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Oral Communications

OC1

A rare heterozygous *IGF1* variant causing postnatal growth failure and offering novel insights into IGF-I physiology

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Section 1: Case history

A 10-year-old girl presented with significant postnatal growth failure. Her birth weight was normal (–0.15SDS) but poor growth was observed from a few months of age. She had no other symptoms. On examination, height was –3.4SDS and head circumference –1.6SDS. She had no dysmorphic features and normal development.

Section 2: Investigations

Baseline serum analyses were unremarkable. Karyotype was normal (46XX). Bone age was delayed by 2.5 years. A high peak GH was observed on glucagon stimulation (17.1 mcg/l). Baseline IGF-I levels were low/normal (144 micrograms/l; –1.3SDS) and responded poorly (increase <15) following IGF-I generation testing, suggesting GH resistance.

Section 3: Results and treatment

RhIGF-I was commenced, and she was assessed for genetic defects in the GH-IGF-1 axis. After 6 months of rhIGF-I therapy (120 micrograms/kg BD), IGF-I levels were exceptionally high (1,044 micrograms/l; +5.9SDS). Height velocity improved from 3.6 cm/year to 6.5 cm/year. Assessment on our unique short stature gene panel identified a novel heterozygous *IGF1* variant (102813333C>T, c.356G>A, p.R119H) which was exceedingly rare (gnoMAD frequency 0.004%) and predicted damaging by SIFT (CADD score 32). The p.R119H variant changes an arginine to histidine. R119, the first amino acid of the IGF-I E domain, is the most critical amino acid for binding furin, an enzyme essential for cleaving pro-IGF-I to mature IGF-I (E domain removal). R119 is highly conserved across species. We hypothesise this variant impairs pro-IGF-I cleavage, reducing available mature circulating IGF-I. Pro-IGF-1 is likely to be less biologically active than mature IGF-I, resulting in postnatal growth failure and GH resistance. Functional work is ongoing.

Section 4: Conclusions and points for discussion

Pathogenic *IGF1* mutations are extremely rare with 5 autosomal recessive mutations, one *IGF1* copy number variant and two heterozygous frameshift mutations reported associated with growth failure. Heterozygous missense *IGF1* mutations have not been previously described. We report the first missense variant identified at the furin cleavage site, predicted to prevent the conversion of pro-IGF-I to mature IGF-I. Since the standard ELISA IGF-I assay cannot distinguish mature IGF-I from pro-IGF-I, the proportion of each IGF-I form in the circulation is unknown. A skewing to increased pro-IGF-I may impact IGF-I function as the functional roles of pro-IGF-I and the E domain are poorly understood. We are currently assessing whether IGF-I p.R119H competitively inhibits mature IGF-I from binding IGF1R and thus act in a dominant negative manner. Characterisation of this naturally-occurring novel mutation will fundamentally enhance our understanding of IGF-I regulation/growth physiology.

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OC2

A novel case of bilateral adrenal hemorrhage and acute adrenal insufficiency due to VITT (vaccine induced thrombosis and thrombocytopenia) syndrome

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Case history

A 23-year-old female with no past medical history, presented with Acute Shortness of breath and Chest pain. CTPA revealed Bilateral Pulmonary Emboli with slightly low platelets. She was discharged on apixaban. Of note, she had received her first dose of Astra-Zeneca Covid vaccine 10 days ago. She re-presented 2days later with worsening chest pain. FBC revealed platelets 27,Hb 80,d-dimer 10,000. She was treated for presumed chest infection and DOAC was converted to heparin infusion on haematology advice d/t Thrombocytopenia for which no cause was found. Multiple platelet transfusions were also given.

Investigations

CT-CAP on admission revealed Left pleural effusion, deemed para-pneumonic.All abdominal viscera normal. Autoimmune profile was negative including lupus-anticoagulant. 5 days post-admission, in view of sudden onset lower backache & worsening infection markers, repeat CT CAP was done which revealed new bilateral adrenal haemorrhages. MRI adrenals revealed B/l adrenal haemorrhages with fat stranding ,no underlying adrenal mass noted. Her 9am cortisol was <25, therefore she was started on IV hydrocortisone for acute adrenal insufficiency. A day later, she developed severe headache and photophobia. MRI head showed multiple cerebellar lesions?cause. She then had 2 grand-mal seizures,therefore was started on antiepileptics and moved to ICU of specialist hospital. MRI was re-reported as PRES (posterior reversible encephalopathy syndrome). Repeat CT AP also revealed splenic vein thrombosis and RT ventricular thrombus.

Treatment

She was finally diagnosed with VITT (Vaccine Induced Thrombosis and Thrombocytopenia) due to Astra-Zeneca vaccine She was treated with 5 cycles of plasma exchange.She was also administered pulsed IV methylprednisolone. She improved clinically and blood parameters wise.She was switched to hydrocortisone 20/10/10 mg. However, she became dizzy, hypotensive on lower dose, therefore dose increased to 20 mg QDS.Her anticoagulation was changed from heparin to Argatroban on suspicion of VITT. She was discharged home with sick-day rules,steroid & mineralocorticoid replacement. She has follow-up planned in Endocrine clinic for SST arrangement.

Conclusion

VITT is a rare syndrome which was recently recognized to be caused by Astra-Zeneca vaccine. It clinically mimics autoimmune HIT with PF4 antibodies. VITTS is extremely rare, but the potential side-effects can be devastating, therefore, UK has now recommended using an alternative vaccine in patients younger than 30 years. We believe this is the first case report of B/l adrenal haemorrhage in association with VITTS. Clinicians should have a high index of suspicion to diagnose VITTS as prompt treatment with IVIG and avoidance of platelets transfusions can be lifesaving.

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OC3

Pyschosis and surgery. A case of thyroid storm treated with emergency non-consensual thyroidectomy

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1. A 48 year old female was admitted to inpatient psychiatry with paranoid delusions, auditory hallucinations and subsequently detained under the Mental Health Act of Scotland. She had been diagnosed with Graves' Disease 5 years previously having presented with anxiety and weight loss but had elected to refuse anti-thyroid drugs in favour of homeopathy and acupuncture. She refused any treatment for Graves' Disease when admitted to Psychiatry even though floridly thyrotoxic. She was found to have new atrial fibrillation with a ventricular rate of 153 beats/minute and was transferred to the Coronary Care Unit. Thyroid storm was confirmed using the Burch and Wartofsky scoring system where she scored 75 points given the presence of psychosis, tachycardia, atrial fibrillation and pulmonary oedema. 2. Thyroid function tests demonstrated thyrotoxicosis with a suppressed TSH, free T4 of 52 pmol/l and total T3 6.1 nmol/l. 3. Despite a multi-disciplinary approach including Psychiatry, Pharmacy, Cardiology and Endocrinology, the patient refused to consider any active treatment including covert Lugol's iodine and amiodarone. As the mortality rate of thyroid storm is substantial at 10–30%, we elected for emergency thyroidectomy in her best interests. This was especially as there is some evidence that neuropsychiatric manifestations portend greater risk of mortality. The patient was intubated under the Adults with Incapacity Act of Scotland and then treated with nasogastric propylthiouracil, hydrocortisone, Lugol's iodine and beta-blocker for 72 hours prior to surgery. She had a fraught post-operative period and remained intubated for 23 days with a tracheostomy formed on day 14 to aid weaning attempts. She sustained ventilator-associated pneumonia and a pulmonary embolism. She made a full recovery with remission of atrial fibrillation and improved psychiatric symptoms, allowing the short-term detention certificate to be revoked. Nine months later, she is managed with aripiprazole and accepts that her emergency treatments were reasonable. She is on 125 micrograms of levothyroxine with well controlled thyroid hormones. 4. Neuropsychiatric symptoms are common in patients with Graves Disease. This may have contributed to our patient's years of non-compliance and ultimate thyroid storm with the florid encephalopathy and psychiatric findings described. This case highlights the necessity of a considered MDT approach with perioperative anti-thyroid medication for stabilisation. Sustained recovery of cardiovascular and psychiatric status can be achieved.

Finally, mental health legislation supports clinicians in making difficult but essential treatment choices where the patient lacks capacity and life is at risk.

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OC4

Synchronous functional heterogeneity of metastatic pancreatic neuroendocrine tumour

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A 65 years old male chef presented with a history of weight loss of 15kg over a 12-month period associated with lethargy, constipation and abdominal pain. His past medical history included epilepsy, hypertension and gastric reflux. He reported no family history of endocrinopathies.At presentation his performance status was 0 and was found to have hepatomegaly. In view of rapid weight loss and hepatomegaly he had a CT scan of the abdomen and pelvis, which showed multiple hypervascular liver metastases, bony metastases, and a heterogeneous enhancing distal pancreas tumour with tiny fleck of calcification over the pancreas body/tail. He underwent a liver biopsy, which was consistent with grade 3 neuroendocrine tumour (strong staining with synaptophysin,chromogranin A and CD56, patchy staining with AE 1/3, p63 and TTF1) with a Ki67 index of 33% with no expression of both insulin and glucagon on immunohistochemistry.A Tc-99m-tektrotyd scintigraphy revealed extensive avidity in liver lesions, retroperitoneal mesenteric nodes and bony lesions. His urine 5- HIAA was normal at 18unol (5–35), HbA1c 31 mmol/mol, PTH 1.7 pmol/l (1.8–6.8), calcium 2.39 mmol/l (2.20–2.60). He was given FCIST chemotherapy [5-fluorouracil, cisplatin and streptozocin] which has minimal impact in tumour progression. After NET MDT discussion, he underwent 3 cycles of Peptide Receptor Radionuclide Therapy (PRRT) with post therapy images demonstrating good tumour targeting. Subsequently, he developed hypoglycaemia during chemotherapy. After a brief fast, his glucose dropped to 1.5 mmol/l, he had raised C-peptide of 1797 pmol/l (<300), insulin 26 mu/l (<3) in keeping with an insulinoma. After his third fraction of PRRT he presented with an erythematous erosive rash with associated desquamation and some annular components affecting the trunk and limbs. He was noted to have glossitis. The clinical features were in keeping with a glucagonoma-related necrolytic migratory erythema and were supported by skin histology. His glucagon was significantly raised at 1465 pmol/l (0–50). The original liver biopsy at diagnosis was reviewed and it was negative for insulin and glucagon staining. Despite the introduction of Diazoxide, octreotide and dexamethasone, he had persistent hypoglycaemia and was admitted for intravenous dextrose infusion. He developed pancytopenia, deteriorated rapidly and sadly passed away 12 months after his initial presentation.

Conclusion

Pancreatic neuroendocrine tumours have varied presentations. Metachronous functional as well as histological heterogeneity have been reported. This case is unique with co-existent glucagon and insulin hypersecretion.We hypothesize this was the result of different metastatic lesions expressing varied differentiation and secretory capacity, adding to the challenges of managing these tumours.

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OC5

A case of parathyromatosis: All options exhausted

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Case history

A 23-year-old woman with no significant past medical history and normal renal function was incidentally found to be hypercalcaemic in 2003. Following investigation, she was diagnosed with primary hyperparathyroidism. She underwent three-gland parathyroidectomy; histology demonstrated hyperplasia. Her bone function remained normal, but 4 years later she was found to have normocalcaemic hyperparathyroidism. Sestamibi demonstrated uptake inferior to the left thyroid lobe and in a 0.7cm right cervical nodule, and she became increasingly hypercalcaemic. Histology following further surgical resection showed parathyroid hyperplasia. Her corrected calcium failed to normalise post-operatively, and repeat Sestamibi in 2009 showed ongoing uptake at the site of the removed cervical nodule and in the superior mediastinum. She continued to be reviewed and her corrected calcium continued to rise. In 2014 she underwent venous sampling, which suggested parathyroid activity lateral to the right carotid artery. Three nodules, again displaying hyperplasia, were removed from the carotid sheath. Her calcium and PTH remained persistently elevated. A trial of cinacalcet was started, but the patient was unable to tolerate because of extreme nausea.

Investigations

CT Chest, MRI neck & Sestamibi (2008): 7 mm enhancing nodule lying just anteromedial to the right jugular vein. Histology: Circumscribed without infiltration but with fibrous septa. No mitotic activity. Microacinar appearance, consistent with parathyroid hyperplasia. Calcium/Creatinine Clearance Ratio (2012): 0.027 mmol/mmol (vitamin D 85 nmol/l). Genetics: MEN1 and HRPT2 negative. Venous sampling (2014) – Highest PTH level obtained from laterally originating tributary of the right internal jugular vein (211 pmol/l). Sestamibi 2017: uptake in the left thyroid lobe and a 10mm nodule superolateral to the right thyroid. Since January 2019: corrected calcium 2.6 – 2.82 mmol/l, and PTH: 16.7–23 pmol/l.

Results/Treatment

Our patient underwent her fourth and final surgery in 2017 with an extensive neck dissection. Histology was again consistent with multiple small foci of hyperplastic parathyroid tissue. Our surgical team feel that there are no further surgeries that they would consider appropriate. She continues to feel very symptomatic but is reluctant to trial further cinacalcet.

Conclusion/Points for discussion

Parathyromatosis secondary to primary hyperparathyroidism is exceptionally rare, with only 22 cases reported in the literature. There are several theories of how it may develop: low-grade parathyroid carcinoma, implantation into surrounding tissue during surgery and stimulation of embryological remnants of parathyroid tissue. Despite multiple surgeries this patient remains symptomatic and cinacalcet, although previously not tolerated, is the only available therapeutic option.

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OC6

A rare genetic cause of phaeochromocytoma

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A 17 year old woman attended the Emergency Department following an episode of chest pain and pre-syncope, coinciding with high blood pressure readings taken at home. Her blood pressure was recorded as 170/101 with no signs of end organ damage on clinical examination. She had no clinical features of Cushing's disease or Neurofibromatosis and her BMI was 22.4. She had been seen at a Cardiology clinic 18 months previously for hypertension and chest pains. A 24 hour blood pressure monitor had recorded an average BP of 140/97 mmHg. She was recommended a 6 month trial of lifestyle changes with weight loss and low salt diet. When this was ineffective she was commenced on Ramipril 1.25 mg and Indapamide 2.5 mg. She was on no other regular medications and had no significant family history. Initial investigations in the Emergency Department showed a troponin of 25 ng/l (ref<14), creatinine 96 umol/l and potassium 4.8 mmol/l (3.5–5.3). An ECG showed sinus tachycardia with no evidence of left ventricular hypertrophy and 24 hour urine protein was normal at 0.1 g/24 hrs. Her chest x-ray showed clear lung fields. A transthoracic echocardiogram showed good left ventricular function with a structurally normal heart. 24 hour urinary metadrenalines were performed in primary care and showed elevated Normetadrenaline at 23.4 umol/24 hours (05–3) with 3-Methoxytyramine 2.39 umol/24 -hours (05–2.8) and Metadrenaline 0.7 umol/24 hours (05–1.8). A 24 hour urine free cortisol was normal at 45 nmol/24 hours (<120). A CT scan of her adrenal glands showed an 8.9−5.6 cm left adrenal lesion with central necrosis and avid enhancement. The right adrenal gland and other abdominal viscera appeared normal. She was commenced on doxazosin and went on to have a laparoscopic left adrenalectomy. Her procedure and stay in hospital were uncomplicated. Histology confirmed a non-invasive pheochromocytoma with Ki67 0%, PASS score 0 and clear margins. Large areas of the lesion showed SDHB staining positivity. Genetic screening was undertaken which identified a heterozygous Fumarate Hydratase gene missense mutation (NM_000143.3:c.908T>c p.Leu303Ser). This is a rare cause of Hereditary Phaeochromocytoma and Paraganglioma Syndrome which results in intracellular accumulation in fumarate. In common with SDH mutations this results in activation of Hypoxia Inducible Factor alpha (HIFα), resulting in an increased lifetime risk of phaeochromocytomas, paragangliomas, uterine myofibromas and renal cell carcinoma. Her specific mutation (L303S) has previously been reported in one patient who presented similarly with phaeochromocytoma, and whose family history was notable for renal cell carcinoma. Her family now await genetic testing.

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OC7

Fulminant cushing's crisis immediately post-partum – challenges of management

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Case history/Investigations/Results and treatment
A previously healthy 36 year old female was admitted to a local intensive care unit with psychosis and intractable hypokalaemia. She had delivered a live preterm baby girl at 33 weeks gestation ten days previously. The hypokalaemia led to an endocrine consultation which revealed onset of symptoms in the third trimester, with no symptoms present pre-conception. Serum cortisol was 2,258 nmol/l with a nadir K+ of 2.2 mmol/l. She was transferred to our ITU to commence an etomidate infusion, and required sedation with olanzepine and propofol. Serum cortisol levels dropped to 300 nmol/l and over the following week octreotide, metyrapone, and ketoconazole were added. An octreotide test had suggested a partial response with ACTH falling from 4200 ng/l to 1800 ng/l at 300 minutes. Cross-sectional imaging revealed a 7.3−4.8 cm anterior mediastinal mass (presumed thymic primary) with widespread mediastinal and axillary lymphadenopathy, bilateral breast masses, and diffusely enlarged adrenal glands (all of which were DOTATATE-avid). An axillary node core biopsy revealed neuroendocrine carcinoma, with Ki-67 hotspots of 40%. Her recovery was complicated by Staphylococcus aureus bacteraemia and Candida albicans fungaemia. A bilateral adrenalectomy was performed due to ongoing hypercortisolaemia, unstable mental state, and hypertension with hypokalaemia despite maximal oral anti-adrenal therapy. This strategy was also felt to simplify future glucocorticoid management when treating the NET. Histology revealed a metastasis within the hyperplastic adrenal tissue, with Ki67 of 20%. All symptoms resolved post-operatively and she was commenced on monthly Lanreotide. Two-weeks post-operatively, plasma ACTH levels were 145 ng/l (pre-hydrocortisone) and 151 ng/l (120 m post-hydrocortisone). CT-scan suggested stable disease. We advised a conservative approach. Repeat scan at 6-months showed mild volumetric reduction in the presumed primary mediastinal primary tumour to 6.4−3.4 cm and at other involved sites.
Conclusions and points for discussion
We discuss how the physiology of pregnancy provided protection from cortisol excess, thus leading to the fulminant presentation. We hypothesise that hCG may have been a driver during pregnancy, stimulating rapid growth and high-grade activity of a previously quiescent NET. We consider whether this provides other therapeutic manoeuvres. We discuss the importance of basing treatment options not solely on markers such as Ki-67, but on the overall clinical picture and presentation. Finally we discuss the regression of the disease which we believe is unlikely due to Lanreotide alone but also removal of a pregnancy stimulus. This opens up discussion on how best to manage the NET in the future.

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OC8

Pregnancy and postpartum clinical course in a woman with a homozygous calcium-sensing receptor mutation

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Section 1: Case history
We present the case of a 21-year-old lady known to harbour a homozygous inactivating mutation of the calcium sensing receptor (CaSR) which led to uncontrolled hypercalcaemia in infancy, necessitating emergency total parathyroidectomy. The CaSR plays an important role in calcium homeostasis. Inactivating mutations result in a higher calcium "set-point" and various degrees of hypercalcaemia based on the severity of functional impairment. In the heterozygous state, a single mutation of the gene presents with a milder phenotype, known as familial hypocalciuric hypercalcaemia (FHH). Neonatal severe hyperparathyroidism is a life-threatening condition occurring when both gene copies are mutated. Following parathyroidectomy the patient developed hypoparathyroidism, requiring treatment with 1-alfacalcidol and sandocal. Aged 21 she became pregnant. Paternal testing showed normal serum calcium, hence the fetus was expected to inherit a maternal mutated copy of the gene and a paternal wild-type copy (and hence be heterozygous for the CaSR mutation). This genotype would result in the fetus having a higher serum calcium, albeit to a much lesser degree than that seen in the homozygous state.
Section 2: Investigations
Following biochemical testing of the maternal grandparents, the fetus' anticipated corrected serum calcium concentration was predicted to be around 2.8 mmol/l. Thus, a maternal serum calcium concentration less than 2.8 mmol/l would likely be perceived by the fetus as being 'low' and subsequently result in fetal secondary hyperparathyroidism. Following birth, this would put the baby at risk of neonatal hypercalcaemia.
Section 3: Results/treatment
Serial growth scans showed normal fetal growth and skeletal architecture. Maternal requirement for calcium increased as pregnancy progressed and extracellular fluid volume expanded. The baby was born by vaginal delivery following induction of labour at 39+4 weeks' gestation, weighing 2.6 kg. At birth, the neonate's corrected serum calcium concentration was 2.87 mmol/l (ref. 2.2–2.6), with a normal phosphate. On day 4, corrected calcium was 2.81 mmol/l, PTH 1.6 pmol/l (ref 1.6–6.9), urine calcium 1.8 mmol/l, urine creatinine 1.2 mmol/l. Corrected calcium aged 4 months was 2.73 mmol/l, PTH 4 pmol/l, urine calcium 0.5 mmol/l, urine creatinine 0.4 mmol/l. Genetic testing on the baby identified a heterozygous mutation of the CaSR, consistent with FHH.
Section 4: Conclusions/points for discussion
We hereby discuss the changing physiology and management of hypocalcaemia in a pregnant patient harbouring a homozygous CaSR mutation and concerns arising for both mother and fetus.

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OC9

Cardiac arrhythmia and ischaemic stroke in a young man with Resistance to Thyroid Hormone beta

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Case history
A 42 year old male teacher presented to the emergency department with an acute right MCA infarct, on a background of paroxysmal atrial fibrillation/flutter and recurrent supraventricular tachycardia. He had chronic palpitations, with previous failed cardiac ablation. He had no other medical history, specifically, no history of ear infections or learning difficulties. There was no known family history of thyroid dysfunction. Previous TSH levels (no FT4 measurements were recorded) were within the normal range.
Investigations
CT brain and angiogram on admission showed an acute right MCA infarct. He was in atrial fibrillation. Repeat thyroid function testing (Roche assay) revealed a discordant pattern; TSH 5.7 mIU/l (0.27–4.2), FT4 34.5 pmol/l (12–22), FT3 7.9 pmol/l (3.1–6.8). Assay interference was excluded by measuring thyroid hormones (TH) on alternate assays [Delfia; TSH 4.16 mIU/l (0.4–4.0), FT4 41.3 pmol/l (9–20); Centaur FT3 10.74 pmol/l (3.5–6.5)], and by demonstrating expected responses to dilution and PEG precipitation of TSH and FT4. SHBG was normal (24.2 nmol/l, RR 16.5–55.9). ALB gene sequencing identified no mutations, however, sequencing of the gene encoding the ? form of the thyroid hormone receptor (*THRβ*) revealed a heterozygous mutation; M313T, known to be pathogenic, and hence confirming Resistance to Thyroid Hormone β.
Management
Initial stroke management included iv thrombolysis but later he developed a further acute cerebral infarct requiring thrombectomy, complicated by haemorrhagic transformation. He had persistent paroxysmal atrial fibrillation, which was difficult to control (no improvement with dronedarone, treated with increasing doses of metoprolol and flecainide). He has significant residual neurological deficits and required prolonged admission to a rehabilitation facility. Given his relative cardiac thyrotoxicosis, he was commenced on carbimazole 10mg od (TRIAC was not available), with biochemical (FT4 reduction from 33.4 pmol/l to 22.1 pmol/l) and clinical improvement (reduced palpitations and ongoing neurological recovery).
Conclusions and points for discussion
This case highlights the need for screening with both T4 and TSH to exclude thyroid dysfunction in patients with a high suspicion of thyroid disease. Patients with RTHβ are known to have tachycardia, and carry a risk of atrial fibrillation. Although there may be some protection from the pro-thrombotic effects of TH (since these are TRβ mediated), patients have dyslipidaemia and increased HOMA-IR, consistent with metabolic dysfunction. Unusually in RTHβ, this patient had very prominent cardiac symptoms, suggesting pronounced cardiac thyrotoxicosis, and required anti-thyroid drug treatment to control these symptoms. Unfortunately, his predisposition to cardiac arrhythmia likely contributed to the development of cerebrovascular disease, with devastating consequences.

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OC10

An unusual case of raised PTH

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60 year old gentleman referred to endocrine clinic from Rheumatology for raised PTH 23.5 pmol/l, in the context of normal calcium 2.2 mmol/l, low vitamin D 27.3 nmol/l, raised ALP 273 U/l, low phosphate 0.57 mmol/l and normal renal function. Past medical history of hypertension, Barrett's oesophagus, cluster headaches and previous left femur fracture secondary to motor cross accident. The ALP isoenzyme for bone was raised. He was complaining of backache which he had for several months which was not precipitated by any injury. Rheumatology had ruled out Paget's disease with a bone scan which showed increased uptake in the ribs and distal third of the left femur. He was started on vitamin D 50,000units once a week, as low vitamin D was presumed to be the cause of the raised PTH. His PSA and myeloma screen were negative. He felt his strength was reducing and though his vitamin D levels came up, his ALP remained elevated and so did his PTH. He went on to have CT chest/abdo/pelvis which showed diffusely sclerotic bones. PET Scan showed deformity and hyperostosis in the distal 2/3rd of the left femoral diaphysis, thought to be due to the previous trauma. His PTH remained up despite normal calcium, vitamin D and renal function. His Sestamibi scan revealed a possible right lower parathyroid adenoma but also reported diffuse bony sclerosis suggestive of renal osteodystrophy but his renal function was still normal. His phosphate had dropped to 0.36 mmol/l and he was started on phosphate replacement. The abnormal bone imaging suggested that this was not PTH driven and he was referred to the metabolic bone department. His Procollagen-1-N-Peptide was raised at 907 ug/l and his FGF 23 levels were high at 175 iu/ml (Normal 0 – 100 iu/ml), suggesting the diagnosis of Oncogenic/tumour induced osteomalacia – which is a mesenchymal tumour secreting FGF23. He had a Ga-68 DOTATATE PET/CT scan which showed a possible lesion in the right femur. He is currently awaiting ablation of this. He currently takes 4 sando phosphate tablets a day and 1.5 mcg alpha calcidol. His phosphate is now 0.86 mmol/l. His PTH is 40.7 pmol/l and ALP is 327 U/l.

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Highlighted Cases

NCC1

Myxoedema Coma precipitated by Diabetic Ketoacidosis

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Section 1: Case History

We present the case of a 52-year-old found female found collapsed at home with a three-week history of polyuria, polydipsia and lassitude on a background of primary hypothyroidism and non-insulin-dependent diabetes. On examination, she was hypothermic at 32°C, hypotensive (blood pressure 90/60 mmHg), newly oliguric, and had a Glasgow coma scale (GCS) of 9/15. A diagnosis of severe diabetic ketoacidosis (DKA) was made on admission.

Section 2: Investigations

Initial ABG demonstrated a pH <6.8 (7.35–7.45), ketones 6.0 mmol/l (<0.1), an undetectable bicarbonate level <5 mmol/l (22–26 mmol/L) and glucose 38 mmol/l. Admission thyroid function showed TSH 9.04 (0.27–4.2 mIU/l) and T4 16.3 (12–22 pmol/l). Initial estimated glomerular filtration rate (eGFR) was calculated at <15 ml/min (90–120 ml/min/1.73m^2) which subsequently normalised. An autoimmune diabetes screen was sent given her ketosis. Computed tomography (CT) Brain was normal. CT thorax abdomen and pelvis ruled out acute pancreatitis and showed bibasal consolidation.

Section 3: Results and treatment

She was admitted to ICU, whereby she was intubated and ventilated for 5 days, treated with broad-spectrum antimicrobials, converted to subcutaneous insulin, and weaned off CVVHD. However, despite the resolution of her DKA, her GCS did not improve post-weaning of sedation. Repeat TFTs, five days off sedation, in the euglycemic state, showed a TSH 87 mIU/l, T4 6.1p mol/l and T3 <2.0 pmol/l (3.1–6.8 pmol/l). Alternative causes of metabolic encephalopathy were excluded. 20 micrograms(mcg) of intravenous triiodothyronine (T3) was given twice daily and titrated to a mid-normal T3 level. This resulted in improved GCS from 9 to 12/15 after three doses and complete resolution to 15/15 after eight doses. Anti-glutamic acid decarboxylase (anti-GAD) antibodies were positive at >2000 units/ml, confirming a diagnosis of latent autoimmune diabetes in adults (LADA). She was discharged home on oral L-thyroxine and a basal-bolus insulin regime.

Section 4: Conclusions and points for discussion

DKA precipitating a myxoedema coma is a rare phenomenon. It can present atypically compared to a classical myxoedema coma, without bradycardia or longstanding history of untreated hypothyroidism. Other expected features can be absent such as hyponatraemia which usually results from excess antidiuretic hormone and inadequate aquaresis. However, in this case, the corrected sodium was only mildly deranged, we suspect, due to her osmotic diuresis and severe kidney injury. Furthermore, hyperglycaemia is known to inhibit TSH secretion, which can mask the diagnosis. This case highlights the challenging diagnosis of myxoedema coma and how DKA can conceal clinical and laboratory features.

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NCC2

Recognizing chronic hypoxaemia as a risk factor for non-hereditary Paraganglioma

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Case history

Hereditary paragangliomas (PGLs) associated with loss of function mutations in *SDHx* and *VHL* genes have revealed a remarkable connection between these conditions and the hypoxia signalling pathway: with a 'pseudohypoxic profile' driving hypoxia inducible factor (HIF) activity and tissue-limited cellular proliferation. We present a case of sporadic, multiple PGL mediated by HIF activation through true hypoxia. A 32 year old female was referred for assessment. She had been born with cyanotic congenital heart disease (tricuspid atresia with single ventricle physiology), treated in childhood with a Glenn shunt. This produced good symptom control but significant, persisting hypoxaemia (peripheral oxygen saturation 80% at rest). In her 20s, the patient had developed unstable SVT, requiring beta-blockade and an ablation procedure. There was no family history of endocrine or renal disease. CT-pulmonary angiogram (CTPA) and liver MRI were performed to assess the impact of cardiac haemodynamic status on pulmonary and hepatic vascular physiology.

Investigations and Results

Imaging revealed hyper-enhancing, high T2-signal bilateral carotid body and a 5.0×4.9 cm retroperitoneal mass consistent with multiple paragangliomas. Plasma metanephrines measured by LC-tandem MS were as follows.

	Result	Reference range
Metadrenaline	520 pmol/l	0-510 pmol/l
Nor-metadrenaline	32590 pmol/l	0-1180 pmol/l
3-Methoxytyramine	131 pmol/l	0-180 pmol/l

Subsequent functional imaging with I-123 MIBG confirmed high isotope uptake limited to only the retroperitoneal mass indicating its secretory nature. Multi-gene next generation sequencing did not identify mutations or sequence variants of uncertain significance in any of the paraganglioma predisposition genes: *SDHAF2*, *SDHA*, *SDHB*, *SDHC*, *SDHD*, *VHL*, *NF1*, *RET*, *MAX*, and *TMEM127*.

Management

Beta-blockers were stopped and incremental alpha blockade was introduced using doxazocin, without development of tachydysrhythmia or hypotension. Further cardiac studies revealed severe functional impairment of the single ventricle, precluding simple excision of the retroperitoneal paraganglioma. Joint congenital heart disease, endocrine and endocrine surgery multidisciplinary team assessments have recommended orthotopic cardiac transplantation, combined with removal of the retroperitoneal paraganglioma.

Conclusion and points for discussion

Data support a diagnosis of multiple paraganglioma driven by chronic hypoxia. Given the role and close association of hypoxia signalling and 'pseudohypoxia' in hereditary PGL disease, this case highlights the utility of having a low threshold for assessing patients with chronic systemic hypoxaemia (such as those with cyanotic congenital heart disease) for occult PGL, supporting the view that paragangliomas are a reflection of chronic systemic hypoxaemia.

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NCC3

Agranulocytosis & contrast – a perfect storm

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A 77 year old female was admitted two weeks after an out-patient CT Pulmonary Angiogram showed a subsegmental pulmonary embolism and retrosternal goitre. History was of ten days of confusion, breathlessness, diarrhoea and reduced intake. On admission, she was febrile, tachypnoeic and in new, rate controlled, AF. Burch-Wartofsky Point Scale: 45, this being highly suggestive of a thyroid storm. TFTs were normal one year prior. Thyroid USS showed a multi-nodular goitre. She was commenced on propylthiouracil (PTU), beta blockers and hydrocortisone, followed by cholestyramine and Lugols iodine, but improved slowly. Nine days passed before free T4 <100 pmol/l. Following discharge after three weeks, she was readmitted with PTU induced agranulocytosis & neutropenic sepsis (Neutrophils 0.04 e^9/l, WCC 2.0 e^9/l) a month later. She was managed with G-CSF and IV antibiotics for cellulitis. Once stabilised, and after further steroids/lugols iodine, thyroidectomy was performed alongside ureteric stent insertion for an obstructing stone. Treatment for contrast induced thyrotoxicosis can be very difficult given the excess formed thyroid hormone present, with resultant reduced efficacy of standard anti-thyroid disease medications including carbimazole / PTU. In our case, treatment difficulties were further exacerbated/limited by PTU induced agranulocytosis. Her elevated TSH receptor/anti TPO antibody levels, and multinodular goitre, suggest pre-existing thyroid disease, with contribution of the Jod-Basedow phenomenon causing her thyroid storm, rather than a contrast induced acute thyroiditis. Contrast administration delivers large iodine loads. Approximately 35,000 mg of Iodine are given for a CTPA. Recommended daily intake is approximately 150 micrograms. Contrast induced thyrotoxicosis is more likely in iodine deficient countries (up to 0.5% vs 0.025%). Those with pre-existing thyroid disease are at increased risk. Screening is not recommended but some studies suggest uptake scintigraphy imaging can be used to stratify patients as high risk. As more CT/MRI/invasive imaging is performed & more contrast administered, we should be aware of the risks of iatrogenic thyrotoxicosis /

Admission bloods:		Reference range
free T4	>100 pmol/l	12 – 22 pmol/l
free T3	36.9 pmol/l	3.1 – 6.8 pmol/
TSH	<0.01 mU/l	0.3 – 4.2 mU/l
Neutrophils	3.09 e^9/l	1.8 – 7.7 e^9/l
WCC	4.8 e^9/l	4 – 11 e^9/l
TSH receptor Ab	8.7 IU/l	0 – 0.9 IU/l
Anti thyroid peroxidase Ab	553 iu/ml	<34 iu/ml

thyroid storms, given the high mortality rates associated with this hypermetabolic state. Avoiding a storm by avoiding unnecessary imaging or optimising disease control ahead of time, is a far preferable concept, for both patient and physician.

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NCC4

A rare case of multiple thrombi and left adrenal haemorrhage following COVID-19 vaccination

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Case history

A 55 year-old female presented to A&E with left iliac fossa pain and vomiting, 8 days following her first dose of the AstraZeneca COVID-19 vaccine. She had a background of hypothyroidism, hypertension and hysterectomy for menorrhagia at age 25 – no prior thrombotic history. She underwent emergency laparoscopy for suspected torsion, which was converted to laparotomy for ovarian necrosis secondary to left ovarian vein thrombosis. Post-operatively, isolated thrombocytopenia was noted (nadir platelet count of 13×10^9/L) leading to ITU admission for cautious introduction of low molecular weight heparin (enoxaparin). Cross-sectional imaging revealed multiple sites of thromboembolism including both lungs, left basilic vein, and left renal vein.

Investigations

CT pulmonary angiogram revealed a 3.5 cm left adrenal mass and repeat CT abdomen & pelvis reported "swollen adrenals", previously reported as normal in appearance on the admission CT. Images were reviewed in the endocrinology clinico-radiology MDT meeting. The left adrenal gland appeared normal on the admission CT abdomen & pelvis, but the subsequent CT 10 days later demonstrated significant enlargement of the left adrenal, suggestive of haemorrhage within the gland. The right adrenal also showed new signs of hyperplasia. Urgent dynamic testing to assess adrenal insufficiency was arranged.

Results and treatment

Short Synacthen Test confirmed suspected adrenal insufficiency with a peak cortisol of 95 nmol/l at 30 minutes, and she was promptly commenced on replacement hydrocortisone. ACTH is currently in progress. She made a good recovery, and was switched to a direct oral anticoagulant (apixaban). Given the clinical course with multiple thrombi and adrenal haemorrhage, we decided to manage her conservatively, with a plan for repeat imaging (CT adrenal protocol) after 3 months, following the SST.

Conclusions and points for discussion

The COVID-19 pandemic and vaccine rollout has presented significant concerns regarding thromboembolic events. Haemorrhage of the adrenal gland is rare, but it must be considered in cases of sudden adrenal enlargement in the context of any underlying coagulopathy. Our differential diagnosis includes Waterhouse-Friderichsen Syndrome. We hypothesise that this is a manifestation of post-COVID immunisation thrombocytopenia. Thus adrenal haemorrhage needs to be considered as a potential complication of this novel vaccine induced thrombocytopenia syndrome.

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NCC5

Grave's orbitopathy – Metastatic breast cancer presenting as orbitopathy, not previously recorded in the endocrine literature

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Case history

A 67-year-old lady was referred to an endocrinologist for autoimmune hypothyroidism diagnosed in 2004. A treatment combination of levothyroxine and liothyronine was used. She had a history of recurrent metastatic ER-positive HER-2 negative lobular breast cancer with liver and bony metastatic involvement. She commenced with Letrozole (aromatase inhibitor) and Palbociclib (CDK inhibitor), later Fulvestrant (antioestrogen) and Crizotinib (tyrosine kinase inhibitor). The patient is on Capecitabine and Denosumab at the moment. She has not been on immunotherapy or checkpoint inhibitors at any time. From April 2020 the patient had what was thought to be progressively worsening thyroid eye disease (TED) with diplopia and exophthalmos. She had bilateral red and uncomfortable eyes, blurred vision and the patient developed a corneal ulcer in one eye. Ocular motility was reduced in all directions. The Clinical Activity Score for TED was 3 out of 7. Both MRI and CT scan of orbits described the picture being most likely secondary to severe TED with muscle enlargement. She received three intravenous infusions of methylprednisolone and rituximab in week two. In February 2021 an orbital biopsy was taken which showed metastatic disease secondary to breast cancer. The patient is scheduled for orbital radiotherapy to prevent a further compression of the optic nerve going forward as well as increasing proptosis.

Investigations

TSH 0,87 mU/l (0,3–4,2); fT4 17,1 pmol/l (9,00–19,00); fT3 4,7 pmol/l (2,60–5,70). Thyroid antibodies negative, TR-Ab negative. CT orbits: marked enlargement of the extraocular muscles bilaterally sparing the left superior oblique. Thought most likely to be secondary to severe TED. MRI orbita: Pattern of bilateral extraocular involvement with sparing of anterior tendon insertions, which is common finding in TED.

Results, treatment

The histology report from the orbital biopsy confirmed metastatic breast cancer involving the orbit. Treatment for autoimmune thyroid disease: levothyroxine 100 mcg four times altering 50 mcg three times a week, liothyronine 5mg twice a day. Treatment plan for orbitopathy: orbital radiotherapy to prevent further optic nerve compression. Treatment for metastatic breast cancer: continuing chemotherapy.

Conclusions, points for discussion

This case illustrates the challenges in patients with autoimmune thyroid disease and breast cancer. This is a rare association. To our knowledge, there are 3 reports in the ophthalmic literature. Breast cancer is the most common tumour to metastasize to the eye. Extraocular muscle metastases are uncommon, representing about 9% of orbital metastases, with bilateral presentation in up to 20% of cases.

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NCC6

An unusual cause of hypokalaemia: Itraconazole induced apparent mineralocorticoid excess syndrome

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Case history

81 year-old female was admitted to hospital with pneumonia. Past medical history included laryngeal cancer (1996), laryngectomy, iatrogenic hypoparathyroidism, hypothyroidism, and pulmonary tuberculosis (2007). She was treated with different antibiotics without improvement. She had positive aspergillus serology, but cultures were negative. She was started on voriconazole which was later changed to itraconazole 100 mg twice daily and discharged home. She was seen in the respiratory clinic one month later and a plan was made to continue itraconazole for another 6 weeks. Subsequently she was admitted again with iatrogenic hypercalcaemia and pneumonia which responded well to antibiotics, but it was noted that her potassium was low and blood pressure was high (215/109 mmHg). There was no confirmed history of hypertension in the past. She also had mild hypomagnesaemia. Patient was not taking any diuretic. Serum potassium level remained low despite oral and intravenous replacement, high potassium diet and correction of hypomagnesaemia.

Investigations

Potassium 2.4–2.5 mmol/l [ref 3.5–5.3 mmol/l] with poor response to oral and IV replacement. Urine potassium excretion was high (32.4 mmol/l) confirming renal loss of potassium. Serum bicarbonate 48.3 mmol/L. Renin and aldosterone levels were checked after optimization of potassium level and found to be low (Renin 0.2 nmol/L/hr [Ref 0.3–2.2], Aldosterone >50 pmol/l [Ref up to 630 pmol/l]).

Results and treatment

She was treated with potassium replacement and the itraconazole treatment was stopped after discussion with the respiratory team. Her potassium levels normalized and she was discharged home with normal potassium.

Conclusions and points for discussion

Apparent mineralocorticoid excess (AME) syndrome is characterized by hypertension, hypokalaemia, metabolic alkalosis and low renin and aldosterone. It is caused by congenital deficiency or acquired suppression of 11-beta hydroxysteroid dehydrogenase type-2 (11-β-HSD-2). Substances that inhibit 11-β-HSD-2 include liquorice, carbenoxolone and flavonoinds (grapefruit). There is growing evidence that triazoles like itraconazole can cause apparent mineralocorticoid syndrome by inhibiting 11-β-HSD-2. Hypokalaemia was reported in context of treatment with itraconazole and data suggest excessive urinary loss of potassium as a mechanism. Association with worsening hypertension, oedema, metabolic alkalosis and low renin aldosterone was also reported. In vitro, suppression of 11-β-HSD-2 was described with itraconazole.

Patients taking itraconazole should there for be monitored for hypokalaemia and hypertension. This case highlights this unusual and less recognized cause of hypokalaemia.

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NCC7

A rare case of metastatic prolactinoma presenting with cervical myelopathy

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Case History
A 52 year old man presented in 2009 with a gradual loss of peripheral vision associated with headaches. Examination confirmed bi-temporal hemianopia. Further investigation revealed elevated prolactin levels and pituitary MRI showed evidence of large pituitary tumour. A diagnosis of macroprolactinoma was made and cabergoline was commenced. Given resistance to medical treatment, the patient required two surgical resections (2011 and 2013) and radical radiotherapy (2013). Between 2014 and 2017, his prolactin levels remained well controlled on cabergoline. However in 2018, prolactin levels increased and were resistant to increasing doses of cabergoline. Repeat pituitary MRI showed no evidence of tumour regrowth. The patient later developed neck pain associated with bilateral upper limb paraesthesia and hypoesthesia of the right upper limb. A spine MRI revealed an intradural extramedullary tumour at C2-C4 level. Surgical resection was performed and a diagnosis of pituitary carcinoma was made. Post-operatively prolactin levels normalised and cabergoline was weaned.
Investigations
Initial prolactin levels were approximately 30,000 mIU/L. MRI showed an invasive pituitary tumour. Histology confirmed a prolactinoma with high mitotic activity. Following surgical treatment and radiotherapy, his prolactin level remained within the normal range on $\leq$0.5 mg cabergoline weekly and MRI confirmed no tumour re-growth. In 2018, his prolactin level rose to 22,000 mIU/l despite 4.5 mg cabergoline/week. Repeat pituitary MRI confirmed no evidence of tumour re-growth. MRI spine revealed a $31\times10\times25$ mm intradural extra-medullary lesion between C2-C4 with cord compression. Histology revealed a pituitary tumour with atypical features including nuclear pleomorphism, increased mitotic activity, raised Ki-67 of 15-20%, and evidence of MGMT methylation.
Treatment
Initial treatment involved dopamine agonists i.e. cabergoline. However, given the resistance to medical treatment, the patient underwent transsphenoidal surgery followed by a craniotomy 2 years later. Post-surgical radiotherapy was initiated after the second procedure. Due to the development of cervical myelopathy secondary to intraspinal metastasis, the patient underwent a cervical decompression procedure followed by cervical radiotherapy. A trial of Temozolomide was ceased after 2 cycles, given intolerance to treatment.
Conclusion and Point for discussion
Pituitary carcinomas are rare neoplasms that metastasize to sites distant from the pituitary, accounting for approximately 0.1% of pituitary tumours. Pituitary carcinomas are challenging as they initially behave in a similar fashion to their benign counterpart at the outset. This case demonstrates the importance of considering metastatic disease in patients with rising prolactin levels and no evidence of sellar recurrence.

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NCC8

Invoking Occam's razor: A case of familial partial lipodystrophy unifying multiple diagnoses

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Case history
A 25 year old primigravid woman was referred through to the Joint Antenatal clinic with a 15-year history of Diabetes Mellitus Type 2 treated with metformin. Her past medical history included polycystic ovarian syndrome, (causing significant hirsutism and amenorrhoea), non-alcoholic fatty liver disease, dyslipidaemia and hypertension (previously investigated for secondary causes). Her HbA1c was well controlled at 30 mmol/mol, and her Metformin had been discontinued. Due to her lack of adipose tissue, muscular appearance and diabetes-onset at a young age, a differential diagnosis of a lipodystrophy syndrome was considered.
Investigations
Initial investigations demonstrated raised triglycerides of 9.06 mmol/l, insulin level 109 pmol/l, a C-peptide level of 949 pmol/l and a random glucose 3.9 mmol/l. She was referred to the National Insulin Resistance team.
Results and treatment
Further investigations showed Leptin levels returned as 5.7 ug/l (normal as her BMI was below 25), however she was found to have a heterozygous missense mutation of her PPARG gene, giving a diagnosis of familial partial lipodystrophy. This diagnosis not only explains the early-onset of her diabetes but also her co-morbidities of PCOS, hypertension and dyslipidaemia. Due to this diagnosis she was referred through to the National Severe Insulin Resistance Service at Addenbrooke's Hospital for further specialised treatment and family genetic counselling.
Conclusions and points for discussion
There are a number of interesting aspects to this lady's case. Her diagnosis of Diabetes Mellitus Type 2 was made at a very young age, and she had this diagnosis for 15 years before further investigation was triggered. Phenotypical lack of adipose tissue in heterozygous individuals is partial and may only become evident following puberty. A diagnosis of familial partial lipodystrophy may therefore elude clinicians, often for many years. This highlights the importance of considering differentials when meeting a patient for the first time, irrespective of the duration of prior diagnosis, especially in atypical cases which do not fit typical cases of Diabetes Mellitus Type 1 or Type 2 or MODY and of young onset. In spite of a borderline leptin level, her genetic tests confirmed a result of partial lipodystrophy, which has unified all her pre-existing conditions under one signal diagnosis. This will now allow her to go on and have more targeted treatment and genetic counselling for her wider family and her new born child, who has a 50% chance of having the condition also.

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NCC9

A rare case of Hypocalcaemia – A diagnostic dilemma

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Case history
A 38-year-old woman presented with blepharospasm, cramping of the hands, and paraesthesia primarily affecting the face and hands. Symptoms had been present for 10 years but had been progressive over the previous 12 months. Symptoms were consistent with neuromuscular instability. Hypocalcaemia and elevated Parathyroid hormone (PTH) were confirmed. Past medical history was notable for anorexia nervosa in remission. Family history was non-contributary. Hypocalcaemia was resistant to oral calcium supplementation and symptoms persisted despite treatment with high doses of vitamin D (cholecalciferol). The patient had normal intelligence and was morphologically unremarkable with normal facies, stature, and metacarpal length. Following full biochemical assessment with a pattern of PTH resistance in the absence of overt skeletal defects, a diagnosis of pseudohypoparathyroidism type 1B (PHP1B) was suspected.
Investigations
On serial testing serum calcium was persistently low [1.6–1.8 mmol/l(ref, 2.2–2.6)]. PTH was elevated at 57.4 pmol/l (ref, 1.6–7.2). Phosphate was 1.41 mmol/l (ref, 0.7–1.45). 25 (OH) vitamin D was replete at 79 nmol/l(ref, $\geq$50). 1,25 (di-OH) vitamin D was low at 51 pmol/l (ref, 55–139). 24-hour urinary excretion was 1.2 mmol/24hr(ref, 2.4–6.5). Renal function and thyroid function tests were normal. Genetic analysis was undertaken to establish a diagnosis of PHP1B.
Results and treatment
The guanine nucleotide-binding protein alpha-stimulating (GNAS) gene locus on chromosome 20q13.3 displayed almost complete loss of maternal methylation

pattern at all four differentially methylated regions (DMRs) analysed. A diagnosis of PHP1B was thus confirmed. The patient was commenced on high doses of alfacalcidol (3 mcg/day) and calcium supplementation (1g/day). Serum calcium level improved significantly (2.08 mmol/l) and the patient has been symptom free for 12 months.

Conclusions and points for discussion

PHP comprise a group of disorders with an estimated prevalence of 0.3–1.1 per 100,000 and are characterised by end-organ resistance to PTH. This is classically associated with the Albright hereditary osteodystrophy (AHO) phenotype of brachydactyly, rounded facies, short stature, central obesity, heterotopic subcutaneous ossifications, and cognitive impairment. Genetic molecular analysis secures a diagnosis in up to 90% of clinically confirmed cases. PHP1B occurs due to methylation defects of the GNAS locus, and manifests as renal resistance to PTH action. Inheritance is autosomal dominant, but most cases present as sporadic. Patients with PHP1B do not typically display features of AHO, respond to high dose activated vitamin D supplementation with alfacalcidol or calcitriol, and have an excellent prognosis. Therefore, it is important to diagnose the condition early and optimize patient care to prevent complications due to long term PTH resistance.

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NCC10

PVLSA – A rare cause of thyroid abscess

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Case History

We present a case of a 24 year old music teacher and who attended our medical assessment unit. The gentleman described a twelve day history of neck pain, malaise, and odynophagia having received treatment one month previously for a PVL positive *Staphylococcus aureus* (PVLSA) lip abscess for which he did not complete eradication therapy. He described associated difficulty swallowing, rigors, vomiting and weight loss. On examination he had a tender, hot goitre and was septic.

Investigations

Chest radiograph showed changes consistent with pneumonia and empirical treatment as per local guidelines was commenced. He was notably thyrotoxic with a raised T4 level of 27, total T3 of 2.2 and partly suppressed TSH of 0.03. Suppurative thyroiditis was suspected and a neck CT revealed a large retro-pharyngeal collection and evidence of thyroid abscesses throughout the gland.

Results and treatment

The patient was transferred urgently to ENT and received further treatment for sepsis-associated coagulopathy. He underwent drainage of the collection and thyroid abscess formation and was monitored in the ICU. Cultures from the drained pus returned positive for PVLSA and anti-microbial treatment was optimised with senior microbiology input. A viral throat swab also returned positive for Influenza A and Oseltamivir was added. Thyrotoxicosis initially worsened with a T4 level greater than maximal assay detection. He continued to receive supportive management on the advice of the Endocrine team and T4 level began to down-trend five days post-operatively. Thyroid receptor and peroxidase antibodies returned negative.

Conclusion and Point for discussion

To conclude, a PVLSA infection progressed to an acute suppurative thyroiditis and retropharyngeal abscess. This occurred in the context of an associated pneumonia and Influenza-A. Further discussion of PVLSA infection, predisposing factors and differential diagnoses or underlying sequelae is prompted. This case highlights the considerations for the on-call Endocrinologist when faced with a rare and potentially fatal presentation of acute suppurative thyroiditis.

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NCC11

A spoonful of sugar helps the lactate stay down

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Section 1: Case history

A 30-year-old Romanian male presented to A&E with symptomatic hypoglycaemia (point-of-care venous glucose 1.8 mmol/l, laboratory value 2.0). He reported 2 days of intermittent left-sided abdominal pain and frequent food craving. Despite eating, he developed dysarthria, hyperhidrosis, somnolence and asthenia, associated with epigastric pain and vomiting. He was recently diagnosed with hepatitis C, discovered incidentally during investigations for chest pain with associated lactataemia. Throughout childhood, he had multiple hospital admissions due to protracted vomiting during intercurrent illness. On one-such occasion, he recalled being hypoglycaemic and requiring intravenous glucose. These episodes persisted into adulthood, and he had identified a maximum fasting period of 15 hours, with symptoms readily responsive to glucose but not fruit. He denied recent alcohol intake. On examination, he was pale, waxy, tachycardic and hypertensive with no other abnormal signs.

Section 2: Investigations

Emergency room investigations showed a severe lactic acidosis (lactate 18 mmol/l, pH 6.9) and marked leucocytosis (neutrophils 17×10^9/l) with a normal CRP. He was hyperkalaemic (6.5 mmol/l), without concurrent acute kidney injury. Liver function testing demonstrated an acutely elevated ALT (163 unit/l), with normal bilirubin and synthetic function. No infective focus was found on bacteriology specimens (blood, urine) or imaging (CT abdomen/pelvis) and toxicology screen was negative. Due to persistent acidosis and hyperkalaemia despite intravenous crystalloid and dextrose therapy, he required haemofiltration, following which he remained euglycaemic without intravenous dextrose.

Section 3: Results and treatment

He was referred to our unit and underwent a supervised fast, developing symptomatic hypoglycaemia after 18 hours. His serum glucose was 1.1 mmol/l with low insulin (< 1 mU/l) and C-peptide (50 pmol/l). He had significant ketosis, as well as elevated free fatty acids (3.16 mmol/l), urate (645 µmol/l) and lactate (10.4 mmol/l). A clinical diagnosis of fructose-1,6-bisphosphatase deficiency was made and he was referred for genetic analysis and expert inherited metabolic disorders (IMD) advice. A homozygous sequence variant in fructose-1,6-bisphosphatase (FBP1) gene, previously unreported, was identified. Functional studies are ongoing; however, this is predicted to be pathological.

Section 4: Conclusions and points for discussion

FBP1 deficiency, a key gluconeogenesis enzyme, is a rare autosomal recessive disorder that commonly presents acutely in early childhood when glycogen stores are limited or exhausted. We speculate that a reduced glycogen reserve consequent upon recently diagnosed hepatitis C precipitated this presentation. Given that around 30% of patients referred to the IMD service are diagnosed in adulthood, this represents an important differential in patients presenting with hypoglycaemia and lactic acidosis.

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NCC12

A rare presentation of parathyroid carcinoma and brown tumours in a young woman with no associated genetic condition

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Case history

A 34-year old Caucasian nurse presented to her GP with a 7 month history of abdominal pain. She was found to have PTH-dependent hypercalcaemia with Stage 3A chronic kidney disease (corrected calcium 3.43 mmol/l, phosphate 0.62 mmol/l, total vitamin D 32 nmol/l, PTH 214.9 pmol/l, creatinine 117 µmol/l and eGFR 45 ml/min/1.73m^2). On direct questioning, she reported fatigue, generalised weakness and intermittent joint pains affecting her lower back and both hips. She had no past medical history and did not take any prescribed or over-the-counter medication. There was no history of malignancy or endocrinopathy in her family.

Investigations

Following urgent referral to otolaryngology, computerised tomography (CT) and ultrasound demonstrated a $25 \times 17 \times 23$ mm left inferior parathyroid lesion. She was diagnosed with severe primary hyperparathyroidism and due to high PTH, parathyroid carcinoma was suspected. There was no evidence of renal calculi on ultrasound. Thyroid function, plasma metanephrines and calcitonin were all normal.

Results and treatment

Oral colecalciferol was commenced and she was admitted for intravenous fluids prior to a left inferior parathyroidectomy and thymectomy, two months after presentation to her GP. Her post-operative course was complicated by mild hypocalcaemia attributed to Hungry Bone Syndrome, treated with alfacalcidol and elemental calcium. Genetic screening for familial primary hyperparathyroidism was negative. Parathyroid histology was consistent with low grade parathyroid carcinoma with multifocal vascular and capsular invasion. Ki67 index was 3%. Thymus histology was benign. Her post-operative staging CT demonstrated multiple large lytic bone lesions replacing her T9 vertebra, right femoral neck and two pelvic lesions all concerning for metastases or brown tumours. There were no other lesions or lymphadenopathy on CT. Magnetic resonance imaging confirmed hypodense lesions

on T1 and bright cystic lesions on T2 – typical for brown tumours. She has been referred for urgent bone biopsy and orthopaedic stabilisation of her right hip and T9 vertebra. She will remain under close follow up with the Endocrinology team.

Conclusions and points for discussion

This is a very rare presentation of parathyroid carcinoma in young person with no associated genetic condition. Parathyroid carcinoma should always be considered in primary hyperparathyroidism with markedly elevated PTH. Brown tumours are bone lesions that occur in relation to excess osteoclast activity and are a type of osteitis fibrosa cystica. Although not neoplastic they can cause skeletal instability and fractures. They are an important potential sequalae of severe long-standing hyperparathyroidism so patients should be counselled appropriately and investigated promptly should they develop focal pain.

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NCC13

Refractory Graves' disease following total thyroidectomy caused by concurrent ectopic thyroid tissue in the anterior mediastinum

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Case History

A 34-year-old Caucasian female patient presented in May 2015 to A&E with symptoms of overt thyroid dysfunction. She was managed medically until June 2016 when thionamide treatment was withdrawn. Unfortunately, this lady had a first disease relapse in July 2018 whilst she was pregnant at 35 weeks of gestation and then further disease relapse in January 2020 during her second pregnancy.

Investigations

Initial biochemistry in 2015 confirmed thyrotoxicosis – TSH: < 0.01 mIU/l, fT4: 22 pmol/l and fT3: 7.9 pmol/l. TRAb titre was undetectable. A^{99} Technitium uptake scan was at the time normal. Despite initial good response to medical treatment, in June 2018 during 3rd trimester of her pregnancy, this lady developed again symptoms of thyroid dysfunction. Repeat biochemistry confirmed thyrotoxicosis relapse with TSH: <0.01 mIU/l, fT4: 27.1 pmol/l and fT3: 12.1 pmol/l. Below are illustrated thyroid function tests at initial presentation and during relapses.

Date	27/5/15	23/2/16	06/07/18	18/12/18	27/4/19	11/9/19	31/1/20
TSH (mIU/l)	0.02	0.88	<0.01	<0.01	<0.01	0.01	<0.01
fT4 (pmol/l)	22	13.3	27.1	23.6	21.8	30.3	37.7
fT3 (pmol/l)	7.9	5.6	12.1				

Treatment

At diagnosis in 2015, Carbimazole 20 mg daily was offered for 12 months and once this lady achieved remission, treatment was withdrawn. During first relapse, it was felt that Carbimazole was the best option as she was at the end of pregnancy. This lady continued following delivery, albeit using just 5mg daily as she was breastfeeding. Definite treatment was discussed, and total thyroidectomy was considered optimal as this lady was breastfeeding and was planning to conceive again imminently. She had total thyroidectomy in October 2019. Histology was consistent with Grave's disease and focal nodular hyperplasia. Surprisingly, she became thyrotoxic after surgery which initially was thought to be due to factitious thyrotoxicosis. She was again pregnant at 27 weeks of gestation. Despite thyroxine withdrawal, clinical and biochemical thyrotoxicosis persisted and thionamide treatment was restarted. This lady was referred for a new ^{99} Technitium uptake scan which demonstrated a large focus of tracer concentration in the left anterior mediastinum accumulating 3.5% of the administered activity. It retrospectively transpired that the 2015 uptake scan had demonstrated the same mediastinal focus. Cross-sectional imaging with CT showed a large anterior mediastinal mass, compatible with thyroid gland tissue.

Conclusion

Ectopic thyroid tissue is a rare entity resulting from developmental defects at early stages of thyroid gland embryogenesis. Ectopic Graves' disease is exceedingly rare and differentiating from eutopic disease can represent a diagnostic conundrum.

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NCC14

Multiple electrolyte disturbances as the presenting feature of MEN-1

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Case history

A 49-year-old teacher presented to his GP with lethargy and lower limb weakness. He had noticed polydipsia and polyuria, and had experienced weight loss albeit with an increase in central abdominal fat mass. He had previously undergone cholecystectomy and colonic polypectomy. He took no regular medications.

Investigations

He had hypercalcaemia 3.34 mmol/l with PTH of 356 ng/l and hypokalaemia 2.7 mmol/l and was admitted for intravenous fluid therapy and potassium replacement. Renal function was normal and phosphate level measured low at 0.42 mmol/l. A contrast enhanced CT Chest/Abdomen/Pelvis imaging revealed a well-encapsulated anterior mediastinal mass measuring 1742 cm × 1142 cm with central necrosis, compressing rather than invading adjacent structures. A neck ultrasound revealed a 242 cm right inferior parathyroid lesion. The patient underwent biopsy of the mediastinal lesion and immunohistochemistry was positive for synaptophysin and CD56 with weak patchy staining for PAX8; Ki67 was 3%. Histology was consistent with an atypical carcinoid-likely thymic. His serum cortisol was 2612 nmol/l. Inadequate cortisol suppression to 575 nmol/l from an ODST was demonstrated and ACTH was elevated at 67 ng/l. Pituitary MRI was normal and remaining anterior pituitary biochemistry was unremarkable. On review of the previous CT imaging, the adrenals appeared normal but a pancreatic lesion was noted adjacent to the uncinate process with internal calcification. The admission was further complicated by an increase in urine output, to 10l/24 hrs with significant thirst, for which a water deprivation test was conducted. Desmopressin was administered at 1700 hrs without significant response. A ^{18}FDG-PET demonstrated high avidity of the mediastinal mass with additionally active bilateral superior mediastinal nodes. The pancreatic lesion was not FDG avid. On ^{68}Ga-DOTA-PET, the mediastinal mass was moderately avid, and the pancreatic mass showed marked uptake with additional peripancreatic lesions likely representing lymph node involvement.

Time	1100	1247	1506	1700	1840	1930	2030	2130
Serum osmolality (mOsm)	300	301	304	304	298	301	294	291
Urine osmolality (mOsm)	253	275	377	348	391	412	355	304
Serum Na+ (mmol/l)	150							

Treatment

Intravenous fluids successfully treated hypercalcaemia. Metyrapone was initiated at 250 mg QDS and uptitrated to 500 mg QDS, with therapeutic cortisol concentration aimed between 100–200 nmol/l. Genetic testing due to MEN-1 phenotype was requested and he was referred urgently for thoracic MDT review and surgery.

Conclusions/Discussion

The underlying unifying diagnosis is clinical MEN-1 with concurrent paraneoplastic Cushing's syndrome most likely secondary to the large thymic neoplasm, complicated further by nephrogenic DI due to multiple electrolyte disturbances.

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NCC15

A case report on rare metastic Paraganglioma with SDHB mutation

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Paragangliomas are rare neuroendocrine tumours that originate from neural crest cells and can arise from any autonomic ganglion of the body. This is a challenging entity given the limited therapeutic options. Here, we present a rare case of metastatic Paraganglioma in a patient with a germline pathogenic succinate dehydrogenase subunit B (*SDHB*) mutation. A 54 year old lady was initially diagnosed with functioning bladder paraganglioma with raised metanephrine and normetanephrine level, which was treated with open radical cystectomy and lymph node dissection after appropriate alpha and beta blockage. Postoperative MIBG scan did not show

any convincing residual or metastatic disease and biochemical work up revealed normalisation of metanephrine levels post operatively. Patient remained under regular follow up and had routine surveillance scans and continued to remain asymptomatic. 3 years after the initial diagnosis, she presented with symptoms of palpitations, pounding sensation in her neck and excessive seating.Surveillance scan picked up multiple lung nodules, a soft tissue nodule in the posterior right para renal space, an acetabular lesion in the left hip and a new lytic lesion in L1 vertebral body with grade 1 pathological fracture. Blood work up showed elevated plasma metanephrine level. Clinically she was hypertensive with resting tachycardia and was commenced on appropriate alpha (Doxazocin)and beta (Bisoprolol) blockage. She was discussed in the MDT with input from multiple specialities and it was decided to treat her with Peptide receptor radio nucleotide therapy (PRRT) using Luteum Dotatate, which is one of the latest modality of treatment There is growing body of evidence that PRRT is highly effective in terms of tumour response, disease stabilisation, symptomatic control and preservation of quality of life with favourable safety profile.. She has currently completed 2 cycles of the therapy and is awaiting FDG PET-CT and Gallium dotatate PET scan to assess response to treatment 8 weeks after the 2 nd cycle. Neurosurgical team advised conservative management of the vertebral fracture. She is also considered for prophylactic radiotherapy to the left acetabular lesion to prevent any fracture in the future. Multi disciplinary team approach remains indispensable given the complex nature of the condition.Patients with *SDHx* mutation, especially *SDHB,* have increased risk of developing metastasis and hence require regular, long-term surveillance. For patients with progressive or symptomatic disease that is not amendable to surgery there are various palliative treatment options like radiotherapy, radio frequency or csystemic therapies like chemotherapy or molecular targeted therapies like PRRT.

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NCC16

AIP-mutated Acromegaly responding well to a first generation somatostatin analogue

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Introduction
Aryl hydrocarbon receptor interacting protein (AIP) mutated Acromegaly is a complex rare disease. AIP mutations are associated with an aggressive, inheritable form of acromegaly that responds poorly to SST2-specific somatostatin analogues (SSAs). Literature reports demonstrate that second generation SSA, Pasireotide LAR, is superior to first generation SSAs in treating acromegaly with AIP mutation. Treating acromegaly with AIP mutation could be quite challenging. We describe an unusual case of acromegaly that has shown a good biochemical and clinical response to first generation Sandostatin LAR and also shows an uncommon histological picture of dense granulations.
Case report
A 19 year old male was referred by his GP after he had been complaining of headaches for 4 years. On examination he looked acromegalic with frontal bossing, thick skin, prognathism and big hands. Initial investigations showed a high IGF-1 1276 mcg/l, an OGTT with a nadir Growth hormone (GH) 33 mcg/l, a high Prolactin of 6724 mlU/l, and a low Testosterone of 3 nmol/l with a low normal FSH 1.5 IU/l and LH 2.5 IU/l. A MRI of the pituitary showed a 16 mm pituitary macroadenoma. Transsphenoidal excision was performed at 8 weeks after presentation. Histology showed a densely granulated somatotroph cell PitNET/adenoma with Ki67 mildly elevated. Post-surgery follow up investigations showed a high IGF-1 512 mcg/l, an average GH of 1.3 mcg/l on a growth hormone day curve (GHDC). Clinical review three months after surgery confirmed improvement in symptoms and facial appearance. Further investigations confirmed on-going evidence of acromegaly with a high average GH of 2.25 mcg/l on GHDC and a high IGF-1 of 526 mcg/l. Genetic testing confirmed AIP mutation which is heterozygous for c.805_825dup. Familial counselling and investigation confirmed maternal and brother AIP gene mutations. Baseline MRI pituitary post-surgery did not confirm a definite residual tumour and a methionine PET scan is pending. An Octreotide test was performed and GH levels improved from 1.8 mcg/l to 0.65 mcg/l after a test dose of 100 mcg Octreotide subcutaneously. Consequently, he was started on Sandostatin LAR 30 mg every 4 weeks. Good biochemical response was noted and IGF-1 returned to within the age and sex specific target range. The patient's average GH on a GHDC is 0.8 mcg/l after 3 months on treatment.
Discussion
Despite the fact that AIP-mutated Acromegaly shows a better response to second generation SSA than first generation SSAs our patient has responded well to a first generation SSA. Further follow up is necessary to confirm whether a long term effect is maintained.

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NCC17

Hyperthyroidism as an under-recognised reversible cause of microcytosis

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Introduction
Hypothyroidism is a well-recognised cause of macrocytosis, but microcytosis is not widely recognised to be associated with hyperthyroidism. Thyroid abnormalities are often associated with various haematological changes and Graves' disease has been reported to be mimicking beta thalassaemia trait in the literature. We discuss two cases of microcytosis related to hyperthyroidism that fully resolved once euthyroidism was achieved.
Case 1
A 24-year-old male with a few years history of hyperthyroidism on intermittent Carbimazole use was referred with relapse (suppressed TSH and elevated Free T4, 48 and Free T3, 18 pmol/l). He was incidentally noted to have microcytosis (MCV 76.1 fL, Hb: 135 g/l). In addition to starting Carbimazole, Ferritin and haemoglobinopathy screen were checked and these were normal. Once he became euthyroid his MCV normalised to 85.4 fL. He again became hyperthyroid (Free T4 66 and free T3 30) a year later and his MCV dropped to 79 fL.
Case 2
A 37-year-old female with symptoms suggestive of long standing hyperthyroidism was diagnosed with Graves' disease (suppressed TSH and Free T4, 45 pmol/l) and was noted to have longstanding low MCV 75 fL. Her ferrin was normal at 23 µg/l and haemoglobinopathy screen was suggestive of delta beta thalassaemia trait. Interestingly after achieving euthyroidism her MCV normalised to 80.5 fL. We are planning to repeat her haemoglobinopathy screen to check if all the abnormalities have resolved.
Discussion and conclusion
Microcytosis is one of several well described but often under recognised haematological consequences of untreated hyperthyroidism. Thyroid hormones have been known to have a key role in regulating bone marrow haematopoiesis and iron utilisation by erythrocytes through a variety of poorly understood mechanisms. Ineffective erythropoiesis with reduced Iron utilisation could explain microcytosis. This change is noted to be more common in those with prolonged hyperthyroidism as in our cases. Incidental microcytosis with hyperthyroidism resolves with treatment and further investigations would only be needed if microcytosis persists after achieving euthyroidism.

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NCC18

A case of iatrogenic Cushing's disease and secondary adrenal insufficiency following a drug interaction between intra-articular triamcinolone injection and ritonavir

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Section 1: Case history
A 50-year-old woman presented to the HIV clinic after suspecting adverse effects following two intra-articular triamcinolone injections to her left hip, administered three and seven months prior. She complained of ongoing leg pain, generalised weakness and lethargy. Her past medical history included HIV infection, mild asthma for which she took inhalers only and had never required oral steroids. Her antiretroviral medications included dolutegravir, darunavir and ritonavir. Her asthma was treated with inhaled beclomethasone and formoterol twice daily for five years. On examination She had increased facial fat, prominent supraclavicular and dorsocervical fat pads, dark abdominal striae and central adiposity with slim arms and legs. On neurological examination she had proximal weakness of the lower limbs.
Section 2: Investigations
A Short Synacthen Test showed a cortisol level that was undetectable at baseline (RR 160-550 nmol/l), 167 nmol/l 30 mins after administering tetracosactide (RR > 450 nmol/l) and 244 nmol/l after 60minutes (RR >600 nmol/l).
Section 3: Results and treatment
She was diagnosed with iatrogenic Cushing's disease and secondary adrenal insufficiency (SAI) following a known interaction between triamcinolone and the CYP450 inhibitor ritonavir. She commenced 4 mg prednisolone once daily. Ritonavir was stopped immediately and darunavir was switched to Triumeq, which does not inhibit CYP450, aiming to facilitate hepatic clearance of triamcinolone.
Section 4: Conclusions and points for discussion
Ritonavir is an HIV protease inhibitor which is primarily used as a 'booster' for other antiretroviral agents. It is a highly potent inhibitor of hepatic cytochrome P450 3A4

(CYP3A4) activity. When given at subtherapeutic doses, ritonavir increases the concentration of other antiretrovirals given in conjunction with it, allowing for decreased dosages and increased dose intervals. However, as exogenous steroids are primarily metabolised via the CYP3A4 pathway, significant interactions with ritonavir may occur. It is now well known that this interaction can cause iatrogenic Cushing's disease and sometimes SAI which occurs due to ACTH suppression by excess non-metabolised exogenous steroids. Patients on CYP3A4 inhibitors such as ritonavir require careful consideration regarding prescribing of new drugs and potential drug interactions. Practitioners should be aware of potential interactions with glucocorticoids in all forms. Following a diagnosis of iatrogenic Cushing's disease in such cases, prompt assessment for SAI is indicated with a low threshold for commencing steroid replacement in patients who are symptomatic. This is particularly crucial for those who have had depot injections, where the exogenous steroid can not be withdrawn.

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NCC19

Conservative management of incidentally detected isolated ectopic papillary thyroid carcinoma: A case report vs possibility of future management protocols?

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Section 1:
25 year old lady presented in 2014 with subacute submental midline neck swelling. Ultrasound neck: thyroid glands noted to be normal in size, shape and echotexture. No foci/nodules/mass lesion noted with normal vascularity. Isthmus of thyroid also noted to be normal in size, shape and echotexture. Neck vessels seen normally. Few hypoechoic lesions noted in submental region with echogenic area within it, on application of color doppler flow showing blood flow in echogenic area (differential ?enlarged lymph node), no evidence of calcification. FNAC only revealed foamy histiocytes and acute inflammatory infiltrate. Normal routine bloods including thyroid function tests except slight increase in CRP therefore diagnosed as inflammatory cyst. Patient started on antibiotics and discharged. Lost to follow up. Represented to ENT 3 years later for cosmetic removal of persisting swelling. Noted to have a 3*3 cm submental swelling, surface noted to be irregular moving with swallowing. Overlying skin normal. Suspected thyroglossal cyst vs lymph node. Planned for sistrunk operation under GA as per patient request.
Section 2:
Specimens sent to pathology – received 4.5*2*2 cm three grey white nodular soft tissue masses measuring together 4.5*2*2 cms. C/S showed 4 cysts with papillary projections arising from the wall projecting into lumen. Microscopically well differentiated papilliferous lesion lying within a cystic space. Incomplete fibrous capsule capsule, closely packed papillae have a core of fibrovascular connective tissue lined by single layer of cuboidal to low columnar epithelial cells. Eosinophilic secretions presented within cysts. Pale staining nuclei with prominent nucleoli. Endocrinology involved retrospectively full thyroid screen (post op), thyroglobulin levels, autoimmune antibodies negative. Asuragen and thyroseq3 testing negative.
Patient Discussion Plan made for active surveillance rather than thyroidectomy as patient denied same. Ultrasound/CT thyroid done serially for 3 years negative. FDG PET scan done 1 and 3 years post op negative
Conclusions/Points for Discussion
Rare case of ectopic thyroid papillary cancer developing in prolonged swelling. No evidence of malignancy in thyroid gland. Authors vary in offering management in patients with thyroglossal cyst carcinoma (or ectopic papillary thyroid cancer) / microscopic papillary thyroid cancer with total thyroidectomy vs active surveillance. Involvement of endocrine is essential in such cases as we may be able to offer patient with a better information background in case the option of thyroidectomy is to be broached. Perhaps, in this case early endocrine consultation and reassurance may have helped in achieving thyroidectomy if needed.

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NCC20

What next when parathyroid surgery fails?

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Case History
Mr AT, a 54 year old male was referred by his GP in 2019 with a two year history of raised calcium. He initially sought medical attention for pain radiating from the left buttock to the knee. He had a background of hypertension and pre-diabetes and was on Nifedipine LA 3 mg OD and Furosemide 20 mg OD. He denied headaches, insomnia, concentrating problems, constipation, polyuria and polydipsia. He had no history of fractures nor renal stones. He was a non-smoker and drank little alcohol. There was no family history of raised calcium or kidney stones.
Section 2: Investigations
In 2014, his corrected calcium was normal. Over the next few years his calcium rose to 2.7, 2.84, 2.85 and 2.88 mmol/l in 2017, 2018, 2019 and 2020 respectively. Correspondingly PTH was elevated at 156 and 192 ng/l in 2019 and 2020. Vitamin D was normal at 52, 62 and 56 nmol/l in 2018, 2019 and 2020 respectively. The first calculated urine calcium: creatinine excretion ratio was 0.0028 in June 2019. Renal ultrasound in 2019 was normal. DEXA scan showed Osteoporosis at the lumbar spine with a T score of –3.1. He had an MRI spine 2019 prior to referral showed multilevel arthritis. NM Parathyroid showed a suspected right inferior parathyroid adenoma. Ultrasound of parathyroid was discordantand did not reveal an adenoma. He was referred for parathyroid surgery.
Section 3: Results and treatment
He underwent four gland exploration and the right inferior pararathyroid gland was excised in June 2020. Histology of the excised gland showed a normal parathyroid. Post surgery his calcium levels were not corrected and remains elevated. Genetic analysis in December 2020 was negative for AP2S1, CASR and GNA11 gene variants. His bisphosphonate were stopped recently and localising scans were requested and if required Choline PET scan and 24 hour urine sample for calcium: creatinine clearance and a parallel blood test same day(sample in lab)
Section 4: Conclusions and points for discussion
Persistent hypercalcaemia post-surgery for suspected primary hyperparathyroidism. 1. Is this primary hyperparathyroidism or autoantibody associated FHH? 2. Does low Ca: Cr excretion ratio make hyperparathyroidism unlikely? 3. What further tests can be carried out to determine the cause of raised calcium and PTH? What is role functional imaging in this scenario 4. How common is autoantibody associated FHH?

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NCC21

Steroid responsive encephalopathy associated with autoimmune graves thyroid disease, a rare presentation

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Case History
We describe a case of a 30-year-old female who presented at 8 weeks postpartum with history of altered behaviour, clouding of consciousness and status epilepticus. She had been diagnosed with autoimmune graves thyroid disease and was commenced on carbimazole prior to this episode. She was treated as meningoencephalitis. Also, consideration was given for possibility of thyroid storm and post-partum eclampsia. She was intubated and ventilated, treated with IV acyclovir, IV ceftriaxone, IV Keppra and IV magnesium. Lugol's iodine and propylthiouracil was also started for thyroid storm.
Treatment
She was extubated after 3 days, but she continued to be confused and noncommunicative. A diagnosis of autoimmune thyroid disease encephalopathy (EAATD) was made, and high dose steroid therapy was initiated. She was also given IV Pabrinex as high metabolic state was considered. Over the next few days, she improved steadily nevertheless continued to have poor short-term memory of events like childbirth. She then recovered fully around 6 weeks. The steroid was weaned and stopped over the period of next six weeks. She was discharged on block and replace regime and Keppra awaiting a thyroidectomy surgery. Five months later she presented again with seizures after consuming alcohol which was treated similarly.
Investigations
At initial presentation, routine blood tests showed normal white cell count, C reactive protein was 25 mg/l, Blood glucose was 6.7 mmol/l, Thyroid stimulating hormone <0.05 mU/l, Free thyroxine-84.2 pmol/l, Free triiodothyronine-15.2 pmol/l, Thyroid peroxidase 344 IU/mL. Anti-Thyroid receptor antibodies were negative. CT Head, MRI Head, Pituitary and MR Venogram was normal, Cerebrospinal fluid looked clear, raised protein 0.74, CSF glucose was 3.7, WCC were zero, microscopy and culture showed no organism, negative for viral screen on polymerase chain reaction.
Conclusion
Encephalopathy associated with autoimmune thyroid disease(EAATD) has been described in the literature with following features: – Neurological/psychiatric symptoms, high levels of anti-thyroid antibodies, raised cerebrospinal fluid protein levels, non-specific diffuse electroencephalogram changes and

responsiveness to the corticosteroid treatment (1). Clinical presentation entails relapsing and remitting course. (1) Makoto et al found out that the serum antibodies against the NH2-terminal of alpha-enolase (NAE) are highly specific diagnostic biomarkers for EAATD. Immunoglibulins and plasma exchange were efficacious other treatments. This case highlights the importance of considering thyroid encephalopathy in all patients with signs of encephalopathy of unknown origin and autoimmune thyroid disease. The need for prompt initiation of steroids. 1. Tamagno et al, BMC neurology 2010,10:27, 2. Makoto Yoneda, Brain Nerve 2013 Apr;65(4):365-76.

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NCC22

Familial hypocalciuric hypercalcemia. Not so benign

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Section 1: Case history

At the age of 18 our patient presented with renal stones and was diagnosed with Primary Hyperparathyroidism (PHPT). At 20 she underwent a right sided nephrectomy for a calculus associated non-functioning kidney. Over the years she has had numerous renal calculi, ureteric obstructions with stents, requiring urology input. Of note she had osteoporosis, hypertension, pancreatitis, gastritis, intracranial hypertension (with shunt in situ) and resistant Vitamin D deficiency. She was partially blind. Her late mother and brother also had renal stones, but no cause was identified. Her offspring remain normocalcaemic and asymptomatic. Referred for parathyroidectomy where she was diagnosed with familial hypocalciuric hypercalcaemia (FHH), a genetic disorder of phosphocalcic metabolism which is usually asymptomatic.

Section 2: Investigations

Between 2001 to 2019 her adjusted calcium varied between 2.4–2.8 mmol/l. Vitamin D persistently remained low. PTH ranged from 32–298 mmol/l. 24–hour urinary Calcium/creatinine ratio: 0.23. No paired bloods were done. Ultrasound parathyroid showed possible ectopic parathyroid lateral to the right lobe of the thyroid gland. Parathyroid SPECT CT showed generally homogenous uptake in thyroid except in the region of the right lower pole. DEXA SCAN showed: Spine T score –3.6, Hip T score –3.6 and Neck of femur T score –3.5.

Section 3: Results and treatment

Cinacalet 30 mg once a day was started but calcium levels remained unchanged. Cholecalciferol 50,000 IU was also started but Vitamin D remained persistently low. Bisphosphonate therapy was withheld due to dental complications. Despite compliance, remained symptomatic. Prior to four gland exploration, genetic testing was requested in 2020. A mosaicism mutation in CASR gene was identified.

Section 4: Conclusions and points for discussion

FHH is generally considered a benign disorder. Our patient was diagnosed with FHH 38 years after her diagnosis of primary hyperparathyroidism. Unusually, she developed multiple complications associated with (PHPT). This case highlights that FHH may not be benign. Points for discussion. 1. Urinary calcium should be evaluated in all cases of PHPT. 2. FHH may not be a benign disease as usually stated. 3. Management of symptomatic FHH is complex and needs MDT input. 4. How should this patient be managed further?

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NCC23

An interesting case of POEMS syndrome with adrenal insufficiency

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POEMS syndrome is rare multi-system disorder characterised by a paraneoplastic plasma cell disorder. The acronym POEMS stands for Polyneuropathy, Organomegaly, Endocrinopathy, M protein, and Skin changes. The underlying mechanisms are poorly understood, but chronic overproduction of pro-inflammatory cytokines have an integral role in the disorder. Diagnosis of POEMS is difficult owing to the variety of clinical manifestations. Mandatory diagnostic criteria are (a) one major criterion of either polyneuropathy or monoclonal gammopathy, in association with (b) one minor criterion including, but not limited to, organomegaly, endocrinopathy or skin changes. Endocrinopathies have been identified in 67-84% of patients with POEMS [1]. While hypogonadism and hypothyroidism are relatively common, primary adrenal failure is rarely reported. We present a 54-year-old woman who was found to have a raised hemoglobin, hematocrit and thrombocytosis on routine blood testing. She was concomitantly investigated for a rapidly-ascending, bilateral peripheral motor and sensory neuropathy. Diagnosis of POEMS was made and she underwent chemotherapy with Lenalidomide and high dose dexamethasone in 2015. Since then, she has not received endogenous glucocorticoids. She had an unplanned admission in April 2020 with a likely viral illness, and was found to be glucocorticoid deplete. A 250-mcg short synacthen test demonstrated an inadequate response in cortisol, from 119 nmol/l to 169 nmol/l, with a raised adrenocorticotrophic hormone (ACTH) level of 66 mU/l. Adrenal antibodies were not detected. CT scan of the abdomen reported no adrenal gland abnormalities. The patient denied symptoms of mineralocorticoid deficiency, with no postural blood pressure (BP) drop – sitting BP 123/69 mmHg and standing BP 131/74 mmHg. Serum electrolytes were normal. Random renin was raised at 107.0 mIU/l, aldosterone was at the lower level of the normal range, 141 pmol/l, and androgen screen was within normal limits. Thyroid stimulating hormone (TSH) was 8.07 mIU/l, free thyroxine (fT4) levels 0.93 ng/dl, and thyroid receptor and thyroid peroxidase antibodies were both negative. The patient is now established on tds Hydrocortisone therapy: 10mg morning, 5mg lunchtime and 5mg evening. In summary, we present a 54-year-old woman with POEMS syndrome with subacute primary adrenal failure, characterised by glucocorticoid deficiency and ACTH excess. Although rare, it is important for all clinicians to be aware of POEMS syndrome as a potential diagnosis if the diagnostic criteria described above are filled, and for endocrinologists to be aware that POEMS endocrinopathies can occur in any gland, including the adrenal glands.

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NCC24

Severe postmenopausal hyperandrogenism with diagnostic dilemma. The source of androgen being unmasked by the adrenal ovarian venous sampling

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Section 1: Case history

A 60 year-old lady presented with a 4-year history of progressively increasing virilisation on the background of right salpingo-oophorectomy for ectopic pregnancy in 1984 (no histology available).

Section 2: Investigations

Testosterone 23.6 nmol/l (NR $<$ 1.7), LH 16 IU/l (7.7–58.5), FSH 33 IU/l (25.8–134.8), androstenedione 3.2 nmol/l (NR 1.4–14.3), DHEAs 1.2 umol/l (0.5–5.6), 17-OHP 2.7 nmol/l (1–4.5), cortisol 372 nmol/l (133–537 nmol/l), plasma metanephrines, CEA and CA-125 were likewise all normal. Urine steroid profile showed very high androgen metabolites, but no characteristic pattern of adrenal carcinoma. Overall, basal biochemistry indicated an ovarian source. The low dose dexamethasone suppression test failed to suppress the testosterone levels, indicating tumourous cause of raised testosterone levels. Treatment with GnRH-analog achieved complete suppression of LH, FSH and testosterone levels, indicating that pathological testosterone secretion was gonadotrophin dependent and, again pointing towards an ovarian source. However, laparoscopic left salpingo-oophorectomy showed a normal postmenopausal ovary, with no evidence of tumour or hyperthecosis

Section 3: Results and treatment

PET scan showed increase FDG uptake in a slightly bulky right adrenal gland, but adrenal protocol CT scan failed to definitively identify an adenoma. Pelvic MRI and transvaginal ultrasound indicated the possibility of an ovarian remnant within the right broad ligament, but laparoscopic removal found only fibrous adipose tissue. In view of ongoing high testosterone levels, imaging was done, which did not indicate towards any obvious cause. We therefore proceeded to sampling of ovarian and adrenal veins (see table below), which indicated right adrenal source of testosterone, and she then underwent right adrenalectomy that achieved biochemical cure (testosterone $<$1.0 nmol/l). Our hypothesis is that the right adrenal contains tumourous tissue that expressed the LHCG-receptor (Luteinizing hormone choriogonadotropin), but histology and staining remains in progress.

Section 4: Conclusions

This is an unusual and complex case of postmenopausal hyperandrogenism with unclear cause of persistently raised testosterone levels, which was only unravelled by the adrenal ovarian venous sampling, which we have never previously performed in Newcastle, that indicating the right adrenal as the source.

- Identification of the source of androgen excess based solely on testosterone, DHEAS and androstenedione may be misleading

• Pure testosterone-secreting adrenal adenomas are extremely rare
• In some selected cases of post-menopausal hyperandrogenism, biochemically proven to be gonadotrophin-dependent, imaging of the adrenals is appropriate and adrenal/ovarian venous sampling may be required.

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NCC25

An adrenocortical carcinoma with distinct features of 21-hydroxylase deficiency

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Adrenal carcinomas are rare with a poor prognosis, highlighting the importance of prompt investigation of adrenal incidentalomas. We report a challenging case of an adrenocortical carcinoma secreting steroids in a pattern characteristic of 21-hydroxylase deficiency, which also proved to be a histopathological enigma. A 36-year-old woman underwent investigation for right-sided loin pain. A CT showed an avidly heterogeneously enhancing circumscribed left adrenal mass measuring 65 × 48 × 76 mm with <60% absolute washout, with fat deposition. She was reviewed in the urology clinic, with discussion in the urology MDT. Radiology was felt to be in keeping either with an angiomyolipoma or an adrenal adenoma. The possibility of a phaeochromocytoma was raised. Following clinical and biochemical assessment in the urology clinic, and liaison with the clinical biochemistry team, she was referred to the endocrinology clinic for urgent review prior to left adrenalectomy. She was normotensive and normokalaemic. She had no features of Cushing's. Plasma and 24-hour urinary metadrenalines, as well as 24-hour urinary cortisol were normal. Grossly elevated levels of testosterone (8.84 nmol/l), 17-hydroxyprogesterone (>300 nmol/l), and androstenedione (63.3 nmol/l) were found. ACTH was elevated at 78 ng/l. She gave a 6 month history of amenorrhoea, severe hirsutism and scalp hair loss. A urinary steroid profile showed significantly elevated levels of 17-hydroxyprogesterone metabolites (11-oxo-pregnanetriol, pregnanetriol and 17-hydroxypregnanolone), which strongly suggested a diagnosis of congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency. However, the short history of hyperandrogenism was not consistent with CAH. Following robotic left adrenalectomy, considered complete, her serum biochemistry normalised and symptoms improved. Detailed histology was unable to differentiate clearly between adrenocortical tumour and phaeochromocytoma. A second opinion was sought, identifying the tumour as a phaeochromocytoma, which conflicted with the biochemistry. A third opinion characterised the tumour as an adrenocortical carcinoma. Although she remained very well, unfortunately, a CT scan 7 months post-operatively showed evidence of liver metastases, with left para-aortic and left renal hilar nodal disease. Serum testosterone and 17-hydroxyprogesterone started to rise again. This confirmed that the tumour was a virilising adrenocortical carcinoma with disrupted steroidogenic enzyme expression comparable to 21-hydroxylase deficiency. She was referred for oncology input.

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NCC26

Rapidly progressing Cushing's syndrome secondary to ACTH producing Parotid Carcinoma

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61 year male presented with productive cough and was noted to have persistent hypokalaemia. On examination he had an elevated blood pressure; previously not known to be hypertensive and significant proximal myopathy in his lower limbs. He also had central obesity. In October 2018 he had a left parotid swelling. He had left parotidectomy and left neck dissection. The histology was an adenocarcinoma. In the following year he had cough, and shortness of breath, which on investigation showed a left pleural effusion. He had a VATS procedure and histology showed metastatic adenocarcinoma to lung from the parotid. His potassium levels ranged from 2.8–3.45 mmol/l litre with raised urinary potassium. Cushing's syndrome was suspected so low dose dexamethasone test(LDDST) was done. 24 hour urine cortisol was also requested, as well as ACTH. The baseline cortisol was 10595 nmol/l and after 48 hrs after LDDST the cortisol was 4425 nmol/l. ACTH was 1105 ng/l which was suggestive of ACTH dependent Cushing's syndrome. MRI pituitary was normal. 24 hour urine cortisol was 11585 nmol/l. Ectopic ACTH production was suspected and patient was started on Metyrapone 250 mg tds. A week later the patient was admitted with hypokalaemia, atrial flutter and fluid overload. The metyrapone dose was increased to 500 mg tds. He had similar admissions with recurrent hypokalemia, oedema and shortness of breath and metyrapone was increased to 1g tds. Spironolactone and losartan was also given. In spite of this 24 hour cortisol kept increasing to 19785 nmol/l. His CT chest also showed progression of lung metastasis. He was admitted to hospice and sadly passed away. Parotid carcinoma producing ACTH is exceedingly rare. Only less than 10 cases have been described in literature. Ectopic ACTH producing malignancies can be very difficult to treat even with rapidly increasing metyrapone doses.

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NCC27

Hyperandrogenism and breast cancer in a postmenopausal woman – treatment challenges

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Introduction
New-onset hyperandrogenism is rare in postmenopausal women and is usually associated with causes such as ovarian hyperthecosis, androgen-secreting tumor or medication. Patients with hyperandrogenism and breast cancer need a special attention when choosing the treatment.
Case history
A 46-year old woman diagnosed with hormone receptor-positive breast cancer at 37 years old, for which she underwent surgery, chemotherapy, radiotherapy and hormonal therapy, until the age of 41, when she had adnexectomy; she presented for hair loss with significant vertex alopecia and upper lip hirsutism developed in 1 year. At the clinical exam she was mildly hypertensive (120/90 mmHg).
Investigations
Hormonal evaluation revealed: postmenopausal levels of serum gonadotroph hormones and estradiol, normal basal and stimulated cortisol, normal basal ACTH and 17 hydroxyprogesterone and hyperandrogenism: mildly elevated DHEAS: 591 mcg/dl (N<282.9), testosterone: 64.17 ng/dl (5–51), low SHBG: 18 nmol/l (26–110) and low 11-deoxicorticosterone: <2 ng/dl (2–15). Other androgens were normal. CT scan showed bilateral adrenal hyperplasia, no ovarian tissue was visible.
Results and treatment
The patient had a suboptimal clinical response at spironolactone and cyproterone acetate. She also received 2 more years of aromatase inhibitor (AI), with the aim of reducing the impact of hyperandrogenism upon the breast. Dexamethasone (DXM) 0.25 mg in the evening normalized DHEAS levels and significantly improved the hair growth. The patient had not developed metastases until the age of 49, but mild osteopenia occurred.
Discussion
With aging, there usually is a dramatic decrease in adrenal androgens, principally dehydroepiandrosterone and its sulfate (DHEA-S), from their peak in early adulthood. Antioestrogens treatment for breast cancer may mildly increase the androgens levels, even in postmenopausal women; in our patient with overt adrenal hyperandrogenism and alopecia, persistant after AI withdrawal, only DXM was efficacious. However, it has been reported that glucocorticoid treatment increases the risk for metastases in patients already having breast cancer. Moreover, glucocorticoid treatment and the lack of the oestrogens due to AI treatment predispose to osteoporosis. In this case, the most important aspect is to prevent a breast cancer recurrence. Therefore, after a succesful course of DXM, a maintenance treatment with an androgen receptor blocker was proposed, associated with calcium and vitamin D. The addition of an aromatase inhibitor may be considered.

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NCC28

Cushing's syndrome and the diagnostic challenge

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Section 1: Case history
This 41 year old lady was seen in the Endocrine clinic with an 8 year history of worsening hypertension, obesity and Type 2 diabetes. She had no conditions

known to cause physiological hypercortisolism, no exogenous steroid use and had clear physical features of Cushing's syndrome.
Section 2: Investigations
Investigations confirmed Cushing's syndrome with two elevated urinary free cortisol assessments (UFC) (934 and 906 nmol/24hr) and failure of cortisol suppression after 1mg overnight dexamethasone suppression (221 nmol/l). An ACTH of 39.1 ng/l confirmed this was ACTH dependent and secondary hypothyroidism (TSH 1.68 mIU/l, free T4 8.2pmol/l) suggested a pituitary origin. The rest of the pituitary panel was normal.MRI pituitary showed no lesion. A CRH test was indeterminate with basal to peak increases of >50% for ACTH (24.1 to 86.5 ng/l) but <20% for cortisol (783 to 806 nmol/l). She was therefore referred to the regional pituitary MDT who recommended contrast pituitary MRI and Inferior Petrosal Sinus Sampling (IPSS).
Section 3: Results and treatment
She was commenced on dose titrated metyrapone and prophylactic low molecular weight heparin to reduce her thrombotic risk. The contrast MRI pituitary showed a small non-enhancing area on the right side which might represent a microadenoma. IPSS assessment (off metyrapone with UFC confirmation of elevated cortisol) however was more suggestive of an ectopic than pituitary origin. The central to peripheral ACTH ratio of <2 prior to corticotrophin releasing hormone (CRH) and <3 post CRH didn't support a pituitary source. A prolactin-normalised central to peripheral ACTH ratio of 0.4, was also suggestive of ectopic ACTH syndrome rather than Cushing's disease.
Section 4: Conclusions and points for discussion
Localisation of ACTH-secreting adenomas is commonly challenging due to their small size. It is however essential to increase the likelihood of successful surgical remission from Cushing's syndrome. This patient has gone on to have a full body contrast CT scan and spoiled gradient echo MRI of the pituitary gland. The latter has recently been described as superior for detecting small microadenomas over contrast MRI. Normalising the central to peripheral ACTH ratio with prolactin also helps to reduce the false negative rate of the procedure. We describe the use of these novel techniques and their benefit in clinical practice in cases where adenoma detection is challenging.

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NCC29

A triumvirate of macroprolactinoma, apoplexy and aneurysm: what is the optimal management strategy?

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Case history
A 57-year-old male with well controlled primary hypertension presented with acute onset severe headache while exercising, associated with nausea and vomiting. He had no visual or other neurological symptoms. The pain settled with analgesics in ED. He reported four transient similar episodes during the preceding 18 months. There were no symptoms suggestive of pituitary or other endocrine dysfunction, including hyperprolactinaemia. Clinical examination was unremarkable with normal cranial nerves, visual field and neurological exam.
Investigations
Routine blood investigations were unremarkable. Urgent unenhanced CT brain imaging revealed possible pituitary apoplexy and CT angiogram excluded a subarachnoid hemorrhage (SAH). Hormone profile revealed significantly elevated serum prolactin (19,730 munit/l), but otherwise normal range values, though ACTH and cortisol levels were sampled post hydrocortisone administration. MRI pituitary and MRA showed an invasive pituitary macroadenoma with intra-tumoural fluid levels consistent with recent hemorrhage/necrosis. The macroadenoma partly encases the cavernous-left internal carotid artery (ICA), and completely surrounds a 9mm aneurysm arising from the ICA side-wall just proximal to the level of the ophthalmic artery origin. There was no appreciable local mass effect on the optic nerves or chiasm.
Results and Treatment
The patient was commenced on hydrocortisone, and transferred to the local neurosurgical centre for further imaging and management. The apoplexy was managed conservatively and endovascular treatment of the cavernous ICA (C-ICAA) aneurysm was prioritized before medical treatment of the macroprolactinoma.
Conclusions and points for discussion
We present a case of pituitary apoplexy in a macroprolactinoma whose management was complicated by the co-existence of a C-ICAA. C-ICAA rarely rupture because of the surrounding bony and dural structures but the risk is observed to be increased when this protection is eroded by invasive pituitary tumour. There was no appreciable evidence to suggest previous bleeding or contained rupture, though the recurrent prior headache episodes may reflect micro bleeds, and the risk of re-bleed in the aneurysm is potentially life threatening. Commencement of dopamine agonist (DA) therapy could cause rapid shrinkage of the tumour with possible de-tamponade effect if there is a micro bleed. DA therapy and cystic degeneration within a pituitary tumour are both recognized predisposing factors in pituitary apoplexy. Caution is needed when initiating DA therapy in this case and definitive management of the C-ICAA was prioritized first.

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NCC30

The management of ectopic ACTH syndrome secondary to a lung neuro-endocrine tumour with metyrapone: Illustration from a clinical case

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Case history
We report the case of a previously healthy 69-year-old female who was referred to our centre after she presented with rapidly progressive weight-gain, hyperglycaemia, hypokalaemia and hypertension. She had no symptoms suggestive of carcinoid syndrome. On assessment, she had pathognomonic features of Cushing's syndrome: central weight gain (peripheral wasting) proximal myopathy, leg oedema, skin thinning, bruising and facial puffiness; this appearance being markedly different to 2 months earlier. Her serum potassium was 2.9 mmol/l (3.5–5.3).
Investigations
A cortisol day curve was performed on the day of first assessment. On this, the baseline serum ACTH was elevated at 159 nmol/L (0–46) with a paired baseline cortisol of 1454 nmol/l. The mean of 7 cortisol measurements taken was 1278 nmol/l. A computed tomography (CT) scan of the thorax, abdomen and pelvis was also performed. This showed a right lung 13×8 mm middle lobe nodule, a small 9 mm hilar lymph node, multiple liver lesions and bilaterally enlarged adrenal glands. Magnetic resonance imaging of her pituitary gland was normal. Histological analysis of a liver biopsy sample revealed a well-differentiated metastatic NET with low grade (II) morphology and a Ki-67 index of 10%.
Results and treatment
Ectopic ACTH syndrome(EAS) was diagnosed due to the suggestive clinical features, biochemical and radiological findings. The patient was commenced on metyrapone considering the need for urgent clinical stabilisation and management. Her dose was titrated according to a 'block and replace' regimen (with hydrocortisone replacement) due to COVID19 pandemic limitations regarding repeated hospitals visits. The conclusion of our regional NET multi-disciplinary meeting, was that the pathology represented a metastatic lung NET. The patient was commenced on Capecitabine and Temozolomide chemotherapy. Following treatment, the patient demonstrated both clinical and biochemical remission of the Cushing's syndrome (mean day curve LCMS-MS cortisol 159 nmol/l). A repeat CT scan, 6 months post-treatment, showed stability of the lung and hepatic lesions as well as a reduction in the size of the adrenal glands.
Conclusions and point for discussion
Our case demonstrates a significant clinical and biochemical improvement in a patient with a grade III ACTH-secreting lung neuroendocrine tumour (NET) following metyrapone therapy. There is sparse data on the effectiveness and tolerability of metyrapone therapy in managing ectopic ACTH syndrome (especially secondary to NETs). This case serves to highlight that in tumours unsuitable for surgery, metyrapone provides an effective means to manage EAS.

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NCC31

Resistance to thyroid hormone receptor-beta: diagnostic pitfalls

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Table 1: trend of thyroid function tests over time, Units = mU/L

	29/3/18	1/10/18	29/5/19	3/7/19	29/7/19	28/10/19	18/2/20	10/3/21
TSH	2.85	3.27	5.41	5.52	4.9	4.09	4.15	
Free T3			7.7	8.4	7.6	7.6		9.9
Free T4			30.2	30.7	28.5	27.7		27.7

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Section 1
A 77 year female was referred by her GP in May 2019 for abnormal thyroid function tests (TFT) which were requested due to new diagnosis of atrial fibrillation. The patient was otherwise asymptomatic and clinically euthyroid. Family History was negative for thyroid abnormalities. On enquiry, the patient revealed that she had abnormal thyroid function tests associated with a large goitre in 1970s and subsequently underwent partial thyroidectomy followed by radioactive iodine treatment.
Section 2
Thyroid profile trend is shown in Table 1. Anti-TSH receptor Antibodies and TPO Antibodies were negative. Full pituitary profile and MRI brain were done to rule out pituitary disease and were normal. Cortisol and sex hormone binding globulin were normal. Thyroid ultrasound and thyroid uptake scan were consistent with nodular thyroid disease. The nodules were considered benign and she was referred to ENT team for further follow up.
Section 3
Genetic testing confirmed pathogenic variant of Thyroid hormone receptor beta (THRB) gene. A single base change c.1312C>T, in exon 10 of THRB was detected that led to abnormal THRB protein p.Arg438Cys, resulting in thyroid hormone resistance. Considering the patient was clinically euthyroid and asymptomatic, conservative management with regular follow up of TFT was implemented.
Section 4
Thyroid hormone resistance (THR) is a rare disorder and should be suspected with atypical TFT. As may have happened in this case, failure to recognise an uninhibited TSH in the presence of elevated thyroid hormones and goitre may lead to unnecessary treatment with thyroidectomy and radio-iodine treatment. When treating these patients it is important to understand that elevation of T3 and T4 are compensatory to the degree of thyroid hormone resistance. Clinical presentation is variable, patients may be clinically euthyroid, hyperthyroid, hypothyroid or mix of hypothyroid symptoms in some organs and hyperthyroid in others. Treatment is largely symptomatic depending on the symptoms (e.g. with beta blockers for tachycardia). Goitre is one of the most common symptoms and tends to reoccur after surgery and radio-iodine treatment. If there are compressive symptoms due to goitre then treatment with thyroid hormone supplementation can be considered with aim to bring TSH level in the upper limit of the normal.

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NCC32

The perils of post prandial paralysis and palpitations

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Section 1: Case history
A 53 year old male of Chinese ethnicity presented to hospital with a fall and a long lie. He had a heavy meal for dinner, and he fell later in the evening after standing from the sofa. He lacked strength in his limbs and could not stand up again. He was on the floor for 7 hours before he could shuffle his way to the phone and call for help. On examination he had MRC grade. power in the proximal arms and MRC grade. hip. flexion. Sensation was normal. He was tachycardic with a heart rate of 130bpm. There were no signs of thyroid eye disease or palpable goitre. He had lost approximately 6 kg of weight unintentionally over the last 3 months. There was no family history of periodic paralysis.
Section 2: Investigations
Blood tests showed a low potassium level of 2.5 mmol/l, an elevated serum thyroxine level of >100 pmol/l, a low serum TSH of <0.01 mu/l. Sodium, magnesium and calcium levels were normal. Serum thyroid peroxidase antibodies were elevated at 138.0 iu/ml and his thyroid receptor antibodies were also elevated 9.4 iu/l. ECG confirmed atrial fibrillation with rapid ventricular response at 130 bpm.
Section 3: Results and treatment
The patient was hospitalised for further treatment and monitoring. He was initially given intravenous and subsequently given oral potassium supplementation. His potassium level improved from 2.5 mmol/l to 4.9 mmol/l within 6 hours. He was also started on propranolol MR 80 mg twice a day for symptomatic relief from thyrotoxicosis and started on 40 mg once a day of carbimazole. His weakness improved with potassium replacement and he was discharged from hospital after 2 days of inpatient care. His thyrotoxicosis is responding to carbimazole therapy and he is being considered for radioiodine treatment.
Section 4: Conclusions and points for discussion
His presentation and investigations were consistent with a first presentation of Graves' Disease and concurrent hypokalaemic periodic paralysis. Concurrent hypokalaemia and weakness should trigger a clinician to assess a patient's thyroid status. These patients should be admitted for monitoring of arrhythmias, potassium levels and muscle weakness recovery. Heavy meals are also recognised to trigger thyrotoxic periodic paralysis. The prevalence of thyrotoxic periodic paralysis is up to 10 times higher in people of Chinese descent compared to people of European descent. The prevalence is estimated to be 2% in Chinese people with thyrotoxicosis.

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NCC33

Pituitary apoplexy in the setting of recent COVID-19 infection

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Section 1: Case history
We present a case of a 75-year-old male with hypopituitarism on the background of recent COVID-19 infection. The patient was COVID-19 swab positive six weeks prior and suffered mild hypoxia, however declined hospital admission at that time. He presented one month later with sudden onset severe headache associated with fever; drowsiness and abdominal pain. He was discharged with antibiotics for suspected diverticulitis. His GP subsequently performed a pituitary panel, revealing hypopituitarism, and advised urgent admission. The patient reported symptoms of lethargy, memory loss, peripheral oedema and light-headedness. Systemic examination revealed no evidence of chronic pituitary insufficiency. There was no neurological or visual deficit on examination. The patient was started on intravenous hydrocortisone replacement pending further investigations.
Section 2: Investigations
A pituitary panel revealed anterior pan-hypopituitarism. Computerised tomography imaging demonstrated a rounded mass within the pituitary fossa of increased attenuation corresponding with a fresh blood clot. A subsequent magnetic resonance imaging scan performed revealed a 12 mm mass located within the pituitary gland, extending into the suprasellar cistern but not compressing the optic chiasm. Within the pituitary there was a large area of high signal on T1-weighted imaging consistent with haemorrhage into a pre-existing pituitary macroadenoma, confirming pituitary apoplexy. Formal assessment of the patient's visual fields was normal.
Section 3: Results and treatment
The patient was treated with hydrocortisone on arrival and later commenced on thyroid replacement. His symptoms improved after two weeks and repeat MRI revealed reduction in size of the haemorrhagic lesion. Multidisciplinary team discussion decided no neurosurgical input was required, and advised continuation of hormone replacement therapy and to monitor the pituitary macroadenoma with a repeat MRI after six months.
Section 4: Conclusions and points for discussion
Our understanding of how COVID-19 affects different bodily systems remain incomplete. This case demonstrates a potential link between COVID-19 and pituitary apoplexy in a patient with no recognised risk factors for apoplexy, although this remains speculative. A growing number of similar cases have been reported in a variety of ages and genders during the pandemic. Speculation on possible links between COVID-19 and apoplexy include haemodynamic instability, direct CNS viral invasion and insulin resistance with glycaemic disarray. Despite the rarity of this pathology, the prevalence of COVID-19 suggests that more patients with underlying pituitary tumours will be exposed to COVID-19, increasing their risk of pituitary apoplexy. We must be vigilant in recognising this endocrine emergency, and further elucidate the underlying pathophysiology.

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NCC34

DDAVP: diagnosis, dentition and arginine vasopressin

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Case History
A 47-year-old man presented to his GP in November 2019 with sudden onset polydipsia, polyuria and large volume nocturia, passing approximately 5L of urine daily. He was drinking to thirst, had no past medical or family history, and was not taking any medication. He had normal serum calcium, sodium and HbA1c. His GP referred to the local endocrinologist. Five months later, he was referred to our tertiary centre for a water deprivation test, as it had not been possible for this to be performed locally.
Investigations, Results and Treatments
The patient was seen in our centre within 2 days of referral. Plasma and urine osmolalities, obtained five months earlier by the GP, were diagnostic of diabetes insipidus (DI): serum sodium 145 mmol/l, plasma osmolality 300 mOsmol/kg, urine osmolality 115 mOsmol/kg. Anterior pituitary function was normal other than secondary hypothyroidism. MRI of the pituitary and skull base CT demonstrated an aggressive destructive skull base process, significant paranasal sinus disease and poor dentition. Oral desmopressin 100 mg am and 200 mg nightly was commenced the same day (without performing a water deprivation test), with immediate improvement and the first full night's sleep in six months. CT of the chest, abdomen, and pelvis; autoimmune and vasculitis screen; immunoglobulin-G subclasses, and Quantiferon tests were all normal. Regional Pituitary MDT case review that week could not ascertain clear aetiology. ENT review advised a 2-week course of co-amoxiclav and fluconazole, then subsequent endoscopic sinus surgery and biopsy, after negative SARS-CoV-2 PCR. During surgery, the sinuses opacified on imaging were clear and overtly normal. Biopsy showed lymphocytes and plasma cells, but no granuloma or neoplasia, and no bacterial, mycobacterial or fungal growth. Repeat imaging 3 and 6 months later showed a significant improvement in the skull base changes. DI however remained, fully controlled with normal sleep and normal serum sodium, except profound aquaresis on delayed desmopressin administration.
Conclusions and points for discussion
1) Cranial DI diagnosis does not require a water deprivation test when the history and baseline biochemistry are diagnostic; 2) Prompt diagnosis of DI prevents prolonged symptoms, and ensures appropriate and timely investigation and management; 3) Early referral to a pituitary centre is important, greatly facilitated in the post-COVID era by almost universal adoption of virtual MDT meetings. the delay could have caused significant morbidity; 4) This case illustrates an unusual, probably infective, aetiology and the importance of expeditious management in all presenting patients.

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NCC35

Challenges in managing toxic multinodular goitre and propylthiouracil-induced anti-neutrophil cytoplasmic antibody associated vasculitis

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Case history
A 53-year-old woman presented with vasculitic rash affecting her limbs. She has a 3-year history of thyrotoxicosis. Having developed intolerance to carbimazole she was maintained on propylthiouracil (PTU) for the last two years. Imaging results were consistent with multinodular goitre. Thyroid stimulating immunoglobulin was negative. A few months prior to this presentation she developed dysphagia. Repeat imaging showed an 8 cm right thyroid nodule that grew significantly from multiple coalescing nodules detected 3 years previously. Tracheoesophageal deviation with right vocal cord paresis was apparent. Cytology following fine needle aspiration was consistent with Thy3a.
Investigations
Admission blood tests showed microcytic anaemia – Hb 98 g/l (normal range (NR) 115–160), MCV 79fl (NR 80–100) and neutropenia 0.89 $\times$ 10^9/; (NR 2–8). Thyroid function tests showed TSH $<$0.02 mU/l (NR 0.27–4.2), free T4 (fT4) 19.0 pmol/l (NR 12–22) and free T3 (fT3) 6.8 pmol/l (NR 3.1–6.8). Vasculitic screen showed atypical anti-neutrophil cytoplasmic antibodies (ANCA), PR3 28 iu/ml (NR 0–1.9), MPO 7.2 iu/ml (NR 0–3.4). Lupus anticoagulant, ANA, ENA, dsDNA and complement levels were normal.
Results and treatment
Prednisolone was commenced with minimal improvement. After PTU was withdrawn, the vasculitic rash improved and neutropenia resolved. Seven days after PTU cessation there was clinical and biochemical evidence of worsening thyrotoxicity; fT4 increased to 66.4 pmol/l. Due to limited medical treatment options available total thyroidectomy was planned to allow symptom control and histopathological evaluation of the thyroid gland. Lugol's iodine and beta blockade were commenced to optimise thyroid function pre-operatively. FT4 subsequently decreased to 47.2 pmol/l, 26.9 pmol/l and 22.3 pmol/l on days 2, 7 and 10 of treatment respectively. Total thyroidectomy was performed on day 11 with no complications. Macroscopically the right thyroid lobe was twice the size of the left. Diffuse hyperplasia of thyroid follicles, cystic changes with calcifications were present microscopically without features of thyroiditis or malignancy. TSH and fT4 were $<$0.02 mU/l and 17.4 pmol/l respectively on Levothyroxine replacement one-week post-op.
Conclusions and point for discussion
PTU-induced ANCA vasculitis (AAV) is an uncommonly encountered complication. Endocrinologists need to be vigilant as it can occur independent of PTU dose or length of exposure. Timely recognition is crucial as prompt PTU discontinuation is key. The conundrum faced in this case reflects the complexity when planning alternative treatment post PTU cessation. The presence of Thy3a nodule made total thyroidectomy a necessity, however the timeframe for surgery was influenced by patient-related factors including variable degrees of thyrotoxicity and AAV treatment such as steroids or immunosuppressive therapy.

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NCC36

Asymptomatic primary hyperparathyroidism-acute deterioration with intercurrent illness-hypercalcaemic crisis

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Case history
80 year old male was referred to endocrine clinic for incidental hypercalcemia picked up on six monthly blood tests for follow up of treated carcinoma of prostate in remission. Patient himself complained only of mild mechanical backache and no other symptoms of hypercalcemia. There was no family history of thyroid or parathyroid related disorders. Drug history did not include thiazides or lithium.
Investigations
serum calcium 2.75 mmol/l, PTH 30.4 pmol/l, Vitamin D 27.7 nmol/l, PSA 0.51 microgram/l Normal ALP, Phosphate and kidney function. 24 hr urinary calcium output 4.92 mmol/l. X-ray pelvis and lumbosacral spine showed osteoarthritic changes but no fracture or bony lesion. No renal calculi on CT KUB. No osteoporosis on DEXA scan. normal serum protein electrophoresis.
Treatment and Follow up:
Initially managed conservatively with six monthly serum calcium and renal functions along wit vitamin D supplementation and advice on optimal fluid intake. Serum calcium at one year follow up was 2.88 mmol/l with normal renal functions. He was admitted two months later following a mechanical fall with long lie leading to rhabdomyolysis and AKI. Biochemistry revealed serum calcium 5.16 mmol/l, PTH 245 pmol/l, creatinine 178 micromol/l, urea 24 nmol/l, eGFR 32 and CK 2792 U/l. Repeat ultrasound KUB and x-rays of pelvis and lumbosacral spine did not reveal any abnormality. He was managed with intravenous pamidronate and fluids which reduced serum calcium to 2.8 mmol/l, PTH 36.3 pmol/l and eGFR improved to 47. He was further referred to surgeons for consideration of parathyroidectomy. An ultrasound and CT neck revealed right inferior parathyroid adenoma with normal thyroid gland and no evidence of cervical lymphadenopathy. parathyroidectomy was done three months after hospital admission. He made an uneventful post operative recovery. Histology of removed gland revealed parathyroid adenoma. Follow up in endocrine clinic six months after surgery revealed a serum calcium of 2.42 mmol/l, PTH 15.8 pmol/l and vitamin D 53 nmol/l.
Conclusion and Points for Discussion
Rarely, Primary Hyperparathyroidism may present with parathyroid (hypercalcemic) crisis, which may occur due to significant fluid loss or dehydration leading to rapid rise in blood calcium. Patients may experience cardiac and renal impairment, rapid deterioration of CNS, vomiting, severe abdominal pain, stomach ulcers and constipation. High index of clinical suspicion is required in acutely ill patients as presentation is varied and mortality is high in patients

treated only conservatively. Prompt surgical intervention should be considered as treatment of choice.

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NCC37

Management of unresectable insulinoma using cloud-based continuous glucose monitoring: a case report

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Section 1: Case history

A 62 year old man presented with a three month history of abdominal bloating and discomfort, loose stools and weight loss. This progressed to hypoglycaemic symptoms that occurred initially after exercise. Symptoms included confusion and light-headedness, fatigue, cold sweats and shakiness. The patient had to eat regularly to prevent hypoglycaemia which resulted in weight gain. Hypoglycaemic episodes increased in frequency to the point where the patient had to live a sedentary lifestyle to avoid becoming symptomatic.

Section 2: Investigations

Fasting capillary glucose fell to 2.3 mmol/L with inappropriately elevated insulin and c-peptide. CT was consistent with T4a, N1, M1 disseminated pancreatic tail malignancy. Liver biopsy demonstrated a well differentiated neuroendocrine tumour, grade 2, likely metastatic to the liver. A whole-body NM tumour imaging SPECT CT scan showed an intense abnormal tracer uptake projected over the pancreatic tail and multiple somatostatin receptor positive hepatic deposits. The disease was unresectable.

Section 3: Results and treatment

Initially, patient was given lifestyle advice. Recurrent hypoglycaemic episodes at home led to hospital admission and trial of short acting somatostatin analogue, Octreotide. Flash glucose monitoring (FGM) was initiated in the form of Free Style Libre to enable monitoring of blood glucose levels. Following an initial positive response to Octreotide, the long-acting somatostatin analogue, Lantreotide was administered and patient was discharged home. Further hypoglycaemia resulted in hospitalisation for IV dextrose and trial of Diaxozide. Everolimus, was then added to his treatment. The use of continuous glucose monitoring with cloud based storage of glucose results provided both the patient and clinical team a detailed record of glucose control and allowed much of his treatment to be provided as an outpatient.

Section 4: Conclusions and points for discussion

It can be difficult to achieve normal glycaemic levels during medical management of insulinoma and can often result in hospital admission. This case is unique because FGM combined with a remote cloud-based diabetes management system has allowed physicians to monitor the patient's glucose levels remotely. Frequent adjustments to patient's medications have overall reduced the frequency of hypoglycaemic episodes. In conclusion, FGM has advantages to both patients and clinicians; patient confidence and quality of life is not only improved but the clinician also has the ability to manage this complex diagnosis as an outpatient. Overall, this reduces patient time in hospital, improves patient safety and maximises clinical outcomes.

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NCC38

Perinatal headaches and the postpartum diagnosis

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Case history

A 42-year old female was urgently referred to the endocrinology clinic. Symptomatology included worsening lethargy, polydipsia, poor appetite, postural dizziness and hypogalactia. Relevant background included the delivery of a healthy baby at term four weeks prior (Emergency caesarean section, 1000 ml blood loss documented). She had undergone an MRI at 39 weeks gestation following a 10-day history of persistent headaches with associated photophobia and dizziness (pre-eclampsia excluded). Her MRI brain was initially reported as normal (antenatal course otherwise uncomplicated). Her GP had identified a secondary hypothyroidism and provided her with steroid cover.

Investigations

Further pituitary axis assessment by the endocrine team demonstrated the following: Na 146 mmol/L, TSH 0.06 (0.3–4.2 mu/l), Free T4 8.0 (9–23 pmol/l), Free T3 5.2 (2.5–5.7 pmol/L), Prolactin 207 (100–500 milliunit/L), IGF-1 18.2 (7.5–35 nmol/L), Oestradiol 207 pmol/L, FSH 3.2 IU/L, LH 1123 IU/L, ESR 46. Short synacthen test (SST): 0 min = 212 nmol/L, 30 mins = 431 nmol/L, 60 mins = 523 nmol/L.

Results and treatment

Steroid supplementation had increased the severity of her thirst, nocturia and polyuria. A 24hour urinary collection yielded 3799 ml. A subsequent water deprivation test demonstrated an inability to concentrate urine, with a partial response to desmopressin (peak serum osmolality – 307 mOsmol/kg, peak urine osmolality pre-and post-desmopressin were 401 mOsmol/kg, and 592 mOsmol/kg respectively). She was commenced on desmopressin and her ACTH axis was further interrogated. The insulin stress test showed an impaired cortisol response to hypoglycaemia (plasma glucose 1.8 mmol/l, peak cortisol response 322 nmol/l, growth hormone axis preserved). A retrospective review of her initial MRI at 38 weeks gestation demonstrated an enlarged pituitary beyond that expected in pregnancy with diffuse T1 signal reduction raising the possibility of autoimmune hypophysitis or pituitary infarction. Her postpartum MRI demonstrated an enlarged pituitary stalk but no further features consistent with hypophysitis. Following investigation, she has been established on long-term levothyroxine, hydrocortisone and desmopressin with good symptomatic response, and has plans for further pregnancies. Eighteen months later, she has needed to continue her supplementation: re-interrogation of her axis has not suggested recovery.

Conclusions and point

Our case demonstrates a significant clinical and biochemical improvement in a patient with a grade III ACTH-secreting lung neuroendocrine tumour (NET) following metyrapone therapy. There is sparse data on the effectiveness and tolerability of metyrapone therapy in managing ectopic ACTH syndrome (especially secondary to NETs). This case serves to highlight that in tumours unsuitable for surgery, metyrapone provides an effective means to manage EAS.

Discussion Points

1. Pitfalls of SST in context of pituitary disease 2. Impact of steroid deficiency on ADH axis 3. Differentiating between Sheehan's syndrome and autoimmune hypophysitis

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NCC39

A rare case of Carbimazole induced peripheral neuropathy

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Section 1: Case history

A 55 year woman presented with a one month history of fatigue, anxiety, tremor and diarrhoea. She was diagnosed with Grave's thyrotoxicosis and commenced on Carbimazole 30 mg daily. Thyroid hormones normalised, but after three weeks of therapy she developed rapidly progressive ascending numbness and weakness predominantly affecting her legs. Examination revealed distal symmetrical lower motor neurone weakness and widespread loss of light touch sensation. Cranial nerves and sphincter function were intact.

Section 2: Investigations

Initial thyroid function showed a TSH <0.02 mIU/l and elevated free T4 of 33.6 pmol/l, which normalised by the time of presentation with neurological symptoms (20.4 pmol/l). Extensive investigations were unremarkable, including potassium, creatinine kinase, paraneoplastic and autoimmune screen and cerebrospinal fluid analysis. There was no suggestion of heavy metal exposure. Neurophysiology showed generalised large fibre sensory motor peripheral axonal neuropathy. She had undergone neurophysiology testing two weeks before commencing Carbimazole for investigation of a nerve palsy following a fractured humerus. This confirmed the diagnosis of ulnar nerve entrapment, but did not show any evidence of peripheral neuropathy.

Section 3: Results and treatment

Investigations excluded Guillain-Barre Syndrome (GBS). The patient had a significant alcohol intake, but the acute nature of her presentation made this an unlikely explanation and there was no indication of alternative aetiology. In view of the temporal association, Carbimazole initiation was identified as the causative agent and she was switched to Prophylthiouracil 150 mg daily. Her symptoms improved within days, and when reassessed at 7 months she had normal power throughout with partial recovery of sensation.

Section 4: Conclusions and points for discussion

Thyrotoxicosis is associated with several pathologies of the peripheral nervous system: myopathy, periodic paralysis and myasthenia gravis. Peripheral neuropathy, usually sensory, is described and there are rare reports of acute severe motor neuropathy, termed Basedow's paraplegia, which is linked to severe thyrotoxicosis and recovers with anti-thyroid treatment. Although the British National Formulary list 'nerve disorders' as a potential side effect of Carbimazole, the literature lists only three historical case reports and a retrospective study quoting the incidence of undefined neuropathies as a side

effect of anti-thyroid drugs as 0.7%. In this case, the normal neurophysiology whilst she was thyrotoxic, the acute onset of neurological symptoms after starting Carbimazole and the rapid resolution once the medication was stopped, in the absence of an alternative explanation, have led to the diagnosis of Carbimazole-induced polyneuropathy.

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NCC40

A Lady with thyrotoxicosis and rapidly growing goiter

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Case history
A 62 years old lady presented with a history of weight loss, sweating, and tremor for 3 months. The diagnosis of thyrotoxicosis was made following biochemical confirmation and she was started on carbimazole 20 mg twice a day. Several weeks later she got admitted with progressive shortness of breath, hoarseness of voice, and a painful neck lump. Examination revealed a firm to hard fixed multinodular goiter with a dominant hard nodule at the left upper pole. There was an enlargement of deep cervical lymph nodes in the left anterior triangle. She had a fine tremor, tachycardia with no features of Grave's ophthalmopathy.
Investigations
The initial thyroid function tests revealed thyroid-stimulating hormone (TSH) of 0.09 miu/l (0.4–4.2) free T4 31.5pmol/l (10–28.2) ,free T3 8.24 pmol/l (4.26–8.1) and negative Thyroid receptor antibodies. At the time of admission which was 8 weeks following anti-thyroid medications, she remained toxic with a TSH of 0.085 miu/l, free T4 32 pmol/l, free T3 7.8 pmol/l. Tc99m thyroid uptake scan showed low uptake in the thyroid gland with markedly reduced uptake over a left upper pole. USS revealed a multinodular goiter invading into the trachea with a heterogeneous nodule of 2.8×3 cm with a hypoechoic rim, increased internal vascularity, and Intralesional microcalcifications. There was ultrasound evidence of background thyroiditis. Fine needle aspiration cytology of the suspicious nodule revealed marked cellular atypia suggestive of poorly differentiated thyroid carcinoma. Chest X-ray revealed multiple cannonball opacifications in bilateral lung fields evident of lung metastasis.
Results and treatment
The multidisciplinary team decided that the surgical debulking of the tumor was not beneficial at this late stage of malignancy. The patient declined any further tests and agreed with palliative management. She was given adequate pain relief and a tracheostomy was performed to support breathing. Her clinical condition deteriorated leading to severe upper airway obstruction. She was started on high-dose steroids and Radiotherapy was planned, however, she passed away after 6 days of admission.
Conclusions and points for discussion
In differentiated thyroid malignancy, thyrotoxicosis is usually due to excessive hormone secretion from functioning cancer cells whereas infiltration causing follicle destruction or nonspecific thyroiditis are the proposed mechanisms in poorly differentiated malignancy. Thyroid malignancy presenting with thyrotoxicosis is a rare occurrence where a high degree of clinical suspicion and early histological evaluation is essential.

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NCC41

A Rare case of abnormal thyroid functions

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52 year old lady was referred to the endocrine clinic with h/o lethargy and tiredness. She also had mild tremors. She denied weight loss, palpitations or diarrhoea. Past medical history includes bipolar disorder. She was on Venlafaxine, Carbamazepine, Pregabalin and HRT. GP has done thyroid functions because of the symptoms and results are as below. TSH: 7.15 mIU/l(0.38–5.50), FT4:24.3 pmol/l (10.0–18.7) on 05.02.2020 TPO: < 10 IU/Ml This was rechecked in a different laboratory to eliminate assay interference and the results were comparable. TSH:7.8 mIU/l(0.38–5.50), FT4:24.9 pmol/l(10.0–18.7), FT3:7.7 pmol/l Additional investigations including a full anterior pituitary profile was also organised. The results are as below. SHBG:>180 nmol/l Alfasubunit 1.78 IU/l(< 3.00) Prolactin: 411 Miu/l(0–646) LH:5.5 IU/l FSH:10.5 IU/l Cortisol:508 nmol/l IGF–1:179 mcg/l (97–292) This was followed by an MRI scan of her pituitary scan. The scan has shown presence of an adenoma measuring 11*9*6 mm solid, cystic lesion within the right side/midline of the pituitary gland with areas of hypo/hyper enhancement. TRH stimulation test was done by injecting 200mcg of TRH intravenously. The results are as below. 0 MIN:TSH 5.75, FT4:20 20 Min:6.37 60 min:6.74 This was highly suggestive of TSHoma and was discussed in local Pituitary MDT. Somatostatin analogues(SSA) were started as initial therapy and monitored response with thyroid function tests. Also referred to a regional centre for genetic testing. Thyroid functions improved after a week of SSA as below. TSH:3.96 mIU/l FT3:3.8 pmol/l FT4:12.1 pmol/l on 24.11.2021 and remained normal thereafter. Unfortunately, she couldn't tolerate the SSA and was referred to neurosurgeons for considering surgery

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NCC42

Lithium-induced polyendocrinopathy in a single patient

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Case history
A 50-year-old lady, on Lithium for 30 years, presented with a history of progressively increasing thirst since 12 months; associated with polyuria and nocturia. She had been having some joint aches and was finding it more difficult to get up and down stairs. She was found to be hypothyroid few months back and prior to that had been falling asleep easily. There had been an improvement in her energy levels after starting Levothyroxine. She gave no history of renal calculi. Her father had been on Lithium and her mother had renal calculi.
Investigations
6 months back, her adjusted calcium was 2.61 mmol/l, phosphate was 0.79 mmol/l with PTH elevated at 9.0 pmol/l. A repeat test done the following month showed an adjusted calcium of 2.71 mmol/l, with PTH 10.0 of pmol/l and a normal 25-hydroxy vitamin-D of 62 nmol/l. Her most recent TSH was 0.84 mU/l and plasma sodium was 144 mmol/l. Ultrasound of the neck showed a mild diffuse goitre with changes consistent with lithium-induced thyroiditis, with normal parathyroids.
Results and treatment
Suspecting Lithium-induced nephrogenic DI, urine and plasma osmolalities were done after overnight water deprivation, which were 153 mOsm/kg and 303 mOsm/kg respectively. Hence, she was started on Amiloride to manage the nephrogenic DI. Elevated PTH was likely secondary to Lithium effect.
Conclusions and point for discussion
Lithium inhibits AVP-stimulated translocation of cytoplasmic urinary aquaporin-2 (AQP2) to the apical membrane. Failure of AQP2 insertion leads to delivery of a hypo-osmotic fluid to the medullary collecting duct, whose capacity to reabsorb water is blunted, resulting in the excretion of large volumes of dilute urine. Long-term exposure to Lithium may also down-regulate AQP2 gene expression. Amiloride inhibits the uptake of lithium in the collecting duct, leading to reduced mean urine volume, increased urine osmolality, and better renal response to ADH. Lithium alters the set point of CaSR in parathyroid cells, thus promoting excess parathyroid release. Lithium affects normal thyroid functioning through multiple mechanisms. At the cellular level, it decreases thyroid hormone synthesis and release. It also decreases peripheral deiodination of thyroxine by decreasing the activity of type-I 5' de-iodinase enzyme. Hypothyroidism and goitre (clinically and/ultrasonographically) are the most prevalent thyroid abnormalities among patients on long-term lithium therapy. Our case was unique since she exhibited 3 different endocrinopathies simultaneously-Lithium-induced nephrogenic DI, hypothyroidism (secondary to thyroiditis) and hyperparathyroidism.

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NCC43

Severe and resistant hypercalcaemia: a diagnostic and management challenge

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Case history
An 81 years old lady with treated follicular lymphoma, hypertension and osteoporosis was admitted to hospital with a fall and was found to have hypercalcaemia with adjusted calcium of 4.9 mmol/l (nr 2.2–2.6 mmol/l). There was history of constipation but no history of excessive thirst or polyuria. The patient was on atorvastatin, amlodipine, bendroflumethiazide, ramipril, calcium and vitamin

D. On examination our patient was dehydrated and mildly confused. There was no palpable neck swelling and rest of the clinical examination was normal.
Investigations and results
Biochemical profile revealed persistently elevated adjusted calcium ranging between 3.5 and 4.9 mmol/l (2.2–2.6), phosphate 4.8 mmol/l (3.4–4.5), PTH 1 pmol/l (1.6–6.9), urea 10.6 mmol/l (2.5–7.5), Creatinine 152 umol/l (59–104) and Vitamin D 40 nmol/l (50 – 125). Multiple myeloma screen, serum angiotensin converting enzyme (ACE) and anti-neutrophilic cytoplasmic antigen (ANCA) were negative. Hypercalcaemia due to malignancy was suspected and the patient underwent CT chest, abdomen and pelvis which did not reveal any evidence of malignancy. Our patient then underwent whole body PET scan which showed 17 + 11 + 8 cm FDG avid mass encasing the left femoral shaft. MRI left femur confirmed the mass and the differential diagnosis was either soft tissue sarcoma or lymphoma. Biopsy of the soft tissue mass revealed a diffuse large B cell lymphoma.
Treatment
Thiazide diuretic and calcium and vitamin D supplements were stopped, and our patient received intravenous fluids. The calcium levels did not normalise with intravenous fluids, however the patient developed sign of heart failure. Frusemide was added on which improved heart failure but had minimal effect on calcium. The patient received intravenous pamidronate and because calcium levels remained high, our patient needed further doses of intravenous Pamidronate over the next 4 weeks. Calcium responded only marginally to pamidronate treatment. Our patient needed 2 doses of desnoumab without significant response. Calcitonin was given with only modest improvement of calcium levels (3.5 mmol/l). After biopsy confirmed the left thigh mass to be a diffuse large B cell lymphoma, prednisolone 1 mg/kg was started.
Conclusion and points for discussion
1. Our case report describes the diagnostic and management challenges in the context of resistant hypercalcaemia. 2. Consider underlying malignancy in the presence of severe resistant hypercalcaemia. 3. We are of the opinion that hypercalcaemia in our patient may settle once lymphoma is treated.

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NCC44

Dose-dependent Carbimazole-induced eosinophilic dermatitis: a rare reminder of potentially serious side effects

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Case History
A 23-year-old Bengali woman with a 2-year history of Graves' disease presented to the endocrine day unit with a widespread, pruritic, vasculitic-looking rash. She was treated with Carbimazole since diagnosis but was poorly compliant. One month prior to presentation, her Carbimazole dose was increased from 20 mg daily to 60 mg daily, as she remained biochemically thyrotoxic (Free T4 79.9 pmol/l, T3 34.8 pmol/l and TSH < 0.01 mU/l). The rash started on her lower legs and spread to the abdomen and arms. She felt systemically well and there was no mucosal or ophthalmic involvement. She had no personal or family history of dermatological issues, no previous drug reactions and no recent travel history. On examination, there was a purpuric, confluent, papular rash affecting her limbs and trunk, with scanty bullous lesions over both lower legs. Carbimazole was stopped with some immediate improvement in symptoms and urgent dermatological review was arranged.
Investigations
Full blood count demonstrated a marked eosinophilia of 1.4 + 10^9/l (0–0.5) with a total white cell count of 7.8 + 10^9/l (4–11). C-reactive protein was 2 mg/l (0–5). Alkaline phosphatase was chronically raised at 257 units/l (30–130). Bilirubin was normal at 6 mmol/l (0–21). Autoimmune serology, complement C3d, anti-streptolysin o titre and immunoglobulins were normal.
Results and Treatment
Punch biopsies taken from arm and leg lesions revealed spongiotic eosinophilic dermatitis with no evidence of vasculitis or leucocytosis. Subsequent fungal stains and direct immunofluorescence testing for immunoglobulins and complement C3 were negative. She was treated with oral Prednisolone, topical Clobetasol propionate and emollients for 4 weeks, with complete resolution of skin lesions and eosinophilia. She became hyperthyroid after cessation of Carbimazole and underwent successful definitive treatment with radioiodine.
Conclusions and points for discussion
• Rashes are a well-recognised side effect of Carbimazole. Although most are mild and self-limiting, severe reactions including ANCA-associated vasculitis can occur.
• Severe eosinophilic reactions to antithyroid drugs are rare and idiosyncratic. Delayed reactions and systemic involvement (DRESS syndrome, eosinophilic pleural effusion) have been reported.
• Important to consider systemic effects and associated symptoms in patients presenting with dermatological reactions to antithyroid medication.
• Definitive treatment for Graves' disease should be considered in cases of drug reaction.
• Prompt dermatological referral and histological examination are imperative in cases of antithyroid drug-induced rash. If dangerous differential diagnoses can be excluded, treatment continuation may be possible.

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NCC45

Opiod induced hypoadrenalism: a increasingly frequent condition, but easily forgotten

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A 57 year-old female patient was admitted for the supervision of supplementary parenteral feeding, due to excessive weight loss and difficulty with gastric motility since having Roux-en-Y gastric bypass surgery a decade ago. During her stay she was noted to have regular episodes of significant resting hypotension, postural hypotension, and tachycardia, which did not respond to fluid replacement or nutritional support. Endocrinology specialist advice were requested by her gastroenterology team because of abnormal test result. Her 9am cortisol level was 227 mol/l, which was abnormal in the context of acute illness, and was also significantly lower than that from 6 months ago (to 858 nmol/l). Subsequent short synacthen test result showed incomplete response: 66 nmol/l at 0-minute (at 9am), 391 nmol/l at 30-minute, and 460 nmol/l at 60-minute. Her baseline 9am ACTH was also abnormally suppressed (15 ng/l). Her other relevant medical history include chronic malabsorption after bariatric surgery, and active musculoskeletal conditions (Sero negative inflammatory arthritis, lumbar vertebral disc prolapse) resulting in chronic pain. As a result, we identified her regular medication include high dose of codeine phosphate (240 mg daily total), morphine sulphate (60 mg daily total), alongside gabapentin, amitriptyline, and sertraline. She also requires long term total parental nutritional support at home, administered via Hickman line. She is not exposed to regular exogenous glucocorticoid therapy. There was no clinical or biochemical feature suggestive of other concerning acute pituitary abnormality. The diagnosis was opiod-induced secondary hypoadrenalism. She was treated with glucocorticoid replacement therapy, which results in significant clinical improvement. Increasing prevalence of both appropriate and inappropriate of long term usage of opiod-based analgesia has been reported in UK and world-wide. The adverse negative side effect profiles has been drawing increasing attention among healthcare community. However, secondary hypoadrenalism appears to remain one of the significant side effects that is still not fully aware by healthcare professionals involved in the care of this particular patient group. Tabet EJ, Clarke AJ, Twigg SM Opioid-induced hypoadrenalism resulting in fasting hypoglycaemia *BMJ Case Reports CP* 2019;**12:**e230551). Rabi, (128) A case of adrenal insufficiency secondary to chronic opioid use-keep this diagnosis in mind!, The Journal of Pain, Volume 15, Issue 4, Supplement, 2014, Page S8, ISSN 1526-5900, https://doi.org/10.1016/j.jpain.2014.01.034. (https://www.sciencedirect.com/science/article/pii/S1526590014000625) https://eje.bioscientifica.com/view/journals/eje/181/2/EJE-19-0154.xml

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NCC46

Recurrence of cushing's disease after several years of remission

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68 Y M Has Background of Hypertension and Asthma. Presented with progressive visual deterioration for 12 months in 2012. VF testing confirmed Bitemporal Hemianopia. He has symptoms suggestive of cortisol excess. Therefore, MRI pituitary and pituitary hormone profile was done. MRI showed pituitary macroadenoma A Pituitary Hormone profile in 2012 showed cortisol excess at value of 755 nmol/l and ACTH 156 ng/l(0–46). IGF-1 17.2 nmol/l which is normal. LDDST was done and cortisol was not suppressed level was 453 nmol/l. At this stage the patient was diagnosed with Cushing's disease secondary to ACTH producing pituitary macroadenoma with partial hypopituitarism. Therefore, he started on Metyrapone 250 mg BD which titrated according to cortisol level, thyroxine 50 mcg and Tostran Gel 2%. In November 2012 he underwent Transsphenoidal surgical debulking of invasive pituitary macroadenoma. Histology showed densely granulated corticotroph adenoma with raised Ki 67 index in excess of 10% raising the possibility of tumor recurrence and

aggressive tumor. Immediate post operative period was uneventful and the patient has had some visual field improvement. He remained off Metyrapone post OP and early morning cortisol level remained significantly elevated (1160 nmol/l) in keeping with tumor residual which was not surprising. Post OP MRI showed good tumor debulking although there was a small part of the suprasellar component extending into the floor of the third ventricle. Hence, Metyrapone 500 mg TDS was restarted and In view of postoperative persistent active cushing and high Ki67 index he was referred for radiotherapy. He completed radiotherapy in 2014 and achieved biochemical remission, confirmed by Post radiotherapy GST and ACTH level, hence metyrapone was stopped. He remains well between 2014 and 2020 with stable tumor residual and biochemistry. Currently, admitted with symptoms and signs of cortisol excess, which confirmed recurrence of Cushing's disease with very high values of ACTH 477 ng/l, cortisol of 1061 nmol/l and LDDST cortisol value of 894 nmol/l. The MRI pituitary showed recurrence of pituitary macroadenoma.

Discussion

1. Recurrence of Cushing's disease after several years of remission 2. Management options are quite limited as no clear surgical Target, specially on background history of radiotherapy 3. Discussion whether to continue with medical treatment or bilateral adrenalectomy

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NCC47

Postpartum isolated cranial diabetes insipidus

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Cranial Diabetes Insipidus is a rare diagnosis and rarer still postpartum. We present the case of 24-year-old woman who developed CDI following pregnancy. The patient had developed polydipsia and polyuria 5 months following pregnancy. The pregnancy had been complicated by Gestational Diabetes Mellitus and a large Postpartum Haemorrhage. The patient reported feeling fatigued, lightheaded and she stated a need to drink water frequently: ~ 8 litres throughout the day and 4 litres overnight. She reported being unable to breastfeed but was otherwise well: she attributed her symptoms of lethargy to sleepless nights with her new born baby, the polyuria as a consequence of vaginal delivery and as such presented for initial review 18 months following delivery. Investigations revealed a fasting blood glucose of 4.9 mmol/l, an Adj. Calcium of 2.23 mmol/l and a fasting urine osmolality of 85 mmol/kg. A diagnosis of DI was suspected and was confirmed by water deprivation test: the patient had an inappropriately dilute urine osmolality of 111 mmol/kg when compared to the serum osmolality of 301 mOsm/Kg at the start of the test and her urine failed to concentrate as water was withheld. Administration of DDAVP resulted in appropriate concentration of urine confirming the diagnosis specifically as Cranial Diabetes Insipidus. The patient was established on DDAVP replacement therapy and her quality of life improved: she enjoyed restful sleep and reported less exhaustion. There was no anterior pituitary hormone deficiency 28 months following delivery. MRI Pituitary revealed an unusually flat and broad pituitary gland with a possible tiny lesion in the posterior pituitary suggestive of an adenoma. DI is a rare diagnosis with an estimated prevalence of 1 in 25 000 people. CDI has been commonly reported as being caused by infiltrative or inflammatory pituitary disease, as an iatrogenic sequelae of pituitary surgery or as a result of a congenital defect in the production of vasopressin. We suspect that in this case the patient's PPH may have resulted in isolated cranial diabetes insipidus though the significance of the MRI scan findings remains unclear. This case highlights that CDI can occur following pregnancy in an isolated form without anterior pituitary hormone deficiency and that patients may misattribute significant symptoms and signs of DI as being a normal part of the postpartum period resulting in a delayed diagnosis.

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NCC48

The pragmatic use of corticosteroids in the diagnosis and treatment of non-PTH driven hypercalcaemia

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A 65-year-old gentleman was referred by his GP because of acute kidney injury and hypercalcaemia, which was associated with low levels of parathyroid hormone. He had been fit and well and was on no regular medications. Whilst his hypercalcaemia was partly correctible with saline rehydration, cautious use of bisphosphonates and cinacalcet were not effective in preventing rebound, and his nephropathy persisted. Curiously, he had longstanding low plasma alkaline phosphatase, but had normal dentition and no pathological fractures. Physical examination was normal. The cause of his hypercalcaemia was not clear despite usual first line investigations. His routine biochemistry was as follows: serum calcium 3.41 mmol/l; phosphate 1.13 mmol/l; ALP 19 IU/L, PTH 0.8 pmol/l. eGFR 20 ml/min/1.73 m^2. Total 25-OH vitamin D nmol/L. 24-hour urine calcium excretion was raised at 16.6 mmol. CRP was 2. Myeloma screen, including skeletal survey was negative. PSA, PTH-related-peptide and other tumour markers were normal. CT scan of whole body showed no evidence for carcinomatosis or significant lymphadenopathy. Serum ACE level was 74 U/L (range 20–70). Renal biopsy showed chronic changes associated with hypertension. We asked our metabolic bone unit for significance of the low ALP, to consider adult-onset hypophosphatasia as cause, but this was felt to be unlikely given normal bone turnover markers (P1NP and CTx) and urinary phosphoethanolamine. Instead, our tertiary-centre colleague recommended pragmatic trial of corticosteroids and focus investigations on possible granulomatous disease. Prednisolone, at dose of 30mg, restored normocalcaemia and renal function, after 4 weeks. Subsequently returned tests showed raised 1,25 dihydroxyvitamin D (318 pmol, reference range 43–144) and serum ACE, four months from presentation, had risen to 117 U/L. Repeat CT scan at this time showed interim development of small volume mediastinal and hilar lymphadenopathy, which was biopsied to yield histological evidence of non-caseating granuloma, indicative of sarcoidosis. This case illustrates the value of corticosteroids in managing patients with refractory hypercalcaemia, where neoplastic and PTH-driven causes have been excluded. Of note is that sarcoidosis can cause significant hypercalcaemia despite presenting with apparent low disease activity.

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NCC49

Diagnostic and management challenges in a case of aggressive PTH-dependent hypercalcaemia associated with malignancy

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A 76 years old previously healthy gentleman presented with severe hypercalcaemia (5.19 mmol/l;, 2.1–2.55) and raised Parathyroid Hormone (PTH, 37 pmol/L, 1.6–7.2) after a three weeks history of confusion, diarrhoea, and weight loss. There were no other focal symptoms and family history was not significant. Other significant findings included mild recent hyponatraemia (132 mmol/L, 136–145), acute kidney injury (urea 16.1 mmol/L, 3.2–7.4, creatinine 177 umol/L, 63–111), low vitamin D (30.1 nmol/L, 80–150), high CRP (39 mg/L, 0–5), and normal Thyroid Stimulating Hormone (1.96 mIU/L, 0.35–4.94). An ultrasound scan was unable to localise a parathyroid lesion, while high resolution CT scan of the neck showed a 2 cm poorly defined lesion adjacent to the right lobe of the thyroid. A CT scan of the chest, abdomen and pelvis showed three sub-centimetre nodules in the lungs and multiple lesions, including one 7.7 cm exophytic heterogenous lesion in the liver. Histology of one of the liver lesions demonstrated poorly differentiated adenocarcinoma. Immunohistochemistry staining showed high index of Ki67 with multiple mitotic figures, positivity for AE1/3, and weak staining for TTF-1. Significantly the tissue did not stain for chromogranin A, synaptophysin, and CD 56. Blood DNA analysis for CDC73, Menin, and RET was requested and results are awaited. The hypercalcaemia was refractory to treatment with intravenous hydration and bisphosphonates. The PTH increased within days from 37 to 96.5 pmol/L and liver function tests became markedly abnormal which was attributed to the burden of hepatic disease. The patient deteriorated rapidly requiring intensive care admission for intubation and ventilation. He had haemofiltration to treat his hypercalcaemia and renal impairment and required inotropic support for hypotension. He continued to decline and died before our investigations could be completed and definitive management instigated. In conclusion we describe a patient with terminal aggressive PTH dependant hypercalcaemia of uncertain aetiology. Differential diagnoses include metastatic parathyroid carcinoma or ectopic PTH secretion from another primary, such as a hepatocellular carcinoma. Parathyroid carcinomas typically follow an indolent course with the cause of death usually attributable to hypercalcaemia rather than tumour burden. This case is remarkable for the speed at which the patient deteriorated, despite his hypercalcaemia being adequately treated by haemofiltration. The absence of staining for chromogranin

A on histology is also unusual for parathyroid carcinoma and raises the possibility of a diagnosis of ectopic PTH secretion from another primary.

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NCC50

Incidental finding of lipaemia retinalis on diabetes retinal screening

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Section 1: Case history
A 37-year-old South Asian woman was referred to our diabetes clinic from the Diabetes Eye Screening Programme. Her retinal blood vessels appeared white, in contrast to the normal pink-red colour. The patient was diagnosed with diabetes secondary to chronic pancreatitis a year prior to this presentation, for which she was on metformin and long-acting insulin but had suboptimal control and multiple hospitalisations with chronic pancreatitis. She was previously genotypically diagnosed with type I hyperlipidaemia aged 18. She had no significant family history. Her marriage was non-consanguineous, and she had five children, none of whom struggled with lipid abnormalities. She was a lifelong non-smoker and did not consume alcohol.
Section 2: Investigations
Upon examination, the patient had multiple naevi on her skin currently being managed conservatively by dermatologists. The rest of her examination was unremarkable. Laboratory investigations showed hypertriglyceridemia of 57.7 mmol/l (ref: <.0 mmol/l) and total cholesterol of 12.5 mmol/l (ref: <5.0 mmol/l), markedly higher than previous results. Her diabetes control was suboptimal, with an HbA1c of 74 mmol/mol (8.9%). Following evaluation, the patient was diagnosed with grade III lipaemia retinalis, secondary to type I hyperlipidaemia.
Section 3: Results and treatment
The patient was initially started on various standalone and combination therapies with fibrates, cholestyramine, orlistat and statin over a year; however, these proved to be ineffective. Dietary prudence consisting fruits, vegetables, whole grains, legumes, nuts, fish, and low-fat dairy products rather than refined or processed foods, red meats, high concentrated sweets, eggs, and butter, strict glycaemic control, omega-3 fish oil, and the use of medium-chain triglyceride oil showed some improvements in her lipid profile. The latter resulted in fat-soluble vitamin deficiency which was subsequently treated with vitamins D and E supplementation. She was also later started on volanesorsen. This lowers her serum triglycerides to single figures with no further admission with pancreatitis.
Section 4: Conclusions and points for discussion
Although our patient initially presented with no visual symptoms, untreated lipaemia retinalis may lead to irreversible visual loss. There is no specific treatment available other than conventional lipid lowering agents. More recent treatment, that was also received by our patient, volanesorsen, has been shown to significantly reduce triglyceride levels. Other management options such as exchange transfusion and surgical intervention may also improve lipid profile in refractory cases. Three years after the inital presentation, retinal images showed a complete resolution of lipaemia retinalis and normalisation of the retina.

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NCC51

"The eyes have it": a case of treatment-induced neuropathy of diabetes

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Case History
A male in his 40's diagnosed with type 2 diabetes in 2011 (BMI:20.7 kg/m^2) was admitted with DKA (Dec 2018) after a period of poor glycaemic control on oral hypoglycaemic agents (Feb 2017: HbA1c-105 mmol/mol, Nov 2018: HbA1c-115 mmol/mol). There was dramatic improvement in glycaemic control after commencing him on subcutaneous insulin (April 2019: HbA1c-56 mmol/mol). GAD65 antibodies were positive (24 u/ml; normal < 5 u/ml) and a diagnosis of latent autoimmune diabetes (LADA) was made. After the initiation of insulin and rapid improvement in glycaemic control, the patient began to experience severe debilitating "burning" and "shooting" pain (10/10) across his abdomen, back, thighs and shins with hyperalgesia and allodynia. On examination the patient had normal strength in all limbs (MRC power grading 5/5), no muscle wasting, and no clinical large fibre deficits. He had an irritable nociceptor phenotype with mechanical brush stroke allodynia.
Investigations
Nerve conduction studies were at the lower end of the normal range (sural/peroneal nerve conduction velocity/amplitude: 42.9 m/s; 7.5μV and 42.9 m/s; 3.9 m/s, respectively). MR brain imaging to rule out a central pain aetiology e.g. thalamic infarct was normal. However, corneal confocal microscopy (CCM), a measure of small sensory nerve fibre pathology was abnormal. Corneal nerve fibre length (CNFL) (6.0 mm/mm^2), fibre density (CNFD) (12.9 /mm^2) and branch density (CNBD) (6.7 /mm^2) were all markedly reduced indicative of small fibre degeneration (normative values CNFL: > 12.5 mm/mm^2, CNFD: > 20.6 no/mm^2, CNBD: > 22.7 no/mm^2).
Results and treatment
A diagnosis of treatment-induced neuropathy of diabetes (insulin neuritis) due to rapid improvement in glycaemic control was made based on sudden onset of neuropathic pain and objective evidence of small fibre degeneration. He received multidisciplinary support in the form of maximal dose anti-neuropathic drug therapy, psychological therapy and physiotherapy. After nine months, there was a significant improvement in pain (3–4/10), CCM measures of small nerve fibres showed regeneration (CNFL: 13.1 mm/mm^2; CNFD: 24.8 /mm^2; CNBD: 18.7 /mm^2) and he returned to work.
Conclusions and points for discussion
Treatment-induced neuropathy of diabetes is a potentially debilitating complication with an unknown prevalence. In contrast to diabetic polyneuropathy secondary to prolonged hyperglycaemia, treatment-induced neuropathy is self-limiting and will resolve with supportative treatment. Treatment-induced neuropathy should be considered as a differential diagnosis in cases of acute-onset neuropathic pain following initiation of therapy which rapidly improves glycaemic control.

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NCC52

Unmasking of hyperthyroidism by Takotsubo cardiomyopathy

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Case History
A 74-year-lady with a background of COPD presented to the emergency department with precordial chest pain radiating to the left arm. The pain had been ongoing since a few hours, and was associated with diaphoresis. She was hemodynamically stable, with no tachycardia
Investigations
ECG showed significant ST-segment elevations, predominantly in the chest leads, with elevated troponins. Assuming it to be STEMI, she was transferred to the tertiary cardiology centre for an urgent PCI. She underwent a PCI which showed moderate LAD disease with no obstruction, hence not stented. She had an echocardiogram which showed ballooning of the apex of the left ventricle, suggestive of Takotsubo cardiomyopathy (TCM)
Results and Treatment
She was started on bisoprolol and was repatriated back to us. She remained pain-free and hemodynamically stable, with a normal pulse rate. We received a call from her tertiary centre, mentioning the results of the low TSH of <0.05 mIU/l (normal range 0.2–4.0 mIU/l), the elevated free T4 of 28.8 pmol/l (normal range 10–20 pmol/l) and the elevated free T3 of 2.8 nmol/l (normal range 0.9–2.5 nmol/l) that were done at their centre as routine tests. She never gave a history of thyrotoxic features. She reported occasional palpitations prior to this presentation. Her clinical examination showed no enlargement of the thyroid gland or exophthalmos. No family history of thyroid disease. Her anti-TPO antibodies were positive, but her TSH-receptor antibodies were negative, suggesting Hashimoto's thyroiditis. She was commenced on carbimazole and the bisoprolol continued
Conclusion and points for discussion
TCM is a condition in which left ventricular dysfunction, patterns of regional wall motion abnormalities and myocardial ischemia occur; in the absence of obstructive coronaries. TCM can occur in patients with Graves' disease, Hashimoto thyroiditis, thyroid storm, after radioactive iodine treatment, following thyroidectomy and

even in hypothyroid/euthyroid states. Elevated levels of thyroid hormones exaggerate the inotropic and chronotropic responses to catecholamines. TCM occurs more commonly in females, and is probably related to the role of oestrogens and the myocardial sensitivity to catecholamines. The treatment of hyperthyroidism-associated TCM involves using beta-blockers to disrupt the positive feedback mechanism between thyroid hormone activation and up-regulated beta-adrenoceptors. Anti-thyroid drugs block the effects of thyroid hormone excess. Our case is unique since she didn't have the classical features of hyperthyroidism and she presented with angina and diaphoresis secondary to TCM

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NCC53

A case of heterophile antibody interference causing a falsely positive thyroglobulin in a patient with non-relapsing thyroid carcinoma

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Case History
We report the case of a 59-year-old lady with a persistently elevated serum thyroglobulin following a total thyroidectomy for multifocal papillary thyroid carcinoma. She subsequently underwent radioiodine therapy following which her serum thyroglobulin remained elevated. However, it was later found to be almost undetectable at 0.3 μg/l after a change in laboratory method. This discrepancy prompted further investigation, and repeat analysis using the original assay showed measurement of detectable thyroglobulin which became undetectable following treatment with a heterophilic antibody blocking tube. Thyroglobulin is frequently measured to monitor disease activity after total thyroidectomy in patients with thyroid carcinoma. All immunoassays are prone to interference, and thyroglobulin assays are susceptible to heterophile antibody (HAb) interference. HAbs have the capacity to bind to animal immunoglobulins used in immunometric assays, bridging capture and detection antibodies and lead to a false positive result in the absence of analyte. In this case our patient's thyroglobulin remained detectable at 48 μg/l following total thyroidectomy. After discussion at the thyroid cancer multidisciplinary team meeting she was referred for radioiodine therapy. Despite this her thyroglobulin remained elevated at 47 μg/l (17/03/20). In April 2020 our laboratory changed method from the Siemens Immulite 2000 high sensitivity thyroglobulin assay to the Beckman Access high sensitivity thyroglobulin assay. Both are chemiluminescent immunometric assays. Following this change, the patient's thyroglobulin was measured at 0.3 μg/l (21/07/20). A further sample was analysed by both methods and measured at 0.2 μg/l by Beckman assay but 27 μg/l by Siemens assay. Following pre-treatment with Heterophilic Blocking Tube (Scantibodies) containing blocking reagent, which binds and inactivates HAbs, the Siemens assay result decreased to <2 μg/l.
Conclusions and points for discussion
Heterophile antibody interference is not limited to thyroglobulin assays. Similar problems have occurred when measuring tumour markers such as human chorionic gonadotropin (hCG), leading to unnecessary adjuvant therapy for choriocarcinomas in women and testicular cancers in men. As in this case, the trend to treat thyroid cancer with radioiodine solely on the basis of high thyroglobulin levels can result in unnecessary and potentially harmful therapy for patients without actual recurrence of disease. The key learning point from this case is that when thyroglobulin elevation does not correlate with the clinical scenario then it is prudent to question the reliability of the assay and consider the presence of heterophile antibodies. It also highlights the significance of continuous communication between clinicians and biochemists in order to avoid unnecessary diagnostic procedures and treatments.

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NCC54

Surgical dilemma in management of hyperparathyroidism in multiple endocrine neoplasia type 1

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Case History
29 year old lady presented with profuse diarrhoea, lethargy and hypokalaemia in 2010. CT scan confirmed mass lesion in tail of pancreas. Chromogranin A and 24 hour urinary 5HIAA were normal. Fasting Gut hormone level showed elevated level of Vasoactive Intestinal Peptide (VIP), suggesting diagnosis of VIPoma. Further investigations confirmed hyperparathyroidism and microprolactinoma.
Investigations
Adjusted calcium 2.98 mmol/l (<2.55), phosphate 0.25 mmol/l (0.81–1.45), Parathyroid hormone 17.6 pmol/l (<6.9), 24 hour urinary calcium 14.6 mmol/24 - hours (<7.5), prolactin 2287 mu/l (<496). MRI pituitary with contrast confirmed pituitary microadenoma. Ultrasound parathyroid and Sestamibi scan confirmed left superior parathyroid adenoma.
Results and treatment
Patient underwent distal pancreatectomy and splenectomy in 2011 and histology revealed pancreatic endocrine neoplasm, with Ki67 stain $<2\%$ cells and cells stained positive for VIP. Genetic testing showed MEN-1 mutation. Later in 2011, she went onto have parathyroidectomy and intraoperative frozen section confirmed left superior parathyroid adenoma and solitary parathyroidectomy was performed. Her calcium and PTH levels normalised and patient improved symptomatically. Cabergoline was initiated for microprolactinoma. She was followed up annually and remained well. In 2020, she noticed symptoms of lethargy and investigations showed elevated calcium at 2.69 mmol/l, elevated PTH of 12.2 pmol/l and elevated 24 hour urinary calcium of 9.5 mmol/24 hours, confirming recurrence of hyperparathyroidism. Further imaging in 2020 with ultrasound scan showed two parathyroid adenomas measuring 0.9 cm and 1.3 cm in right mid pole and right lower pole and confirmed on Sestamibi scan. She has been referred to tertiary centre for subtotal (3.5 gland) parathyroidectomy.
Conclusion
Recurrent hyperparathyroidism in patients with multiple endocrine neoplasia type 1 is frequent if fewer than 3 glands are removed at initial parathyroidectomy. Since all glands in patients with MEN1 have the menin mutation, any parathyroid tissue left is at risk of developing into hyperfunctioning gland. To achieve lowest possible rate of recurrence, surgeons advocate subtotal (3.5 glands) or total parathyroidectomy with forearm auto transplantation. However this risks permanent hypoparathyroidism, which can greatly affect quality of life. Several reports also show some patients do not develop recurrence despite solitary adenoma removal, especially with ability to preoperatively localize lesions and some surgeons have begun less aggressive initial parathyroidectomy.

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NCC55

A case of adrenocortical carcinoma in a female with rapid virilisation and mild Cushing's Syndrome

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Section 1: Case history An 86 year old female presented to hospital after being found on the floor and had profound lower limb oedema. She was treated for a urinary tract infection and possible heart failure. On examination she had significant hirsutism and bruised skin. She had a past medical history of BCC removal and primary hyperparathyroidism. Her ECOG performance status was 1–2. There was a family history of pancreatic cancer (father) and pancreatic neuroendocrine tumour (niece). Section 2: Investigations Her 1–mg overnight dexamethasone test demonstrated a cortisol of 505 nmol/l. Her other biochemical test demonstrated: serum androstenedione 99.8 nmol/l (2–5.4), DHEAS >40.7 umol/l (0.7–12.5), total testosterone was 26.3 nmol/l (0.101–1.42), SHBGat 21 nmol/l (17.3–125) and albumin 30 g/l (35–52). Her electrolytes and urinary metadrenalines were normal. 24 hour urinary steroid profile was consistent with an adrenocortical carcinoma (ACC). Her adjusted calcium was 3.10 mmol/l (2.20–2.55) and her plasma PTH was elevated at 7.36 pmol/l (1.6–6.9). Serum NT pro-BNP was 8121 pg/ml (0–738). Ultrasound of her urinary tract found a 191 mm heterogenous mass in the right upper quadrant. This was further characterised with a CT chest, abdomen and pelvis confirmed a 19.2 + 10.1 cm suprarenal mass with a necrotic centre with liver involvement and partial inferior vena cava compression. Echocardiogram demonstrated normal LVEF of 55–60%. Section 3: Results and treatment Patient was diagnosed with ACC with biochemical evidence of cortisol and androgen excess. Her case was discussed at the specialist MDT. It was recommended to start prophylactic low molecular weight heparin. Given her functional status, it was felt that surgical resection of the lesion was not appropriate. She was started on Mitotane. Genetic testing for multiple endocrine neoplasia type 1 (MEN1) was also undertaken due to her family history and past medical history. Section 4: Conclusions and points for discussion ACC are rare but aggressive tumours. They can present as an incidental finding or an abdominal mass or rapid progressing Cushing syndrome with or without virilisation. Our patient had rapid virilisation but only some clinical features of Cushing's syndrome. Surgery is the mainstay treatment option for ACC. However, our patient was not a candidate for surgical resection was started on Mitotane. This will act on the adrenal gland to shrink the tumour, prevent its progression and block excess cortisol and testosterone. The majority of ACC are

sporadic. However, it is important to consider ACC can develop as a part of familial disease like MEN1.

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NCC56

Thyroidectomy for recurrent sub-acute thyroiditis

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A 21-year-old woman presented in 2015 with palpitations, weight and hair loss, mood swings and diarrhoea. She was diagnosed with thyrotoxicosis (Table). On examination, thyroid was normal and no evidence of opthalmopathy. Treatment with Propranolol and Carbimazole was commenced. Ultrasound neck revealed moderate diffuse enlargement of the thyroid with uniformly abnormal echotexture, consistent with thyroiditis. A month later, she developed profound hypothyroidism, therefore Carbimazole was stopped and Levothyroxine started with subsequent normalisation of thyroid function tests. Later on, Levothyroxine was paused. She has not required treatment and remained asymptomatic until April 2017, when she suffered a relapsed thyrotoxicosis. Technetium (Tc) scan showed normal homogenous uptake. Thyroid receptor antibodies (TRAbs) were undetectable. She was commenced on Propranolol and within weeks made a full recovery with no additional treatment. In September, 2019, she had another relapse of severe thyrotoxicosis. Treatment with Propranolol and Prednisolone was started for a diagnosis of recurrent subacute thyroiditis (SAT). She has developed hypothyroidism, which required Levothyroxine treatment and remained stable on 125 mcg OD. In December 2019, the patient fell pregnant. She was euthyroid throughout pregnancy on 75/100 mcg Levothyroxine. Twelve weeks post-partum, in November 2020, she again, presented with thyrotoxicosis. Her Tc scan showed low uptake consistent with postpartum thyroiditis. In 2019/2020, her TRAbs were undetectable. Her Levothyroxine was paused. By December, 2020, she became hypothyroid and since then is on Levothyroxine 100mcg and remains well and stable.

Results

	TSH mIU/l	FT4 pmol/l	FT3	Anti-TPO Ab IU/ml
July, 2015	<0.03	45.7	13.3	63
August, 2015	>100	1.9	1.6	
September, 2015	3.15	21.7	5.0	
April, 2017	<0.03	83.6	27.4	17.7
June, 2017	7.61	10.9	4.6	
August, 2017	3.7	14.7	5.6	
September, 2019	<0.01	91.8	29.8	
November, 2019	3.95	12.6	4.7	
November, 2020	<0.01	72	22.4	36
January, 2021	23	9.9	3.2	
March, 2021	4.82	15.1	3.7	

Treatment

Given 4 relapses of severe thyrotoxicosis as a presentation of SAT (1 episode occurred while the patient was on Levothyroxine) and patients request, she was referred for thyroidectomy.

Conclusion

This case represents an unusual form of thyroiditis where the patient fluctuates between severe hyperthyroidism and hypothyroidism; last episode occurred post-partum. SAT is a rare disease with a recurrence frequency of 20–30%. The reason for SAT relapse is unknown, but an association with HLA-B*18:01 and -B*35 was reported. In such high-risk patients, the steroid treatment regimen should be intensified with a slower dose reduction.

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NCC57

"BED IS BAD" – Finding the unusual cause of hypercalcaemia

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Section 1: Case history

A 78 years old lady presented to Emergency Department with two weeks history of lethargy and confusion. She had background of advanced destructive Rheumatoid Arthritis diagnosed 30 years ago, multiple joint fractures, osteoporosis, long-term urinary catheter, recurrent UTI and renal calculi. She was recently discharged from hospital for urosepsis. She was bed-bound for the last 15 years after crushing vertebrae C2 C3 pressing on spinal cord. Her regular medicines included gabapentin, methenamine, senna and paracetamol. On admission, her observations and physical examination were unremarkable apart from features of long-standing rheumatoid arthritis.

Section 2: Investigations

Her biochemical profile on admission revealed marked hypercalcaemia with adjusted Calcium 3.88 mmol/l (2.20–2.60), phosphate 1.2 mmol/l (0.65–1.50) ALP 162 U/l (40–150), 25 OH Vitamin D 87 nmol/l (70–150), PTH 0.8 pmol/l (1.6–7.2), TSH 3.13 mU/l; (0.30–4.20), Free T4 12.3 pmol/l (7.0–17.0), urea 6.4 mmol/l (2.5–7.8). Myeloma screen and urine MSU were negative, ACE levels were <12 U/l. CT TAP did not reveal any evidence of malignancy. No clear cause for hypercalcaemia was identified after these investigations apart from prolong immobilisation.

Section 3: Results and treatment

Aggressive IV fluid replacement was commenced with close monitoring of calcium levels. Later on, intravenous pamidronate was added which resolved hypercalcaemia and she improved clinically. She was assessed by physiotherapy but had no rehabilitation potential and needed hoist transfers. She was discharged home with routine electrolyte monitoring as outpatient.

Section 4: Conclusion and points for discussion

Hypercalcemia is a common metabolic disorder in hospitalised patients. The common causes of inpatient hypercalcaemia are primary hyperparathyroidism and malignancy. Immobilisation hypercalcaemia is among the rare causes but its diagnosis requires an exhaustive evaluation to rule out common causes first. Prolong immobilisation stimulates osteoclastic bone resorption, osteopenia, osteoporosis and bone remodelling disorders. This induces resorptive hypercalciuria and suppression of the parathyroid 1,25-vitamin D axis. If untreated, patients may develop dehydration, personality changes, calcium oxalate nephrolithiasis and renal failure. Treatment is aimed at early mobilisation, hydration, and restoration of the balance between calcium excretion and resorption with a gradual bone metabolism reduction. Bisphosphonates and denosumab are also beneficial. Our patient was a difficult case as she developed severe hypercalcaemia and no obvious cause was identified. It was only when other causes of hypercalcaemia were ruled out and further investigations confirmed unexplained hypercalcaemia. Timely treatment of hypercalcaemia is a critical step for rapidly control of symptoms.

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NCC58

Challenging management of type II amiodarone induced thyrotoxicosis AIT

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Case history

20 year old man with a complex cardiac history of Shone's syndrome, out of hospital cardiac arrest 2015 (CRT-D implant) and multiple previous episodes of fast atrial fibrillation was admitted to hospital (28/11/2019) with 3 weeks history of intermittent palpitations and shortness of breath. His regular medications included amiodarone and bisoprolol. Examination revealed a fine tremor of outstretched hands, no obvious goitre or thyroid eye disease. Thyroid function testing (TFT) on admission revealed hyperthyroidism; TSH < 0.01 munit/l (0.3–4.20), FT4 61.1 pmol/l (9–19), FT3 17.9 pmol/l (3–5.4), TFTs from 2018 were normal. Impression was of amiodarone induced thyrotoxicosis (AIT). He was commenced on carbimazole 40 mg and prednisolone 30 mg OD.

Investigations

Findings on thyroid ultrasound were suggestive of type II AIT, TSH receptor antibody were negative. The TFTs gradually started improving by 12/12/19 with FT4 47.8 pmol/l and FT3 9.0 pmol/.

Treatment

The patient was discharged with weekly TFT monitoring. Due to pre-syncpoal episode and worsening biochemistry (28/12/19 (FT4 >64.35 pmol/l, FT3 19.1 pmol/l)) he was readmitted. Prednisolone and Carbimazole were increased to 50 mg and 60 mg respectively. Diuretics were adjusted to clinical fluid status. He developed deranged liver function, felt to be due to the combination of hepatic congestion and potentially a complication for the high dose carbimazole. His thyroid uptake scan confirmed the ultrasound finding of type II AIT, the carbimazole was stopped. Due to his overall thyrotoxic state and exacerbating

heart failure on steroids, a thyroidectomy was considered, but anaesthetic review deemed him a poor surgical candidate with 70% mortality risk. Other medical therapies were trialled including Colestyramine and lithium; both had to be stopped due to intolerance Lithium due to toxicity. The prednisolone was gradually reduced with improvement in patient's fluid status and FT3 values (FT3 11.9 pmol/l). He was discharged with outpatient monitoring of thyroid function, which continued to improve. Once TFTs were normal the prednisolone was weaned and stopped. His TFTs remain normal off prednisolone.

Conclusion

This is an example of management of complex case requiring discussions both within the departmental team and with national experts seeking opinions early. This patients' significant cardiac history meant thyroidectomy was deemed too risky but should be considered as a treatment option in AIT. The differentiation between AIT type I and II can be difficult, starting treatment for both maybe required in clinically unwell patients. Medical treatments are options but can take time to be effective and have side effects.

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NCC59

Fresh pair of eyes for peri-menopausal lady

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A 50-year-old peri-menopausal lady has had a background history of hypertension on single-agent antihypertensive medication (ACEI), chronic headache, recurrent collapses, and panic attacks for the past 14 years. She has been visited by her GP frequently and performed countless blood tests including FSH, LH, and TSH which confirmed that her symptoms were neither related to menopause nor hyperthyroidism. She also presented to the Emergency Department a dozen times and called paramedics 8 times for similar symptoms. She was diagnosed with panic attacks or investigated for meningitis. Her symptoms have never been resolved or getting better after discharge from the hospital. Unfortunately, her chronic catecholamines symptoms were controlled with anti-depressants and analgesics. Subsequently, she was relocated to a new place in 2014 and registered with a new GP for symptom relief medications. The GP reviewed her before issuing a repeat prescription and re-investigated the unresolved symptoms. 24-hour urine catecholamines were markedly elevated which were evident by urine volume of 3.7L, Noradrenaline 54327 nmol/24 hours (0–570 nmol/L), Adrenaline 78 nmol/24 hours(0–100nmol/l), urine dopamine 1468 nmol/24 hours (0–2500 nmol) respectively. Finally, she was referred to the endocrine clinic for further evaluation and management. She was a slim and well-presented lady with a slightly anxious disposition on examination. Her BP was 150/90 with a pulse rate of 100 beats /min. Hypertensive retinopathy grade 1 was detected in fundoscopy. There was no postural drop and no thyroid nodules. MRI adrenals showed 39 mm high intensity right adrenal lesion. Alpha blockade with Phenoxybenzamine was used before surgery. She underwent laparoscopic right adrenalectomy in January 2015 and the histology reported encapsulated tumour without lymphovascular invasion and low risk for malignancy. The adrenergic symptoms were entirely resolved postoperatively. She became normotensive and Urinary catecholamines were dramatically normalized although she required hydrocortisone replacement for a few months due to the suboptimal short synacthen test. It was stopped subsequently as her adrenal response has recovered fully thereafter. She has been followed up in endocrine outpatient clinic from 2015 to 2020 with 6-monthly urinary catecholamine and there is no biochemical as well as clinical features of pheochromocytoma relapse.

Discussion

The diagnosis of a very rare and potentially life-threatening endocrine tumour was made by a General Practitioner instead of an endocrinologist. This case also highlighted that the definitive treatment is not only curative and reducing cardiovascular risks, but also improving her quality of life.

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NCC60

Learning to weather the storm: a case highlighting the challenges of managing a thyrotoxic crisis in a ventilated, co-morbid patient

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Section 1: Case history

A 60-year-old woman was transferred to the receiving hospital after thrombolysis for a left-sided total anterior circulation stroke. Her past medical history was significant for alcohol dependence (70 units/week), atrial fibrillation (not anticoagulated but rate controlled with propranolol), seizures and severe mitral regurgitation. This lady underwent a successful thrombectomy, but subsequently developed haemorrhagic transformation and hydrocephalus. She was transferred to ICU for an external ventricular drain insertion which was removed after improving radiological imaging. The patient remained intubated and ventilated. During this time she became pyrexic, had multiple seizures and increasingly fast AF, consistent with a thyroid storm.

Section 2: Investigations

On admission to hospital thyroid function tests were sent as part of her assessment for atrial fibrillation, showing TSH <0.02 mIU/l, and free T4 36.2 pmol/l. Unfortunately, the results were not checked and no action was taken. Following her clinical deterioration with pyrexia and seizures her TFTs were repeated which revealed a TSH <0.02 mIU/k, Free T4 70.7 pmol/l and Free T3 25.3 pmol/l. Treatment was commenced with IV propranolol, propothyouracil, iodine and hydrocortisone. However, following this episode the patient developed a significant lactic acidosis (4.0 mmol/l to 12.5 mmol/l), and hyperkalaemia (3.4 mmol/l to 11.0 mmol/l) over the course of 4 hours. She also became increasingly hypotensive despite aggressive fluid resuscitation and vasopressor support.

Section 3: Results and treatment

Clinical examination revealed a soft abdomen producing liquid stool. A CT angiogram was requested for suspected mesenteric ischaemia. During transfer to CT this lady had a cardiac arrest and resuscitation efforts were unsuccessful. Subsequent pending TRAb results were measured at 13 IU/l, supporting a diagnosis of Grave's disease.

Section 4: Conclusions and points for discussion

This lady displayed symptoms consistent with a thyrotoxic storm including: pyrexia, tachycardia, seizures and diarrhoea in addition to deranged TFTs. Her Burch-Wartofsky score was later calculated at 95 points, further supporting this diagnosis. Despite medical management, disease progression resulted in a fatal outcome. Even with targeted treatment, the mortality rate for a thyroid storm remains high. This reinforces the need for prompt investigation and management of suspected hyperthyroidism, particularly in vulnerable patient groups where existing co-morbidities may mask acute progression of symptoms. Additionally, this case highlights the difficulty of diagnosing a thyroid storm in a ventilated, co-morbid patient with previously undiagnosed thyroid disease. It also underlines the importance of having reliable hospital systems to prevent abnormal results being missed.

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NCC61

An unusual cause of hypercortisolism: Adrenal carcinoma

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Case History

A 76 year old woman presented to the Accident & Emergency Department with persistent hypokalaemia, hypertension and metabolic alkalosis. She complained of ongoing muscle fatigue and tiredness and denied any headaches or vision problems. On examination, she had evidence of centripetal obesity, proximal myopathy, pink striae and bruises on her abdomen. No visual field deficit on confrontation and neurological examination was normal. She had a past medical history of hypertension on Amlodipine 5 mg, Ramipril 5 mg and Doxazosin 4 mg daily. She reported two months history of hyperkalaemia managed by her general practitioner with regular potassium supplements.

Investigations

Blood tests and CT adrenal glands were requested to exclude adrenal pathology.

Results and treatment

Her potassium level was low at 2.4 mmol/l with a pH of 7.55 on venous blood gas. Early morning cortisol was elevated at 1885 nmol/l. Plasma metanephrine was normal at 21 ng/l. ACTH level was suppressed. Aldosterone to renin ratio was normal at 2 and HbA1c was 41 mmol/mol. CT adrenals with contrast demonstrated a large right adrenal mass likely to be an adrenal cortical adenocarcinoma with local infiltration into the right renal vein, IVC, right lobe of the liver with multiple lesions in the lung bases keeping in with metastatic lung deposits. She was treated with intravenous potassium replacement with cardiac monitoring and Metyrapone 500 mg twice a day. She was discussed at the local Adrenal MDT and an adrenal biopsy was recommended. Because of the risk of seeding, adrenal biopsy isn't usually recommended but in this case it was thought that a tissue diagnosis would have potentially helped to confirm the diagnosis and guide chemotherapy. She was subsequently discharged with potassium of 3.3 mmol/l and an early morning cortisol of level 657 nmol/l. She

was reviewed in the Endocrinology Clinic a week later and Metyrapone was increased to 750 mg three times a day. Adrenal biopsy confirmed adrenocortical carcinoma. She was offered palliative chemotherapy. WHO performance status was 3. Her condition deteriorated very quickly and she died after several weeks.
Conclusions and Points of Discussion
Endocrine causes of persistent hypokalaemia should always be considered when managing potassium disorders. This case highlights the importance of careful physical examination to pick up subtle clinical signs to build up a diagnosis. In the current pandemic, telephone appointments can be challenging and it is easy to misdiagnose rare conditions. In complex cases with difficult diagnoses, face-to-face appointments should be offered to patients.

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NCC62

A case of pseudohyperkalaemia in a patient with myeloproliferative disorder and acute kidney injury

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Introduction
Pseudohyperkalaemia is one of the most common testing errors that occur in clinical practice. It's commonly due to pre-analytical factors many of which are clinically well recognised. These include incorrect sampling, delay in sample processing and haemolysis to name a few. However non-recognition of some rarer causes like thrombocytosis often results in initial inappropriate, potentially dangerous treatment. Here we present one such case of pseudohyperkalaemia in a patient with myeloproliferative disorder in the context of acute kidney injury.
Case
A 70-year-old gentleman was admitted to hospital with abdominal pain and vomiting. This was later diagnosed to be due to cholecystitis. He was also found to have severe hyperkalaemia of 7 mmol/l, acute kidney injury with an eGFR 48 (68 about a month ago), Hb: 106 g/l, Platelets: 1,035 10^9/l, WCC: 54.6 10^9/l and Neutrophils: 52 109/l. Although his point of care (POC) venous blood gas potassium was 5.4 and ECG was normal, he was treated with intravenous insulin dextrose infusion due to two lab K levels being $\geq$7 mmol/l. He was not on any medications that could raise potassium. He had a past medical history of JAK2 + ve myeloproliferative disorder, hypertension, gout, and glaucoma. It was then noted that his hydoxycarbamide was stopped about a month ago, before his hip fracture surgery, but was not restarted due to oversight. This was promptly restarted and a possibility of pseudohyperkalaemia was considered. A repeat serum and plasma K with Lithium heparin tube were sent and the results were 6.7 and 5.5 mmol/l respectively confirming pseudohyperkalaemia due to thrombocytosis. Subsequently, POC potassium was used to make clinical decision. His K came down to 3.8 mmol/l along with platelet count of 404 10^9/l and normal WBC, on day 5 of restarting hydroxycarbamide.
Discussion and conclusion
Hyperkalaemia is a potentially fatal condition and should be managed promptly. However, pseudohyperkalaemia must be excluded particularly when there is evidence of thrombocytosis as it could lead to inappropriate corrective treatment that may cause hypokalaemia an equally dangerous condition. Pseudohyperkalaemia in the context of thrombocytosis is due to in vitro release of potassium from activated platelets during the process of clotting in serum tubes. Literature suggests considering pseudohyperkalaemia when platelet count is more than 500 + 10^9/l, and measuring plasma K using heparinised tube or whole blood K with POC venous blood gas analyser for making appropriate diagnosis and to avoid unnecessary and potentially harmful treatment.

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NCC63

Diagnostic conundrums: Severe hypoglycaemia in a non-diabetic individual

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Case history
A 26-year-old female with a past medical history of migraines was admitted to the Emergency Department (ED) with severe hypoglycaemia after drowsiness was noted by her partner in the early hours of the morning. On initial paramedic assessment, the patient had a reduced Glasgow Coma Scale (13/15), hypoglycaemia (capillary blood glucose of 0.9 mmol/l [16.2 mg/dl]), hypothermia (34.3 degrees Celsius [°C]) and bradycardia (heart rate 41 beats per minute). The patient quickly recovered during transfer to the ED following the administration of 250 ml intravenous 10% dextrose. Full clinical history in the ED noted the patient had consumed alcohol (gin and tonic) the evening before the episode with nil else of note reported. A full clinical examination was unremarkable.
Investigations
Venous blood glucose was 6.6 mmol/l on arrival to the ED. Renal profile, C-reactive protein and liver profile were normal. Neutrophilia of 16.7 + 10^9/l was noted. Urine microscopy and β-HCG were negative. The patient was discharged with advice and safety netting.
Results and treatment
Three months later, follow-up in endocrinology clinic yielded little further diagnostic information. Investigations showed a fasting glucose of 4.2 mmol/l, HbA1c of 29 mmol/mol (4.8%) and a random cortisol of 349 nmol/l (lab reference range 145–619). Thyroid stimulating hormone (TSH), anti-tissue transglutaminase (anti-tTG), vitamin B12, folate and ferritin were all normal. The patient had been asymptomatic and well following the episode. Capillary blood glucose monitoring in the weeks leading up to the appointment were between 4.5 and 8.5 mmol/l (81–153 mg/dl).
Conclusions and points for discussion
This is a challenging case with no immediately obvious cause identified for such profound hypoglycaemia. As an isolated singular episode of severe hypoglycaemia, the clinical presentation was not in the pattern seen in insulinoma nor consistent with post-prandial reactive hypoglycaemia. Literature searches have revealed a limited number of case series and case reports on the association between mild hypoglycaemia and quinine infusion (in therapeutic doses, 5–10x the quantity seen in 1L of typical tonic water). Further review of the literature demonstrated a small number of case reports noting the "perfect storm" of combined sucrose, quinine and alcohol ingestion inducing hypoglycaemia. The mechanisms of hypoglycaemia proposed are via hyperinsulinaemia (quinine-mediated beta cell stimulation, sucrose-mediated hyperglycaemia), alcohol-mediated counterregulatory hormone suppression (growth hormone and adrenaline) and resultant increased insulin sensitivity. To our knowledge, this is the first case report of severe hypoglycaemia in response to ingestion of a mixed sucrose-quinine-alcohol beverage.

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NCC64

A case of sight threatening pituitary macro-adenoma in pregnancy

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Introduction
Pituitary adenomas account for 10% of intracranial tumours and are almost always benign. In some individuals, who may have a pre-existing adenoma, the pituitary gland undergoes remarkable hyperplasia especially during pregnancy, due to increase in oestrogen levels leading to increase in the tumour volume causing mass effects. This case report reviews a pregnancy with incidental finding of pituitary macro adenoma causing visual field defect, its management and further follow up.
Case Presentation
We present a 32 years old pregnant female of 37 weeks gestational age (G1, P0) presenting to the emergency department with 1 week history of sudden deterioration in visual acuity. Visual field examination revealed a supero-temporal defect in the right and left eyes. MRI showed a pituitary macro adenoma measuring 16 + 12 + 15 mm, extending to suprasellar region causing upward displacement and compression of optic chiasma. Blood tests including pituitary profile were within normal reference range except mildly raised prolactin. She underwent elective lower caesarean section under hydrocortisone cover in view of her visual field defect. Following the delivery, her visual acuity improved significantly. A follow up MRI pituitary with contrast done 2 months later showed a reduction in the size of adenoma measuring about 9 mm. Patient was started on cabergoline and has been advised to use contraceptives and to seek help before planning for next pregnancy.
Discussion
Managing macro adenoma during pregnancy is challenging. Symptomatic macro adenoma should be an indication for caesarean section. In our case, the tumour was diagnosed after conception. Hence for the future pregnancies, an MRI should be done before conception to document tumour size with a monthly follow up and visual field examination at every trimester. Patients must be informed about the

relatively higher risk of tumour enlargement and the importance of treatment before conception. Patients with large macro adenomas and those with suprasellar extension are strongly discouraged from conceiving until definitive therapy is undertaken. Surgery is an option in cases with no tumour reduction with medical treatment, or in those who developed tumour growth in a previous pregnancy. What can be more challenging in planning for the future pregnancies is that surgery of the gland can lead to infertility whilst future pregnancy may again cause macro adenoma which may even lead to blindness as pituitary once enlarged, never shrinks back to its normal size.

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NCC65

Multi-disciplinary management of the diabetic foot: putting patient choice at the forefront of clinical decision making

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Case History
A 54 year old man with type 2 diabetes mellitus was referred in 2014 to our multi-disciplinary foot care service for the management of ulcers. One year previously he had undergone a left hallux amputation due to underlying osteomyelitis. Over the period 2015 through 2021, he required multiple admissions for management of limb threatening foot sepsis with exposed necrotic mid and hind foot bone. In 2016 he suffered a cerebrovascular infarct and in 2019 an episode of AKI.
Investigations
Arterial duplex scans in 2014 and then angiography in 2015 showed severe peripheral arterial disease. Bacteriology across this time period yielded a range of positive cultures with variable antimicrobial sensitivities. In 2018, cultures were positive for carbapenem resistant organisms.
Treatment
Clinical decision making was undertaken by a multi-disciplinary team comprised of diabetic physicians, vascular surgeons, microbiologists, specialist diabetic nurses, podiatrists as well as those involved in the patient's wider social care needs. Issues addressed by the MDT included whether the patient might have an undiagnosed learning difficulty. There was disagreement amongst health professionals as to whether he had mental capacity. Bone and soft infection worsened significantly in 2019. The patient refused to consider the possibility of below knee amputation – the only surgical option if revascularization and medical management failed. Successful angioplasty, six months of intravenous antibiotics and intensive nursing and podiatry care has enabled him to avoid below knee amputation and maintain independent mobility. Non-clinical staff played a critical role by getting him to appointments and coordinating his care.
Conclusions and points for discussion
The 2014 Lancet Commission on Culture and Health has emphasised how inseparable health is from cultural perceptions of well-being. A range of initiatives, for example the City Changing Diabetes Project, are intended to address the social and cultural factors which can increase type 2 diabetes vulnerability amongst certain people living in urban environments. Our case report highlights the efforts required by a team of health professionals to support a patient at risk of losing limb, mobility, independence and dignity arising from complications of the diabetic foot. Also, how multi-disciplinary team decisions taken across a period of 7 years have helped our patient live with his diabetes. The culture of clinical decision making, care giving and how to best take into account patient wishes within diabetic service delivery is worthy of its own study.

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NCC66

Diagnostic dilemma of cushing disease

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57 year old female physiotherapist, diagnosed with osteoporosis following a fibula fracture from a low impact stretch and a wedge vertebral fracture at age 51 with a metatarsal fracture age 54. With associated history of easy bruising, increase abdominal girth although her weight remained stable at 48.5 kg with BMI 19.9 and proximal myopathy. Blood pressure was constantly normal.
Investigations
Early morning random Cortisol 564 and ACTH 6.6 (2–11), cortisol after overnight 1 mg Dexamethasone Suppression test 35. Long Dexamethasone Suppression Test (2 mg QDS) baseline cortisol level 353 post-test cortisol suppressed to 38.6 9 am salivary cortisol 183(5–46). MRI showed a bulky pituitary and no macroadenomas although a microadenoma could not be excluded. Pituitary MRI with contrast showed two focal area of hypo-enhancement within the left anterior aspect of the pituitary which measured 2.7 + 5.2 and 2.5 mm + 6.0 mm and was cystic in nature. Repeat ACTH was 9 pmol/l. CT Thorax, abdomen and pelvis demonstrated no adrenal masses. 24 Hour Urinary free cortisol 479 and 274 a few months apart when she had maximal symptoms (Ref range <165). The rest of the pituitary profile was normal. Electrolytes were consistently normal. IPSS done showed significant gradient between the right side of the pituitary and peripheral ACTH. She had transsphenoidal surgery unfortunately her symptoms persisted. Post transsphenoidal surgery MRI head showed a hypo enhancing focus within the pituitary gland anteriorly at and just to the left of the midline. Appearance compatible with residual recurrent adenoma. 24hour Free Urinary cortisol was 467. She was commenced on Metyrapone awaiting second transsphenoidal surgery. Metyrapone was adjusted according to hydrocortisone day curve. The second transsphenoidal surgery was successful, ACTH 0.7 24 hour urinary cortisol 72.7 TSH 1.1 early morning cortisol 22.5. Histology showed corticotroph adenoma. She was commenced on replacement hydrocortisone. Generally, her symptoms improved, unfortunately she never regained her health.
Discussion
Cushing's disease is challenging to diagnose and manage. Transsphenoidal surgery provides initial cure for 75 to 90% and recurrence in 5 to 20% of cases. Residual tumour on MRI repeat transsphenoidal surgery 50 -70% cure 1. Residual tumour which is non resectable, pituitary irradiation and steroidogenesis inhibitor with 85 to 100% cure rate. Bilateral adrenalectomy, in cases of severe hypercortisolism or women desiring pregnancy with a potential cure rate of 100%. Patients with mild hypercortisolism can be treated with corticotrope-directed medical therapy (pasireotide or Cabergoline) with possible 20 to 40% remission.

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NCC67

A challenging case of lithium induced thyrotoxicosis and thyroid storm

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Case History
A 69-year-old woman with bipolar schizoaffective disorder of 11 year's duration and recent diagnosis of atrial fibrilation was admitted with acute onset of delirium, lethargy, shakiness and confusion. On admission, the patient was restless and non-compliant. Her skin was warm and sweaty, clinically dehydrated. Her heart rate ranging between 75 and 100 /min. The rhythm was irregular, consistent with atrial fibrillation on ECG and was afebrile. She was oriented to time/place/person but trying to climb from bed. Her speech was dysarthric. She had coarse tremors generally and brisk tendon reflexes but no ataxia. Her recent medication were lithium 600 mg a day (started since 2009 with dose titration recently), valproate, clomipramine and procyclidine. At care home, the patient's ability to perform self-care had worsened over the previous year. There was no family history of thyroid illness. Patient's thyroid function was normal 2 months prior, checked by her psychiatrist/mental health team.
Investigation
FBC, U/Es, LFTs and Urine MSU results-normal, CRP: 28, CT head NAD, LP – NAD. Her TFTs on admission was consistent with hyperthyroidism with FT4: 62.2 pmol/l (7.86–14.41), TSH: <0.02 mU/l (0.35–5.5). Lithium level: 1.50 mmol/l (0.4–1.2), TRAB and TPO antibodies were normal.
Results/Treatment
Given history, symptoms and investigations patient was treated as Lithium induced hyperthyroidism and started on carbimazole 20 mg BD and lithium was stopped as per Psychiatry team. Next day patient became very agitated, developed temperature and became drowsy. She was not compliant with oral medications and hasn't had her carbimazole doses. O/E: GCS: 10/15, HR:160 irregular, BP: 160/90, temp: 39. On Burch-Wartofsky Point Scale (BWPS) for Thyrotoxicosis, she was scoring 80 (highly suggestive of thyroid storm). Patient was treated as Thyroid storm secondary to Lithium and moved to ITU for the management. She was Started on PTU and beta-blocker via NG tube and IV hydrocortisone. Also given temperature she was covered with IV Antibiotics. Clinical and biochemical improvement noted 5–6 days post treatment. On day 9: FT4: 28.5 pmol/l, TSH: $<$ 0.02 mU/l. PTU was switched to oral carbimazole.
Conclusion and Point of Discussion
Hyperthyroidism is an uncommon side-effect of lithium compared to hypothyroidism but may have clinical implications. As this case suggested that early recognition of thyroid problem/Thyrotoxicosis in confused and agitated

patient, especially if they are on offending agent like lithium is important and can be lifesaving.

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NCC68

An interesting case of pan-hypopituitarism associated with empty sella syndrome

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Background
Empty Sella syndrome (ESS) is caused by the herniation of the subarachnoid space into the sella turcica, causing compression of the pituitary gland. Patients may be asymptomatic or exhibit different degrees of pituitary hormone deficiency. Pan-hypopituitarism can occur if there is decreased or absent secretion of all of the anterior pituitary hormones.
Case
We report the case of a 68 year old female of Pakistani background who was visiting the UK. She presented with a 2 day history of lethargy. She reported feeling this way thrice during the last 5 years when her sodium levels were found to be low. Her past medical history included hypertension, renal stones and chronic hyponatraemia. Blood pressure was 157/70 mmHg. Clinical examination was unremarkable, with visual fields full to confrontation.
Investigations
Sodium 119 mmol/L (133–146). Paired Osmolalities: Serum Osmolality 258 mOsm/kgH2O (275–295), Urine Osmolality 339 mOsm/kgH2O, Urine Sodium 139 mmol/L. 9 am cortisol 61 nmol/L (185–624). Short Synacthen test: 30 minute Cortisol 207 nmol/L, 60 minute Cortisol 256.80 nmol/L. ACTH – Outstanding. Serum Glucose 6.4 mmol/L (3.5–5.4). CT Head – Enlarged fluid-filled pituitary fossa. Anterior Pituitary Hormone testing: Prolactin 45 mIU/L (58–416), LH 0.3 I.U./L (>16), FSH 1.9 I.U./L (>30), IGF-1 3.8 nmol/L (4.8–21.6), TSH 1.57 mIU/L (0.30–4.8). TFTS: Free T4 <3.2 pmol/L (7.7–20.6), Free T3 3.3 pmol/L (4.2–6.9). MRI Pituitary – empty sella with no fat or tumour seen within the pituitary fossa and normal enhancement of pituitary stalk.
Treatment
As the available anterior pituitary hormone levels were low we suspected pan-hypopituitarism. She was initiated on Hydrocortisone, and Levothyroxine replacement as her free T4 level was undetectable. Her sodium level improved from 119 mmol/l to 131 mmol/l over 4 days and her symptoms completely resolved. She was discharged on Hydrocortisone (10 mg – am and 5 mg – pm) and Levothyroxine (50 mcg). ACTH level later returned as 18 ng/l. She was referred for Ophthalmology review. As she returned to Pakistan, we advised her next of kin that she contact her local doctor for follow up, including repeat thyroid function testing.
Conclusion
This is an interesting case as this post-menopausal lady had suffered from chronic hyponatraemia due to pan-hypopituitarism associated with empty sella syndrome. Her sodium levels improved and symptoms resolved after hormone replacement was initiated.

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NCC69

How novel is Dapagliflozin?

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Case history
This 55 years old gentleman has past medical history of obesity, type 2 diabetes (since age of 27 yrs.), hypercholesterolemia, hypertension and osteoarthritis. He recently suffered from myocardial infarction discharged 2 days back and presented to emergency department with central chest pain radiating to both arms in the morning.
Investigations
ECG reported as normal and venous blood gas showed pH- 7.10, pCo2- 3.84, pO2- 5.54, glucose- 10, lactate-1.8, bicarbonate- 8.5, base excess 19.2, anion gap 25. And dapagliflozin was stopped as a part of discharge planning and followed up in our diabetes clinic. Urine dipstick revealed Glucose +2, ketone +4, pH 5.
Results and treatment
He was diagnosed to be suffering from euglycemic diabetic ketoacidosis & treated as per protocol. When he recovered from (Diabetic ketoacidosis) DKA his insulin was optimised and dapagliflozin was stopped as a part of discharge planning and was followed up in our diabetes clinic.
Conclusions and points for discussion
In patients on dapagliflozin, cases of euglycemic diabetes ketoacidosis are increasingly being reported. Diagnosis of euglycemic diabetes ketoacidosis can be easily missed in the emergency department due to absence of marked hyperglycemia, often leading to delayed diagnosis and treatment. Mechanism of action of dapagliflozin is by selectively inhibiting the transporter protein SGLT2 (Sodium-glucose co-transporter-2) in the renal proximal, which prevents glucose reabsorption and subsequently induces the elimination of filtered glucose via urine, the process is known as 'glycuresis' which reduces the blood glucose levels. SGLT-2 inhibitors should be initiated by a clinician cautiously and only after adequately weighing the risks and benefits of treatment. It is advisable to do urine test on patient taking dapagliflozin on admission which will help diagnose euglycemic DKA early. To prevent this potentially dangerous complication, patients taking SGLT2 inhibitors who become ill should discontinue the medication, undergo ketone evaluation, and start basal insulin, if ketones are positive. In addition, patients should be educated to stop their SGLT2 inhibitor at least 1 week prior to elective procedures.

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NCC70

Omeprazole induced hypomagnesemia leading to hypocalcemia

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Case History
A 58 year old female was referred by the GP to hospital for symptoms of tingling and numbness in fingers and toes, muscle cramps in arms and legs and swollen legs. The patient had a history of gastroesophageal reflux disease (GERD), irritable bowel syndrome (IBS), hypertension, fibromyalgia, iron deficiency anaemia, knee osteoarthritis, and heart failure.
Investigations
On admission, a corrected calcium level was 1.9 mmol/l and serum magnesium 0.37 mmol/l. Her Parathyroid hormone (PTH) was 7.6 pmol/l and Vitamin D-level was 48 nmol/l.
Results and Treatments
She was treated with intravenous calcium and magnesium and there was improvement in the electrolytes. However, the calcium levels still didn't normalise till she had magnesium infusion. Calcium and magnesium replacements were continued till she managed to maintain the levels within normal reference range without any replacement. It was identified that she was taking Omeprazole for a long time and she recently had worsening of reflux symptoms two months ago and the dose was doubled. Therefore, omeprazole was immediately stopped and replaced with famotidine (H2 blocker), and then serial calcium and magnesium levels became stable. Calcium levels normalised to 2.35 mmol/l from 1.9 mmol/l after stopping omeprazole. Magnesium levels were increased to 0.74 mmol/l from 0.3 mmol/l. She was discharged on Vitamin D and calcium supplement. A repeat set of bloods was done one month later, and all electrolytes levels were normal without Omeprazole.
Conclusion and next steps
Omeprazole is quite effective in gastric acid suppression by inhibiting the parietal cell H+/K+ ATP pump. Intestinal magnesium absorption occurs via both passive and active transport mechanisms. Firstly, magnesium is passively absorbed through a paracellular pathway between the enterocytes of the intestine across a concentration gradient. Secondly, a transcellular active transport mechanism occur by means of a combined action of magnesium channels in the apical membrane of enterocytes on the luminal surface, particularly transient receptor potential melastin (TRPM) 6 and 7. It has been proposed that increased luminal pH in the intestine caused by proton pump inhibitors may alter the affinity of the TRPM6/7 channel for magnesium, resulting in reduced active transport of magnesium. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the drug. Serious adverse events of omeprazole include tetany, arrhythmias, and seizures. The field which needs further research and analysis is the one where hypocalcemia develops inspire of normal PTH hormone in patients with long term omeprazole use.

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NCC71

Polycystic ovarian syndrome-atypical presentation with severe hyperandrogenism

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Case History

27 year old female was referred to endocrine clinic with complaints of excess hirsutism over face, chin and neck accompanied with oligomenorrhea and acne for three years. The hirsutism was worsening gradually and she had to shave or wax her facial hair on daily basis. She was born at full term and had menarche at 12 to 13 years of age with regular periods. She had no symptoms of galactorrhea, headache, visual problems or recent weight gain. There was no family history of diabetes but her elder sister had mild PCOS. Examination revealed BMI of 24.4, marked hirsutism over face, chin and neck but no features of virilization, Cushing's syndrome or acromegaly.

Investigations

Serum testosterone 7.6 nmol/l. LH 9.1 IU/l, FSH 5.9 IU/l, Estradiol <92 pmol/l, SHBG 16 mmol/l. Serum Prolactin, 17-OH Progesterone, Androstenedione and DHAS levels normal. HbA1c 6.0%, TSH 0.82 mu/l, mildly deranged lipid profile with triglycerides 3.4 nmol/l. Electrolytes, renal, liver and bone biochemistry normal. Trans vaginal ultrasound revealed bilateral multiple small peripheral follicles, up to 20 seen, with a central echogenic stroma. right ovarian volume 14 ml and left ovarian volume 12 ml. MRI scan of abdomen and pelvis did not reveal any focal adrenal lesion or free fluid in abdomen. An ovarian suppression test using GnRH analogues was performed to establish ovarian origin of androgens but unfortunately proper protocol was not followed to look for suppression of androgens following GnRH. However, results were appropriate with adequate rise in estradiol levels with LH and FSH levels.

Treatment An Follow Up

A diagnosis of PCOS was made and she was started on metformin and COCP(Yasmin) which made her cycles regular but had little effect on hirsutism. She was also given a trial of topical eflornithine cream with little effect. Subsequently spironolactone was started as hirsutism was her main concern and she did not have any active plans to conceive in near future. She was advised to avoid pregnancy for six months after stopping spironolactone. On subsequent follow ups, her serum testosterone decreased to 1.1 nmol/l, SHBG increased to 12 mol/l and her shaving frequency reduced considerably.

Conclusion

In diagnosing PCOS, other causes of androgen excess, such as non classical CAH and Cushing's disease, should always be excluded. Severe hyperandrogenism of recent onset should always lead to exclusion of androgen secreting tumors of ovarian or adrenal origin.

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