with cyclical ACTH-dependent Cushing's syndrome since 2002. She has two-yearly relapses with proximal myopathy, candidiasis, facial swelling and hypokalaemia that have been biochemically confirmed with Overnight and Low Dose Dexamethasone Suppression tests. Although her initial cycles were brief and uncomplicated, her most recent episodes led to prolonged hospital admissions. During her last admission, she became septic complicated by a bleeding pseudo-aneurysm in the liver, a right peroneal artery occlusion and bilateral deep venous thrombosis.
Investigations
Prior to admission, an MRI Pituitary in 2014 showed no clear adenoma. A subsequent MRI in 2017 showed no change. Inferior petrosal sinus sampling was inconclusive. A Ga68 DOTATATE whole body PET-CT was unable to locate any lesions as a source for ACTH. A CT chest, abdomen and pelvis demonstrated normal adrenal glands and stable calcified lung nodules. During her second admission, she had a fall in haemoglobin with deterioration in liver function tests. CT abdomen confirmed a 10 cm bleeding lesion in the left lobe of the liver. Following this, she developed necrosis of her right toes. A vascular duplex scan confirmed the presence of occlusions of bilateral superficial femoral vein and the right peroneal artery.
Results and Treatment
Her clinical deterioration coincides with rising cortisol levels (up to 2273 nmol/l). She became intolerant of Metyrapone and was switched to Fluconazole, which was uptitrated to 600 mg BD. There were concerns that her liver lesion could be a mycotic pseudo-aneurysm secondary to sepsis. She had an emergency embolization, the pseudo-aneurysm was micro-coiled and required no further intervention. Given her bleeding risk, she was commenced on a heparin infusion for her thrombosis and thereafter, long-term treatment dose tinzaparin. Her necrotic toes were conservatively managed. Due to her frailty, a biopsy was not possible to ascertain whether the lung lesions could be a source of ectopic ACTH.
Conclusions and Discussion
This case illustrates the complexity of managing cyclical Cushing's; the challenges in identifying the source of ACTH, and its management. Fluconazole was effective in the medical management of Cushing's syndrome, acting on the same pathway as ketoconazole. Definitive treatment with bilateral adrenalectomy may be considered in the longer term. An established link between Cushing's and pseudo aneurysms has been demonstrated in previously published clinical cases. This unusual case highlights the potential for serious adverse vascular sequelae of Cushing's syndrome and the need for awareness of such complications.

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P36

Severe necrotising pancreatitis secondary to hypertriglyceridaemia in pregnancy

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Case history
A 35-year-old woman with known hypertriglyceridaemia presented with a one day history of abdominal pain, vomiting and fever. She was 14 weeks pregnant having conceived spontaneously following a period of infertility. She had discontinued her lipid-lowering medication and was managed with diet alone. On examination, she was pyrexial, tachycardic (HR = 100 bpm), normotensive (BP = 111/71 mmHg), oxygen saturation was 96% on air and she had a tender distended abdomen. A fetal US confirmed a viable pregnancy. She was diagnosed with acute pancreatitis. Initial management was conservative but she developed acute respiratory distress syndrome (ARDS), requiring respiratory support and transfer to the intensive care unit.
Investigations
Venous blood gas showed a mild acidosis (pH 7.338), raised lactate (3.2 mmol/l) and glucose of 7.6 mmol/l. Blood investigations were limited by high levels of triglycerides precluding automated measurement. After multiple dilutions, triglyceride level was confirmed at 115 mmol/l and lipase level at 293 U/l. A CT abdomen demonstrated extensive peri-pancreatic fluid collections and peri-pancreatic fat stranding in keeping with acute necrotising pancreatitis presumed secondary to hypertriglyceridaemia.

Results and treatment
Initial management was focused on lowering the triglyceride levels. She was started on an intravenous insulin and heparin infusion and transferred to a tertiary centre for consideration of plasmapharesis. Her triglyceride level fell to 5.1 mmol/l with insulin and heparin alone. Plasmapheresis was not required. She was started on Fenofibrate, high-dose Omega3 and a low-fat diet which has maintained her triglyceride level below 5 mmol/l (currently 2.8 mmol/l). She subsequently developed a distended gallbladder and septicaemia requiring intravenous Tazocin, a gallbladder drain and a period of parenteral nutrition. Medical termination of pregnancy was discussed as a potential option to ensure maternal survival. She is currently 23 weeks gestation, approaching viability, with a growth scan showing normal growth but reduced uterine-artery-dopplers suggesting an increased risk of fetal-growth-restriction and placental insufficiency. Her care is being co-ordinated by a multidisciplinary team including hepatobiliary, obstetrics and metabolic medicine teams.
Conclusions and points for discussion
Acute pancreatitis in pregnancy has a high morbidity and mortality rate for both mother and fetus. Due to medical and ethical challenges, such cases must be managed via the multidisciplinary team. This case highlights the efficacy of insulin and heparin in lowering triglyceride levels. Plasmapheresis remains an option where triglycerides do not fall. It also highlights the importance of preconception care and effective use of diet, Omega3 and Fenofibrate in lowering triglyceride levels during pregnancy.

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P37

A rare case of congestive heart failure caused by idiopathic hypoparathyroidism

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Clinical Case
A 48-year old male presented with gradual onset of shortness of breath and atrial tachycardia requiring admission to intensive care unit. He was normally fit and well and did not have any history of thyroid/neck surgery. He was an ex-smoker who drank more than 40 units of alcohol per week.
Investigations
Laboratory tests revealed low serum calcium of 1.03 mmol/l (2.15–2.6 mmol/l), high serum phosphate of 2.77 mmol/l (0.9–1.50 mmol/l) and low serum magnesium of 0.53 mmol/l (0.65–1.05 mmol/l). His potassium, alkaline phosphatase and renal function were normal. Electrocardiogram at admission showed atrial tachycardiawith ventricular rate of 180 bpm, left ventricular hypertrophy, T wave depressions in leads V4-6 and prolonged QT interval. Chest x-ray showed cardiomegaly and features of pulmonary oedema. Urgent echocardiogram showed dilated and hypokinetic left ventricle with left ventricular ejection fraction of 27%. His parathyroid hormone was undetectable and he had normal thyroid function tests and vitamin D. He also underwent a coronary angiogram which was normal.
Treatment
Hypocalcaemia, hyperphosphataemia and undetectable parathyroid hormone is consistent with the diagnosis of primary hypoparathyroidism. He was initially treated with intravenous calcium gluconate and magnesium for several days until normalisation of serum calcium and serum magnesium. Following this, he was commenced on long term alfacalcidol and calcium supplementation. An echocardiogram done after three months of treatment showed improved left ventricular ejection fraction and normal left ventricular size. This patient is under long term follow-up with the cardiologist and the endocrinologists.
Conclusions
Dilated cardiomyopathy is a dangerous condition that can be associated with reversible conditions such as alcoholism, peripartum cardiomyopathy and various metabolic conditions. Hypoparathyroidism results in hypocalcaemia and hypomagnesaemia. Hypocalcaemia can cause prolongation of QT interval, ventricular arrhythmias and dilated cardiomyopathy. Calcium ion is important for the excitation of the myocardium and consequently its contractibility. Cardiomyopathy associated with hypoparathyroidism can be reversed when it is adequately treated with calcium and vitamin D supplementation. In these cases, recombinant parathyroid hormone is rarely required. It is important to identify hypocalcaemia as a treatable cause of cardiomyopathy as this can prevent the development of life threatening sequelae.

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P38

A case of pheochromocytoma with SDHA mutation

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A 58-year-old gentleman who was otherwise well presented with urinary symptoms. As part of his investigation for this he underwent a CT scan which showed an incidental 6 cm right adrenal mass compressing the inferior vena cava and superior pole of the right kidney with a 6-mm pulmonary nodule. He was subsequently found to have a raised urinary normetanephrine of 48.81 (normal range 0–3.3) suggestive that the mass was a pheochromocytoma. Retrospectively he reported episodes of flushing, sweating, headaches and diarrhoea. Examination was unremarkable with a blood pressure of 136/84 and he did not take any medications including anti-hypertensives. An MIBG scan showed uptake within the adrenal mass. Having been established on phenoxybenzamine he underwent a radical adrenalectomy with right nephrectomy as there was invasion into the perinephric fat. On histological review the excision appeared complete and the tumour cells strongly expressed CD56, chromogranin, synaptophysin and NSE and S100 highlighted sustentacular cells, all of which supported a diagnosis of pheochromocytoma. The Ki-67 proliferation index was $<2\%$ suggesting low mitotic activity within the tumour. However, the tumour showed focal extension through the capsule and into the perinephric fat with lympho-vascular invasion within the large vessels of the perinephric fat and within the surrounding fibrous capsule. This histology gave an overall PASS of 6/20 with a score of <4 indicating a tumour will behave in a benign fashion. A gene panel test was performed which revealed a variant of unknown significance in the SDHA gene. Immunostaining showed loss of SDH expression suggesting this was pathogenic. Post-operatively he has had follow-up CT scans with 24 hour urinary normetanephrine and gut hormone measurements at 2 months and 1 year. These have shown no evidence of residual or recurrent disease and stable appearance of the 6mm pulmonary nodule. He reports complete resolution of his symptoms.
Conclusions
Genetic predisposition to pheochromocytomas and paragangliomas is well recognised. The SDHA gene codes for one of the four subunits of the succinate dehydrogenase enzyme which converts succinate to fumarate. It is a tumour suppressor gene and alterations in this gene have been associated with pheochromocytomas and paragangliomas. The particular variant in this case has not previously been reported so it is therefore uncertain whether this alteration is associated with an increased risk of tumour development, however loss of immunostaining suggests it is pathogenic. This case also suggests that SDHA mutation associated pheochromocytoma can exhibit malignant behaviour.

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P39

Management of acromegaly in pregnancy and post-partum

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Case history
A 39 year old female presented reporting a 5-year history of swollen face, hands and feet, with associated joint pain. She was initially investigated for rheumatoid arthritis. She had no significant past medical history except for a previous miscarriage in 2014 and treatment for hypertension in a subsequent successful pregnancy. Post-partum she breastfed with no difficulty for 18-months but remained amenorrhoeic during this time. During 2016 she noticed increase in shoe and ring size, snoring and sweating. She felt increasingly tired, with a reduction in libido and experienced recurrent headaches with deterioration in her peripheral vision.
Investigations
Investigations demonstrated elevated IGF-1 level of 71 nmol/l (8.5–30.7 nmol/l) with growth hormone of 15.3 mcg/l. Her prolactin was 1717 MU/l. An MRI scan in August 2016 confirmed a large pituitary macroadenoma compressing the optic chiasm and eroding the fossa with right cavernous sinus invasion. She was advised to stop breast feeding, commenced on Lanretoide and Carbergoline, and referred to our centre for Transphenoidal surgery.
Results and treatment
She underwent transphenoidal adenomectomy in December 2016. Post operatively there were no significant complications. Histology showed a somatotroph pituitary adenoma with a mixed densely and sparsely granulated pattern, no evidence of atypia, and a MIBI index $<$ 1%. Lanretoide was continued post-operatively in view of the known residual tumour within the

cavernous sinus. This was then confirmed on the post-operative MRI at 3 months. Biochemistry (on Lanretoide) showed IGF-1 of 24.3 nmol/l (6.4–31.0 nmol/l), growth hormone 1.2 mcg/l, LH 2.3 IU/l, FSH 5.9 IU/l and prolactin of 129 MU/l. In April 2017 her IGF-1 level was 20 nmol/l and random growth hormone was 2.3 IU/l. Prior to a complete biochemical post op assessment, she was keen to extend her family. Following discussion around the evidence of Lanreotide in pregnancy she and her husband chose to stop treatment. She conceived in May 2017 and the pregnancy is progressing without complication. She has expressed the wish to complete the pregnancy and breast feed off somatostatin analogue therapy.

Conclusion

This case highlights the potential challenges in monitoring and treatment of acromegaly during pregnancy and the post-partum period. There is limited evidence on the use of somatostatin analogues in pregnancy, largely based upon anecdotal evidence and case reports. This case highlights the importance of pre-natal discussion and tailoring treatment to the individual.

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P40

Diagnostic challenges in a patient with hitherto unexplained hyperinsulinaemic hypoglycaemia

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- In healthy adults, hyperinsulinaemic hypoglycaemia is rare and therefore needs further investigation. Such a state invariably indicates endogenous insulin secretion after a careful history has ruled out Sulphonylurea abuse. Optimal diagnostic and management strategies remain a challenge. A recent observational study in a tertiary Centre in Cambridge has identified 29 cases over a 13-year period and has found great value of the 48-h fast in diagnosing insulinoma and Endoscopic Ultrasound in pre-surgery localisation of tumour.
- Our patient is a 62-year-old otherwise fit and well handyman who initially presented with collapse with loss of consciousness leading to occipital fracture and contre-coup brain contusions. Diagnosis remained somewhat uncertain for 6 months when he was seen by Cardiologist and then Neurologist as outpatients. He re-presented with difficulty in rousing in the morning after drinking whisky and lager at night without food. Capillary glucose of 1.4 was noted by ambulance crew. GP review after 4 days with capillary glucose 2.0 with no symptoms and admitted under medicine.
- Capillary glucose of 1.9 at 0515 following admission to the Acute Medical Unit at 2,200 prompted blood sampling for glucose, insulin and C-Peptide. Glucose was 2.4 mmol/l, insulin 5.6 mU/l and C-Peptide 1,010 pmol/l. A second lot a few days later on the ward yielded glucose 2.4 mmol/l, insulin 10.3 mU/l and C-Peptide 1,288 pmol/l. Although a 0900 h Cortisol was 175, a Short Synacthen Test showed a good cortisol response. Other hormones including gut hormones were normal. CT and MRI Pancreas showed complete fatty replacement of Pancreas except for head and uncinate process and two small indeterminate nodules adjacent to spleen. Octreotide scan has shown no octreotide-avid focus involving the pancreas nor any octreotide avid disease elsewhere. Endoscopic Ultrasound has not shown any lesion. Since starting on Diazoxide 100 mg BD, there have been no hypoglycaemic episodes so far.
- This is case is still posing great challenges with regards to the cause of hypoglycaemia despite biochemical confirmation with high insulin, C-Peptide with laboratory glucose of 2.4 mmol/l. The patient has now been referred to a Tertiary Centre and a Selective Arterial Calcium Stimulation with hepatic venous sampling is planned. Differential diagnoses remain as Insulin Autoimmune Syndrome or occult Insulinoma.

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P41

A not so sweet glucagonoma

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Case history

This 33-year old Scottish female presented in February 2017 with a 3-month history of vomiting, erythematous vesicular pruritic rash and three stone weight loss. The rash started 1 day postpartum in January 2015 and migrated from dorsum of feet to both lower legs, upper thigh and torso. A negative biopsy for pemphigus led the team to suspect necrolytic migratory erythema (NME) in November 2016. Her past medical history includes gestational diabetes with her third pregnancy (January 2015).

Investigations

In February 2017, a CT chest, abdomen and pelvis revealed a 4.1 cm pancreatic tail mass and an extensive right pulmonary embolus. Endoscopic ultrasound showed brisk arterial phase uptake (Sonovue contrast), in keeping with a neuroendocrine tumour (NET). Fine needle aspirate of the pancreatic mass was consistent with glucagonoma. Plasma glucagon and chromogranin B levels were elevated (202 pmol/l ($n < 50$), 312 pmol/l ($n < 150$) respectively). Vasoactive intestinal peptide, pancreatic polypeptide, gastrin, somatostatin, chromogranin A, plasma catecholamines, CA 19-9 and CEA were negative. Micronutrient screen, albumin and liver function tests were normal. Blood and capillary glucose remained within normal range since February 2017.

Results and treatment

Prior to her Octreotide scan, she received some symptomatic relief from subcutaneous octreotide infusion. As such, despite the negative Octreotide scan, subcutaneous octreotide injections were continued until her laparoscopic distal pancreatectomy in March 2017. This was complicated by a splenic infarction. In August 2017, she developed a pancreatic pseudocyst requiring pigtail stenting. Pathology showed an encapsulated Grade 1 well-differentiated NET with stage T3 N0 M0, R0. The pancreatic transection margin was free of tumour (Ki-67 proliferation index 3.4%). The tumour stained positive for CD 56, chromogranin and synaptophysin with variable positivity for glucagon. Postoperatively, her plasma glucagon (66 and 116 pmol/l) and chromogranin B remained elevated. This has since been managed with watchful observation.

Conclusions

Her case resembles most glucagonoma cases; with the delay in diagnosing NME, thromboembolism and severe weight loss. She meets two of the major criteria for glucagonoma; NME and pancreatic lesion. Unusually, she did not display any insulin resistance apart from gestational diabetes prior to development of NME. Despite the negative Octreotide scan, she had some symptomatic response to subcutaneous Octreotide prior to surgery. Some theories have suggested that Octreotide may stabilise glucagon levels, regardless of tumour octreotide uptake. Interestingly, her symptoms resolved completely following distal pancreatectomy, albeit the elevated post-operative glucagon level.

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P42

Abstract withdrawn.

P43

SDH mutation and prolactinomas: case series

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Succinate dehydrogenase (SDH) mitochondrial enzyme complex mutations are associated with hereditary paragangliomas and phaeochromocytomas. Of late, there has been more awareness of the development of other tumours in this patient cohort. There is limited evidence of propensity for development of Prolactinomas and other pituitary tumours in patients harbouring mutations in the SDH complex genes. We present three cases attending our center with a diagnosis of prolactinoma and *SDH* complex mutations.

Case 1

61 year old gentleman, presented with a large right-sided carotid body tumour. Three years previously he had been diagnosed with a macroprolactinoma and continues to be managed on Cabergoline. Upon further review, the patient reported that his nephew had been diagnosed with two Phaeochromocytomas. There was no other family history. Genetic testing confirmed an *SDHB* mutation.

Case 2

40 year old gentleman was found to have a macroprolactinoma. On extensive history taking he reported a strong family history of phaeochromocytoma. Consequently, he underwent genetic testing, resulting in a diagnoses of *SDHB* mutation. He was also found to have a large right lung mass, which was confirmed to be a carcinoid tumour following resection. His investigations pre-surgery

identified mildly elevated metanephrines He underwent surgery after appropriate alpha and beta blockade and subsequently metanephrines normalised.
Case 3
A gentleman diagnosed with a macroprolactinoma in his early 20's. His mother was noted to have a confirmed paraganglioma syndrome secondary to a mutation in *SDHC* gene. His genetic testing has confirmed the same genetic mutation. His investigations including metanephrines and radiological scans have proved normal, apart from a small (6 mm) lung nodule that is under surveillance.
Discussion

Our case series highlights the potential propensity for development of pituitary tumours in patients who have mutations in the SDH complex genes. This would inform the follow up that they currently receive to include pituitary imaging and biochemical profiling. In our patient cohort, macroprolactinoma was diagnosed prior to the development of phaochromocytoma or paragangliomas. Larger case series would be needed to confirm the association and the clinical course.

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Clinical Update

Workshop A: Disorders of the hypothalamus and pituitary (I)

Diabetes Insipidus

WA1

Nephrogenic diabetes insipidus one year following discontinuation of lithium

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Lithium-induced Nephrogenic Diabetes Insipidus is the commonest type of Nephrogenic Diabetes Insipidus. Management remains challenging even when Lithium is discontinued as non-reversibility of Diabetes Insipidus can be irreversible. Possible treatment options include Hydrochlorothiazide, Amiloride or Acetazolamide. We report a case of possible Nephrogenic Diabetes Insipidus 1 year after discontinuation of Lithium. Our patient is an 85-year old lady who was referred for an Endocrinology opinion as she was noted to have polydipsia and polyuria on the ward. It was noted that prior to this admission with a fall, she had been on Lithium therapy for 20 years and this was stopped 1 year previously due to declining renal function. On admission, she had an acute on chronic kidney injury with urea 26.9 and creatinine 349. Baseline creatinine was around 240. Her fluid balance was on average negative 1,900 ml in a day and she passed more than 3 l of urine per day. A random serum osmolality was 317 mosm/kg with urine sodium 53 mmol/l and urine osmolality 265 mosm/kg. Following an overnight water deprivation period, her morning plasma sodium was 143 mmol/l, serum osmolality was 322 mOsm/kg and urine sodium was 48 mmol/l and urine osmolality was 290 mOsm/kg. She also passed 1,800 ml of urine over those hours. She has been booked for a formal water deprivation test as an outpatient.

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WA2

A complex case of diabetes insidipus in a patient with septo-optic dysplasia

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An 18 year old gentleman was first reviewed in our endocrine adolescent transition clinic. He had been under the care of the paediatricians since birth, where he initially presented with developmental delay. This triggered investigations which led to the diagnosis of septo-optic dysplasia. At aged 12 he developed cranial diabetes insipidus (DI) and secondary hypothyroidism. This was managed with intranasal DDAVP (20 ug BD) and thyroxine 125 µg. Due to an abnormal thirst threshold he was required to take up to 2.5 l/day of fluid to maintain sodium levels within the normal range. This was only achievable through the heroic efforts of his caring family. At that point his family were worried about his 'lack of vitality' and energy. Several 0900 h serum cortisol levels of <100 nmol/l were measured therefore he was commenced on hydrocortisone replacement (5 mg BD). This however caused him to become hypernatraemic (Na 151 mmol/l). His fluid 'prescription' and DDAVP dose had to be adjusted accordingly, until a new equilibrium was established. A previous glucagon stimulation test documented evidence of growth hormone deficiency (GHD). However treatment was not initiated until the family raised concerns of his increasing lethargy, somnolence and increasing central obesity, 6 months after starting hydrocortisone replacement. He was commenced on GH replacement (0.3 mg OD). Although this greatly improved his level of alertness and short term memory, it led to decompensation of his DI, resulting in severe hypernatraemia: peak Na169 mmol/l. Disturbance of sodium balance with GH had been predicted, but the extent was unexpected and required inpatient correction. Septo-optic dysplasia is a congenital condition characterised by optic nerve hypoplasia, hypopituitarism and other midline brain defects. The evolving nature of the various endocrinopathies over time makes management of sodium and water balance especially challenging. ACTH deficiency is known to cause hyponatraemia. This may have been partially masked DI, which was revealed when he was commenced on hydrocortisone. The sodium-water equilibrium was again disrupted when he was started on GH replacement. Patients with GHD have sodium and water depletion. When GH replacement is initiated, there is usually stimulation of thirst, triggering an increase in fluid intake to match the sodium retention to keep serum sodium concentrations constant. However, due to hypothalamic dysfunction in our patient, this compensatory mechanism was lost, resulting in severe hypernatraemia. This case highlights the complex nature of sodium homeostasis and the profound effects the anterior pituitary hormones can have on that delicate balance.

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WA3

Lymphocytic hypophysitis in a pregnant patient with type 1 diabetes

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A 34-year old female with type 1 diabetes presented to the antenatal clinic complaining of polydipsia, polyuria and nocturia. She was 12 weeks pregnant with adequate glycaemic control on a basal-bolus insulin regime. She reported new onset headaches but no deterioration in vision. On examination, her visual fields were full to confrontation with red pin. She was eunatraemic (Na 138 mmol/l), had an early morning cortisol of 332 nmol/l and normal thyroid function tests (FT4 16 pmol/l, TSH 1.73 munit/l). A formal water deprivation test was not undertaken due to the potential risk of significant dehydration to the pregnant mother. She was, therefore, commenced on oral Desmopressin for suspected diabetes insipidus, advised to drink to thirst and referred for a non-contrast pituitary MRI to exclude a mass lesion. This showed a slightly bulky pituitary gland with a visible posterior bright spot. Although her osmotic symptoms improved after starting Desmopressin, she was becoming disproportionately fatigued to the stage of pregnancy, necessitating a small dose of Hydrocortisone, with good symptomatic benefit. A provisional diagnosis of lymphocytic hypophysitis was made. Regular scans confirmed good fetal growth throughout the pregnancy and she subsequently delivered a healthy baby boy at term. Her pituitary function was reassessed post-partum. A pre-hydrocortisone cortisol level was satisfactory at 439 nmol/l and she reported no polydipsia or polyuria after omission of her Desmopressin. A repeat MRI pituitary showed a reduction in the size of the gland and basal pituitary function returned to normal, consistent with resolution of the hypophysitis. She was discharged from clinic on her pre-pregnancy doses of insulin and off all pituitary hormone replacement. She has recently, however, represented in the first trimester of her second pregnancy with polyuria and polydipsia and is currently undergoing assessment by her local endocrine team. Lymphocytic hypophysitis is well reported to occur in pregnant women, particularly when there is a history of autoimmunity, and may well be transient. Diabetes insipidus in pregnancy is associated with diagnostic challenges especially as standard dynamic pituitary function tests are unsafe. The diagnosis is, therefore, often presumptive and this case highlights the importance of close monitoring during pregnancy and early assessment of the pituitary axis post-partum.

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WA4

Extreme polydipsia as an emergency presentation of chronic undiagnosed central diabetes insipidus

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Isolated Central Diabetes Insipidus is a rare condition characterised by deficiency of arginine vasopressin (AVP) which presents with polyuria and polydipsia. The reported prevalence of diabetes insipidus is 1 in 25,000. The pathogenesis of central diabetes insipidus is often uncertain however the known causes can be divided into acquired, through trauma or vascular injury as well as infiltrative including malignancy, and congenital abnormalities which accounts for less than 10% of cases. Patients with this condition can often compensate through water consumption and therefore any disruption in their usual routine may lead to potentially fatal electrolyte disturbances. We present a 16 year old female patient who presented to the emergency department with increased water intake and lethargy. There was no previous medical history however it was reported that from the age of 3 years she had been obsessed with drinking water and the amount had steadily increased over the years where she was now consuming up to 15 litres per day. Her initial biochemistry was within the normal reference range (Sodium 144 mmol/l (133–146), potassium 4.1 mmol/l (3.5–5.3) and creatinine 51 umol/l (45–84)) and a provisional diagnosis of psychogenic polydipsia was made with paired osmolalities requested. She was limited to 4 l of fluid per day and following this her sodium level steadily increased over the subsequent 4 days to 156 mmol/l. The urine and serum osmolalities along with a water deprivation test revealed the diagnosis of central diabetes insipidus, the aetiology of which remains uncertain. MRI pituitary was performed measuring $5\times7.5\times13$ mm, with normal stalk. She was commenced on desmopressin 100 mg three times per day and since has had no further polyuria, polydipsia or nocturia. A detailed history and physical examination can often unmask clues within the underlying aetiology and provide a timescale as to when the patient may have developed diabetes insipidus. Biochemical analysis and water deprivation test remain the gold standard for diagnosis. This case highlights the potential complications of

misdiagnosis and treatment of patients with central diabetes insipidus. It is also important to identify the changes in fluid intake that can occur through concurrent illness which requires monitoring in these individuals and can often be challenging manage with adjustments in fluid balance and DDAVP dose required to prevent extreme electrolyte changes.

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WA5

Selective-Serotonin-Re-uptake inhibitor induced SIADH on a background of post-operative Diabetes Insipidus

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We present a case of a 79 year old gentleman who attended the emergency department with a one day history of acute confusion and hallucinations. His background included trans-sphenoidal surgery for a gonadotrophic pituitary macro-adenoma in 2012 with subsequent panhypopituitarism and post-operative diabetes insipidus. He also had a history of restless-leg-syndrome for which he took Amitriptyline chronically, COPD and tablet-controlled diabetes mellitus. Of significant note, the patient had been discharged the previous week following an admission with painful legs and diagnosed with peripheral vascular disease thus commenced on Duloxetine as part of a conservative management plan. Blood tests showed an acute hyponatraemia with sodium 109 mmol/l and a normal full blood count, potassium, creatinine and urea. His baseline sodium was between 129 and 135 mmol/l over the previous year. There was no evidence of infection. On initial assessment the patient was confused without any lateralising neurology. He was clinically euvolaemic and normotensive. A palpable bladder was noted. CT head and chest X-ray did not reveal acute pathology. The initial management plan was to hold Desmopressin, (DDAVP), commence intra-venous Hydrocortisone and catheterise. Paired osmolalities revealed a serum osmolality of 234 mosm/kg/H20 (normal value: 275–295), urinary osmolality of 583 mosm/kg/H20, and urinary sodium of 103 mmol/l. He was managed with 2.7% hypertonic saline requiring two 100 ml infusions to raise the sodium above 5 mmols. The rate of correction exceeded 10 mmols within total 24 hours and therefore Desmopressin was re-commenced, initially at a lower dose. Acute hyponatraemia secondary to syndrome of Inappropriate anti-diuretic hormone, (SIADH), was diagnosed and deemed a consequence of recent commencement of Duloxetine, a dual re-uptake inhibitor of serotonin and norepinephrine. This patient was on long-term Amitriptyline, also a selective-serotonin re-uptake inhibitor, as well as Omeprazole and Desmopressin. Both SSRI agents were permanently discontinued; Omeprazole another agent frequently associated with SIADH was switched to Ranitidine. Sodium was carefully monitored and slowly corrected to 135 mmol/L over a period of 72 hours, (low end of normal reference range). His cognitive impairment improved to baseline and he was discharged on his regular dose of oral Desmopressin and steroids. This case highlights how SSRIs potentiated the action of synthetic anti-diuretic hormone in a patient with central Diabetes-Insipidus. It is important to have awareness of SIADH as a side effect of common prescription medications and the cautions necessary for patients with polypharmacy, particularly the elderly.

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WA6

Primary CNS lymphoma as a cause of diabetes insipidus

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A 38 female patient with a diagnosis of primary CNS lymphoma was admitted for MATRIX (methotrexate, rituximab, thiopeta, cytarabine) chemotherapy. Prior to chemotherapy and while on steroids she became increasingly polydipsic and polyuric with blood biochemistry demonstrating a sodium of 164 mmol/l. An endocrine review of the patient was requested and a diagnosis of cranial diabetes insipidus was suspected due to the extent of infiltration of the hypothalamus and pituitary stalk by the CNS lymphoma. Formal testing for diabetes insipidus was not possible due to the patient's condition. A pragmatic trial treatment with Desmopressin was initiated with good effect while closely monitoring fluid balance and serum sodium levels. Further blood testing demonstrated hypothyroidism and a suppressed gonadal axis. A diagnosis of pan hypopituitarism was made and Levothyroxine initiated with plans to review gonadal and adrenal axes following chemotherapy. During the second cycle of MATRIX chemotherapy the patient developed methotrexate toxicity. This resulted in a severe acute kidney injury requiring dialysis after which her renal function returned to baseline. Protocols to avoid Methotrexate toxicity require intravenous fluid at up to 250 ml/h so that a significant diuresis is achieved. Methotrexate toxicity was in part exacerbated by Desmopressin treatment which reduced the anticipated diuresis. Following chemotherapy and prior to discharge the patient's Desmopressin was adjusted to achieve a normal fluid balance with stable sodium levels. Further cycles of chemotherapy are planned with down titration of Desmopressin under strict fluid input/output and serum sodium monitoring. How does this route to diagnosis differ from outpatient assessment of patients with possible diabetes insipidus? How would you coordinate future treatment with Desmopressin and chemotherapy?

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WA7

When opposites are one and the same

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Water balance disorders following neurosurgery are well recognised and may give rise to both hypo- and hypernatraemia. We present the case of a 42-year-old male who developed a triphasic response after extended transsphenoidal surgery for a pituitary stalk lesion. The patient presented with a 4 month history of unremitting frontal headaches and dizziness. MRI confirmed a 15×15 mm stalk lesion. Clinical examination including formal visual perimetry was unremarkable. Blood tests revealed primary hypothyroidism but were otherwise normal. His past medical history included hypertension and alcoholism. He was referred to the UK where he underwent extended transsphenoidal surgery. In the immediate postoperative period, he developed polyuria (670 ml/h) and polydipsia (500 ml/h) which led to a negative fluid balance (of 2 L over 12 hours), serum sodium of 142 mmol/l, high serum osmolality of 299 mOsmol/kg and low urine osmolality of 131. The patient was normoglycaemic and did not receive any diuretics. Desmopressin (initally subcutaneous then desmotabs) reduced the polyuria and, together with intravenous fluids (2 L of 5% dextrose/day between days 1 and 2) and ad libitum drinking, restored normonatraemia. Hydrocortisone 10-5-5 mg was started on the 6th postoperative day in view of a morning cortisol of 25 nmol/l. On the 7th day post-op he developed severe SIADH with a serum sodium of 120 mmol/l, which was managed conservatively with fluid restriction (1.5 l/day). He was clinically euvolaemic, with normal kidney function (creatinine 53 Umol/l). Despite fluid restriction, fluid intake exceeded urine output (19 ml/h) producing a positive fluid balance of $+1.5$ l and a further fall in serum sodium to 119 mmol/l. Here the patient complained of headaches, unsteadiness and lethargy but no confusion or seizures. On day 12 the patient redeveloped polyuria (250 ml/hour) for which desmotabs 100mcgs daily were started. In anticipation of a triphasic response he was continued on ad libitum fluid intake and desmopressin was further increased to 100–200 mcgs as the patient was still waking up hourly to micturate. He was advised to omit one dose a week to allow excess water to be offloaded. On the 13th postoperative day he developed a serum sodium of 138 mmol/l, serum osmolality 299 mOsm/kg and urine osmolality of 79 mOsm/kg. Histology confirmed a pituicytoma (WHO grade 1); Ki-67 $<1\%$.

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WA8

Challenges in management of cranial diabetes insipidus in critically ill patient

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Cranial diabetes insipidus in critically ill patient increases the complexity of fluid management. Well patients with cranial diabetes insipidus can drink enough fluid to replace their urine losses driven by their thirst mechanisms. In critically ill patients the thirst response cannot be relied upon. When fluid input is not adequate it results in hypernatremia. Here dextrose, water or hypo-tonic intravenous fluid is used. Complications related to this are high glucose levels, fluid overload and quick correction of hypernatremia. Treatment with desmopressin cause low urine output and anti-diuresis. Frequent monitoring serum sodium, urine osmolality and volume is very important. 39-year-old lady admitted to critical care with major haemorrhage following liver biopsy. Background Germinoma age 15, had a combination of chemotherapy and radiotherapy) craniospinal irradiation) which has left her with pan hypopituitarism with Diabetes insipidus. She takes Desmopressin 100micrograms in afternoon and 200 µg in the evening On

admission she had hypotension, low urine output and positive fluid balance while on desmopressin normal dose. The fluid balance further increased and on fifth day, and one desmopressin dose was omitted and evening dose halved to facilitate diuresis. She also had hyponatremia at this stage. Next day, sodium normalised and had negative fluid balance and desmopressin was restarted. On day 7 of admission, she was still in negative fluid balance, but was clinically noted to be overloaded. Her sodium was normal, and frusemide was given for fluid overload. She then had large diuresis and hypernatremia. She was also started on NG feeds mixed in sterile water. As the urine output increased, she was given additional NG water with frequent sodium monitoring. Hydrocortisone was reduced to facilitate free water clearance. She continued to be in negative fluid balance with Na 158 mEq/l and 10% dextrose boluses were given. More strict fluid replacement strategy was employed with NG water and 10% dextrose replaced hourly by monitoring urine output. Sodium normalised and urine output in normal range and desmopressin continued at admission doses on discharge. This case outlines the intricacies in fluid management in CDI patients. The scope for improvement in this specific case is aggressive rationalisation of desmopressin doses, strict monitoring of urine osmolality or urine specific gravity, accurate recording of fluid intake and output and fluid replacement to match urinary losses. This might have to be done every hour.

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WA9

Acute onset DI in a young woman

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A 31 year-old lady presented to clinic with an acute, three-week history of rapidly worsening polyuria and polydipsia. She described an eighteen month history of dysmenorrhoea with no galactorrhoea and reported no change in her vision. Her past medical history included alopecia areata one year previously from which she made a full recovery. Clinical examination was normal including full visual fields to red-pin confrontation. Biochemistry identified serum sodium of 141 mmol/l, serum osmolality 292 mOs/kg and urine osmolality 84 mOs/kg. On the basis of the history and these investigations she was diagnosed with diabetes insipidus, felt likely to be cranial due to the acuity of onset. She was started on DDAVP with good effect on her symptoms and this was titrated to a dose of 200 µg bd orally to achieve full control. Anterior pituitary function was normal (T4 of 14.5 pmol/l, TSH 4.1 mIU/l, 0900 h cortisol 238 nmol/l, LH 3.6 IU/l, FSH 4.1 IU/l, oestradiol 289 pmol/l, prolactin 383 mIU/l and testosterone 0.8 nmol/l). MRI scan of the pituitary showed a normal-size pituitary but without a posterior bright spot correlating with diabetes insipidus. There was diffuse thickening within the pituitary stalk, in keeping with an inflammatory process such as histiocytosis, sarcoid or infundibular hypophysitis. Epithelial tumour markers were checked in serum and CSF and were within normal limits. CSF was clear with low protein and normal glucose levels. Auto-antibody testing revealed a positive anti-smooth muscle antibody. Based on her history, biochemistry and imaging characteristics she was diagnosed with probable infundibular lymphocytic hypophysitis. Her symptoms have remained well controlled on oral DDAVP and interval imaging has shown no progressive hypothalamo-pituitary lesion. However, she developed secondary amenorrhoea with biochemical evidence of gonadotrophin insufficiency. She was started on transdermal oestrogen application and referred to the fertility service for assistance with conception. She conceived with gonadotrophin injections and with close endocrine input required an uptitration of her DDAVP during the early stages of pregnancy to account for extra thirst. Her pregnancy was uncomplicated and she delivered a healthy baby via caesarean section. Her periods have now returned, although irregularly, and her diabetes insipidus remains well controlled on 100 µg DDAVP qds. This is a case of acute onset cranial diabetes insipidus secondary to presumed lymphocytic infundibular hypophysitis. It highlights the diagnostic considerations in investigating this presentation as well as the management of DI in pregnancy.

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WA10

Rapidly progressive polyuria, polydipsia and headache – an unusual case of central diabetes insipidus

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A previously well 49 year old woman was referred to our endocrine service with a compelling 4 month history of polyuria and polydipsia. Her 24 h fluid intake was estimated to be 12 l with 4 l of this taken overnight; these estimates had doubled in the 2 months since referral. Due to the development of an increasingly severe frontal headache, her GP organised a CT head scan which was largely unremarkable aside from a 'slight fullness' to the pituitary gland. Pituitary function tests at this time were normal with elevated gonadotropins. Urgent outpatient investigations including short Synacthen test, MRI pituitary and water deprivation test were arranged. Before any of these investigations were completed, however, the patient was admitted to the acute medical unit 2 weeks after her clinic appointment due to worsening of her symptoms. While monitoring her fluid balance and checking urine osmolality it became clear that she did indeed have diabetes insipidus. Despite being a non-smoker and having no respiratory symptoms, the admission CXR revealed a large right upper lobe mass consistent with a primary lung tumour. An inpatient MRI brain showed multiple metastases including one in the pituitary fossa. Her symptoms responded well to the introduction of both dexamethasone and desmopressin. Prior to discharge she underwent bronchoscopy which confirmed a diagnosis of adenocarcinoma of the right lung. She was ultimately treated with whole brain radiotherapy and palliative chemotherapy. During follow-up she became progressively more Cushingoid due to the high-dose dexamethasone required for symptom control and was diagnosed with steroid-induced diabetes mellitus. This case demonstrates the rarely encountered scenario of central diabetes insipidus due to pituitary metastasis. The possibility of this diagnosis was considered in the first clinic appointment hence the necessity of arranging more urgent investigation than for most suspected/possible DI cases.

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WA11

Cranial diabetes insipidus, beyond polyuria & polydipsia

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Cranial diabetes insipidus (CDI) is commonly idiopathic but can also be due to tumours of the pituitary & hypothalamus or surgery to remove these tumours. It can also occur due to infiltrative processes including metastatic malignancy. Pituitary metastases are not a common clinical entity although it can be a common finding in autopsy in advanced cancer when the pituitary & the sella have been evaluated. In this abstract, I will discuss two cases of CDI as a presentation of metastatic lung cancer compared to a case of known breast cancer that developed CDI. Weight loss can be a main presenting feature in DI due to malignancy. Our patients had normal or high Na, partial or Panhypopituitarism & adequate response to Vasopressin. It is important that a careful history & a thorough clinical examination are conducted in all cases of DI. The examination should not be only focused on signs of an endocrinopathy. Neuroimaging does not always differentiate vey well between different aetiologies of CDI & doubtful cases need to be discussed in an MDT. Treatment with Desmopressin can improve symptoms and quality of life but the prognosis is guarded with poor survival rates even in patients who had intervention.

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WA12

Diabetes mellitus ketoacidosis, diabetes inspidus clinical diagnosis and hypophysities

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A 47 years old gentelman was admitted as a case of DKA. She was kept on insulin infusion protocol despite hydartion her Na remained to be high so she was kept on Na 18% her glucose was controlled but her sodium remained on the higher side so they used clinical disgnosis to start her on miniril tablet twice dialy. MRI pituitary showed thickening of pituitary stalk no adenoma she was discharged on insulin Three doses mix insulin. Her blood tets shows anemia of normochromic normocytic anemia with high ESR, she has ANF positive and thrombocythemia. however she has later well controlled blood sugar, MRI report reported again shows hypophysities. Opinion from rhematology suggested Plaquinel 200 mg bid. After 6 months of tretment ESR reteurn to normal CBC corrected blood sugar was well controlled. Patient can not stop miniriel. 1) What is diagnosis; 2) what is next step of mangemnt regarding miniril and plaquinel; 3) patient refused water Deprivation test.

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WA13

Cushing's disease relapse associated with central diabetes insipidus

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Introduction
Central diabetes insipidus (DI) is a frequent complication of transfenoidal surgery for Cushing's disease (CD). It can be transient or, more infrequently, permanent. The most common mechanism results from surgical neurohypophyseal damage rather than local mass effect from the pituitary adenoma.
Case report
A 40 years old woman was referred to our Endocrinology outpatient clinic at the beginning of 2015 for new onset hypertension, significant weight gain, mood disturbance, proximal muscular weakness and amenorrhea. After a year of follow-up, she was formally diagnosed with cyclic CD, hypogonadotrophic hypogonadism, central hypothyroidism, as well as a pituitary macroadenoma ($12\times16\times15$ mm) with pituitary stalk enlargement. She had surgery in March 2016, with no post-operative complications. Histology confirmed an ACTH positive adenoma. Her initial symptoms resolved, except for central hypothyroidism. She required hydrocortisone treatment for 5 months, with no adrenal insufficiency afterwards. About two years after surgery, the patient started complaining of increased thirst and water intake (3 to 4.5 l of water/day) and 24-hour urinary output. She also noted weight gain again. Further evaluation confirmed hypercortisolism relapse and revealed a new onset partial DI. MRI showed an increased thickeness of the pituitary stalk ($7\times7\times10$ mm), more significant than before, associated with a residual lesion at this location. Other infiltrative disorders of the pituitary stalk were excluded. The patient was started on desmopressin and a new surgical procedure is under consideration.
Conclusion
This case illustrates a rare form of CD relapse, with associated DI, possibly related with the location of the residual lesion at the pituitary stalk. It should alert the clinicians to be aware for DI symptoms during follow-up, even a long time after surgery.

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Workshop B: Disorders of the hypothalamus and pituitary (II)

Management of Acromegaly

WB1

Gigantism presenting with visual failure

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A 22 year old man was referred to the endocrine unit at St Barts following an abnormal visual field test with his optician and subsequently with ophthalmology at Moorfields eye hospital. At presentation he was noted to be very tall (194 cm), with facial features of growth hormone excess. Despite starting puberty at the age of 12–13 he had experienced continued vertical growth - he was the tallest in his family and his parents had commented that he was continuing to grow, even at the age of 22. He was also still outgrowing his clothes lengthwise year on year. Over the last 3–4 years he had experienced severe intermittent headaches, growth in his shoe size by 2 sizes and a growth in his hand size - he had been able to play the guitar 4 years ago and when he tried to start playing again recently he was unable to get his fingers between the guitar strings. He also reported a reduction in his libido. Significantly he had been for an optician's eye test 3 years ago due to headaches and visual field testing had been abandoned as he had found it difficult to see the object without shifting his gaze. Examination was remarkable for tall stature, the presence of mutiple skin tags, large doughy hands, a prominent brow and an enlarged nose. Testicular volume was 12 ml bilaterally but the testes were soft. IGF1 was raised at 1093 mcg/l (normal 113–320), testosterone was low at 5.1 nmol/l (normal 8.6–29) with normal range LH and FSH. 9AM cortisol was 330 nmol/l ACTH 36 ng/l. OGTT was indicative of growth hormone excess. Formal Goldman perimetry demonstrated a bitemporal hemianopia. MRI pituitary showed a large pituitary macroadenoma with distortion of anterior visual pathways, but there was no extension into the cavernous sinuses. He has now started Lanreotide and an urgent referral for Transspheonidal surgery has been made to our local neurosurgical centre.

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WB2

A case of successful conception in a patient with acromegaly, post TSS after pre-treatment with a somatostatin analogue

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A 35 year old lady presented to endocrine services with a background of attempted conception and oligomenorrhoea. Presenting features were typical of acromegaly including sweating, acne and median nerve entrapment. Growth hormone day curve showed unrelenting high levels of growth hormone. Serum IGF-1 was elevated at 154 nmol/l (normal 14.2–36.9). Other pituitary blood tests were within normal limits. A pituitary macroadenoma measuring 1.5×1.5×1.3 cm was found on MRI. There were no neuro-ophthalmic signs to suggest compression of the optic chiasm and the blood pressure was normal. The patient strongly desired future fertility and so a decision was taken to try and shrink down the pituitary tumour using somatostatin analogue therapy. It was hoped that this would better delineate the tumour from normal pituitary tissue, so that surgical resection might be less traumatic and would hopefully avoid damaging gonadotroph function. She underwent uncomplicated Transsphenoidal surgery in 2012. The operation note mentions that a tumour was visualised on the left hand side of the pituitary gland as seen on the pre-op MRI. Histology showed a pituitary adenoma with cells staining strongly for growth hormone. Ki 67 = 1%. Appearances were consistent with a densely granulated somatotroph adenoma. Soft tissue changes associated with acromegaly disappeared after the surgery and the patient was left with normal pituitary function –the growth hormone level fell by 90% (compared to pre-op values). Normal menses returned and the patient subsequently had two successful pregnancies. Post-op MRI had shown a 6 mm area of tissue with reduced enhancement in the surgical bed which was thought to represent post-surgical change. Her serum IGF-1 remained mildly elevated (355 ng/ml, normal 109–284) and latterly she was put onto cabergoline (which proved ineffective) and more recently back onto a small dose of somatostatin analogue to control residual, very mild, symptoms.

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WB3

Big hands result in a good catch

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A 36 year old gentleman with a BMI of 22 was seen in diabetes clinic. He had a 1 year history of type 2 diabetes (and no family history of diabetes). He was on insulin but had later been started on metformin and had been able to reduce his insulin dose. He was advised to continue reducing his insulin dose and the consultant decided that due to the patient's morphology he would request an IGF-1 level. At his next follow up the patent had vastly reduced his insulin doses and his glycaemic control was very good. His IGF-1 result had come back significantly elevated at 175 nmol/l (reference range 8.3–29.2). On further questioning the patient had not noticed any particular change in his facial features or in the size of his hands or feet over the years. He had no problems with dentition but did tend to get quite sweaty. He had no history of hypertension. He felt generally very well and had no headache. On examination he had morphological features of acromegaly. His hands were large, especially for his height. He had slight bossing of the forehead and moderate macrognathia. Visual fields were normal as was cranial nerve examination. His blood pressure was normal. The patient had the significance of the elevated IGF-1 level explained to him. He was booked in for a growth hormone suppresion test and an MRI of his pituitary was requested. He was referred to the joint pituitary clinic. In due course he had the growth hormone suppression test and his growth hormone production failed to suppress having had a glucose drink (GH 14.27 ng/ml at 0 minutes, 10.69 ng/ml at 60 minutes and 12.96 ng/ml at 120 minutes). The rest of his biochemical pituitary profile was normal. The MRI showed a 8 mm by 9 mm by 10 mm poorly enhancing lesion on his pituitary gland. There was no chiasmal involvement. The findings and options were discussed in the joint pituitary clinic and the patient agreed to have a trans-sphenoidal adenectomy. The surgery was performed 6 months later and the adenoma was resected endoscopically (endonasally). Aside from elevated blood glucose levels in the aftermath of the surgery, his recovery was unremarkable. Histology reported a pituitary adenoma with production of growth hormone and prolactin. Recent IGF-1 at 3 months was 63.8 nmmol/l and the patient is due to be seen in clinic very soon.

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Workshop C: Disorders of the thyroid gland (I)

Goitre and Thyroid Nodules

WC1

Management of solitary toxic thyroid nodule

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Background
Toxic thyroid nodules are difficult to manage medically. Surgical versus radioiodine therapy can be chosen in light of risk and benefit for individual cases.
Clinical case
72 years old woman presented with 3 months history of hands tremor. There was no associated palpitations, weight loss, sweating, diarrhoea or mood change. She reported mild tiredness. She had never noticed any lump or pain in her neck. There was history of cold intolerance which had been a long standing problem and did not change recently. Her thyroid function was tested and showed fT_4 of 25.4 (12–22 pmol/l) with suppressed TSH <0.01 (0.27–4.2 mU/l). She was started on carbimazole 5 mg daily by her GP and was referred to the Endocrine clinic. On treatment her tremors improved but did not settle completely. Clinically she was euthyroid. Her heart rate was 80/minute and regular. There was no tremor or sweaty palms. There was no evidence of thyroid eye disease. Thyroid gland was not enlarged. The rest of systemic examination was unremarkable. Her repeated thyroid function on carbimazole showed TSH of 0.02 (0.27–4.2 mU/l) and FT_4 12 (12–22 pmol/l). Her TSH receptor antibodies and thyroid peroxidase antibodies were negative. Thyroid uptake scan was performed to evaluate the cause of hyperthyroidism which showed localised increased uptake consistent with a solitary toxic nodule. Definitive treatment of her toxic nodule in form of surgery or radioiodine treatment was discussed with patient and she opted for surgery.
Conclusion
For solitary thyrotoxic nodules, surgical approach can be considered a better management option as it would preserve thyroid function but decision is dependant on patient's preference.

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WC2

Toxic nodule: wait or treat?

Saba Hafeez, Rakshit Kumar, Anand Velusamy, Jake Powrie & Paul Carroll

68 years old female initially referred to endocrine clinic in November 2016 for assessment of fluctuating thyroid function. She had a history of long standing primary hypothyroidism, stable on treatment with 100 mcg Levothyroxine. In last one year, Levothyroxine was tapered and stopped due to persistent suppression of TSH and high normal Free T4. Last tests showed TSH of <0.01mIU/l and Free T4 of 27.1 pmol/l. She had ongoing complaints of feeling increasingly tired and generally unwell. She was clinically euthyroid with no evidence of thyroid eye disease. There was asymmetrical thyromegaly on right side with no compressive symptoms. Her thyroid function tests (TFTs) were normal with negative thyroid antibodies. Her TSH was 0.31 (0.27–4.20 mIU/l), T4 11.1 (10–23 pmol/l) and T3 5.9 (3.1–6.8 pmol/l). However, thyroid ultrasound showed a 2.7×3.5 cm right lobe nodule, characterised as U2. Repeat blood test revealed suppressed TSH (0.06 mIU/l), normal T3 (5.8 pmol/I) and T4 (12 pmol/l). Pituitary profile was normal for age. Suppressed TSH with increased T3/T4 ratio raised suspicion of a toxic nodule. She had a thyroid technetium uptake scan which confirmed dominant nodule in the right lobe of the thyroid. She was planned for Radio Active Iodine treatment but her thyroid function normalised and a decision was made to keep her under active surveillance. Over last 6 months, she had normal TFTs twice with improvement in symptoms. This is good learning case showing fluctuating toxic features in a thyroid nodule.

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WC3

Indeterminate thyroid nodule in a patient with Graves' disease

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Grave's disease is an autoimmune mediated thyrotoxicosis which accounts for 50–80% of cases of hyperthyroidism. In addition to non-thyroid organ involvement, presence of thyroid stimulating hormone receptor antibodies (TRAb) or increased uptake on a nuclear scan are diagnostic. Ultrasound typically shows a diffuse enlargement of the thyroid with increased vascularity, but up to 23% of patients are known to have thyroid nodules. Thyroid nodules carry a 4–6% risk of malignancy and therefore it is recommendations that patients undergo fine needle aspiration (FNA). Cytology helps differentiate between benign and malignant nodules but may be limited by the quality of the sample. A hemi-thyroidectomy is indicated where FNA fails to resolve uncertainty. Recent studies have indicated a higher risk of thyroid malignancy in individuals with Grave's disease irrespective of the presence of nodules. We present the case of a 53-year-old female who was referred to clinic with a persistently elevated free triiodithyronine (fT3) 8.3 pmol/l and suppressed thyroid stimulating hormone (TSH) <0.01 mIU/l. This was an incidental finding following a coronary angiogram 5 months earlier. The patient was initiated on carbimazole 5 mg once daily and referred for a Tc99 thyroid uptake scan. She declined the scan, did not attend further appointments and was subsequently discharged from clinic. The carbimazole was stopped 2 years later and the patient remained clinically and biochemically euthyroid off anti-thyroid medication. The patient relapsed the following year with evidence of thyrotoxicosis - TSH <0.01 mIU/l, free thyroxine (fT4) 30.2 pmol/l and fT3 12.1 pmol/l. An ultrasound scan showed a large 5 cm solitary nodule on the right lobe with internal vascularity reported as U3. A nuclear scan showed low uptake in the nodule. FNAC was reported as Thy3a. She was restarted on carbimazole and the local thyroid MDT recommended total thyroidectomy as a definitive treatment for relapsed Grave's and further assessment of the nodule. Serial repeat TFTs were markedly improved and the carbimazole was gradually reduced and eventually discontinued to reflect this. She has remained biochemically euthyroid. This is an interesting case of a patient with Graves' disease and an indeterminate thyroid nodule. The risk of thyroid cancer in Graves' is twice as that of general population and the risk increases to approximately five fold in Grave's disease patients with thyroid nodules. In patients with a Thy3a nodule, 20–52% will be malignant. The British Thyroid Association (BTA) has subdivided the Thy3 group into Thy3a and Thy3f. They recommend hemi-thyroidectomy for Thy3f and repeat FNA in 3–6 months with MDT discussion for Thy3a.

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WC4

A common case of goitre, thyroid nodules and thyroid carcinoma

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A 31 year-old woman is referred into the Endocrine clinic with a palpable mass in her right anterior neck that was found incidentally by her GP. She had no known past medical history, did not take any medications and had not noticed any dysphagia, neck pain, or compressive symptoms. On clinical exam, there was an enlarged thyroid with a 1.5-cm left-sided thyroid nodule that moved on swallowing. There was no palpable cervical lymphadenopathy. TSH was 2.5 mIU/l (0.29–5.1 mIU/l). Thyroid ultrasound showed a mildly enlarged multi-nodular goiter with a complex nodule in the left midpole with solid and cystic components and several subcentimeter nodules throughout both thyroid lobes. None of the nodules had suspicious ultrasonographic characteristics. Fine Needle Aspiration (FNA) of the left thyroid nodule showed cytology consistent with a "nodular goiter." The patient was then lost-to-follow-up for 5 years. She re-presented upon noticing an increase in the size of her neck and an occasional "pressure" sensation when lying supine. On clinical exam, she had an enlarged thyroid with a 2.0-cm nodule in the left lobe and an another more indistinct nodule of 1.5 cm in the right lobe, that both moved on swallowing. There was also a nontender, enlarged right cervical lymph node. An Ultrasound showed a multinodular goiter that had increased in size. The nodule in the left lobe was reported as unchanged in size and appearance. A number of other nodules were noted: a 2.1-cm solid hyperechoic nodule to the right of the isthmus. Color Doppler Ultrasound revealed no internal blood flow in this nodule and it was completely surrounded by a sonolucent ring. There was a 1.3-cm solid hypoechoic nodule in the right superior pole that had microcalcifications and chaotic internal blood flow. There was also an enlarged 1.4-cm cervical lymph node measuring in the right anterior cervical chain.FNA biopsy of the 1.3-cm right superior pole nodule was carried out and the cytology reported as "cannot

rule out follicular neoplasm". The patient had a total thyroidectomy and right lateral neck dissection. Pathology showed follicular variant of papillary thyroid carcinoma in the 2.1-cm nodule on the right of the isthmus with lymphatic invasion. The 2.0-cm nodule in the left midpole and 1.3-cm nodule in the right superior pole were follicular adenomas. One lymph node was positive for follicular variant of papillary thyroid cancer. The patient was treated with Radioactive Iodine. Subsequent Whole body Radionuclide scanning was negative for metastatic disease.

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Workshop D: Disorders of the thyroid gland (II)

Thyroid Cancer

WD1

Abstract withdrawn.

WD2

An unusual route to the diagnosis of medullary thyroid cancer

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We describe a 68 year lady who was found to have bilateral adrenal masses (7 cm on the right side and 1.3 cm on the left) during investigations for gastrointestinal symptoms, in early 2016. Biochemistry revealed high urinary normetanephrines of 41.7pmol/24h (ref 0–3) and metanephrines of 40pmol/24h (ref 0–1.8). A PET and MIBG scan revealed uptake in both adrenals and therefore a diagnosis of bilateral phaeochromocytoma was made. The patient had complained of occasional palpitations and headaches, but no paroxysmal sweating or flushing. She had long-standing borderline hypertension not requiring treatment, and diet-controlled type 2 diabetes. In 1988 she had had a sub-total thyroidectomy for a large goitre at another hospital. The patient had a family history of thyroid disease. Her paternal aunt had a goitre removed and one of her sisters has autoimmune hypothyroidism. Her identical twin also has type 2 diabetes. Her mother had a stroke and osteoarthritis and her father died of a myocardial infarction. She has two daughters aged 38 and 41 years old. The patient underwent bilateral adrenalectomy in August 2016. Subsequent histology confirmed a right sided phaeochromocytoma, with a PASS 9, and a left sided phaeochromocytoma, with a PASS 4. Genetic screening revealed a previously reported ATA level C pathogenic *RET* variant (p Cys634Tyr)confirming a diagnosis of MEN 2A. This varian is associated with more aggressive form of medullary thyroid carcinoma. In light of these findings an ultrasound scan of her thyroid was performed in September 2016. This revealed two nodules measuring 13mm and 4mm in the right lobe, and a 10mm nodule in the right-sided isthmus. These nodules had entirely benign ultrasound appearances. Calcitonin and carcinoembryonic antigen (CEA) levels were normal. We were able to obtain the histology slides taken from the patients' previous sub-total thyroidectomy. These had initially been reported, in 1988, as benign multi-nodular changes, but in retrospect a clear focus of medullary thyroid carcinoma was found. The question therefore was raised about whether the patient should now proceed to completion thyroidectomy, despite there being no definitive evidence of malignancy on ultrasound and 30 years having passed since her original thyroid surgery.

What intervention, if any, would you recommend in this situation?
What investigations, if any, would you look to perform prior to making your recommendation?
If you decided against completion thyroidectomy, what monitoring would you put in place?
How would you council the patient and her family?

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WD3

A case of medullary thyroid cancer

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Case
A 61 year old female, presented to ENT in July '17 with 6 month history of left sided neck swelling, gradually increasing in size over the last 1 month prior to presentation. She complained of tenderness over the swelling and pain and discomfort around her left shoulder. She denied any problems with her voice, breathing or swallowing. Her past medical history consisted of recurrent UTI's, renal stones and medullary sponge kidney. She smokes 15 cigarettes per day and no family history of thyroid cancer. Examination-Left sided level V lymph nodes were hard and tender. An ultrasound guided fine needle aspiration was suggestive of medullary thyroid cancer (MTC). Despite a recent chest radiograph showing clear lung fields a CT neck and chest showed multiple lung nodules and adrenal deposits suggestive of metastatic disease. She was referred to Endocrinology in August '17 for further investigations; Two urinary metadrenalines, U&Es, TFTs and calcium were all within normal range. CEA – 417 (0–3 mg/l) and calcitonin - 9,000 (0–15 ng/l) were both grossly elevated. Her case was discussed at the regional thyroid cancer MDT and she underwent bilateral neck dissection and total thyroidectomy in October '17. Histology confirmed metastatic medullary thyroid cancer and an incidental 1.2 mm papillary microcarcinoma. She has made an excellent post operative recovery and her calcitonin 2 months post operatively has improved to 4,970 (0–15 ng/l). She is on Levothyroxine, alfacalcidol and calcichew post operatively. In view of her normal PTH we would aim to wean her off calcichew and alfacalcidol. Her MEN2 genetic testing was negative. She is awaiting a follow-up CT neck and thorax.
Discussion points
i) What is the most common presentation of MTC?
ii) What is the most important pre-operative investigation in patients with MTC?
iii) What percentage of MTC is thought to be genetic?
iv) What is the role of TSH suppression or high dose radioactive iodine in MTC?

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WD4

A thyroid lump presenting in pregnancy

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Peter, Tassone, UK; Joanne, Randall, UK.

A 34 weeks pregnant woman was reviewed in the joint antenatal clinic with over a month history of neck swelling. Her thyroid function tests showed TSH of 1.39 mU/l and a free T_4 of 11 pmol/l. An initial ultrasound of the neck revealed a solitary heterogeneous nodule in the right lobe of the thyroid consistent with U3 morphology (indeterminate). She was reviewed by ENT consultant and had a fine needle aspiration (FNAC). Cytology was consistent with features of papillary thyroid cancer (THY5). It has been discussed during Thyroid MDT with the recommendation to allow for completion of pregnancy first before offering any definitive thyroid treatment and to reconsider treatment 3 months postpartum. It was felt that she was a borderline candidate for hemithyroidectomy versus thyroidectomy as the tumour was less than 4 cm. She had a delivery in December 2016. When assessed 4 weeks postpartum in the beginning of January 2017 she described globus type symptoms and felt the swelling of the neck has increased. On examination there was a 4:3 cm right thyroid nodule with no palpable lymph nodes. A repeated ultrasound of the neck showed an increase in size since the previous study. She underwent a total thyroidectomy in March 2017. A postoperative calcium and PTH were 2.32 mmol/l and 0.9 pmol/L respectively. Thyroid histology described a 40 mm encapsulated follicular variant papillary thyroid cancer with extensive vascular invasion pT2, R0. On follow up she has made an excellent recovery. The neck wound has healed well and her vocal cords were mobile on nasendoscopy. In April her thyroglobulin was less than 0.2 ng/ml, anti-thyroglobulin 28 IU/ml, TSH above 100 mU/l. There was no evidence of distant metastases on radioiodine scan. Her case was discussed at Thyroid MDT again and it was felt that she could either opt for therapeutic radioiodine or wait and see approach with ongoing oncology follow up.

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WD5

Hashimoto's Thyroiditis and Thyroid cancer

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A 40 year old lady presented to GP with few months history of palpitation, anxiety, frequent stools in April'15. Clinical examination revealed moderate sized goitre, more prominent on right side, mobile, non-tender and no lymphadenopathy. Blood tests consistent with T_3 toxicosis with FT_3 10 (3.5–6.5), FT_4 21 (9–25), TSH <0.05 (0.3–5.0) and thyroid peroxidase antibody positive at 562 IU/ml (0–60). Initiated on Carbimazole 20 mg once daily. US Thyroid (May'15) showed features consistent with multinodular goitre. Right largest nodule solid cystic 3.8×2.2 cm. Left sided largest nodule 1.5×1.9 cm. FNA not performed due to hyperthyroidism. NM Thyroid Scan with uptake Technetium (July'15) – cold nodule corresponding with the right largest nodule. Repeat US thyroid (September'15) in view of above findings showed U2 nodule and FNA was benign (thy2). Carbimazole stopped in view of FT_4 8.3, TSH 8.6.

She presented with worsening left neck pain in 2016. Repeat US thyroid reported no significant interval change in the right lobe nodule. There were two iso to hyperechoic nodules in the left lobe and ENT assessment was suggested. Reviewed in the ENT clinic August'16 and patient reported dysphagia for few months. US thyroid – no interval change. BTA U2 (benign) nodule. No FNA performed. ENT review again in May'17 with left otalgia and neck pain. MRI neck showed only multinodular goitre. Repeat US thyroid revealed right solid cystic nodule slightly increased in size, course calcification and FNA was thy4 (suspicious for malignancy). Underwent right hemi thyroidectomy (pT2 follicular variant PTC). The background thyroid tissue shows features consistent with Hashimoto's thyroiditis (diffuse lymphocytic inflammation with occasional secondary lymphoid follicles). As per MDT decision went for completion left hemi thyroidectomy (pT2(m)NXMX) and rreferred for radioiodine treatment.
Discussion points

- Is there any association between Hashimoto's thyroiditis and thyroid cancer?
- Should clinicians consider the higher risk of TC in patients with HT?

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WD6

Advanced medullary thyroid cancer with metastatic disease at diagnostic in young patient negative for RET mutation- to treat or not to treat with tyrosine-kinase inhibitors

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We report a 21-year-old man who referred to endocrinologist following biopsy of a left-sided cervical mass. The pathological examination was diagnostic for medullary thyroid carcinoma (MTC). Physical examination was remarkable for a firm 3-cm nodule in right thyroid lobe and another 3 cm. firm nontender mass in left thyroid lobe. The calcitonin was 15,324 pg/ml, and carcinoembryonic antigen was 415 ng/ml. The calcium level was 10.3 mg/dl ($<$10 mg/dl) with unsuppressed parathormone of 37.1 pg/ml (15–65) and negative screening for pheochromocytoma. The ultrasound of the cervical region shows both thyroid lobes occupied by hypoechoic irregular masses with macrocalcifications and blood flow and metastatic bilateral adenopathies. The tomography of the chest revealed multiple bilateral nodular lesions (maximum 10 mm.) suggestive of pulmonary metastasis. The tomography of abdomen described hepatic lesions ($>$20) of sizes up to 22/17 mm. The patient was negative for germline RET mutations. The total thyroidectomy with central and cervical compartment dissection was carried out by a thyroid surgeon, as well as the exclusion of three out of four parathyroid glands. The patient received thyroid substitution therapy and active vitamin D supplement. A nadir for calcitonin of 16,646 pg/ml was registered three months following surgery. The follow up with repetitive tumor markers, and evaluation of tumors showed a slow progressive increase of calcitonin of 21.55% in 0.83 years (52% increase in 24 months) with the stable size of the pulmonary and hepatic metastasis and no tumor tissue in the cervical region.
Discussion
The study by Wells establishes the efficacy of Vandetanib in patients with locally advanced or metastatic MTC. This study included 15% patients that the progression of the disease was not documented before entry. The response rate to Vandetanib with sporadic MTC seems to correlate with RET mutations with better responsive rate (54.5%) when the mutation is present compared with the 32% in the patients who were negative for mutations (or have unknown mutation status). The relatively indolent tempo of disease in some patients with MTC makes the risk: benefit ratio of treatment unfavorable in patients with a low disease burden who experience slow progression and surviving rates of 100% at ten years when the doubling time of calcitonin is more than 24 months. In contrast, patients who are symptomatic, have a high disease burden or have rapidly progressing disease stand to benefit the most from treatment with Vandetanib.

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WD7

A challenging case of progressive follicular thyroid cancer

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A 60 year old gentleman with a history of renal stones presented 5 years ago with left sided flank pain. A CT of his renal tract showed an unexpected metastatic deposit in the left iliac crest. Cross-sectional whole body imaging, performed to locate the primary, also identified an expansile soft tissue mass in the T8 vertebral body and a predominantly cystic looking left sided thyroid nodule. He proceeded to have an iliac crest biopsy which was consistent with metastatic follicular thyroid cancer. A dedicated thyroid ultrasound scan showed a malignant looking thyroid nodule with no suspicious lymphadenopathy. He was referred for an urgent thyroidectomy. Post-operative histology was reported as widely invasive follicular thyroid cancer with evidence of vascular invasion and tumour necrosis. He was commenced on suppressive doses of Levothyroxine and was referred to our centre for radioiodine. A repeat look at his pre-operative spinal imaging was worrying for impending spinal cord compression from the T8 metastatic deposit. He, therefore, received urgent radiotherapy to this lesion and to the left ilium. After completing the radiotherapy he received radioiodine ablation. Post-ablation I-131 scan showed iodine avidity in the thyroid bed, T8 and the left ilium. Over the next two years he received four therapy doses of radioiodine with good concentration in the metastatic deposits. His stimulated thyroglobulin fell from 6,840 μg/l to 3,544 μg/l. However, in May 2016, four months after his last radioiodine therapy dose, he reported worsening bone pain. His unstimulated thyroglobulin rose to $>$5,000 μg/l and a repeat MRI scan showed new acetabular deposits and a left pubic ramus pathological fracture necessitating more radiotherapy to this site. A repeat look at his post-therapy scans confirmed these sites as being non-iodine avid. In view of this, a PET scan was arranged to look for other non-iodine avid sites. Unfortunately, this identified multiple spinal and lung metastases. He was given bisphosphonate therapy and his case was brought back to the thyroid multi-disciplinary team meeting where funding for Sorafenib was discussed. However, the patient had done some of his own research and was keen to enrol in a clinical trial that specifically looked at treatment options which may restore iodine avidity to his advancing disease first. Differentiated thyroid cancers are usually responsive to radioiodine therapy. Refractory follicular thyroid cancers are rare and treatment options are limited. This case highlights the role of the multi-disciplinary team in managing these complex patients.

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Workshop E: Disorders of the adrenal gland

Mineralocorticoid Hypertension & Phaeochromocytoma

WE1

Lumps and bumps, fears and phaeos: Infrequent symptoms and conflicting test results in a man with three lesions in three organs

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A 42 year old gentleman was referred to endocrinology clinic by a consultant urologist due to an incidental finding of a 14 mm adrenal nodule on the patient's right adrenal gland. He was originally seen by gastroenterology having been referred due his 7 year history of twice yearly attacks lasting around 30 min, comprising of flushing of the face, palpitations, burning sensation in his stomach, sweating, vomiting and loose bowel motions. The gastroenterology consultant did not feel this was a gastro problem and arranged CT chest/abdo/pelvis for exclusion of carcinoid and phaeochromocytoma. The CT scan showed a 13 mm left lower lobe lesion (likely bronchocele – suggested respiratory follow up), a left lower pole renal lesion (possible early neoplasm – for ultrasound and MDT follow up) and a right adrenal soft tissue nodule measuring 14 mm (referred to endocrinology). The urology consultant saw the patient who had now had an MRI and the renal lesion had been identified as a Bosniak 3 cyst (50% chance of malignancy). The plan was to monitor the cyst and likely excise it but only once the adrenal lesion had been dealt with. The MRI had shown this to not have characteristics typical of an adenoma with phaeochromocytoma being possible. A 24 hour urine collection for metanephrines had been sent with results awaited at this stage. The urologist organised an MIBG scan to further image the adrenal lesion. The patient was then seen in clinic in the endocrinology department. He and his wife were understandably anxious about all that was going on. The urine collection had demonstrated normetanephrine output of 2.15 (reference range 0–3.00), metanephrine output of 1.52 (reference range 0–1.40) and 3-methoxytyramine output of 2.52 (reference range 0.57–2.30). Chromogranin A and B results were also available and were within the reference ranges. A set of plasma metanephrines had been taken and these too were well within the reference ranges. The various results were explained to the patient and he was referred to the endocrinology MDT meeting. A repeat set of 24 hour urinary metanephrines was requested. The MIBG result was available not long after the clinic appointment and this showed an MIBG avid right adrenal nodule consistent with phaeochromocytoma. The endocrinology MDT meeting concluded this was an early phaeochromocytoma. The patient was referred for excision and alpha and beta blocking arranged. The lesion was excised uneventfully and histology confirmed the phaeochromocytoma diagnosis.

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WE2

Challenges in managing primary hyperaldosteronism

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Background
A 59 year old man was referred to Endocrinology from Neurology with a 2 year history of hypertension, and a 1 year history of mild hypernatraemia (146–148 mmol/l) and hypokalaemia (3.2–3.4 mmol/l). He had a past history of a cerebral aneurysm and superficial siderosis. His main complaints were severe fatigue, poor balance and tinnitus. His medications at diagnosis were Amlodipine 5 mg and Sertraline 50 mg.
Investigations
Blood pressure at his first attendance to the Endocrine Unit was 150/87. Aldosterone level was raised at 834 pmol/l with a suppressed renin <5 mIU/l. A saline infusion test failed to adequately suppress aldosterone levels (932–628 pmol/l). A 24 hour urine free cortisol was normal at 112 nmol/24 hours. A CT of the adrenal glands showed a 25×18 mm fatty nodule (Hounsfield units -5) within the left adrenal gland. The patient was referred for and underwent adrenal vein sampling however this was unsuccessful as the levels from both samples were the same as in peripheral serum, therefore it is likely that the adrenal veins were unsuccessfully cannulated.
Progress
Antihypertensive medication was changed to Spironolactone 50 mg and titrated up to 100 mg. His blood pressure at the last clinic visit was 147/68 and potassium level was 4.0. Nine months after commencing spironolactone he had developed gynaecomastia, 3–4 cm bilaterally. If this persisted or progressed, other medical options such as Epleronone or Amiloride were to be considered.
Discussion points
This case illustrates the workup of a patient with primary hyperaldosteronism and the challenges of decision making when adrenal vein sampling is inconclusive. Newer imaging modalities show potential but are not widely available. Should surgery be considered in the absence of confirmatory AVS in view of the adrenal nodule and side effects with Spironolactone? What is the audience's experience with second line medical agents?

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WE3

***Pheochromocytoma*: A reversible cause for hypertension**

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The case
The case described is a 49 year old lady referred to emergency department with history of episodic palpitations, headache and sweating with possible weight loss for last 14 years but symptoms now worse in the past few days. Past medical history was significant for modest hypertension with retinal changes treated with Lisinopril. Patient stopped going to the gym recently as it seemed to exacerbate the symptoms. Patient recently registered with a new GP who in view of the above symptoms correctly organised 24-hour urine catecholamines and referred the patient to A&E. Systemic examination was unremarkable at time of admission with BP of 140/90, pulse rate of 72/min and RR of 14/min. However, patient seemed anxious. There was AV nipping and silver wiring on fundoscopy but no papilloedema or retinal haemorrhages. Rest of the systemic examination was unremarkable.
Results and management
The initial blood results were normal including sodium 139 mmol/l and potassium 4.3 mmol/l. Patient was referred to ambulatory care from A&E as clinically well. In view of strong suspicion of pheochromocytoma, patient was commenced on Phenoxybenzamine 10 mg twice daily and referred to urgent endocrine clinic. 24-hour urine catecholamine results showed grossly elevated urine noradrenaline 5427 nmol/24 h with normal urine adrenaline 78 nmol/24 h and urine dopamine 1468 nmol/24 h with a 24-hour urine volume of 3.7 l. The TFTs were unremarkable and ODST suppressed the cortisol to <30 nmol/l. Patient was booked for an urgent MRI adrenals which showed 35×32 mm mass arising from the right adrenal gland. The left adrenal gland appeared normal. Urgent referral was made to King's College London and patient underwent a successful right laparoscopic adrenalectomy next month. Postoperatively blood pressure was 120/70 at next follow up and patient was not on any anti-hypertensive. She had a short Synacthen test post-operatively which showed adequate response of cortisol at 30 and 60 min and normal 24-hour urine catecholamine profile on few occasions since the surgery.
Discussion
The case describes a textbook presentation of pheochromocytoma. However, in our patient the symptoms although florid were present for many years before the diagnosis was made. Luckily for the patient it did not cause any significant morbidity or mortality. Also the case highlights the fact that pheochromocytoma is a rare but reversible cause of hypertension and patients can completely come off the antihypertensive medications after successful therapy as in the case of our patient.

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WE4

Challenging diagnosis of phaeochromocytoma

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A 64 year old female with a background history of hypertension resistant to dual therapy had recurrent admissions to the local emergency department with pulmonary oedema and chest tightness over the preceding 3 months associated with fluctuations in Troponin I levels. This led to multiple cardiac investigations including invasive coronary angiogram which did not report any abnormality. Her blood pressure was elevated at 200/120 mmHg and an electrocardiogram demonstrated sinus tachycardia on return of her chest pain. Investigation with a CT chest, abdomen and pelvis for ongoing back pain revealed a possibility of an incidental 3.5 cm right adrenal adenoma. Significantly elevated 24 hour urinary catecholamines confirmed the diagnosis of phaeochromocytoma (24 hour urinary metadrenaline of 13.19 umol/24 hour (normal reference range <1.20), 24 hour urinary normetadrenaline 10.89 umol/24 hour (normal reference range <3.30), total metadrenalines 24.08 umol/24 hour (normal reference range <4.50)). The MIBG scan correlated with the findings; demonstrating extensive uptake within the mass. Following referral to the tertiary centre she underwent an open right

adrenalectomy with normal post-operative levels of catecholamines and remains asymptomatic with a blood pressure of 133/80 mmHg on annual reviews and has discontinued all of her anti-hypertensive medications. There are important considerations when evaluating resistant and unusual cases of hypertension. Electrocardiogram changes with phaeochromocytoma are common and up to 12% of patients will present with coronary syndromes. Elevated cardiac enzymes can be a prognostic indicator for those at risk of developing myocardial damage. It is therefore an important consideration when managing patients with chest pain including those with ischaemic ECGs. The general prevalence of phaeochromocytoma in people diagnosed with hypertension is around 0.5% and this increases to 1.7% in the paediatric population. Less than 5% of incidental adrenal lesions prove to be phaeochromocytoma. Of the cases identified approximately 30% will have a genetic predisposition which may alter treatment and surveillance. This patient did not have any features suggestive of syndromic association including multiple endocrine neoplasia, Von Hippel Lindau syndrome or neurofibromatosis however the case raises the importance of considering when and who to screen for genetic testing with a confirmed phaeochromocytoma.

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WE5

Case report of malignant hypertension secondary to Renal Artery Stenosis due to Fibromuscular Dysplasia in a young female patient

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Secondary causes for Hypertension account for 5% of hypertension cases. Renal Artery Stenosis due to Fibromuscular Dysplasia is an uncommon cause of Secondary Hypertension. This is a case of a 35-year old lady who presented with headache and vomiting and was found to have malignant hypertension with resultant acute left caudate nucleus infarct in the brain. A mild hypokalaemia on admission prompted measurement of renin and aldosterone which were both elevated. She also had elevated plasma normetadrenaline. This prompted an Endocrinology referral. It was noted that she was on SSRI and this could account for the slightly elevated normetadrenaline. An Ultrasound scan of the kidneys was reviewed and there was 3 cm difference in the size of the kidneys with the left kidney being smaller. Magnetic Resonance – angiogram of renal arteries confirmed features in keeping with left renal artery stenosis secondary to Fibromuscular Dysplasia. The patient was successfully treated with renal artery angioplasty.

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WE6

From hyper- to hypoaldosteronism: a rare but important complication to recognise post adrenalectomy

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A 69-year-old retired pharmacist was referred to our endocrine clinic with an incidental finding of hypokalaemia noted during recent spinal fusion surgery. He has been hypertensive for 6 years. His blood pressure was well controlled on Diltiazem 240 mg and Doxazosin 4 mg, but required 8 tablets of SandoK daily to maintain normokalaemia. His past medical history includes type 2 diabetes, diabetic retinopathy, chronic kidney disease, hypercholesterolaemia and benign prostatic hypertrophy. A diagnosis of Primary Hyperaldosteornism was made on the basis of a high aldosterone: 2684 pmol/l and suppressed renin <0.2 nmol/l/h. CT adrenals revealed a 30×28 mm left adrenal adenoma. He underwent adrenal vein sampling. Cortisol levels in the IVC, right and left adrenal veins were 1439 nmol/l, 1486 nmol/l and 16 840 nmol/l respectively, suggesting unsuccessful cannulation of the right adrenal vein. He therefore underwent a metomidate PET CT scan which suggested not one, but two, aldosterone-producing adenomas (APA) in his left adrenal gland. He successfully underwent a laparoscopic left adrenalectomy. Blood pressure and potassium levels normalised post-operatively. He was however discharged home on hydrocortisone replacement (10/5/5 mg), in view of a non-suppressed cortisol (60 nmol/l) after a LDDST performed pre-operatively. On reassessment 9am cortisol was 393 nmol/l, hence hydrocortisone replacement was stopped. At 1-month follow-up, he reported a 1-week history of feeling generally unwell with symptoms suggestive of viral gastroenteritis. Although the diarrhoea had settled he was still extremely lethargic. Blood tests revealed an acute on chronic renal failure, Na128 mmol/l, K7.4 mmol/l. He was urgently admitted for IV fluids, insulin-dextrose and IV hydrocortisone. Originally we presumed this gentleman had adrenal insufficiency due to cortisol co-secretion from his APAs which were suppressing his contralateral adrenal. However cortisol levels were reasonable: 625 nmol/l (01100 h sample). Most likely this gentleman has hyporeninaemic hypoaldosteronism as a result of his longstanding diabetes. Removal of his left APA(s) unmasked his underlying mineralocorticoid deficiency. Clinically and biochemically he responded promptly to fludrocortisone replacement (50 μg BD). Isolated mineralocorticoid deficiency post adrenalectomy is rare, observed in $<5\%$ of studied populations, but usually associated with high renin levels. However awareness of this complication is vital due to its potentially life-threatening consequences. In retrospect, when our patient was started on spironolactone pre-operatively, deterioration in his renal function, associated with a mild hyperkalaemia and hyponatraemia, was noted. This resolved promptly on reducing the dose of spironolactone. Was this a warning sign of the impending problems to come?

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WE7

A hypertensive emergency post massive phaeochromocytoma resection: catecholamines not to blame

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Case history
A 26 year-old lady was admitted from clinic with severe hypertension and bilateral papilloedema. Six weeks prior to admission she had undergone resection of a massive right upper quadrant lesion that was felt to be of hepatic origin. Histological analysis of the lesion revealed it to be an adrenal phaeochromocytoma and she was thus referred to the endocrine service. Pre-operative biochemical assessment had not been performed but there was no evidence of any blood pressure abnormality or variation pre- or peri-operatively. Two weeks post-operatively she began to experience episodes of palpitations, sweating and hypertension and had attended the emergency department of her local hospital on a number of occasions and been commenced on doxazosin.
Results and treatment
Review of the surgical pathology confirmed the diagnosis of a phaeochromocytoma with tumour present at the resection margin. Immunohistochemistry for the SDHB protein was negative, suggestive of a germline SDHx mutation. She was admitted to the High Dependency Unit for invasive blood pressure monitoring and commenced on IV labetalol alongside oral phenoxybenzamine given the previous diagnosis and incomplete resection. Urine and plasma metanephrines were subsequently normal. She was hypokalaemic on admission (K 3.2 mmol/l) and given the large size of the original lesion (18 cm), renovascular mediated hypertension was considered. This was confirmed biochemically and hyperreninaemic hyperaldosteronism demonstrated (renin 18.3 nmol/l/h, aldosterone 1,014 pmol/l). Imaging confirmed infarction of the right kidney due to ligation of the renal artery with a DMSA scan confirming only a 5% contribution from the right kidney. Serum creatinine was normal. Her oral anti-hypertensives were rationalised to doxazosin and losartan. This combination was chosen to provide mechanism direct treatment of the current driver of hypertension, whilst providing alpha blockade given the incomplete phaeochromocytoma resection and risk of local recurrence. The results of genetic analysis for germline mutations in phaeochromocytoma-predisposing genes (and particularly SDHx given the negative SDHB immunohistochemistry) are awaited.
Conclusions and points for discussion
This is an unusual and interesting case of acute secondary hyperaldosteronism due to inadvertent surgical ligation of the renal artery. The fact that the original operation was for an undiagnosed phaeochromocytoma, which was incompletely resected, further complicates matters and led to an initial assumption of catecholamine-mediated hypertension. It provides an excellent opportunity to discuss:

- Non-catecholamine-mediated causes of hypertension following phaeochromocytoma surgery
- The mechanism and management of renin-mediated hypertension and particularly whether, in this instance, nephrectomy might play a role

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WE8

A pressing diagnosis in an adolescent

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Case history
A 17 year old previously healthy male presented to his local emergency department with a generalised tonic seizure associated with severe hypertension (systolic blood pressure 240 mmHg) and tachycardia. He was intubated and admitted to the Intensive Care Unit. Antimicrobials to cover meningoencephalitis were commenced and his hypertension was managed with intravenous labetalol. He was extubated the following day. He had experienced headaches on a monthly basis for two years. They had become more severe and frequent in the weeks prior to presentation and were associated with paroxysms of sweating and palpitations. There was no suggestive family history. A 24 h urine collection was sent for metanephrines, however, given the significant suspicion of a phaeochromocytoma, he was commenced on phenoxybenzamine and abdominal imaging was undertaken prior to diagnostic biochemistry becoming available. He was subsequently transferred to our centre for ongoing investigation and management.
Results and treatment
Initial blood tests demonstrated haemoconcentration with an acute kidney injury and active urinary sediment. CT and MRI demonstrated cerebral oedema within the occipital lobes and brainstem consistent with a diagnosis of posterior reversible encephalopathy syndrome (PRES). Urine normetanephrine was significantly elevated with a normal metanephrine and 3-methoxytyramine. The magnitude of normetanephrine elevation was significantly higher at presentation ($\times$8.8 upper limit of normal) compared to on transfer ($\times$2.4). Abdominal imaging demonstrated a 4.1 cm left phaeochromocytoma that was invading the renal vein. This lesion was MIBG-avid. Two small indeterminate pulmonary nodules were identified on thoracic imaging. Low molecular weight heparin was commenced in light of tumour thrombus in the renal vein. Phenoxybenzamine dose was uptitrated and propranolol subsequently added. After a number of weeks of outpatient blockade he underwent an open adrenalectomy and nephrectomy. His post-operative course was complicated by pneumonia and wound discharge. Anti-hypertensives were successfully discontinued post-operatively. Histology confirmed the diagnosis of a phaeochromocytoma, which was completely excised. Immunohistochemistry for the SDHB protein was negative, highly suggestive of a germline mutation in an SDHx gene and confirmation of this is awaited.
Conclusions and points for discussion
This case of a locally invasive phaeochromocytoma in an adolescent who presented with PRES provides an excellent opportunity to discuss:

- The acute management of a phaeochromocytoma crisis (particularly given the discontinuation of intravenous phenoxybenzamine)
- How pre-operative suspicion of a germline predisposition to phaeochromocytoma development might influence imaging and surgical strategy
- Optimal surveillance strategy for this patient in particular and those with confirmed SDHx mutations generally

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WE9

The case of a young man who originallypresented with severely derranged electrolyes aged four days

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We would like to present the case of a twenty-six year old gentleman whose first presentation to hospital was aged 4 days old. At that time he was thought to be generally unwell with poor feeding and excessively somnolent. During his resuscitation he was found to have extremely deranged serum electrolytes with sodium 122 mmol/l and potassium 14 mmol/l. His electrocardiogram (ECG) was initially noted to be bizarre, with no clear rhythm. After resuscitation with IV fluid, glucose and insulin his potassium improved to 10 mmol/l and the ECG reverted back to sinus rhythm. Further investigations following his stabilisation showed that he had excessively high aldosterone and renin levels with a biochemical picture more in keeping with hypoaldosteronism. On this basis a presumed diagnosis of pseudohypoaldosteronism was made. It took a number of weeks to ascertain the daily sodium requirement given his very high urinary and sweat sodium concentrations. Once stable he was converted to a regime of oral slow sodium and calcium resonium, both at high doses: slow sodium 16 tablets per day and resonium 16 g daily. He has 3 younger siblings the elder two of which are unaffected. His youngest brother was noted by his mother to have excessively salty sweat and has gone on to have the same clinical diagnosis, although less severe in phenotype. There is no evidence to consanguinity. He has maintained a nearly normal life on the basis of intermittent additional dosing of calcium resonium and sodium when his potassium levels rose. Additionally he once needed hospital treatment during excessively hot weather and he became hyponatraemic due to profuse sweating. He has never had recurrent lung infections or skin disorders as a results of high sweat sodium content. In adult life he underwent screening for genetic causes of his condition and was found to have a homozygous mutation in the amiloride sensitive sodium channel subunit alpha. The c.1339dup pathogenic variant is predicted to case a frameshift mutation and premature truncation p.(Tyr447leufs*13). This is a mutation known to cause pseudohypoaldosteronism type 1. The disorder is estimated to affect 1 in 80,000 children and can be inherited in an autosomal dominant or recessive fashion depending on the gene affected. We aim to undertake further genetic testing in members of his family and continue genetic counselling. He continues to need careful management of electrolytes during intercurrent illness.

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WE10

A case of mineralocorticoid hypertension with low postoperative cortisol

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66 year old man who had hypertension treated with Amlodipine 5 mg, Perindopril 10 mg, Nebivolol 5 mg, Doxazosin 8 mg and a Thiazide diuretic from the age of 45 with previous history of subarachnoid haemorrhage and DVT presented to emergency department with episode of weakness, nausea and dizziness. His serum potassium at initial presentation was 2.3 mmol/l. After stopping thiazide diuretic and beta blocker for 4 weeks and being commenced on Amlodipine 5 mg, Doxazosin XL 12 mg for BP control his potassium was 3.1, plasma aldosterone was 1497 pmol/l (194-970 pmol/l with plasma Renin activity of 1.0 ng/ml/h (1.0–4.2), giving an ARR of 1497. Saline suppression test showed a baseline aldosterone of 2099 pmol/l with undetectable plasma Renin activity and following saline suppression his aldosterone suppressed to 548 pmol/l. His morning cortisol was undetectable post 1 mg overnight Dexamethasone. His initial CT adrenal showed a 7-mm left sided adrenal adenoma with normal MRI adrenals. Subsequently, he went for adrenal vein sampling but unfortunately the radiologist was unable to cannulate right adrenal vein. He was referred to Addenbrooke's Hospital, Cambridge for a 11C –metomidate PET–CT scan of adrenals that showed 12 mm nodule in right adrenal gland. He went for a right adrenalectomy based on 11C-metomidate PET–CT scan finding. He had an uncomplicated right laproscopic adrenalectomy. Two days post operatively he complained of profound tiredness and his morning cortisol came back as 24 nmol/l. His Bisoprolol, Doxazocin and eplerenone were stopped and he has remained on Amlodipine 5 mg and his blood pressure remained stable. His sodium was 136 mmol/l and potassium was 4.0 mmol/l. He was covered with steroids and a short synacthen test done 5 days post operatively that showed 0 min value cortisol of 217 nmol/l and 30 mins value 617 nmol/l. Based on this result his steroids were stopped. He was seen in clinic 5 weeks post surgery, he was well with a blood pressure remained stable of 130/72 on Amlodipine 5 g and Bisoprolol, 2.5 mg. Serum potassium was 4.7 mmol/l.
Learning points:
1) Investigation of mineralocorticoid hypertension
2) What to do when your radiologist fails to cannulate both adrenal veins
3) Did this patient have 'Connshings' syndrome given the recent data and low cortisol post operatively

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WE11

You can lead a patient to hospital, but you can't make him have an adrenalectomy

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A 42 year old man was referred to the acute medical unit with accelerated hypertension in March 2015. He presented with headache and blurred vision due to hypertensive retinopathy. Pre-treatment BP was 186/131 mmHg. Initial treatment included amlodipine, bendroflumethiazide and losartan. Prior to discharge, a 24 hour urine collection showed a significantly elevated urinary

noradrenaline level (3091 nmol/d, reference 0–473). Referral was made to the cardiovascular risk clinic for further investigation. Unfortunately, due to several missed appointments he was not followed up until May 2015. It transpired that the patient had a long-standing history of depression and substance misuse. He had previously taken alcohol to excess but more recently had replaced this with amphetamines in the form of 'base', the potent base form from which amphetamine ('speed') is manufactured. At review, 24 hour ambulatory BP measurement revealed severe, uncontrolled hypertension (mean daytime BP 164/104) with loss of the nocturnal dip. An ECG also showed LVH. A second 24 hour urine collection again showed elevated urinary noradrenaline (6445 nmol/d) and plasma normetanephrine was >25 000 pmol/l. The patient attended for an abdominal MRI scan in July 2015 which showed a large left adrenal lesion measuring 7.3 × 7.4 × 7.0 cm. Despite having the consequences of severe hypertension due to untreated phaeochromocytoma explained, this did little to encourage regular engagement or adherence to medication. In addition to substance misuse and the chaotic lifestyle ensuing, the patient also had anxiety issues around attending hospital. He eventually began to attend the endocrine service where he was offered weekly appointments – most of which were not attended. He was often found to be symptomatic of postural hypotension when he did attend. Biochemistry showed the development of mild non-PTH dependent hypercalcaemia. He declined to attend hospital on two occasions for adrenalectomy. He was eventually persuaded to attend on the third occasion where he had a short admission under endocrinology for pre-operative management prior to transfer to the surgical unit where he underwent adrenalectomy in November 2016. Histopathology confirmed this to be a phaeochromocytoma with a PASS of 9. No genetic mutations were found. Since adrenalectomy the patient has been lost to follow-up. This case demonstrates the extraordinary challenges of managing a patient with a phaeochromocytoma who also abuses amphetamines and has other mental health problems. It remains to be seen if the patient will re-present with recurrent metastatic disease given his elevated PASS.

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WE12

The octagenarian with a phaeochromocytoma: a new management dilemma

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Increased use of abdominal imaging has resulted in vast numbers of adrenal incidentalomas being identified (Bovio *et al.*, 2006). Guidelines exist for identifying hormone excess and diagnosing malignancy but there is little evidence about how to manage phaeochromocytoma in patients who are poor surgical candidates. We present the case of a frail 88 year-old lady who was found to have a right adrenal incidentaloma during assessment for abdominal pain. Mrs R is able to mobilise short distances with a frame. She has a history of falls associated with a postural hypotension, hypertension, previous transient ischaemic attacks, diverticular disease, fractures and a mastectomy for breast cancer. She was found to have a 28 mm right adrenal mass on CT-abdomen. Biochemical work-up showed significantly raised plasma metanephrines. A repeat supine resting sample confirmed a raised plasma normetanephrine at 2678 pmol/l (<720 pmol/l) and raised plasma metanephrines at 984 pmol/l (<450 pmol/l). Other biochemistry was normal. In Endocrinology clinic she described several years of symptoms, including a peculiar feeling in her head, a recurrent sensation of doom and intermittent palpitations. She was also found to be significantly hypertensive. She was not felt to be a surgical candidate in light of frailty and co-morbidities, and was equally not keen on embarking on an operation. The decision was made to manage her phaeochromocytoma conservatively. Doxazocin was chosen, due to its lesser side-effect profile compared to phenoxybenzamine. It was started at a low dose and slowly titrated, with weekly assessment in the Day Unit. Her blood pressure slowly improved but controlling her symptoms remains problematic. With gradual titration and encouraging good salt and water intake, postural symptoms have been minimal and she has not experienced falls. This case illustrates a new population in which phaeochromocytoma diagnoses are being made. Little data is available regarding prognosis when such conditions are managed conservatively long-term, although some comparisons may be possible from looking at patients with metastatic phaeochromocytoma and familial paraganglioma syndromes in whom surgery is no longer feasible. Alpha-blockade is often poorly tolerated and it remains to see if we will achieve adequate blood pressure control without significant side-effects. In this case, we are balancing the risks of adrenalectomy against the risks of ongoing normetadrenaline excess. We suggest there is a need to develop a conservative care pathway to help appropriately manage these patients, balancing quality of life with the burden of symptoms and medications, and collect data on outcomes.

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WE13

Primary hyperaldosteronism presenting following a miscarriage

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Case history
A 35-year-old female was found to be significantly hypertensive (181/91 mmHg) following a first trimester miscarriage (at 8 weeks gestation) during her first pregnancy.
Investigations
Blood tests demonstrated moderate hypokalaemia (2.6 mmol/l) with a normal serum sodium (140 mmol/l) and eGFR (>90 ml/min). ECG showed hypokalaemic changes with prolongation of the PR interval and T wave flattening. To avoid potential misinterpretation, additional blood tests were performed prior to commencing antihypertensive therapy. Her potassium was replaced intravenously and an aldosterone: renin ratio was performed.
Results
Aldosterone 940 pmol/l, Renin <0.2 nmol/l per h with a ratio of >4700. Testing was repeated a week later, Aldosterone 1180 pmol/l, Renin <0.2 nmol/l per h with a ratio >5900. A saline infusion test (with 2 litres of 0.9% NaCl) was undertaken and further bloods drawn. Aldosterone 1380 pmol/l, Renin <0.2 nmol/l per h with a ratio of >6900 supporting a diagnosis of primary hyperaldosteronism. Adrenal MR imaging identified a 2 cm right adrenal lesion with loss of signal on the out of phase image in keeping with benign, lipid-rich adenoma.
Management
Given her suitability for a laparoscopic adrenalectomy, adrenal venous sampling (AVS) was undertaken in order to localise the source of aldosterone hypersecretion (results pending).
Conclusion
This patient was asymptomatic and her hypertension and hypokalaemia only identified following early pregnancy loss (with progesterone acting as a potential aldosterone antagonist). Whilst her MRI is suggestive of an adrenal adenoma, it is important that her initial blood results and imaging are interpreted in concert with AVS in order to guide targeted removal of the appropriate gland. 35% of cases of primary hyperaldosteronism are caused by a unilateral adenoma whilst 60% are the result of bilateral adrenal hyperplasia (bilateral idiopathic hyperaldosteronism). Whilst a laparoscopic adrenalectomy is the treatment of choice for unilateral aldosterone-secreting adenomas (with around 70% of patients being cured for hypertension following surgery); medical management (with Aldosterone antagonists such as Spironolactone/Eplerenone) should be considered in the management of bilateral disease.

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WE14

Hyporeninaemic hypoaldosteronism in surgically cured Conn's syndrome

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A 53 year old gentleman from Ghana was referred to our clinic for further management of his Conn's syndrome. This had been diagnosed at another hospital 3 years previously when he presented with hypertension and hypokalaemia on the back of 14 years of poorly controlled hypertension. Serum aldosterone was raised at 3178 pmol/l and serum renin mass was 3.9 mU/l. MRI revealed a 5 mm nodule in the medial limb of the right adrenal gland. He was initially commenced on medical treatment with spironolactone and then eplerenone but although these medications controlled his blood pressure and hypokalaemia well, caused him troublesome gynaecomastia. Repeat biochemistry, imaging and adrenal venous catheter studies re-affirmed the diagnosis and strongly pointed to the right adrenal lesion as the source of his hyperaldosteronism without evidence of cortisol co-secretion. Referral was made to the endocrine surgical service for consideration of adrenalectomy. However given this gentleman's morbid obesity with a BMI >50 kg/m^2 with uncontrolled OSA, the anaesthetic and surgical risk was considered too great in the context of a medically controllable condition (albeit with averse side-effects). He was seen in the obesity clinic and with little improvement on oral weight control agents went on to have a gastric banding procedure. This precipitated weight loss of 40 kg and enabled a successful laparoscopic right adrenalectomy the following year. Post-operatively he still required two antihypertensive agents for presumed non-aldosterone mediated hypertension. In the follow up to this, he was admitted to our hospital from clinic when follow up biochemistry revealed hyperkalaemia of 7.7 mmol/l. Venous blood gases revealed a normal anion gap metabolic acidosis (HCO3 17 mmol/l, pH 7.306). Reassessment of his renin-aldosterone axis showed hyporeninaemic

hypoaldosteronism (renin activity serum 0.41 pmol/ml per 1 (1.15–4.37), aldosterone <58 pmol/l (135–400)), presumed secondary to long-term type 2 diabetes mellitus. He was commenced on fludrocortisone replacement which was titrated up to 100 mcg bd. His blood pressure and potassium are now well controlled on this dose with additional beta and calcium channel blockade. The case describes the rare occurrence of hyporenininaemic hypoaldosteronism in a patient with surgically cured Conn's syndrome secondary to an aldosterone producing adenoma. The autonomous aldosterone excess 'masked' the diabetes-associated underlying renin insufficiency which was exposed following the adrenalectomy. It highlights the issues of managing both primary aldosteronism and non-aldosterone mediated hypertension in complex patients with comorbidities and also the management of hypertension in aldosterone deficiency.

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WE15

A case of hypertension and palpitations with a suspicious adrenal mass

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A 41 year old man was referred to the endocrine service at St Barts hospital. He had previously had a GP check-up and was found to be hypertensive, this led to him having an ultrasound KUB, an abnormality was detected which resulted in a CT abdomen being performed. The CT abdomen showed a 38×33 mm well defined right adrenal lesion and the patient was referred to endocrinology. Upon review, the patient had been having palpitations for the past year - particularly when straining on the lavatory but also unprovoked when resting - and episodes of sweating. The palpitations had provoked mutliple attendances to A + E and he had had a 24 hour Holter monitor, which was unremarkable. Examination was unremarkable aside from a blood pressure of 140/90, HR 100bpm on Verapamil. A 24 hour urinary metanephrine measurement was performed, which showed elevated 24 hr normetadrenaline of 11,544 nmol/day (normal <4,400) and 24 hr metadrenaline of 2,203 nmol/day (normal <2000). 3-Methoxytyramine levels were normal. Plasma calcitonin was subsequently found to be raised at 21 ng/l (normal <9.52). Gut hormones were within normal limits, but HbA1c was elevated at 45 mmol/mol. The patient was admitted for alpha blockade with phenoxybenzamine and IV fluid filling, he was subsequently beta blocked with propranolol. He also underwent an ultrasound of the thyroid, which showed some small nodules, but none were felt to display any worrying features. The patient is currently awaiting a right sided adrenalectomy.

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WE16

Challenging case of recurrent phaeochromocytoma and metastatic paraganglioma

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Background
A 59 year old woman presented with recurrent symptoms of catecholamine excess (episodic headache and sweating). She was initially diagnosed in another centre to have a right adrenal phaeochromocytoma in 2002. She had suggestive symptoms, elevated urine catecholamines and a right adrenal mass on CT Adrenals. MIBG was however negative and they had proceeded with a right adrenalectomy and histology confirmed a phaeochromocytoma. She also had type 2 DM, anxiety and degeneratvive lumbar spine. In 2010 she presented to our centre with recurrent symptoms. Urine adrenaline was found to be elevated at 404 nmol/24h (Normal <100). CT abdomen revealed 16mm recurrent right adrenal mass but no uptake on MIBG. However PET scan shown mild metabolic activity in the nodule. Genetic screen didn't find any known mutation for VHL1, SDHB, SDHD, RET, MEN 2, TMEM127 genes. The recurrent adenral mass was resected and histology shown benign phaeochromocytoma with lesion extending to excision marigins. Subsequent 24h urine metaadrenalins were normal. The patient started complaining of episodic recurrance episodic of her symptoms two years later and intermittently thereafter. However urinary and plasma catecholamines were within normal limits. Neurological investigations (MRI brain, CSF, EEG) didn't reveal significant abnormality. In 2015 urinary collection shown new elevation of urinary meta-adrenaline at 1.96 (Normal <1.4) Repeat samples were similar after stopping amitryptyline. In March 2016 CT abdomen revealed a new 13x16mm nodule in upper pole of right kidney. However yet again in July 2017 SPECT CT MIBG images show no abnormal foci of uptake. Urinary meta-adrenaline elevated at 2.7. Phenoxybenzamine titration was commenced and she had resection in September 2017. Histology has shown incomplete excision of metastatic paraganglioma and she has expressed unwillingness for a fourth operative procedure. Subsequent urinary catcholamines and meta-adrenalines returned to normal level.
Discussion
This case illustrates the challenges in diagnostic process and identification of phaeochormocytoma and paraganglioma due to inconclusive functional investigations (MIBG and PET CT). Given incomplete excision further reoccurrence is very likely and there will be challenges ahead in choosing further surgical therapy(given her reluctance) and limitations in medical management options including 131I-mIBG therapy.

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WE17

Back to the basics!

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A 42 year old lady initially presented in Poland with haematuria while she was on holiday over Christmas. She had some tests including an ultrasound of the kidney which showed a mass adjacent to the left kidney. The haematuria had settled and she was feeling well apart from non-specific back ache. She worked in a cake factory which she continued to do here in the UK. Her GP requested another ultrasound of her kidneys which showed a solid mass adjacent to the left kidney and a CT abdomen was advised (Feb 17) which found a mass anterior to the left kidney. The radiologists suspected this was arising from the tail of the pancreas. As it was part cystic and part solid, a diagnosis of probably pancreatic cyst adenoma was made. An MRI was requested which demonstrated a 5-cm complex solid and enhancing left retroperitoneal mass but the origin was uncertain, differentials included solid pseudo-papillary pancreatic tumour or retroperitoneal sarcoma. She was reviewed in the Sarcoma MDT and they recommended a laparoscopic biopsy or a surgical excision. She then went on to have a FNA under EUS which stained like an NET. She then was discussed at the hepatobiliary MDT and a NET MDT referral was made who suggested an MIBG scan and 24-hour urine metadrenaline. Meanwhile, she was referred to Endocrinology. In our clinic, on direct questioning she had no symptoms related to adrenaline excess. Her past medical history included an appendectomy, a resected meningioma and high cholesterol. There was no family history suggestive of MEN or a genetic paraganglioma syndrome. On examination, her blood pressure was 213/103 mm Hg. She appeared a fit lady with no stigmata of underlying illness. Her pulse rate was regular. She was commenced on Phenoxybenzamine and slow sodium at this point. An MIBG scan done a month later confirmed the diagnosis of left actively secreting adrenal phaeochromocytoma. She successfully underwent a left laparoscopic adrenelectomy.
Discussion
We did not find any mention of her high BP recordings in any of the correspondence from the GP and various MDTs. If they had noted a finding of significantly raised BP in a previously fit lady with a lesion around the kidney, a possibility of a pheochromocytoma would have been considered much earlier than it was- a simple test which cost nothing would have saved a lot of time and resources.

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Workshop F: Disorders of the gonads

Gynaecomastia and Sex Steroid & Sex Steroid Replacement in Females

WF1

Sex steroid replacement in primary amenorrhoea due to Turner's syndrome

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Case history
FK is an 18 year old female, who attended the Turner's syndrome clinic in our tertiary centre with primary amenorrhoea. Her family are originally from Ghana but she was born in Italy and lived there until moving to the UK in 2016. She was born full-term by normal delivery and Turner's syndrome was diagnosed at 3 months of age due to characteristic phenotypic features. She was managed by the paediatric endocrinologists in Italy and was on growth hormone injections for around 10 years until it was stopped at age 16. She was on the Evorel 25 patch whilst in Italy for a few years and had 1 episode of slight spotting at age 14 years. There has been no further menstrual bleeds. Since coming to the UK, she did not received any further hormonal treatment, until her first appointment in the Turner's syndrome clinic when she was started on Ethinylestradiol. She has not had any menstrual bleed since this was commenced 4 months ago. She has no other developmental issues or past medical history. She was doing a Diploma in Childcare in college. Drug history: Ethinylestradiol 10 mcg OD, Cholecalciferol 800 IU OD. On examination: height 147.5 cm, weight 60 kg, BP 120/78. No webbed neck or swollen hands or feet.
Investigations
TSH: 1.11 mU/l (NR 0.27–4.2); Free T4: 17.0 pmol/l (NR 9.0–26.0); TPO antibodies: 9; FSH: 55 IU/l (postmenopausal 26–135); LH: 11 (postmenopausal 8–58); Fasting blood glucose: 4.4 mmol/l. 25-hydroxy vitamin D: 29 nmol/l; USS pelvis: Both kidneys appear normal in sizes and echogenicity. Normal sized anteverted uterus, endometrial thickness 1 mm. Echo: Bicuspid AV with no stenosis or regurgitation detected. Non-dilated aorta with no evidence of coarctation seen. Audiology: Seen by ENT, reports normal.
Treatment
Since she did not have a menstrual bleed with ethinylestradiol 10 mcg, we increased the dose to 20 mcg OD. During telephone review 4 weeks later, this had resulted in 2 occasions of breakthrough bleeding. Therefore a note was sent to her GP to prescribe Norethisterone 5 mg BD for 5 days for endometrial protection. During her next clinic appointment, we plan to discuss with her about starting the combined oestrogen-progesterone pill or patch.
Conclusions and points for discussion
This is a useful case to highlight the optimal sex steroid replacement in a girl with Turner's syndrome, primary amenorrhoea and premature ovarian insufficiency, who has attained final height.

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WF2

Diagnosis and management of functional hypothalamic amenorrhoea – a case report

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Functional hypothalamic amenorrhoea (FHA) is an endocrine disorder secondary to a deficiency of pulsatile gonadatrophin-releasing hormone (GnRH) secretion. It is not related to hypothalamus-pituitary organic lesions, endocrine or systemic disease. The clinical profile is dependant on the degree of GnRH suppression – it can range from an inadequate luteal phase to hypothalamic amenorrhoea. The incidence of FHA ranges from 15% to 48% of the secondary amenorrheas. We present the case of a 21-year-old female of Romanian origin referred to clinic with amenorrhoea. She attained menarche between the ages of 11–13 years and had regular periods for a year. After this time, her periods became more irregular and this was thought to be secondary to weight gain. The patient subsequently lost around 3–4 kg but continued to suffer from oligomenorrhoea (less than 4 cycles per year). In 2013/14 she was amenorrhoeic for one year at which time she was started on the oral contraceptive pill. This was discontinued after a year due to intolerable side effects. In 2016, she had 4 periods. There was no history of galactorrhoea, hirsutism or hot flushes. The patient was anxious about a familial cause for her symptoms as her sister also struggled with fertility issues. When reviewed in clinic, she was asymptomatic with a stable weight 58.3 kg and blood pressure 107/74 mmHg. Clinical examination was unremarkable. Blood tests showed low follicle stimulating hormone (FSH) (<1 IU/L), low luteinising hormone (LH) (<1 IU/L), oestradiol <44 pmol/l, normal prolactin (155 mIU/L), testosterone (0.8 nmol/L, sex hormone binding globulin 68 nmol/l, dehydroepiandrosterone 5 micromol/L, androstenedione 2.2 nmol/L, free thyroxine (T4) 14.6 pmol/L, thyroid stimulating hormone 1.23 mIU/L, cortisol 233 nmol/L, adrenocorticotrophic hormone 14.1 pg/mL and insulin-like growth factor 1 (IGF-1) 17.5 nmol/l. In addition, her full blood count, renal function and liver function were within normal range. A pituitary MRI showed no abnormality and transvaginal ultrasound showed normal ovaries with follicles measuring between 2–4 mm. She is awaiting a dual-energy X-ray absorptiometry (DEXA) scan. Her results were in keeping with a diagnosis of functional hypothalamic amenorrhoea. She was given life-style advice, offered psychology review for stress management and started on short-term treatment with transdermal oestrogen patches and cyclical oral progesterone (as per the Endocrine Society Clinical Practice Guideline, 2017) to protect bone health. Functional Hypothalamic Amenorrhoea is a form of chronic anovulation not due to identifiable organic causes. There is a functional reduction in GnRH drive which causes reduced LH pulsatility. The mechanisms responsible for FHA are yet to be definitively determined. Recent research indicates a role for hypothalamic neuromodulatory signalling pathways mediated by kisspeptin, a family of peptides stimulating GnRH secretion. Loss of kisspeptin signalling is associated with hypogonadotrophic hypogonadism. FHA is often associated with stress, weight loss, excessive exercise or a combination of these. It remains a diagnosis of exclusion requiring a comprehensive assessment of both systemic and endocrinologic aetiologies. Long term complications such as bone loss and infertility need to be addressed. Oral contraceptive pills (OCPs) have not shown any benefit for improving bone mineral density. On the other hand, transdermal oestrogen showed an improvement in the bone mineral density. In patients wishing to conceive, treatment with pulsatile GnRH is first line. A multidisciplinary approach is necessary and includes medical, nutritional and psychological support.

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WF3

Honesty is always best

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A three year old boy was referred for surgical correction of an undescended right testis. Intra-operatively he was found to have a hyperplastic right gonad which was in continuation with a unilateral fallopian tube, prompting analysis of his karyotype. This showed 46XX/XY mosaicism with 88% of the cells being XX and 12% XY. The post-operative histology confirmed mixed testicular and ovarian tissue in the right gonad. He appeared phenotypically male and had blaschko lines consistent with the diagnosis of genetic mosaicism. Although a HCG stimulation test showed some testicular function in his left gonad, this was insufficient to allow normal progression through puberty. He commenced regular Sustanon injections aged 12 years with good effect. Over the next few years, his left testicular volume gradually increased to 8–10 mls, after which there was no further enlargement raising the possibility of a dysgenetic testis. Ultrasound imaging showed a single small left testis with slight heterogeneity but no malignant features. At the completion of puberty, he reported no symptoms suggestive of erectile dysfunction, had a muscular physique and was referred for a right testicular implant. Sustanon was discontinued and since then his serum AFP, HCG and testosterone levels have remained within the normal ranges. He is currently 25 years old and married. On clinical examination, the left gonad remains soft, in keeping with a degree of germ cell failure, but there are no palpable worrying features. Recent semen analysis shows persistent severe oligospermia. He remains off testosterone replacement (serum testosterone level 18 nmol/l) with the aim to freeze his sperm, as soon as the levels are sufficient to allow this, for potential intracytoplasmic sperm injection, should he wish to pursue this. This case describes a rare cause of hypogonadism. It emphasises the role and treatment aims of testosterone replacement in young hypogonadal males, the impact this can have on spermatogenesis and the complex fertility issues that may arise in adulthood.

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WF4

Klinefelters and testosterone replacement

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A 27 year old was referred to endocrine clinic for investigation of longstanding gynaecomastia. He had noticed loss of early morning erections. He never fully grew a beard and had no children. This was associated with temporal hair recession and intermittent headaches. On examination he appeared to be of asthenic built and youthful. He was tall with his upper body being longer than lower. He had widely spaced breasts and long arms. His testicular volume on examination was 1–2 ml bilaterally. His visual fields were full on confrontation. His bloods showed an FSH of 44.0 μ/l (1–12) and LH of 22.4 μ/l Testosterone levels of 3.7 nmol/l (8.64–29), sex hormone binding globulin levels of 41 nmol/L (18.3–54.1) and a Free Androgen Index of 9.0 (42–200). He was investigated for hyper-gonadotrophic hypogonadism and consented for genetic testing for Karyotyping. His genetic testing confirmed a diagnosis of Klinefelters and he was commenced on testosterone replacement therapy. As he was unable to make testosterone, replacement was required to alleviate the symptoms that he had long suffered with including mood problems, lethargy and sexual dysfunction plus the long term benefit on bone and cardiovascular health, also reducing the risk of developing type 2 diabetes. Review a few months later showed a noticeable improvement in energy levels, mood elevation, and hair growth on arms and increased sex drive. His repeat blood tests showed Testosterone levels of 45.2 nmol/l (8.64–29). He generally felt much better and was terrified of any deviation from this relief and asked for the IM equivalent after being told that Testogel supplies were extremely scant. It was therefore agreed to start him on IM Nebido (Testosterone Undecanoate 250 mg/ml) 1gm every 12 weeks. Dosing will be varied on the basis of trough levels and regular full blood count monitoring during the course of treatment.

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

Hypocalcaemia Including Vitamin D Deficiency

WG1

Calcium homeostasis after parathyroidectomy

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We describe a 82 year old patient with background history of thyrotoxicosis (had total thyroidectomy), primary hyperparathyroidism (had parathyroidectomy 12 years back at another hospital – two glands removed). She was on L-thyroxine, alfacalcidiol 1 μg/day and $CaCO_3$ 500 mg BD. She remained stable for 7 years on this cocktail. In February 2017, she was admitted with acute confusion and was found to have adjusted ca level of 4.57 with AKI, normal magnesium. No recent changes in medications and there was no obvious precipitating event (apart from AKI although this may well be the other way round). Other workup for hypercalcemia was negative (including CT CAP). She was discharged prior to Endo review (CCa 2.68) with no alfacalcidiol/$CaCO_3$ at all. Her renal function was back to baseline. Understandably, she was readmitted after 3 days with paresthesia, pins and needles in both hands and her Adj Ca was 2.01. She was re-started on $CaCO_3$ 500 mg bd and alfacidiol 500 ng once daily with improvement in calcium levels (Adj Ca 2.2). However, 10 days post-discharge, she was readmitted with hypocalcemia (1.82; Mg 0.56). She was treated appropriately and discharged on $CaCO_3$ 500 bd, alfacalcidiol 1mcg daily. In April 2017, she was re-admitted with Adj calcium of 3.33. Her alfacalcidiol was reduced to 750 ng, $CaCO_3$ to 500 mg OD and Ca levels have been stable since (2.1–2.25). Corrected calcium levels: 4.57-3.30-2.68-2.01-2.2-1.82-1.90-3.33-2.21-2.18

Conclusion

This case clearly showed that dose requirements can change even after many years + the difficulties in maintaining calcium homeostasis post parathyroidectomy.

Questions

1. What are the ideal calcium levels in patients with post-parathyroidectomy hypoparathyroidism?
2. What are the reasons for changes in dose requirements?

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WG2

Refractory hypocalcaemia due to pseudo hypoparathyroidism

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A 27 year old, Caucasian female was admitted with vomiting and found to have severe hypocalcaemia. On clinical examination she had a normal stature, oval face; she was not brachydactylic and did not have dental hypoplasia. Biochemically she had serum Ca of 1.49 mmol/l (2.15–2.50), a high serum Phosphate of 1.50 mmol/l (0.9–1.45) and Vitamin D levels of 59 nmol/l (>50 sufficient for majority population). Her serum parathyroid hormone was elevated at 304.5 ng/l (15–65). She had a 24-h urine collection which showed a urine creatinine of 9.46 mmol/l (3–18), Urine Calcium 0.42 mmol/l, 24-h Urine Calcium of 0.3 mmol/d (0–7.5) and Calcium/Creatinine ratio of 0.04 mmol/mmol. She was treated with IV calcium infusion and diagnosed as Pseudo hypoparathyrodism. On taking a further history we find out that she had symptoms of severe hypocalcaemia including perioral paraesthesia, numbness/tingling in the fingers, severe muscle cramps. Her mother had taken her to GP severally since the age of 9 with symptoms of severe hypocalcaemia, when her arms will go in a spasm, with tingling around her mouth and opthalmoplegia. She was advised to be fed sugary drinks and was told this was due to low blood sugars and that she has a squint at times. She had no other medical problems, no family history and not found to have developmental delay. The first time she had her blood tested was age 21, two weeks after her son was born when she presented to ED as she was unable to cope at home due to severe muscle cramps and lethargy. On that occasion she was discharged home with oral calcium tablets. From age 21–27 she was seen in ED six times, admitted for IV calcium infusion twice. Three years since diagnosis she continues under endocrine follow up and is being treated with Calcichew D3 and Alfacalcidiol. She is now age 30 and the management of her hypocalcaemia remains a challenge. With oral therapy we have been unable to achieve serum calcium above 1.80 mmol/l despite being Vitamin D replete. She is asymptomatic when her serum calcium levels are between 1.6 and 1.8 mmol/l. She is now also hypothyroid Free T_4 11.1 pmol/l (12.0–22.0) and TSH 9.95 miu/l (0.27–4.20) thyroid antibodies are awaited. She is waiting genetic testing.

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WG3

Parathyroid hypoplasia - an uncommon cause of hypocalcaemia

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A 23 yr old lady was admitted with a generalized tonic clonic seizure in May 2016. Her corrected calcium was 1.47 mmol/l (2.05–2.6 mmol/l) She was initially treated with intravenous calcium gluconate and subsequently switched to oral calcium carbonate tablets and one alphacalcidol tablets once her calcium improved. The patient gave a history of a prior seizure in 2013. At this point she was not investigated for any electrolyte imbalances. She was initially treated with the antiepileptic leviteracetam but this was later stopped. On further history taking it was noted that the patient had a history of developmental delay – she walked at 1 year 9 months and started talking at 5 years of age. On examination she had dysmorphic facial features with a long face, low set ears and retrognathia. We suspected she might have DiGeorge syndrome and further investigations revealed the following:

PTH**:** 10 pg/ml (15–65 pg/ml)
Vitamin D: 27 (30–100 ng/ml)
Flow Cytometry:
CD3 (T Lymphocytes): 609 cells/l (723–2,737 cells/l)
CD4 (Helper/Inducer T lymphocytes): 418 cells/l (404–1612 cells/l)
CD8 (Suppressor/Cytotoxic T-Lymphocytes): 174 cells/l (220–1,129 cells/l)
CD3: 56% (56–86%)
CD4: 39% (33–58%)
CD8: 16% (13–39%)
CD4/CD8: 2.4 (1–3)

A 22q11.2 deletion de novo mutation was confirmed on genetic studies. A diagnosis of DiGeorge syndrome was reached as this female patient had a reduced number of CD3 T cells, a deletion of chromosome 22q and hypocalcaemia which required therapy. The patient remains well on one alphacalcidol 0.5 μg daily and calcium carbonate 2,500 mg daily. Calcium levels are currently regularly monitored at outpatients and are now within normal limits. 24-h urinary calcium excretion is also satisfactory. She was reviewed by a clinical immunologist who suggested to check serology for pneumococcal antibody, Haemophilus influenza B antibody and tetanus antibody which were all positive, indicating adequate immunity. DiGeorge syndrome is caused by gene deletion at chromosome 22 at location q11.2 The microdeletion causes disruption during the embryonic development of the heart, head and neck, thymus and parathyroids. This leads to a variety of different signs and symptoms such as characteristic facial features, cardiac abnormalities, thymic aplasia with immunodeficiency and parathyroid hypoplasia. In this case parathyroid hypoplasia led to life threatening hypocalcaemia causing seizures.

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WG4

Generalised convulsions as a presentation of severe hypocalcaemia secondary to Vitamin D deficiency: An uncommon presentation of a common condition

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Maidstone Hospital, Maidstone, UK.

A 36 year old female patient presented to the emergency department with a generalised tonic-clonic seizure. She had a past medical history of epilepsy and tuberous sclerosis. Her medication prior to hospital admission was Tegretol which had controlled her seizures well for many years. On admission, the adjusted calcium level was 1.4 mmol/l with a raised ALP 508 U/l and a phosphate within the normal reference range at 1.1 mmol/l. Magnesium was also within the normal reference range at 0.8 mmol/l. On further investigation there was an elevated

parathyroid hormone level 39.2 pmol/l (1.6–6.9) and her Vitamin D was undetectable at <30 nmol/l. Despite repeated IV calcium gluconate infusions and vitamin D supplementations calcium levels did not improve consistently. X-ray of her hands demonstrated periosteal new bone formation around the proximal phalanges which was in keeping with the features of Tuberous Sclerosis. After calcium levels supplemented with IV replacement she was discharged with Alfacalcidol 1.5micrograms twice daily and sandocal 1,000 four times a day. Ergocalciferol 300,000 IU was administered as an intramuscular injection. Epilepsy is a common disorder and the medications administered to prevent recurrent seizures often have multiple side effects. Tegretol, carbamazepine, is a cytochrome P450 inducer and as a consequence of this action can lead to changes within in bone mineral density, including deficiency of vitamin D and hypocalcaemia. It is reported that approximately half of the people treated with such medications develop bone metabolism abnormalities and therefore it is important to initiate surveillance in these patients to prevent fractures as well as seizures from electrolyte disturbance. This case highlighted the difficulties in managing hypocalcaemia and also stressed the importance of looking for a secondary cause. In addition, we raise an important issue of pharmacovigilance in antiepileptic therapy especially for induced Vitamin D deficiency and consequent electrolyte balance.

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WG5

Multifactorial hypocalcaemia in a patient presenting with sepsis

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Hypocalcaemia is one of the common metabolic abnormalities found in hospitalised patients. The most common cause of hypocalcaemia is Vitamin D deficiency. Others causes include hypoparathyroidism, chronic kidney disease and hypomagnesemia. Multiple factors can co-exist in the same patient. We present here a case of hypocalcaemia caused by multiple factors in the same patient. The patient we present probably had multiple factors contributing to hypocalcaemia. Our hypothesis is that a combination of proton pump inhibitor therapy plus alcoholism induced hypomagnesaemia. This caused functional hypoparathyroidism (release of PTH from the chief cells of the parathyroid glands requiring adequate serum magnesium concentrations) which, in combination with vitamin D deficiency, caused severe hypocalcaemia. Additionaly there may have been impaired of activation of vitamin D in the context of the acute kidney injury.

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Workshop H: Miscellaneous endocrine and metabolic disorders

Hypoglycaemia & Neuroendocrine Tumours

WH1

A daughter's diagnosis

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Case
An 89 year old gentleman was admitted to hospital following a collapse at home. His capillary blood glucose was found to be 1.4 mmol/l by the paramedics. The patient had experienced multiple collapses at home in the preceding 2 weeks. Each time, he had been found to be hypoglycaemic but treated and discharged from A&E. He complained of reduced appetite, weight loss and change in bowel habit. The patient's past medical history included a large fibroma of the left pleura which was being managed conservatively. He was also known to have atrial fibrillation, COPD, bronchiectasis and CCF with severe systolic impairment.
Investigations
Blood tests revealed an elevated CRP (45 mg/l) with normal WCC (7.9×109/l), mild anaemia (Hb 116 g/l), elevated ALP (146 IU/l) and normal renal function. A CT scan showed the known large pleural fibroma and a new smaller lesion in the right upper lobe of uncertain aetiology. Following transfer to the endocrinology ward, the patient experienced a further episode of hypoglycaemia and the venous glucose was found to be 1.9 mmol/l. Insulin and C-peptide levels were also found to be low at 11 pmol/l and <94 pmol/l respectively. A SST was normal and IGF-1and IGF-2 levels analysed. Results showed IGF-2:IGF-1 ratio 16.7 (<10). Despite regular feeding, supper and overnight snacks he remained significantly hypoglycaemic especially overnight with no awareness of symptoms. He was commenced on Prednisolone 30mg daily and his hypoglycaemia improved.
Discussion
Doege-Potter syndrome is a rare cause of hypoglycaemia. In this condition, hypoglycaemia is mediated by the secretion of IGF-2 from a fibrous tumour. Prompt recognition and management is essential. Surgical resection of the lesion is curative, but management can be difficult in patients that are not fit for surgery. Options include chemotherapy, embolisation, glucocorticoids or growth hormone.

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WH2

An unexpected cause of hypoglycaemia post-bariatric surgery

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Case history
A 54 year-old gentleman was transferred as an inpatient from another centre for investigation and management of refractory hypoglycaemia following a revision gastric bypass. He was requiring a continuous infusion of 20% dextrose on transfer to maintain normoglycaemia. He had a complex bariatric surgical history dating back 7 years. His initial procedure had been a sleeve gastrectomy that was subsequently converted to a gastric bypass which had then been reversed prior to this most recent operation. He had been particularly troubled by acid reflux, requiring multiple OGDs and dilatations of the gastro-oesophageal junction. He had long-standing symptoms suggestive of hypoglycaemia that developed approximately 2 years after his bypass, which had been investigated on a number of previous occasions. Results had been consistent with endogenous hyperinsulinaemic hypoglycaemia (detectable insulin and c-peptide), in keeping with dysregulated glucose regulation post bariatric surgery. Dietary and medical interventions had been of limited success.
Results and treatment
Initial management was with a phased reduction of IV dextrose infusion with the addition of diazoxide and octreotide that, over a number of days, reduced the frequency and severity of hypoglycaemia. Laboratory hypoglycaemia (glucose <2.2 mmol/l) was confirmed at both the referring hospital and our centre. During these episodes, plasma insulin was undetectable when using the Roche assay (which does not cross-react with exogenous insulin), but elevated when measured on the Mercodia platform (which does). Corresponding c-peptide concentrations were low in all instances. A urine sulphonylurea screen and insulin antibodies were negative. These results were consistent with exogenous insulin administration and he was discharged following input from the psychiatry service. He has attended post discharge follow up and reported a reduction in instances of hypoglycaemia at home, which were no longer interfering with his life.
Conclusions and points for discussion
Endogenous hyperinsulinaemic hypoglycaemia is a rare but well recognised and significant complication of gastric bypass surgery. Exogenous insulin administration is an important cause of hypoglycaemia and requires a high threshold of suspicion to detect. The co-existence of both is highly unusual and this case provides an excellent opportunity to discuss:

- The biochemical assessment of insulin and c-peptide during hypoglycaemia
- Differences in cross-reactivity in commonly used assays and the importance of close collaboration with the Biochemistry department
- Appropriate re-evaluation of an existing diagnosis when the clinical situation changes or treatment response is not as expected

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WH3

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

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Case history
An 11 year old girl was diagnosed with von Hippel-Lindau disease (VHL) on cascade genetic screening due to a positive family history and was enrolled in a VHL surveillance programme. She developed bilateral phaeochromocytomas and underwent staged bilateral adrenalectomies at the age of 12 and 14. At the age of 16, she was discovered to have a 2.5 cm tail of pancreas pancreatic neuroendocrine tumour (pNET) on routine surveillance imaging. This enlarged during follow up and additional smaller pNETs in the pancreatic body became visible. At the age of 19, she underwent a distal pancreatectomy and splenectomy. Her mother had a progressive metastatic pNET and there was considerable understandable family anxiety surrounding the diagnosis.
Results and treatment
Histology confirmed a 35 mm grade 2 pNET with a Ki67 index of 10%. Tumour was present at the resection margin with no evidence of lymph node metastases. A second 1 mm grade 1 pNET was also present and was completely excised. During post-operative imaging surveillance, three new pNETs developed within the tail, body and uncinate process which all grew on sequential examinations. She was asymptomatic and chromogranin A and fasting gut peptides were normal. All lesions were avid on Gallium DOTA-TATE imaging confirming somatostatin receptor expression. Given the rate of lesion growth, in combination with her family history of malignant disease, intervention was deemed necessary. However, given the lesion locations, there was a high risk of pancreatic insufficiency with further surgical resection and there were significant concerns about her ability to manage the resultant pancreatic insufficiency. She therefore underwent a trial of primary somatostatin analogue therapy which was well tolerated without adverse effects. After 6 months of treatment, reimaging demonstrated that all pNETs had significantly reduced in size and met RECIST criteria for partial response. This response has been maintained for over 18 months.
Conclusions and points for discussion
This case of a young woman with recurrent multifocal pNETs in the context of VHL provides an excellent opportunity to discuss:

- pNET management within the context of predisposing germline mutations when the potential for multifocal and metachronous disease (including extra-pancreatic sites) complicates management decision making
- the roles of somatostatin analogue therapy in pNETs.

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WH4

A tricky case of hypoglycaemia

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A 50 year old lady was referred with a two year history of recurrent spontaneous hypoglycaemic episodes. She had put on a stone in weight over this time period.

She was otherwise fit and well and took no regular medications. She had a past medical history of treated melanoma. None of her family members had diabetes mellitus. Neither she nor her husband worked in a healthcare setting but her daughter was a district nurse. Prior to referral, she had a normal short synacthen test and CT chest/abdomen/pelvis showing no evidence of malignancy. She was admitted in July 2017 for an extended fast. Initial glucose level was 6.7 mmol/l, c-peptide 0.24 nmol/l (reference range 0.34–1.8) and insulin 22.2 pmol/l (12 150). Nine hours into the fast, she developed mild symptomatic hypoglycaemia, with a capillary glucose of 3.7 mmol/l – by 16 hours, plasma glucose was 1.8 mmol/l with more convincing symptoms. Simultaneous c-peptide level was suppressed at 0.16 nmol/l, with insulin level of 17.4 pmol/l. Sulphonylurea screen was negative; and anti-insulin antibody levels were negative at 2.5 mg/l (0–5). Initial results seemed to suggest exogenous insulin use, and samples were in the process of being sent externally for differential insulin assays. Meanwhile, she underwent 2 further extended fasts and on both occasions developed hypoglycaemia of <2.0 mmol/l, with suppressed c-peptide (0.17 nmol/l; 0.32 nmol/l) and detectable insulin levels (20.8 pmol/l; 30.4 pmol/l). Unexpectedly, 3-hydroxybutyrate and non-esterified fatty acids were increased on both occasions. However, proinsulin levels were inappropriately high for the degree of hypoglycaemia (29 pmol/l, range <10). Following the third admission, she was commenced on diazoxide 50 mg twice daily, which was increased to three times daily, to good effect. In terms of imaging, octreotide SPECT CT showed a 12 mm focus of moderate uptake projecting over the pancreatic tail. A dual phase CT pancreas was normal. Endoscopic ultrasound showed a 9 mm hypoechoic lesion in the pancreatic tail. FNA of the lesion was done, and histology confirmed a well differentiated pancreatic neuroendocrine tumour with insulin expression, Ki-67 $<2\%$. She underwent robotic enucleation of the insulinoma. The tumour was graded as pT1 N0 (NET G1), Ki-67 $<1\%$. This case illustrates that the diagnosis of an insulinoma is not always straightforward. In our case, there was apparent discordance of biochemical results despite repeat extended fasting tests. Interpretation of results and work-up of difficult cases of hypoglycaemia will be discussed.

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WH5

NET or Not? A case illustrating potential difficulties in detecting neuroendocrine tumours

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A 68-year-old lady presented with a right-sided breast lump detected on routine mammography. Past medical history included type 2 diabetes, asthma, and hypothyroidism following radioactive iodine for toxic multinodular goitre. Staging CT showed 2 presumed metastases in the left lung, and one in the right lung. She was referred for biopsy and/or resection of these lesions. Histology of the left lower lobe lesion showed a typical carcinoid tumour with an adjacent neuroendocrine tumourlet; Ki-67 index $<5\%$. Unfortunately, the left upper lobe lesion was too close to the pulmonary artery to safely excise. She then had an OctreoScan which was negative. Her breast carcinoma was removed and tamoxifen was commenced. An incidental thyroid nodule was also noted and further work-up organised. Her case was discussed in the Neuroendocrine MDT. Histology from her breast resection was reviewed and negative for TTF1 and neuroendocrine markers. Meanwhile, FNA of her thyroid nodule showed Thy1, repeat FNA showed Thy 3f so she proceeded to have a left diagnostic lobectomy. Histology showed a 20 mm papillary thyroid carcinoma with capsular and vascular invasion and extrathyroidal extension, hence completion thyroidectomy was performed. Post-operatively she received 3.7GBq of radioactive iodine. Initial post-ablation scan did not show any extrathyroidal uptake, and stimulated thyroglobulin was 166 ug/l, with negative thyroglobulin antibodies. A year later, thyroglobulin levels started to increase markedly, which raised the suspicion of thyroid cancer recurrence. Repeat radioiodine scan showed no uptake in the neck but showed two areas of uptake in the left lung; USS neck showed no local recurrence; and repeat OctreoScan showed non-specific activity in the left lung. Serial CTs showed a 4 mm increase in the left-sided lesion, with stable appearances of the right-sided nodule. Rediscussion in the MDT concluded that the lung nodules were probable metastases from thyroid cancer all along. The diagnosis was explained to the patient, and due to her lack of symptoms and slow progression of the lesions, further surgery or radioactive iodine was withheld. She remains under close monitoring. This case highlights the potential diagnostic difficulties in diagnosing tumours of neuroendocrine origin, and illustrates various diagnostic modalities and multidisciplinary expertise available. Patients with neuroendocrine tumours may have separate multiple malignancies, and there is a possible association documented in the literature. It is of paramount importance to involve patients in decision-making and consider their symptoms and expectations, as it may be inappropriate to offer treatment when the benefits are uncertain.

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WH6

Insulinoma presenting with nocturnal seizures

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A 29 year old lady presented to an outside hospital with 1 year's history of episodes of confusion in the mornings. The patient's partner had noticed that 2–3 times a week she awoke with episodes of confusion, minimal communication, stereotyped lip smacking and winking lasting up to 20 min. She had one nocturnal tonic-clonic seizure abroad, requiring A + E attendance. She was then seen by a neurologist, had a normal sleep deprived EEG and was diagnosed with focal epilepsy and started on lamotrigine. She subsequently had two further episodes of nocturnal/early morning tonic-clonic seizure whilst in the UK, on anti-epileptic medications. A CBG of 1.2 mmol/l was recorded by the ambulance service after one of these seizures. After this, she would wake herself in the night to consume a banana and a can of Coca Cola, which prevented further seizures. She had experienced some weight gain. Family history was remarkable for type 2 Diabtes Mellitus in a grandmother and thyrotoxicosis in her mother. Physical examination was unremarkable. A 72-hour fast was planned, however, the patient had an episode of hypoglycaemia prior to the test starting, with a lab glucose of 1.6 mmol/l, insulin was inappropriately detectable at 9.8 mu/l with a c-peptide of 765.6 pmol/l. A urinary sulphonylurea screen was negative. Results were compatible with insulinoma. Other blood parameters were normal. MRI pancreas showed a 1 cm soft tissue lesion arising from the pancreatic tail, this lesion was avid on a ^{68}Gallium-Dotate PET-CT. No evidence of metastatic disease was seen. The patient was referred for surgery. Management of the hypoglycaemia was challenging. The patient had a disappointing response to escalating doses of diazoxide, still requiring a midnight snack to prevent hypoglycaemia. Octreotide was unhelpful and resulted in nausea and reduced intake, leading to re-admission with further hypoglycaemic episodes. Symptoms persisted despite the addition of anti-emetic medication and the octreotide was stopped and prednisolone commenced and the dose gradually increased to 10 mg morning, 5 mg evening until the hypoglycaemic episodes were abolished. Diazoxide induced oedema was managed with Bendrofluazide. The patient underwent a distal pancreatectomy and splenectomy. Histology showed a completely excised 13mm NET, Ki67 $<5\%$ with no evidence of vascular invasion. Immunohistochemistry showed expression of chromogranin and synaptophysin with weak staining for insulin. Post-operatively, there have been no further hypoglycaemic episodes.

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WH7

A rare cause of funny turns and weight gain

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Introduction
Symptomatic hypoglycaemia unrelated to the treatment of diabetes is rare. As symptoms of hypoglycaemia are non-specific, investigation should only be instigated if Whipple's triad can be fulfilled- signs and symptoms of hypoglycaemia, a recorded low plasma glucose and resolution of symptoms after treatment.
Case history
A 37 year-old woman presented to the emergency department with fatigue and lightheadedness. She has modified her diet to alleviate her symptoms and gained over a stone. She has a daughter and family history of Type 1 and Type 2 diabetes but has no access to diabetes medications or insulin. She has no family history of Multiple Endocrine Neoplasia (MEN). Blood glucose recorded during admission was 1.6 mmol/l. After treatment, her symptoms resolved rapidly. Two fasting samples of glucose done by her own GP were 3.6 mmol/l and 1.8 mmol/l. Further investigations showed early morning cortisol of 465 nmol/l, calcium 2.71 mmol/l (2.2–2.6), parathyroid hormone of 13.2 pmol/l (1.3–6.85), IGF-1 48.9 nmol/l (14–37), normal prolactin and thyroid function. She was admitted for a 72-h fast and developed hypoglycaemia just after 12 h with blood glucose of 2.1 mmol/l. Insulin and c-peptide at the time were inappropriately elevated, 3.3 mu/l (<3)

and 0.36 nmol/l (<0.2) respectively. Although insulin was only mildly elevated, proinsulin was markedly elevated at 72 pmol/l (<5). Serum sulfonylurea screen and insulin antibodies were negative. CT scan revealed well-defined low attenuation lesion in the superior aspect of the head of pancreas measuring 5×3 cm and incidental left adrenal adenoma. MRI pancreas showed multi-focal pancreatic lesion and PET scan showed metabolically active pancreatic lesion with no metastases. Further testing showed negative urinary metadrenalines, elevated chromogranin A 71 pmol/l (0–59) and chromogranin B 173 pmol/l (0–149) which is consistent with neuroendocrine tumour. She has multiple conditions compatible with a diagnosis of MEN-1 and genetic testing for MEN-1 was positive. She is currently awaiting total pancreatectomy and further work up of her primary hyperparathyroidism and pituitary imaging will be required.

Discussion

An insulinoma is the commonest endogenous cause of hyperinsulinaemic hypoglycaemia and second most common pancreatic islet cell tumour associated with MEN-1. Patients with insulinoma should receive counselling for potential lifelong requirement for insulin after pancreatectomy. MEN-1 is autosomal dominant with high penetrance and the finding of this mutation has implications on the patient and family members who will require screening for associated tumours.

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WH8

Multiple endocrine neoplasia type 1: Can we talk about day-to-day 'routine' patients?

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A 35-year-old patient was referred to a tertiary referral unit for further investigation of severe watery diarrhea. Infectious agents had already been excluded. Biochemistry revealed a strikingly raised serum calcium concentration of 4.09 mmol/l (NR 2.1–2.65 mmol/l), chromogranin A was grossly elevated at 293 U/l (NR 2–18 U/l) and vasoactive intestinal peptide (VIP) was also raised at 130 pg/ml (NR 10–60 pg/ml). Computed tomography (CT) of the abdomen demonstrated an eight-centimeter mass in the body of the pancreas which led to the working hypothesis of a VIP producing neuroendocrine tumour as the cause of this patient's condition. Molecular genetic testing showed a deletion of 4 base pairs in exon 2 resulting in a termination of the Menin protein at codon 116, leading to a diagnosis of MEN1, with a suspected VIPoma and primary hyperparathyroidism. Screening for other manifestations of MEN1 did not reveal any pituitary abnormalities, however genetic testing of family members revealed that the patient's 9 year old son carried the same mutation. As a bridging therapy to surgery somatostatin-analogues were administered which led to a cessation of diarrhea and allowed the patient to undergo a total pancreatectomy. Histology demonstrated VIP-positivity in the known tumour and numerous other neuroendocrine tumours throughout the organ. All tumours were graded as G1, with lymph nodes unaffected. After recovery the patient underwent bilateral neck exploration with subtotal parathyroidectomy. Intraoperatively an incidental lymph node metastasis of papillary thyroid cancer was found in the central neck on frozen section; adequate surgery for the thyroid malignancy was therefore performed in the same session. The patient has been followed up for over 10 years with infrequent biochemical and radiological investigations every two to three years. Screening 7 years post-diagnosis did not reveal any new manifestations of MEN1, however, when he next attended for screening, nine years post-diagnosis, a new incidental 7-centimeter mass arising from the left adrenal was demonstrated on CT. The patient went for surgery and histology confirmed adrenocortical carcinoma. Follow-up scans have not shown any residual or recurrent disease 18 months after surgery. This case demonstrates that patients with MEN1 may not necessarily present with the classical manifestations of the syndrome, 'occult' tumours may be found incidentally on screening and may develop after patients have been disease-free for years. Life-long regular biochemical and radiological screening of MEN-1 patients is therefore necessary to improve morbidity and mortality in this patient group.

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WH9

Persistant hypoglycaemia post bariatric surgery

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Postprandial Hyperinsulinaemic Hypoglycaemia reportedly occurs in 0.1 to 0.3% of patients after Roux-en-Y Bypass procedures. In our Bariatric Surgery Service we seem to be seeing this complication more frequently. Most patients can be managed in a step-wise approach, but we have a few patients who appear refractory to conventional treatment. This case illustrates one such patient. Mrs P was referred to the Weight Management service in 2011, aged 45. She weighed 108 kg, with a BMI of 40 kg/m^2. She had type 2 diabetes, but no other past medical history and was working in a high profile job. A Roux-en-Y bypass was performed in November 2011, with no immediate complications. She successfully lost 25% of her body weight and by April 2012 weighed 79.2 kg. Towards the end of 2015 she was re-referred with symptoms of severe fatigue, poor concentration and mood changes. She had been signed of sick by occupational health. Investigations revealed no evidence of anaemia, or vitamin deficiency and a normal cortisol response to synacthen. Treatment with a course of thiamine and Pabrinex initially improved her symptoms but they then returned. Despite denying symptoms of dumping syndrome and hypoglycemia, a decision was made to proceed with Continuous Glucose Monitoring (CGM). This revealed hypoglycaemia 2–3 hours after meals. A clinical diagnosis of hyperinsulinaemic hypoglycaemia was made and she was referred to the dietitian. Changing her diet initially improved her symptoms but they then returned. Acarbose and diltiazem were next tried without success. Liraglutide, followed by octreotide, were then trialled, which resulted in only temporary improvement. Due to the persistence of her hypoglycaemia a CT-pancreas, 72 h fast & octreotide scan were performed ruling out an insulinoma. In early 2017 she successfully returned to work on Prednisolone, quick-acting insulin with meals, Octreotide and with a CGM funded through exceptional funding. In the last 3 months however, her hypos have returned and she has had to take early retirement. Her most recent CGM download shows she spends 19% of her time with a blood glucose <4 mmol/l and 5% <3 mmol/l. She is adamant that she does not want further surgery. Various options have now been discussed including trialing a dual insulin and glucagon pump. This case illustrates the devastating effects that Hyperinsulinaemic Hypoglycaemia can have on someone's quality of life. More evidence is needed to support new treatments to reduce hypoglycaemia in this cohort of patients who appear refractory to conventional therapy.

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WH10

Insulin independent hypoglycaemia in malignancy: An unusual case

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Hypoglycaemia is often referred to Endocrinology for investigation and management. Occasionally, these referrals are in the context of malignancy and we seek to exclude ectopic insulin secretion, as well as other causes. This case highlights a less recognised cause for hypoglycaemia in haematological malignancy. The patient, a 78 year-old man with advanced Mantle Cell Lymphoma presented with hypoglycaemia and was admitted under Haematology, who had been treating with chemotherapy. Alongside profound hypoglycaemia (glucose), his biochemistry showed significant lactataemia (18 mmol/l). He was treated with intravenous Dextrose and, whilst euglycaemic, remained asymptomatic and well. The patient had Type 2 diabetes and was treated with Metformin, however his biochemical derangement persisted despite discontinuing this. Investigations excluded insulin hypersecretion as a cause; Addison's disease (cortisol >350 nmol/l), acute liver failure (no other features), tumour lysis syndrome (urate normal) and rapid tumour progression (assessed via CT scan) were also excluded. Of note, both his glucose and lactate levels normalised following further chemotherapy implying a correlation between the tumour load and the biochemistry. The patient remained intermittently dependent upon IV dextrose until his eventual death. It has been hypothesised that anaerobic metabolism of glucose by the highly metabolically active tumour cells resulted in both hypoglycaemia and markedly elevated lactate levels. There is some evidence in the literature to support this as similar presentations have been reported in the past. This case provides a presumed further example and may encourage others to consider this process as a differential in patients with haematological malignancy, significant tumour load, hypoglycaemia and lactic acidosis.

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WH11

Pancreatic Neuroendocrine tumor - would you recognise it?

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Pancreatic neuroendocrine tumors are rare neoplasms of this organ. The majority of them are tumors without hormonal activity. Approximately 35% of the pancreatic neuroendocrine tumors (pNETs) are functional, the most common of which is an insulinoma. We present a 57 year old lady with dyspepsia, nausea and Fe deficiency anaemia for more then a year. On examination had a epigastric mass, endoscopy was consistent with a well differentiated endocrine grade 2 tumor. Octeotide scan showed increased uptake. CT abdomen: large enhancing mass with calcification extending from pancreas to stomach, spleen and portal vein. Discussed with wessex carcinoid MDT. Underwent a left upper quadrant clearance: Total gastrectomy, distal oesophagectomy, pancreatectomy, spenectomy, Roux-en-y reconstruction, portal vein resection and anastomosis. Histology confirmed a well differentiated pancreatic endocrine carcinoma with nodal, vascular and perineural invasion, staging PT3N1R1 excision. Post operatively developed diabetes, hypo unawareness, and malnutrition, treated with insulin pump and dexcom G4 CGM and high dose creon. Timely and right intervention saved patients life. We would like to emphasize that in this case Octeotide imaging & contrast CT can be effectively helpful especially in conjunction with other useful diagnostic methods which are handled in pancreatic tumor's. We put emphasis on corrected and extended histopathological report which determines further management according to prognostic and prediction factors of patients with neuroendocrine pancreatic tumor.

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Additional Cases

CB1

Hyperthyroidism in an elderly patient with normal thyroid on USS, negative antibodies and dilemma following liver toxicity

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An 82 year old lady was admitted with acute stroke on 3/1/18, confirmed on MRI. She was found to be in AF and had thyroid function tests checked on 4/1/2018, with TSH 0.01 (0.27–4.20) mIU/l and FT4 52.8 (12.0–22.0) nmol/l. She was commenced on Carbimazole 20 mg OD. TPO and TSH-receptor antibodies were both negative. An ultrasound scan confirmed a normal thyroid without any features of Grave's disease or thyroid nodules. Clopidogrel 75 mg OD and Atorvastatin 40 mg ON were also started. She was discharged on 17/1/2018, to a rehabilitation unit for further physiotherapy input. She progressed satisfactorily, but on routine bloods done on 26/1/2018, she was found to have acutely deranged LFTs, with ALP 700 (35-104) IU/l (81 on 5/1/2018), ALT 147 (10–35) IU/l (12 on 5/1/2018), bilirubin 6 (0–20) μmol/l (7 on 5/1/18). The patient was clinically well. Her statin was discontinued, but she remained on Clopidogrel 75 mg OD and Carbimazole 20 mg OD. She was re-admitted on 29/1/2018 for further investigations. ALP had improved slightly to 522 IU/l, ALT 52 IU/l and Bilirubin 4 μmol/l. The γ-GT was 949 IU/l. The liver ultrasound showed a thin-walled gallbladder with a 1.5 cm gallstone and it was felt that this was most likely a cholestatic picture due to a passed gallstone in view of rapid resolution. By 29/1/2018, TSH was 0.60 (0.27–4.20) mIU/l and FT4 16.3 (12.0–22.0) nmol/l just over 3 weeks after commencing Carbimazole 20 mg OD. There is suspicion that this may have been Thyroiditis (not contrast-related as CT-angiogram on 3/1/2018 and deranged TFTs on 4/1/2018). Given the recent history of AF and stroke, she was continued on Carbimazole but at a much reduced dose of 5 mg OD. She has returned to the rehabilitation unit and remains clinically well. Given the patient had been recently commenced on a number of medications with potential effects on liver function, including statins (hepatitis; jaundice; hepatic failure) and clopidogrel (hepatitis and acute liver failure), as well as Carbimazole (cholestatic jaundice) there was a dilemma about how to proceed, especially given that an alternative option would be PTU (hepatitis; hepatitic disorders; hepatic failure; hepatic necrosis) that would be potentially much more toxic to the liver. On balance, it was felt that given that statins offer more secondary prevention than short-term therapy, it would be safer to discontinue atorvastatin and monitor closely as well as arranging urgent imaging.

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CB2

Diagnosis and management of male hypogonadism

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Gonadism is a medical term for decreased functional activity of the gonads (ovaries or testes) producing hormones and gametes. Male hypogonadism is characterised by a deficiency in testosterone – a hormone critical for sexual, cognitive and body function as well as development. Low testosterone levels can be due to hypothalamic, pituitary or testicular abnormalities. Hypogonadism is classified as primary (primary testicular failure) and secondary (a problem in the hypothalamus or the pituitary gland). Diagnosis requires the presence of symptoms and signs suggestive of testosterone deficiency as well as biochemical evidence. A testosterone level above 12 nmol/l does not require replacement. Patients with testosterone levels below 8 nmol/l will usually benefit from treatment. We present the case of a 58-year-old father of two referred to clinic with a one-year history of erectile dysfunction, reduced libido, absence of morning erections and gynaecomastia. He had a past medical history of hypertension and hypercholesterolaemia. Of note, the patient had been under significant stress relating to the breakdown of his marriage. His blood tests showed vitamin B12 270 ng/l, haemoglobin A1C 41 mmol/mol, serum follicle stimulating hormone 86 IU/l (0–19), serum luteinising hormones 25.9 IU/l (1.2–8.6), ferritin 53 μg/l, prolactin 247 mIU/l, serum testosterone 5 nmol/l, normal thyroid function tests/urea and electrolytes/full blood count/liver function tests and prostate specific antigen. On review in clinic, the patient weighed 90 kg with an elevated blood pressure 147/79 mmHg and pulse rate 86 beats per minute (regular). On examination, he had bilateral non-tender gynaecomastia and small volume testes without any palpable masses. An ultrasound (US) testes confirmed small volume testicles (right testicular volume 3 ml, left testicular volume 4 ml) with a hypoechoic avascular lesion in the right testicle measuring 3.9×3.1×3.1 mm. The patient was referred for urology review and repeat scrotal US in 3 months for interval assessment of the lesion. The patient was diagnosed with primary hypogonadism with a plan to initiate testosterone replacement therapy (the primary treatment option). Current guidelines on the management of sexual problems in men advocate pre-treatment assessment to rule out prostate cancer in men over the age of 40 years. Men with erectile dysfunction and/or diminished libido and documented testosterone deficiency are candidates for testosterone therapy once a diagnosis of hypogonadism is confirmed. After the initiation of therapy, total testosterone, sex hormone binding globulin (SHBG) and albumin levels should be monitored. The aim of therapy should be a total testosterone level of at least 15 nmol/l.

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CB3

A case of asymptomatic hypocalcaemia...

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We present a case of a 54-year-old man who was urgently referred to A&E by his general practitioner with very low calcium of 1.32 mmol/l (normal 2.20–2.60 mmol/l). His only past medical history of note was of recently diagnosed multiple sclerosis (MS), which presented as optic neuritis six months ago. His initial investigations included high phosphate level of 2.0 mmol/l (normal 0.8–1.5), normal vitamin D levels (76 mmol/l) and a very low 24-hour urine calcium of less than 2.2 mmol/24 hours (normal 2.5–7.5). His PTH levels were undetectable i.e. <0.3 pg/ml (normal 1.6–7.2), confirming primary hypoparathyroidism. As no underlying cause was found, this was labelled as idiopathic hypoparathyroidism. Calcium was replaced intravenously initially and the patient was discharged on oral calcium supplements, aiming to keep the calcium in the lower normal range. Interestingly, after noting his new diagnosis of primary hypoparathyroidism, neurologists reviewed their earlier diagnosis of MS. As his lumbar puncture results were normal including negative oligoclonal bands, his MRI scan which had shown generalised white matter changes, was discussed in neuroradiology MDT, who thought that these changes were likely secondary to chronic hypocalcaemia rather than MS. Therefore the diagnosis of MS was reversed. Although papilloedema and raised intracranial pressure have been reported with hypoparathyroidism in the literature, optic neuritis has been very rarely reported, (1) however there could be an association between the two conditions.

Reference

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CB4

Curious case of hypercalcemia in pregnancy

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Hypercalcaemia during pregnancy is unusual and primary hyperparathyroidism is the commonest cause: we present a more unusual case.

Case history

29-year woman, 34 weeks pregnant, was admitted with hypertension and oedema. She had gestational diabetes managed with diet alone. Initial calcium level was normal; it gradually increased in the next few days though this was not noted. She was diagnosed with preeclampsia and treated with steroids for foetal lung maturation. Calcium level normalized after steroids but on the day of delivery was 2.74. She had an induced vaginal delivery at 35 weeks. Six days later she was readmitted due to high blood pressure. Calcium on admission was 3.09. This was treated with iv fluids and then, when calcium rose to 3.19, a dose of pamidronate. She felt well and her only symptom was constipation. Examination was normal except for a flow murmur. Calcium fell into the normal range 2 weeks after pamidronate and remained normal subsequently. She was on 400 units of Vitamin D supplements as per RCOG guidelines, during pregnancy.

Investigations

PTH was 12 (15–60) and 25-OH vitamin D was 115.8 reflecting supplementation. Serum ACE was normal A PTHrP was undetectable, however this was taken

21 days after delivery. A low dose CT scan of chest Abdo-pelvis was done to rule out occult malignancy: this was normal except focal thickening of the gall bladder wall which ultrasound suggested was adenomyomatosis.
Results and treatment
Calcium remained normal during puerperium after treatment with a single dose of pamidronate.
Conclusions and points for discussion
A diagnosis of humoral hypercalcaemia of pregnancy was made in this case based on the acute rise in late pregnancy, suppressed PTH, and no malignant cause found. We feel vitamin D toxicity is less likely as she was not on high dose of Vitamin D supplementation. Vitamin D binding protein levels increases during pregnancy showing elevated levels of 25(OH)Cholecalciferol. Placental PTHrP production is thought to drive this unusual condition: unfortunately, we could not test PTHrP during the puerperium. Recurrence risk for this condition is not known and we have recommended monitoring of calcium levels in her next pregnancy.

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CB5

Post-operative hypocalcaemia in a patient with a metastatic pancreatic neuroendocrine tumour

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Case history
Mrs SC, a 56 year old female was referred to the endocrine registrar with hypocalcaemia (corrected calcium 1.93 mmol/l). She was day 3 post-hemihepatectomy for liver metastases from a primary pancreatic tail neuroendocrine tumour (NET). She had paraesthesia and numbness of her fingers and toes but no spasms. Chvostek's sign was negative and there were no ECG changes. Past medical history includes severe hypercalcaemia in September 2016 which was found when she presented acutely with abdominal pain. CT abdomen done as a part of the work-up showed a 4.5 cm lesion in the tail of the pancreas and 3× liver metastases, which was subsequently confirmed to be a primary pancreatic NET on SRS octreotide scan and biopsy. She had an open distal spleno-pancreatectomy in 2017 for resection of the primary tumour. Aside from this she had previous breast cancer (in remission) and oesophagitis. Drug history: Octreotide 200 µg TDS S/C, Cinacalcet 30 mg BD, Alendronic acid 70 mg weekly and Colecalciferol 800 IU OD.
Investigations
At diagnosis (09/2016)
Corrected calcium: 4.01 mmol/l (NR 2.1–2.58)
Phosphate: 0.63 mmol/l (NR 0.8–1.4)
PTH: $<$0.6 pmol/l (NR 1.1–4.2)
PTHrP: 3.2 pmol/l (NR $<$1.9)
25-hydroxy vitamin D: 24 nmol/l
eGFR: $>$60 ml/min per 1.73 m^2

Pre-operative (29/12/2017)
Corrected calcium: 2.50 mmol/l
PTH: 0.8 pmol/l
25-hydroxy vitamin D: 27 nmol/l

Day 3 post-operative (5/1/2018)
Corrected calcium: 1.94 mmol/l
Phosphate: 1.46 mmol/l
Magnesium: 0.80 mmol/l (NR 0.7–1.0)
eGFR: $>$60 ml/min per 1.73 m^2
Treatment
The sudden post-operative hypocalcaemia was due to loss of PTHrP secretion after removal of the liver metastases. This confirmed the suspicion that her initial hypercalcaemia was due to PTHrP secretion from a NET, which has been described in case reports. This paraneoplastic syndrome tends to occur with metastatic pancreatic NETs and is often responsive to somatostatin analogue therapy or peptide receptor radiotherapy causing hypocalcaemia. In the acute setting, she was given IV calcium gluconate until her calcium increased to $>$2.1 mmol/l. The Cinacalcet and Alendronic acid was stopped and she was started on Adcal D3 2 tablets TDS. Her calcium on discharge was 2.19 mmol/l.
Conclusions and points for discussion
This is an unusual case of a PTHrP secreting metastatic pancreatic NET causing hypercalcaemia initially and then hypocalcaemia after surgical resection. It is important to monitor calcium levels closely in such patients in the post-operative period.

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CB6

A case of primary hypoparathyroidism with hypocalcaemia

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A 55-year-old man known primary hypoparathyroidism, presented with recurrent episodes of collapses. Past Medical history of CVA, Recurrent episodes of collapse, Secondary Polycythaemia. His S Calcium ranges from 1.5 to 1.7. Not always symptomatic. Occasionally, c/o pins and needles. But having recurrent episodes of collapses with loss of consciousness. Each Episode lasts for 10 to 15 seconds. This is going on for more than 15 years. In 2013 his Calcitriol supplement was increased and eventually, he developed AKI with Hypercalcaemia. His calcium gradually came back to his baseline of 1.6 after 3 months but his kidney function took more than 2 years to come back to normal. At that time, he was under the Nephrologist. Usually, he is on Calcitriol 1.5 µg twice daily with Calcium supplements. According to the patient, he is compliant with medication. The Neurologist has also reviewed him for his recurrent collapses, but no diagnosis could be confirmed. MRI head: Established right frontal lobe and left periventricular infarcts. The patient is very reluctant to increase his Calcitriol dose as it may impair his renal function. His current blood test shows S Ca-1.7, Normal U&E's with PTH-19.9. Still having recurrent episode of collapses with LOC. He is also known to have secondary polycythemia with repeated venesection. He is under the hematologist.
Questions for the panel:
1. Are these collapses related to Hypocalcaemia?
2. How can we get the calcium to normal level as there were an episode of AKI with hypercalcemia
3. Was the AKI related to Hypercalcemia?

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CB7

A case of hypercalcemia with normal 25-OH vitamin D levels, post-treatment with high dose cholecalciferol for low vitamin D levels

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79 year old male had been admitted due to multiple falls within a space of 24 hours. On admission, he had a full set of bloods which showed hypercalcaemia and no other significant abnormality. His past medical history included Prostate Cancer, Type 2 Diabetes and Urinary retention for which he had a long-term catheter *in situ*. His current medications were Linagliptin, Apixaban, Bicalutamide and simple analgesia. Initially, he was fluid resuscitated, which seemed to improve his calcium slightly but his calcium levels remained well above 3 despite fluid rehydration so he went on to have intravenous Pamidronate as per trust protocol. Despite this his calcium levels stayed above 3 mmol/l even after 48 hours, so he went on to have a 2nd dose of Pamidronate which also had little effect on his calcium level.
Urine BJP- Negative
Serum protein Electrophoresis- Negative
Serum ALP – 68 IU/l
HB 128 g/l
ACE level – 38U/l (8-52)
Normal SST
TSH 5.1 mIU/l
T 4-15.3 pmol/l
PSA – 3.5 µg/l
PTH (on admission) – 1.4 pmol/l (1.6–6.9)
Total Vitamin D 63 nmol/l
Adjusted Calcium 3.27 mmol/l (on admission) (2.2–2.6)
CT Chest/Abdomen/Pelvis – No evidence of Malignancy
Missing link?
During a recent admission, he had a Vitamin D level checked and found to have very low levels. He was loaded on 50 000 Units of Cholecalciferol and was discharged with instructions to take 50 000 units once a week for 5 weeks. However, he was back in the hospital within 3 weeks of discharge and his Vitamin D box was empty. Looking through this patient's previous calcium levels it was noted he had never had high calcium levels and in fact, if anything at times it was low prior to admission. However, Vitamin D levels at 63 nmol/l they were certainly not very high. We went on to check a 1,25 OH vitamin D level. This level came back at 199 pmol/l (55-139) which was much higher than the normal range.

Discussion
A normal CT scan, as well as a negative serum protein electrophoresis and negative urine BJP, excluded malignancy as a possible cause of his hypercalcaemia. A suppressed PTH at admission prior to treatment also excluded Hyperparathyroidism as a cause. In conclusion, this was a patient with hypercalcaemia due to Vitamin D toxicity with normal serum 25-OH Vitamin D levels and raised 1-25 OH Vitamin D levels.

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CB8

Peripartum calcium conundrum in a lady with pseudohypoparathyroidism

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Pseudohypoparathyroidism during pregnancy can lead to challenging calcium fluctuations and can lead to maternal and foetal morbidity. There are limited case reports and no established management guidelines. Maintaining calcium level in healthy range during pregnancy is required to minimise the risks of associated complications. We report a case of Pseudohypoparathyroidism type 1a in 30 year old lady, who was initially referred to us by her general physician with calcium, of 1.63 mmols/l, raised phosphate levels of 1.71 mmols/l and raised parathyroid hormone; she volunteered the symptoms of feeling non-specifically tired for few years, and it was only over the last few months that she had experienced carpopedal spasm and symptoms that would relate specifically to hypocalcaemia. On examination she had a short stature, rounded face and a short 5th metacarpal; all indicating pseudohypoparathyroidism type 1a. She had no evidence of subcutaneous calcification and the rest of the examination was unremarkable. She was referred for genetic counselling and was started on Alfacalcidol and Sandocal to improve her symptoms, MRI brain was arranged as she mentioned balance issues which revealed symmetrical pathological mineralisation of the globi pallidi, heads of caudate nuclei and cerebellar dentate nuclei. In due course she conceived spontaneously and maintaining calcium in optimum range became even more challenging then pre-conception. Her Alfacalcidol was increased to 1.5 µg BD. She was seen in joint endocrine anti-natal clinic and was found to have high blood pressure and her USS revealed polyhydramnios and had to be given IV Calcium Gluconate to optimise the calcium levels, despite fluctuating calcium levels she delivered a healthy female baby at term but her calcium was ever so resilient it plummeted to 1.58 mmols/l two months after delivery, despite being non-lactating mother. Her Alfacalcidol was increased to 1.5 µg TDS in order to raise the serum calcium. This case highlights the implications of mother's conditions on developing foetus and re-emphasises the importance of close monitoring not only during pregnancy but also in post-partum period and necessitates the genetic workup of new born.

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CB9

An unusual case of hypocalcaemia

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Case history
A 34 year old Chinese male was referred by GP as routine blood test which was done as part of investigation for ongoing hair loss that revealed hypocalcaemia. Patient was asymptomatic with no tingling sensation, numbness or anaesthesia. There was no history of carpopedal spasm, muscle pain or cramps. He does not give any history of symptoms suggestive of malabsorption. His PMH include Mild asthma and Eczema for which he was not on any regular medication. Social history of note he lives with his parents and have no partner. He works in IT and stays mostly indoors. He does not smoke or drink alcohol. There is no family history of problem with calcium or any bony deformity. On examination Chvostek's and Trousseau's sign was negative. No bony deformity noted. Systemic examination was essentially normal.
Investigations
FBC- Normal, Normal renal function, Adjusted calcium- 1.57, PTH 75.7, Phosphate 1.0, Magnesium 0.81, Vitamin D 16.ALP 117 TSH 2. ECG-Normal sinus rhythm and QTc. Vitamin B12, folate and ferritin- Normal.
Results and treatment
The results supported a clinical diagnosis of secondary hyperparathyroidism due to vitamin D deficiency. Patient was started on Cholecalciferol 40 000 units once a week for 8 weeks then 20 000 units once a week for 8 weeks. He was also started on Calcium carbonate 1000 mg three times daily for 3 months. Patient was subsequently followed up in the endocrine clinic for 2 years where he missed couple of his appointments. His Vitamin D level normalised after initial replacement and remained between 71 to 87. His Adjusted calcium remained low between 1.9 and 2. The patients PTH remained high and was 24.2. After initial vitamin D replacement patient was on Cholecalciferol 10 000 units OD and Calcichew 2 tablet daily which was continued for 2 years with patient denying any compliance issue. His most recent blood test showed PTH 15.5, Adjusted calcium 2.1 and Vitamin D 135. All other biochemical test was normal.
Discussion
Differential diagnosis includes 1) Hypocalcaemia due to Vitamin D deficiency with secondary hyperparathyroidism or Pseudohypoparathyroidism Type 2 or 1b.Point for discussion-1) Is there any other test will be helpful to confirm the diagnosis like PTH infusion and measurement of urinary cAMP(where done in UK) or Xray hand or measure 1 25 OH Vit D and genetic test for Pseudohypoparathyroidism. 3) Is there any other treatment that can achieve normocalcaemia like alpha-calcidol.

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CB10

A 60 year history of recurrent hypoglycaemia

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A 69 year old male was referred with a 60 year history of recurrent hypoglycaemia. Over the previous 12 months he had several episodes of severe hypoglycaemia, which necessitated emergency treatment from paramedics. He had been diagnosed with a hypoglycaemic disorder at the age of 9 years, but no underlying cause had been identified. He had no other previous history of note, though he was macrosomic at birth with a birth weight of approximately 5.9 kg. His mother was diagnosed with diabetes shortly after delivery. His maternal grandmother also had diabetes. The patient's younger son was diagnosed with diabetes aged 33 and was treated with metformin; he was not overweight. His son weighed approximately 4.3 kg at 38 weeks and had issues with hypoglycaemia after birth. The patient was fitted with continuous flash glucose monitoring which confirmed interstitial glucose levels below 4 mmol/l virtually every night and sometimes unrecordable levels associated with symptoms of hypoglycaemia. Genetic testing confirmed that both the patient and his son were heterozygous for a pathogenic nonsense mutation (c.421C>T;p.(Arg141*)) in exon 4 of the *HNF4A* gene. The patient was commenced on Diazoxide therapy which had a transformative effect and abolished all episodes of severe hypoglycaemia. In offspring with *HNF4A* mutations birth weight is increased by an average of 700 g, and 50% are born macrosomic. Transient neonatal hyperinsulinaemic hypoglycaemia is reported in 10% of cases. After a period of normoglycaemia Maturity Onset Diabetes of the Young (MODY) develops in adolescence or early adulthood and is sensitive to low dose sulfonylurea therapy. Our patient's phenotype of severe hypoglycaemia in adulthood without diabetes is not one that has been previously described. There are reports of two other families with this nonsense mutation; one family had no history of hyperinsulinaemia and the other proband had a child with macrosomia and transient neonatal hypoglycaemia. Nonsense mutations in *HNF4A* are not expected to have a genotype-phenotype correlation since they will result in degradation of the *HNF4A* mRNA transcript as a result of nonsense-mediated decay. However, the severity and duration of hypoglycaemia can be highly variable in individuals with different *HNF4A* mutations due to other modifying genetic effects and environmental factors. This very unusual case highlights that some genetic causes of neonatal hypoglycaemia can be associated with diabetes or hypoglycaemia in later life or in other family members and detailed family history and genetic studies can prove useful in establishing the diagnosis.

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CB11

Spontaneous hypoglycaemia in an elderly man with suspected bladder cancer

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An 87 year old man was referred to our endocrine service from the medicine for the elderly team for investigation of suspected hypoglycaemia. He had several

co-morbidities but did not have diabetes mellitus. There was a 6 month history of 'funny episodes' characterised by lethargy, profuse sweating and confusion. The symptoms resolved a few minutes after eating. One such episode occurred while attending his GP who arranged for blood to be drawn. The plasma glucose was 1.9 mmol/l hence satisfying Whipple's triad. A CT chest, abdomen and pelvis performed prior to referral to investigate unexplained weight loss revealed an endoluminal lesion in the bladder thought to represent a localised tumour as well as pleural thickening (secondary to asbestos exposure) and a possible small left sided empyema. Considering the patient's relative frailty and already proven hypoglycaemia, it was decided to arrange an immediate inpatient stay on our ward to complete the necessary investigations. A short Synacthen test showed a peak cortisol of 1008 nmol/l thereby excluding adrenal insufficiency. A few hours into an overnight fast he became hypoglycaemic and blood drawn at the time demonstrated hyperinsulinaemic hypoglycaemia – plasma glucose 1.8 mmol/l, insulin 36 mU/l (ref. range 3–17) and c-peptide 3.19 nmol/l (0.36–1.12). The sample was delayed in reaching the laboratory for at least a few hours which may have led to degradation of insulin and c-peptide prior to analysis. The elevated results, however, still supported a diagnosis of endogenous insulin excess. The respiratory physicians reviewed his radiology and attempted an US-guided pleural aspiration but the tap was dry. The patient was followed up as an outpatient thereafter. A follow-up CT scan showed no change in the thorax but did reveal a 13 mm rounded lesion in the tail of the pancreas possibly representative of a small insulinoma. Investigation by our urology colleagues confirmed a high-grade transitional cell carcinoma of the bladder. This was successfully treated with intravesical BCG immunotherapy. Due to the patient's frailty and wish not to undergo surgery, the hypoglycaemia has been successfully managed with diazoxide alone. This case demonstrates a (probable) insulinoma in an elderly patient presenting with spontaneous hypoglycaemia. Insulinoma has been described at the extremes of age and cannot be thought of exclusively as a condition of middle age. The case also highlights the need to investigate and manage patients taking into account their own wishes and co-morbid state.

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CB12

Recurrent hypoglycemia, post sleeve gasterectomy, new approach

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A 29 years old lady she has Diabetes mellitus type II, and obesity so she did sleeve gasterectomy and she was happy that her sugar was well controlled then later in complete remission. She has later recurrent symptomes of hypoglycemia and intloerable,when Hba1c done was hab1c 6.8%. She was started on Glucobay tablet 50 mg before each meal. Next visit she come, she was happy that her sugar is well controlled with treatment but her medicines is finished. After requiring how many tablet she took per day she was using before every simple meal or snack and total of 6–10 tablet per day. Her Hba1c was 6.1. She was tolearting 10 tablet per daywith out troubles.
Q1, how many times we prescribe Glucobay per day to be allowed?
Q2, studies of symptomatic hypoglycemia post sleeve should be employed.
q2 whether should give limit of tablet of Glucobay precribed.

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CB13

Insulinoma – atypical response to tests and uncommon adverse effects to medical treatment

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Background
Insulinoma is the most common cause of hypoglycaemia due to endogenous hyperinsulinemia. However, they can sometimes present with atypical features. Some of the patients can also develop serious adverse effects to medical treatment. We present a case with atypical features and further developed serious adverse effects with medical treatment for insulinoma.

Case presentation
A 42-year-old Caucasian female presented with recurrent episodes of weakness and confusion, increasing in frequency for 5 years. She was previously diagnosed with type 1 vasovagal syncope, cephalic migraine and temporal lobe epilepsy for these symptoms; none entirely explaining the whole phenomenon. Patient's capillary glucose incidentally measured during one such episode was 1.9 mmol/l and hence referred to the endocrine department for further evaluation. There was no history of chest pain, palpitations, presyncope or syncope during these episodes. There were no specific triggers or relationship with meals. Apart from Parkinson's disease in some family members, rest of the medical history was unremarkable.On examination, the patient was hemodynamically stable and clinically unremarkable with a BMI of 20.9 kg/m^2. 24-hour fasting test demonstrated low but detectable levels of insulin (14 pmol/l) and c-peptide (121 pmol/l) with suppressed ketones (0.2 mmol/l) while the patient was hypoglycemic (2.2 mmol/l); sulphonylurea screen was negative. However, the patient had abnormally high insulin (187 pmol/l), c-peptide (1797 pmol/l) with hypoglycaemia (2.2 mmol/l) during mixed meal test. Rest of the endocrine hormonal assessment including gut hormone profile was within normal limits. CT scan of her abdomen revealed a 4.0×3.1 cm mass within the head and uncinate process of the pancreas.
Management and outcome
Patient developed a severe rash with diazoxide and life-threatening hypoglycaemia with octreotide when used as medical treatment for insulinoma. Medical therapy was hence discontinued and the patient went on for surgical resection of the mass following discussion with the neuroendocrine multidisciplinary team. Histology confirmed benign insulinoma and patient reported no further hypoglycemic episodes since the surgery. Genetic testing was not considered as this was a single lesion with normal serum calcium and no family history of neck operations.
Conclusion
Detectable levels of endogenous insulin with severe hypoglycaemia should prompt further investigations to rule out insulinoma. One should consider a possibility of insulinoma with an exaggerated insulin response to a mixed meal test. A close watch is recommended when patients are initiated on medical treatment for insulinoma.

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CB14

Insulinoma – a cause of recurrent hypoglycaemias

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A 72 year old lady presented to endocrine clinic in January 2016 with a history of frequent episodes of feeling increasingly lightheaded, tremulous, sweaty and hungry. All symptoms resolved after eating. Her family doctor had twice documented a capillary glucose lower than 4 mmol/l. Continuous blood glucose monitoring was performed but there were no episodes of hypoglycaemia picked up. She was admitted for a 72 h fast in September 2016. Her capillary blood glucose readings never dropped to below 2 mmol/l during the test. At the end of the fast, a plasma glucose, insulin, C peptide, pro insulin, beta hydroxybutyric acid levels and urine for sulphonylurea were taken revealing:
Fasting Glucose: **2 mmol/l** (3.88–6.38 mmol/l)
Insulin: **7.8 μU/ml** (2.6–25 μU/ml)
C peptide: **1.5 ng/ml** (1.1–4.4 ng/ml)
Pro Insulin: **12.1 pmol/l** (<11 pmol/l)
Beta hydroxybutyric acid: **1687 μmol/l** (Up to 270 μmol/l)
Urine for sulphonylurea: negative
These results were diagnostic of an insulinoma. Magnetic rsonance (MR) imaging of the pancreas in December 2016 failed to show any pancreatic lesions. An endoscopic ultrasound (US) of the pancreas was performed showing a 13× 6 mm hypoechoic homogenous lesion at the body of the pancreas. Pancreatic core biopsies confirmed a Grade 1 (low grade) neuroendocrine tumour. A repeat MR pancreas in May 2017 showed a 9mm focus of restricted diffusion at the junction of the body and tail of the pancreas which probably corresponding to the neuroendocrine tumour seen on endoscopic US. Subcutaneous Octreotide was prescribed to prevent hypoglycaemia. The patient underwent successful distal pancreatectomy in July 2017. Localisation of tumour was guided by on table intra-operative US. She was noted to have high capillary blood glucose readings post operatively and an oral glucose tollerance test confirmed a diagnosis of diabetes mellitus (fasting blood glucose of 10.44 mmol/l, second hour 21.9 mmol/l. She is currently managed on oral glucose lowering agents and is doing well. Insulinomas are the commonest neuroendocrine tumours. They arise from pancreatic islet cells and may secrete insulin in short bursts thus causing

rapid fluctuation in blood glucose levels. 90% are benign tumours. 5% are malignant. Diabetes mellitus is one of the main complications post operatively.

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CB15

A rare cause of elevated testosterone levels in an adult female

Shazia Hussain, Anju Sahdev & William Drake
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A 49 year old Russian lady was found to have an elevated testosterone level (9 nmol/l) when investigated for hair loss. This was first detected some years ago when she apparently was given a provisional diagnosis of polycystic ovarian syndrome. When assessed in her local endocrine unit she did not report any excessive body hair growth or symptoms of virilisation. She claimed to reach the menopause aged 45 years and reported a family history of early menopause. Initial blood tests confirmed normal adrenal androgens and sex hormone binding globulin. A plan for extensive endocrine work-up and pelvic imaging was recommended, however, the patient subsequently requested a referral to our unit for a second opinion. Here she gave a significantly different history. She reported primary amenorrhoea which had previously been investigated in Russia. Although not available for review at the time of consultation, pelvic imaging there had shown an absent uterus and possible gonadal tissue in both inguinal canals. Clinically she appeared phenotypically female with no signs of virilisation. This in combination with an absent uterus and serum testosterone levels within the male reference range would be consistent with a potential diagnosis of androgen insensitivity syndrome. This was confirmed on karyotype, which returned as 46XY. A MRI pelvis showed a normal vaginal vault but there was no cervix or uterus seen. Surprisingly, the patient was also found to have mixed ovarian and testicular tissue. Due to the risk of future malignant transformation she has been referred for a gonadectomy. Pre-operative germ cell tumour markers (AFP and HCG) have returned as mildly elevated (13.9 and 4 unit/l, respectively), although Ca-125 is within the reference range. She awaits whole body cross-sectional imaging to ensure there are no distant sinister findings or associated urological abnormalities before proceeding with surgery. This case highlights the need for careful assessment of patients with elevated androgens; some of the sensitivities that accompany the assessment of reproductive disorders; the importance of considering androgen insensitivity syndrome in adult patients as a potential differential diagnosis; and the fact that, after her gonadectomy, oestrogen replacement in this patient can be unopposed in the absence of a uterus.

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CB16

DHEA: is it fountain of youth or medical need?

Rakshit Kumar, Saba Hafeez & Anand Velusamy

We present here a case of 70 year old female, seen in endocrine clinic for Hypothalamic-Pituitary-Adrenal (HPA) axis suppression after prolonged glucocorticoid use. History revealed that she had prolonged use of prednisolone for her asthma in the past. In 2011, Prednisolone was stopped but she had to be started on Hydrocortisone replacement due to HPA axis suppression. She was taking Hydrocortisone 20 mg BD. Trials to wean her off Hydrocortisone failed due to ongoing tiredness and dizziness. She, generally, had very low energy levels and was struggling with daily activities. She had to quit her demanding job as an Event Manager. There was no other confounding medical history. Her care was transferred to us in 2015, Short Synacthen test showed inadequate response with peak cortisol level of 216 nmol/l at 60 min (normal >420 nmol/l) and ACTH <5 ng/ml (10–50 ng/ml). Other investigations for tiredness including pituitary profile, TFT, haematinics and bone profile were normal. She subsequently had a Hydrocortisone day curve that showed excess replacement of Hydrocortisone with 60 min Cortisol of 859 nmol/l. Several attempts were made to decrease her hydrocortisone dose but she failed to cope with any reductions. In October 2016, she was switched to Prednisolone 5 mg OD, as a trial therapy, but no improvement in her symptoms was observed. In April 2017, it was noticed that her Dehydroepiandrosterone Sulphate (DHEA-S) level was <0.4 μmol/l (0.9–11.6 μmol/l) and she was given a trial of DHEA 25 mg once a day. On further follow up, she reported significant improvement in her energy levels and performance. She also managed to wean her Prednisolone from 5mg to 3mg and returned to work, active as before. Although, clinical evidence is debatable, this case signifies individualised role of DHEA replacement in HPA axis suppression.

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Aslam, MW CB8
Avari, P WC3 & WF2
Aylwin, SJB OC3

Bakhit, M OC3
Bano, G OC1 & P11
Banu, Z OC5 & P07
Baple, E WD2
Bastos, F WA13
Beirne, PA P19
Berney, D OC4
Best, J P18
Beynon, J WH1
Bhake, R WD5
Bhatt, D WD3
Bidmead, J OC3
Bisambar, C P03
Bitat, S CB9
Bondugulapati, L WG1
Boot, C WH4
Brackenridge, A P18
Bravis, V P24 & P30
Brennan, C WD7
Brown, M OC2, P14, WE6 & WE7
Burgess, N P34

Calvo-Latorre, J P10
Carpenter, R WE14
Carroll, P WC2
Carty, D OC6
Chan, K P35
Charles, D WG2
Cheow, H P14
Chicco, M P30
Chika-Ezerioha, DI WF4
Chok, YL P07
Chong, ZM P41
Chung, TT P14 & P15
Church, D OC8
Clark, J P37
Colclough, K CB10
Collier, A P03
Coppack, S WE14 & WH2
Cordeiro, MC WA13
Cordiner, R OC6
Crabtree, T WH10
Cranston, T P13
Cross, S P28

Daly, S WH6
Dawson, A P29
Dede, A P13
Dhere, A OC9
Diaz-Cano, S OC3
Drake, W CB15, P14, P15, WA2, WA3, WA9, WB2, WD7, WE14, WE6, WE9, WF3 & WH3
Drake, WM WB1
Druce, M WH6
Du, Y OC7
Dunn, J WD2
Duthie, F P03
Dymott, J WE16

Ehrenstein, M OC8

Ferreira, A WA13
Field, B P37
Flanagan, D WD2
Foteinopoulou, E CB10
Fox, J P20
Francis, L P35
French, J WH4

Gannon, D P07
Garg, S OC2
George, A P38
Gibney, J WC4
Gibson, J OC6
Gilroy, M WA6 & WD2
Giulea, C WD6
Glyn, T WE12 & WH9
Goodchild, E P14 & WE6
Gorvin, CM P27
Graham, J P36
Grant, J P09
Graveling, A WD3, WE2 & WH7
Green, F WA11
Gruppetta, M WA7
Gulfam, T WH4
Gunganah, K P36
Gurnell, M P15 & P32

Hafeez, S CB16 & WC2
Halsall, D OC8, P09 & P32
Hameed, A OC1 & P11
Hannan, F P13
Haq, M OC3
Hasan, F WE17
Hassoun, S WA11
Hatfield, E P35
Hodgson, S OC1
Houlford, B WB3 & WE1
Howat, I P41
Huang-Doran, I P32
Hussain, S CB15, WA3, WD7 & WF3

Ilangaratne, C WA4, WA5 & WE4
Isenberg, D OC8
Issa, B WH1

Jacob, P WE9
Jafar-Mohamadi, B OC9
Jafar-Mohammadi, B P27, P39 & P43
James, RA WH5
Jayamanne, G CB3
Johnson, A WE17
Joshi, R OC7

Kaltsas, G CB5
Kang, S CB3
Kariyawasam, D P18
Kauser, S CB13
Kaushal, R CB2 & P04
Keat Cheah, S P09
Kempegowda, P CB13
Kim, D P11
Kirresh, O P15
Klepacki, J WE16
Kline, G P26
Koulouri, O P32
Krishnan, S P09
Kulendran, V P35
Kumar, J WG4
Kumar, R CB16, WC2 & WG1
Kummaraganti, S P19
Kurzawinski, T P14
Kyriakakis, N P19
Kyrodimou, E WD2

Lakshmipathy, K P37
Lam, F OC8
Lawrence, V OC4 & P10
Leeds, J WH4
Levy, M CB8 & WD5
Lewis, D OC3
Li, APZ P18
Lindsay, R OC6
Lines, KE P33
Lunken, C P36
Lynch, J P19

MaCinerney, R P05
Mackenzie, F OC6
Mackie, A WA10 & WE11
Maltese, G P18
Manita, I WA13
Mannion, R P32
Manohar Rao Balmuri, L WH1
Manova, Y OC8
Margari, N OC10
Martineau, M P01 & WE13
Mathews, A P09
Matson, M P14
May, C P39 & P43
Mcinerney, R CB4
Meeran, K P35
Mehta, S OC10
Menon, R OC5
Millar, K P04
Millar, L P38
Millson, V P29
Mohamed, M WA11
Mohandas, C WA4, WA5 & WE4
Montebello, A CB14 & WG3
Morganstein, D OC7, P25, P31 & P38
Morris, L WH1
Mumby, C WH1

Muralidhara, K WC3 & WF2
Murray, RD P19
Myint, KS P34

Naeem, A WF1
Nayyar, V P37
Newbold, K WD7
Nizar, R CB7
Nobeebux, A OC8

O'Donovan, D P32
O'Toole, S WE7, WE8, WH2 & WH3
Oddie, P P04
Oddy, S P32
Ogunko, A WA4, WA5 & WE4
Outas, MC WD6

Pagnamenta, A P33
Pal, A P39 & P43
Parsad, M P40, WA1 & WE5
Parvanta, L OC4 & WE8
Pasieka, J P26
Patel, A WD2
Peasey, S P29
Perros, P WH5
Petrides, G WH5
Pettengell, R P11
Pillai, S P05
Pillais, S CB4
Pittaway, J WA9 & WE14
Plichta, P WD4
Plowman, N WD7
Portugal, J WA13
Powls, A OC6
Powrie, J WC2
Premawardhana, L P12 & P17

Quader, M CB6
Quinn, P P31
Qureshi, S P20 & WE13

Rajakumar, L WG4
Rajkumar, S WG5
Ramli, R P35
Rathore, A WE7
Ravindran, R P12 & P17
Redford, C WD2
Rehman, T OC1 & P11
Richardson, T P33
Robinson, R P21
Robinson, T CB7
Rogers, R P34
Ronneberger, R OC8
Ross, C P34
Rumsby, G OC8
Ryan, F P27

Saeed, T P39
Sahdev, A CB15
Salsbury, J P14
Samarasinghe, S CB2, P01, P04, WC3 & WF2
Sankar, S WF1
Saqib (ST4 Queen Elizabeth Woolwich), A WF4
Saqib, A WG2
Sawhney, N WE2
Schofield, C CB11
Scott, A OC6
Seejore, K P19
Seguna, D WA7
Selberherr, A WH8
Semple, R OC8
Seshadri, S P09
Shahriar Huda, M WA3
Shakeel, M WD3
Sharma, A P16, P24 & P30
Sharma, S P22
Shepherd, L CB13
Shine, B P33
Shotliff, K P13
Siddaramaiah, N WH4
Siddiqui, M P31
Silva, T WA13
Silveira, M WH11
Simon, G CB9
Simpson, H CB1 & OC8
Sithamparanathan, N P37
Sivappriyan, S WG4
Smith, A WG5
Snape, K OC1
Srirangalingam, U P36
Stevenson, M P33
Stiles, CE WB1, WB2, WE15 & WH6
Stokes, V P27, P33 & WH8
Storr, H WF3
Strachan, M CB10
Stratos, E P22
Suh, Y-e P25
Sukumar, N CB5 & WF1
Sze, C WE15

Tadman, M OC9
Tan, G OC9
Tan, SH P41
Tana, A P35
Tang, A P26
Tansey, DJ WC4
Taylor, J P33
Tee, SA WH5
Thakker, R P13 & WH8
Thakker, RV P27 & P33
Theodoraki, A P25
Thomas, J WE12
Thomas, S P18
Thurston, L P20 & WE13
Thurtell, C CB11, WA10 & WE11
Timms, R P43
Todd, J P35
Toth, P P21
Tremble, DJ WF4
Tremble, J WG2
Tufton, N OC10, P28 & WE8

Uchambally, M WA8

Vaidya, B WD2
Vakilgilani, T P16
Vamvakopoulos, J WD1
van Heeswijk, I P21
VanAs, N P25
Vella, S CB14 & WG3
Velusamy, A CB16 & WC2
Vithian, K OC10
Vogazianou, A CB1

Wadhwani, R P24
Waterhouse, J OC4
Weickert, M CB5
Williams, D P36
Witczak, J P12 & P17
Woodward, G OC8
Wotherspoon, F WH11
Wren, A P31
Wu, X OC2, P14, WA2 & WE6

Yap, PS WH7
Youn, S WA4

Zachariah, S P37
Zia-ul-Hussnain, HM WE10