

Hammersmith Abstracts

15th Hammersmith Multidisciplinary
Remote on zoom
Endocrine Symposium 2020



Hammersmith Hospital 15th Multidisciplinary Endocrine Symposium

Provisional programme Fri 4th Dec 2020

On zoom

- 2.00pm Reversible pan-hypopituitarism in a case of un-resected non-functioning pituitary adenoma **Dr Shoily Nath** (Ashford and St Peters) **(A001)**
- 2.12pm A rare case of cranial diabetes insipidus in a patient with orbital xanthogranulomatous disease
Hsiu Yap (Imperial College Healthcare NHS Trust) **(A007)**
- 2.24pm Idiopathic Diabetes Insipidus – a diagnosis of exclusion
G. Wordsworth (Bristol, UBHW) **(A013)**
- 2.36pm A rare case of hypercalcemia in pregnancy- a diagnostic conundrum.
Tasneem LADHA (Imperial College Healthcare NHS Trust) **(A004)**
- 2.48pm Dual pathology leading to hypercalcaemia: the issue with confirmation bias. **Htet Htet Aung and Nyan Lin**, (The Lister Hospital, Stevenage). **(A015).**
- 3.00pm A case of iatrogenic Cushing's disease and secondary adrenal insufficiency following a drug interaction between intra-articular triamcinolone injection and ritonavir. **Shaila Khan** (Imperial College Healthcare NHS Trust). **(A012).**
- 3.12pm A case of adrenal tuberculosis mimicking non-functioning adrenal incidentaloma. **Dhruti Hirani** (Imperial College Healthcare NHS Trust). **(A014).**
- 3.24pm A case of metastatic paraganglioma on a background of SDHB mutation.
Luke Boyle (Chelsea and Westminster Hospital). **(A006)**
- 3.36pm Is there a role for 18F-FDG PET/CT in the diagnosis of painless sub-acute thyroiditis? **Harriet Esdaile and Kavita Narula** (West Middlesex Hospital). **(A005)**

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A011	A case of autoimmune thyroid disease with Alemtuzumab therapy
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A013 and OC3	Idiopathic Diabetes Insipidus – a diagnosis of exclusion
A014 and OC7	A case of adrenal tuberculosis mimicking non-functioning adrenal incidentaloma
A015 and OC5	Dual pathology leading to hypercalcaemia: the issue with confirmation bias

A016	A Case of Funny Thyroid Function Tests
A017	Hypothyroidism causing Hypercholesterolemia
A018	Hypothyroidism causing prolonged QTc
A019	An interesting case of autoimmune hypopituitarism associated with myasthenia gravis
A020	Case study of aggressive MEN-1, complicated by non-adherence to routine follow-up

A001 and OC1

Reversible pan-hypopituitarism in a case of un-resected non-functioning pituitary adenoma

S Nath, G Das, Department of Endocrinology, Ashford and St Peters Hospital NHS Trust

Abstract: Glucocorticoid replacement therapy is the 1st line treatment in a case of Panhypopituitarism. Administering the right dose and reproducing the pulsatile release of cortisol is still a major challenge. Hyponatremia can occur with worsening hypocortisolemia, but the mechanism is likely multifactorial and also due to inhibition of renal free water clearance. We present a case with on and off subclinical symptoms of cortisol insufficiency for about 10 years before presenting to emergency department with hyponatremia.

Case history: This 56 year old man presented to the emergency department with worsening central abdominal pain, vomiting and loss of appetite for four days. He had a history of on and off abdominal pain and general malaise for about 10 years with no other past medical history. His only medication was Omeprazole which he took when needed. General physical examination revealed slight epigastric pain. His initial blood biochemistry revealed a sodium of 122mmol/L, potassium of 4.2 mmol/L, creatinine 86micromol/L and urea 4.0mmol/L. He was discharged home, but he represented to the emergency department with the same symptoms four days later and was given intravenous fluids. His repeat blood biochemistry revealed sodium of 114mmol/L, potassium of 4.6mmol/L, creatinine 70micromol/L, urea 4.4 mol/L and plasma osmolality-241mmol/kg. Abdominal x-ray was found to be normal. His urine test revealed osmolality of 746mmol/kg and urine sodium of 110mmol/L. On examination he appeared physically exhausted and dry. He was treated with intravenous fluids and his sodium dropped further to 109mmol/L over next 2 days. Further tests revealed his cortisol level was <30nmol/L, TSH 0.21mU/L. FT4 -8.6pmol/L. FT3 -3.0pmol/L, FSH <1IU/L, LH 0.6IU/L, testosterone <0.24nmol/L. Pituitary imaging revealed a pituitary macro adenoma with supra-sellar extension without touching the chiasm.

This patient was then started on hydrocortisone replacement which corrected his sodium to normal levels over the next few days. Interestingly all his gonadal and thyroid hormones recovered with adequate cortisol replacement. Clinically he improved, gained appetite and discharged from hospital.

This patient likely had a very gradual onset cortisol insufficiency due to enlarging non-functioning macro adenoma leading to general decline in health which improved with corticosteroid replacement. The likely explanation for his recovering pituitary-gonadal and pituitary- thyroid axis after hydrocortisone replacement is due to hypocortisolemia affecting the thyrotrophic and gonadotrophic cellular function rather than compression due to tumour. or pituitary stalk effect causing hypogonadism as commonly seen with enlarging pituitary tumours.

A002

MRKH syndrome and microprolactinoma co-presentation: an unusual cause of primary amenorrhoea

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Mayer-Rokitansky-Kustner-Hauser (MRKH) syndrome, otherwise known as Mullerian agenesis is a congenital disorder characterised by aplasia of the uterus and upper part of the vagina in females with otherwise normal secondary sexual characteristics and normal female karyotype. It is the most common cause of primary amenorrhoea, affecting 1 in 5000 live female births. There are two subtypes; type 1 is limited to utero-vaginal agenesis whereas type 2 is associated with additional extragenital anomalies, which most commonly include renal, skeletal, cardiac, digital malformations and hearing impairments. The most severe type of MRKH type 2 is Mullerian hypoplasia, Renal agenesis and Cervicothoracic somite dysplasia (MURCS) association.

The aetiology of this condition remains unknown but is currently considered to be sporadic with a multifactorial, polygenic inheritance pattern. As in-vitro fertilisation using surrogacy and uterine transplantation become increasingly available, it is hoped that more affected women will be able to have their own biological children and that further genetic linkage may subsequently be revealed.

We present the case of a 17 year old female referred to endocrinology by GP (via gynaecology team) for mild hyperprolactinemia, primary amenorrhoea and pre-pubertal uterus on pelvic US.

Her past medical history was unremarkable; she was not sport enthusiast and was on no regular medications. She had a normal BMI and age appropriate normal secondary sexual characteristics. Her pituitary profile in August 2019 was as follows; TSH 2.3, FSH 6.2, LH 5.8, prolactin 647 (102-496), testosterone 1.5, SHBG 55. In February 2020; FSH 6.2, LH 5.1, prolactin 1048 (macroprolactin negative), Oestradiol 103pmol/l. Genetics showed normal female karyotype 46XX. US pelvis demonstrated a pre-pubertal uterus and repeat US pelvis after 6 months of oestrogen therapy showed no meaningful changes in pelvic organs. Pelvic MRI showed features suggestive of MRKH syndrome: agenesis of the uterus and upper two thirds of vagina, with minimal lower vaginal vault and normal kidneys. Left ureter was dilated and there was pseudo-arthrosis at L5/S1 level. MRI pituitary showed incidental curvilinear lipoma of corpus callosum with no evidence of hypoplasia. The pituitary gland showed asymmetry, with more tissue on the left side. X-rays confirmed adult bone age. Diagnosis of MRKH syndrome in association with pituitary microprolactinoma is secured. Literature search showed two previous case reports of this unusual co-presentation. The aetiology of this concurrence, whether it is a mere co-incidence or if there is a genetic linkage, remains elusive. Further research is needed.

Further plans for this patient's follow up include: 1) ECHO and cardiac MR, 2) hearing test, 3) referral to MRKH MDT clinic for counselling and attend forum meeting, 3) gynae to discuss optimization of existing vaginal structure and family planning options, 4) treatment for hyperprolactinemia, 5) urologist review and 7) whole spine MRI and 8) DEXA.

A003

Hypopituitarism due to Chondrosarcoma: 8-year journey

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Introduction: Hypopituitarism is a chronic disease state that is caused by several aetiologies one of which is tumour compression of the pituitary gland. Hypopituitarism has a varied clinical manifestation and is often of gradual onset. Depending on the severity of hormone effect it can be associated with increased mortality and morbidity.

Chondrosarcomas are malignant mesenchymal tumours made up of cartilage producing cells. They are the second leading cause of bone malignancies and present with challenges in both diagnosis and therapy. Intracranial arising chondrosarcoma is rare and presents diagnostic dilemma as it may mimic radiological features of common lesions in this region such as non-functioning pituitary tumour, chordoma, craniopharyngioma, meningioma, or paraganglioma.

Case review

56-year-old man presented with episodes of retro-orbital headaches and blurred vision. Clinical examination revealed diplopia on right lateral gaze and pronator drift on the left side. Subsequent CT and MRI scans showed a right petrous apex lesion extending through the skull base with an approximate size of 3x4cm, with a large medial temporal component and an extension into right jugular foramina. The lesion encases the carotid artery on the right and is lying partly within the cavernous sinus causing right sided 6th nerve palsy and abuts the middle ear structures which caused the patient to have hearing impairment. The lesion in the right jugular foramina extending into the middle cranial fossa and Sella. The patient blood results revealed evidence of hypopituitarism: Cortisol was 38, FT4 6.4, FT3 3.4, TSH 1.85, testosterone less than 0.1, prolactin 1451, IGF1 124, and PSA less than 0.1. His current medications are Hydrocortisone 10mg BD, Levothyroxine 50mcg OD, Testosterone (tostran) 2 squirts and he has had proton beam radiotherapy for the lesion.

Discussion/conclusion: Chondrosarcoma is often a diagnostic challenge. As a result of its malignant nature, it can spread and cause new manifestations. Sellar chondrosarcoma is a rare manifestation of this malignancy that can present similarly to non-functioning pituitary tumour. In the present case the patient had chondrosarcoma that spread from right petrous apex to the Sella. Once it reached the Sella the patient developed severe manifestations of hypopituitarism which presented with abnormal thyroid function, low testosterone, and ACTH which in turn caused cortisol dysfunction

A004 and OC4

A rare case of hypercalcemia in pregnancy- a diagnostic conundrum

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Abstract: Hypercalcaemia in pregnancy is a rare but important phenomenon, given the potential associated risks to mother and baby. These include hypertension, pancreatitis, nephrolithiasis and renal failure in the mother and intrauterine growth restriction of the foetus, neonatal hypoparathyroidism/hypocalcaemia together with stillbirth (1).

We present the case of a 26-year-old female with a background of PTH-independent hypercalcaemia of unknown aetiology. This was initially detected at the age of 6 months when she was investigated for frontal bossing in Poland. Relevant family history includes that of her two siblings who have chronic kidney disease with renal cysts.

Following confirmation of a pregnancy, her biochemistry was repeated, and her calcium was incidentally found to measure 3.55mmol/L (reference range 2.20- 2.60mmol/L, pre-pregnancy levels in the community 2.62mmol/-2.65mmol/L, PTH <0.2pmol/L). The patient was initially treated with intravenous fluids, encouraged to establish a low calcium diet and maintain hydration. In view of a creatinine of 122umol/L, renal obstetric input was sought, and an ultrasound demonstrated evidence of medullary nephrocalcinosis. Further investigations demonstrated the following: 25-OH Vitamin D 250 nmol/L, 1,25-OH Vitamin D 267pmol/L. PTH-Related Peptide and Fibroblast Growth Factor 23 are pending.

Subsequent targeted genetic testing demonstrated a compound heterozygous mutation in CYP24A1, confirming the diagnosis of idiopathic infantile hypercalcaemia (2).

This case is consistent with infantile idiopathic hypercalcaemia, a cause of PTH-independent hypercalcaemia. Hypercalcaemia in this individual was exacerbated by pregnancy-induced physiological changes, including increased vitamin D driven calcium absorption in the gut and 1-alpha hydroxylase expression by the placenta (1). With her diagnosis, maternal calcium of 3.55mmol/L and the possibility of fetal/neonatal hypoparathyroidism, she has been commenced on subcutaneous calcitonin with excellent response. She will require close monitoring and regular growth scans throughout pregnancy and the postpartum period.

References:

1. Arnold, N. et al. (2019) 'Intractable hypercalcaemia during pregnancy and the postpartum secondary to pathogenic variants in CYP24A1', *Endocrinology, Diabetes & Metabolism Case Reports*, 2019. doi: 10.1530/EDM-19-0114.

2. Schlingmann, K. P. et al. (2011) '*Mutations in CYP24A1 and Idiopathic Infantile Hypercalcemia*', *New England Journal of Medicine*, 365(5), pp. 410–421. doi: 10.1056/NEJMoa1103864

A005 and OC9

Is there a role for 18F-FDG PET/CT in the diagnosis of painless sub-acute thyroiditis?

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Abstract: Whilst focal and diffuse FDG uptake in the thyroid gland is one of the incidental findings encountered during the routine clinical use of 18F-FDG PET/CT, there are few cases where 18F-FDG PET/CT scans have been performed on patients with subacute thyroiditis (SAT).

We present a lady treated for SAT who had incidentally had a surveillance 18F-FDG PET/CT for breast cancer just before the onset of her symptoms.

A 55 year old lady presented to the emergency department with a 5 week history of palpitations, fever and anxiety after finishing a two week course of antibiotics. Her Covid19 screen was negative and she denied any neck swelling or pain. No infective cause was identified. She was taking Exemestane and Zometa for her HER2 receptor positive breast cancer with metastases in her spine. She had not received immunotherapy in the past. Her routine surveillance 18F-FDG PET/CT 6 weeks previously described bilateral focal thyroid FDG uptake, and the appearances of an ultrasound organised in primary care a week previous to the presentation described diffuse changes in the thyroid in keeping with a likely post viral granulomatous thyroiditis. There were no visible nodules or any suspicious radiological features on imaging. She was febrile (39.1 degrees centigrade) and tachycardic on admission with an elevated free T4 46.8 p mol/l, free T3 11.6 p mol/L and a suppressed TSH < 0.01 m IU/L. Her CRP and WCC count were both elevated and her TSH receptor antibodies were negative. She was initiated on Prednisolone 20 mg orally daily, in addition to Propranolol for SAT. Her symptoms resolved within 48 hours and she was discharged. After two weeks her T4 had improved to 18.7 p mol/L and free T3 to 5.6 pmol/L. Her oral steroids were subsequently weaned off.

Painful SAT associated with De Quervain or granulomatous thyroiditis is normally characterised with a painful swelling in the thyroid and resolves spontaneously. Painless SAT is less frequent and is mainly associated with post-partum, Hashimoto's, or drug associated thyroiditis. 18F-FDG PET/CT has an established role in oncology imaging but may be useful to ascertain inflammatory activity in painless SAT. In this latter group of patients, case reports have observed that appearances are generally of diffuse, occasional focal, asymmetrical uptake in the thyroid on 18F-FDG PET/CT, even in patients who have concurrently undergone a Tc-99m pertechnetate scan showing no uptake. Our case illustrates utilization of 18F-FDG PET/CT for differentiating between different forms of painless SAT associated with thyrotoxicosis, which can be difficult to establish with standard diagnostic radiological procedures

A006 and OC8

A case of metastatic paraganglioma on a background of SDHB mutation

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Abstract: We present the case of an SDHB mutation carrier with metastatic paraganglioma, which exemplifies the importance of multidisciplinary working when faced with diagnostic uncertainty.

This 55 year old lady (with a PMH of HTN with white coat effect, T2DM & dyslipidaemia) underwent surgical resection of a retroperitoneal functional paraganglioma in September 2010. Post-op urinary catecholamines and fasting gut hormone profile were normal.

In 2014 urinary normetadrenaline was marginally elevated (2.34 $\mu\text{mol}/24\text{h}$), raising the suspicion of recurrence or a second paraganglioma. Neither MIBG nor MRI were suggestive of recurrence, although there was signal change adjacent to the right ovary – subsequent pelvic US showed normal ovaries but one 25x24x21mm focal posterior fundal subserosal fibroid. HTN continued to be managed by standard approaches. By December 2016 normetadrenaline was 3.79 $\mu\text{mol}/24\text{h}$.

She experienced back pain while gardening, and MRI spine in February 2017 demonstrated some oedema at L5, thought secondary to disc degeneration. Given SDHB mutation status, Ga-68 DOTATATE PET/CT was arranged in July 2017. There was DOTATATE uptake at L5 and in the right humerus. Plain radiographs of the humerus were normal, and our expert musculoskeletal radiologist felt appearances on subsequent serial MRI scanning of her spine were not typical of metastasis.

During 2018 normetadrenaline climbed to 5.9 $\mu\text{mol}/24\text{h}$ and she was discussed in both the Royal Marsden Neuroendocrinology MDT and Spinal MDT at St George's. Repeat Ga-68 DOTATATE PET/CT showed stable L5 disease, but a new aortocaval node. The L5 soft mass was biopsied in June 2018 and confirmed a metastatic NET. By then an MRI humerus was also suspicious for a mass in the humeral diaphysis, but she was asymptomatic with Mirels' score <9 when reviewed by T&O.

In February 2019, the Spine Clinic noted that the L5 tumour had grown from 21 to 29mm, was intruding into the spinal canal, and may have been largely responsible for a plasma normetanephrine of 3792 pmol/L, consistent with urinary normetadrenaline levels at 2-3 times the upper limit of normal. Her L5 disease was resected, and metastatic paraganglioma with low proliferation index confirmed. Her BP normalised to the extent that antihypertensive therapy could be withdrawn. With no evidence of

residual disease in L5, after discussion at the CyberKnife MDT, stereotactic body radiotherapy was commenced in July 2019.

In April 2020 a DOTATATE PET scan showed mild progression at the known sites of disease, and she was commenced on Lanreotide, with a dose reduction to 60mg monthly due to side effects. A repeat DOTATATE PET in November 2020 has shown minor progression at T6 with the other sites stable.

This case illustrates a number of challenges in long term follow up of patients with paraganglioma, including interpreting the significance of imaging findings and distinguishing metastatic disease from other non-paraganglioma pathology. We will also discuss the available therapeutic options.

A007 and OC2

A rare case of cranial diabetes insipidus in a patient with orbital xanthogranulomatous disease

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Abstract:

Case Study: This 46 year old gentleman came to the attention of the endocrine team when his astute GP asked for advice on further investigations into his symptoms of polydipsia and polyuria. The patient had had these symptoms for 3 months and had not presented earlier as the country was in the middle of COVID lockdown, and the patient was shielding. He complained of feeling thirsty all the time and was drinking in excess of 22 pints of fluid daily. He was frequently passing large volumes of urine and estimated passing at least 3 to 4 litres of urine daily.

His past medical history was relevant for peri-orbital xanthogranulomatous disease, which was first diagnosed in 2007 and previously debulked with bilateral orbital decompression in 2011. He developed proptosis of his right eye in 2011 and had initially failed to respond to Methotrexate, 6-Mercaptopurine or Ciclosporin. He was then started on Tacrolimus with good response, however his disease relapsed when weaning of Tacrolimus was attempted. He had further extension of his periorbital disease (predominantly the left eye), enlargement of his left submandibular gland and left nasal septal deviation in 2017. He was subsequently listed for a left lid, lacrimal duct and orbital decompression, as well as excision of his left submandibular gland lymph node in 2018/2019. Interestingly, histology from the left lacrimal gland showed a lymphocytic infiltrate with no particular features of granulomatous change or IgG4 disease, but histology from the left submandibular gland showed chronic sclerosing sialadenitis, with total IgG4-positive plasma cells of 82/hpf and an IgG4:IgG ratio of 200%, consistent with IgG4 related disease. Apart from Tacrolimus, he was also taking a steroid inhaler for asthma and a steroid nasal spray. He had a family history of diabetes mellitus; his father had type 2 diabetes and was previously on dialysis (now deceased), and his sibling had type 1 diabetes.

Investigations: Initial investigations excluded diabetes mellitus as a cause for his symptoms, HbA1c was 40 mmol/mol and fasting plasma glucose was 6.3 mmol/L. His sodium level was 139 mmol/L, creatinine 83 μ mol/L and eGFR >90 ml/min/1.73m². His pituitary profile showed normal thyroid function, prolactin, growth hormone and IGF-1 levels. Short SynACTH test had a normal response, with baseline cortisol of 301 nmol/L, rising to 631 nmol/L at 30 minutes and a normal ACTH level of 19.8 ng/L. However, he had secondary hypogonadism with a low testosterone level of 1.2 nmol/L (normal SHBG of 28.8 nmol/L), low normal FSH levels of 2.4 u/L and low LH levels of

1.3 u/L. He denied erectile dysfunction or other symptoms of hypogonadism. A water deprivation test was carried out and this confirmed cranial diabetes insipidus, with dehydration causing excessively concentrated plasma above 300 mOsmol/kg alongside inappropriately hypotonic urine, and DDAVP administration resulting in concentrated urine to above 150% of previous highest level. He was started on Desmopressin DDAVP and testosterone replacement.

He went on to have a pituitary MRI which was discussed at the Imperial Pituitary multidisciplinary team (MDT) meeting. It was felt that there was mainly inflammatory tissue with posterior stalk thickening, rather than a pituitary adenoma. There was also paranasal sinuses involvement but no dural thickening.

Discussion: The working diagnosis includes an inflammatory IgG4-mediated process infiltrating the pituitary gland, resulting in cranial diabetes insipidus and secondary hypogonadism. This patient's hypophysitis is likely to be related to his peri-orbital xanthogranulomatous disease, which is thought to be a rare non-Langerhans histiocytosis¹. Peri-orbital xanthogranulomatous disease has recently been found to be associated with systemic IgG4-related disease¹. The often chronic and relapsing nature of IgG4-related disease commonly requires immunosuppressive treatment with steroids and steroid-sparing agents such as Rituximab to maintain long-term remission^{2, 3}. We have organised a further MDT meeting between the endocrine, dermatology, vasculitis, radiology and histopathology specialties to discuss this gentleman's further management/treatment, especially since he has previously failed to respond to other immunosuppressants.

References:

1. Burris CKH, Rodriguez ME, Raven ML, Burkat CN, Albert DM. Adult-onset asthma and periocular xanthogranulomas associated with systemic IgG4-related disease. *Am J Ophthalmol Case Rep.* 2016; 1: 34-37.
2. Boharoon H, Tomlinson J, Limback-Stanic C, Gontsorova A, Martin N, Hatfield E, et al. A case series of patients with isolated IgG4-related hypophysitis treated with Rituximab. *J Endocr Soc.* 2020; 4(6): 1-9.
3. Smith C, Hameed S, Rose GE, Wernig F. A 61 year old man with pancreatitis, pituitary dysfunction, and painful exophthalmos. *BMJ.* 2019; 364: I93.

A008

Type B Severe Insulin Resistance Syndrome presenting to the Young Adult Diabetes Clinic and Rheumatology Team

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Abstract

Clinical Presentation: A 22 year old patient was diagnosed with diabetes mellitus after urinalysis detected glycosuria when attending a rheumatology clinic for possible SLE. Blood glucose 25 mmol/l, HbA1c 101 mmol/mol, blood ketones 2.5 mmol/l with no acidosis. She was started on subcutaneous insulin after education from diabetes nurse team and reviewed in diabetes clinic. Despite escalating insulin doses her ketosis settled only slowly over a number of weeks. Her blood glucose levels also remained high (range 8 mmol/l – ‘Hi’) and even worsened despite no apparent intercurrent infection nor use of corticosteroids. When she was using 160 units of insulin daily with ongoing poor diabetes control she was admitted for inpatient assessment.

Clinical Investigations: Clinical examination showed mild synovitis of small joints. BMI 24 kg/m². There was acanthosis nigricans of neck and axillae. There was no evidence for lipodystrophy nor hirsutism. There were no clinical features of Cushing’s syndrome nor acromegaly.

Diabetes auto-antibodies were negative (anti-GAD, islet cell antibodies, anti-Zinc finger domain antibodies). Fasting insulin c-peptide was raised at 12.2 mcg/l (Ref 1.1-4.4). Anti-nuclear and Ro antibodies were positive. Complement C3 was low 0.6 (Ref 0.9-1.8) and C4 borderline low 0.11 (Ref 0.1-0.4).

During an intravenous insulin infusion 8-10 units insulin per hour were required to lower blood glucose to less than 15 mmol/l. The patient was started on high strength subcutaneous insulins with Toujeo (U300 insulin glargine) and Humalog 200 (U200 insulin lispro) (and metformin) with a total daily insulin dose of 220 units.

A blood sample was sent to the UK National Severe Insulin Resistance service at Cambridge which returned positive for anti-insulin receptor antibodies.

Clinical Progress: The patient was seen at the National Severe Insulin Resistance service and treated with immunosuppression therapy including prednisolone and rituximab. One year after starting this therapy she has stopped all treatment for diabetes and her HbA1c 45 mmol/mol.

Conclusions: Type B severe insulin resistance is a rare autoimmune disorder most frequently associated with SLE. Poor diabetes control is common in the young adult clinic, but clinicians should remain vigilant to physiological rather than behavioural causes for this.

A009

Acute Respiratory Distress Syndrome in a patient with new onset Addison's Disease

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Abstract: Primary adrenal insufficiency, Addison's disease, is a rare endocrine disorder with a UK prevalence of 1 in 10,000. Early diagnosis is often difficult, and the presentation is commonly only recognised after a life-threatening adrenal crisis. Fortunately, with appropriate early treatment further complications are uncommon in the acute setting.

We present a case of a 19 year old man who presented to ED with lethargy, dyspnoea on exertion and a one month history of hyperpigmentation. He had a history of nocturnal enuresis for which he was taking desmopressin. On examination he had tanned skin, buccal pigmentation and borderline hypotension. Admission bloods revealed hyponatraemia and hyperkalaemia. After establishing a working diagnosis of first presentation with Addison's disease, treatment was started including fluid resuscitation and IV hydrocortisone (100mg QDS). The diagnosis of primary adrenal insufficiency was supported by inadequate response on short synacthen test and positive adrenal cortex antibodies.

Two days after admission he developed sudden onset respiratory distress and hypoxia. Bi-basal crepitations were present. CTPA reported bilateral predominantly central ground glass and confluent opacities with no evidence of pulmonary embolus. Of note there was CT evidence of right heart strain. An echocardiogram showed good systolic function with estimated ejection fraction 60-65%. Pulmonary artery pressures were elevated. COVID-19 throat swab was negative. Troponin was mildly elevated though ECG showed sinus tachycardia with no ischaemic changes. He rapidly improved with CPAP for several days.

Further endocrine investigations confirmed the diagnosis of primarily adrenal failure (ACTH levels 688, Aldosterone levels <60, grossly atrophic adrenals on CT). He was successfully converted to oral therapy prior to discharge.

The reason he developed ARDS following treatment of adrenal insufficiency remains unknown. A literature review conducted to identify links between cases of Addison's disease and ARDS reports few cases. One (1) presented a very similar, though more severe, history and course of illness. For our patient, previous desmopressin use may be a contributor, exacerbating the rapid changes in fluid balance as steroid deficiency is corrected. This case highlights a rare, though potentially life-threatening, complication of acute adrenal crisis and the necessity for increased awareness of such cases among treating physicians.

1. Wolff, B., Machill, K., Schulzki, I., Schumacher, D. and Werner, D., 2007. Acute reversible cardiomyopathy with cardiogenic shock in a patient with Addisonian crisis: A case report. *International Journal of Cardiology*, 116(2), pp.e71-e73.

A010

A case of metastatic neuroendocrine tumour with co-existing TSH-secreting pituitary tumour

D Hirani, S Khan, S Jarvis, M Moriarty, T Ladha, Z Halil, A Mahmood, V Bravis, F Wernig. Affiliations: St Mary's Hospital Endocrinology Department, Imperial Healthcare NHS Trust, London

Abstract: Neuroendocrine tumours (NET) account for <1% of all malignancies, with common primary sites being the gastrointestinal tract and the lung. Presentation with metastatic disease is not uncommon but well-differentiated tumours are associated with a good prognosis (1).

We present the case of a 61-year-old man, who was referred with abnormal thyroid function tests (TSH 1.51miu/L, free T4 23.3pmol/L, T3 7.2pmol/L). On history taking, he reported a 1.5-year history of persistent diarrhoea, facial flushing and self-resolving palpitations associated with alcohol consumption only. He had had a normal colonoscopy. He denied any weight loss and was clinically euthyroid.

Tests showed raised serum chromogranin A (104pmol/L), urinary 5-HIAA (144.3µmol/day), raised Free T3 (7.9pmol/L) and inappropriately non-suppressed TSH (1.80 miu/L). MRI pituitary showed 1.6cm pituitary macroadenoma. TRH stimulation results are shown in *Table 1* below, with an alpha subunit pituitary polypeptide level of 0.14UI/L. DOTATATE PET CT showed metastatic neuroendocrine disease involving septal myocardium, peritoneum, liver and bone, with likely primary in small bowel. Liver biopsy confirmed presence of NET with a Ki-67 index of 1% (Grade 1). He was started on Lanreotide and Denosumab injections with good effect. He has also been referred for neurosurgical review towards likely surgery and is awaiting cardiology and genetics follow up.

Time	Serum free T4 (pmol/L)	Serum TSH level (miu/L)
0min	16.4	0.10
30min	16.9	0.10
60min	17.1	0.10

Table 1: Thyroid-releasing hormone stimulation test results

Conclusion: This patient presented following incongruent thyroid function tests that were subtle and certainly raised the differentials of thyroid hormone resistance and TSH secreting tumour. His carcinoid was diagnosed following the history he provided, which was unusual. He indeed had an unusual combination of metastatic neuroendocrine disease, and TSH secreting pituitary macroadenoma. Further genetic testing will help determine if these two findings are connected. This case highlights the importance of accurate history taking, repeating endocrine tests appropriately and the accurate interpretation of them in rational sequence, as well as the need for multi-disciplinary input in the diagnostic and management process.

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A011

A case of autoimmune thyroid disease with Alemtuzumab therapy

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Abstract: We present the case of a 42-year-old female with a history of relapsing-remitting multiple sclerosis. She received a course of Natalizumab between 2013 and 2015, followed by Alemtuzumab in 2015 and 2016. Her monitoring blood tests with the multiple sclerosis clinical nurse showed TSH <0.01 mU/L, T3 5.5 pmol/L, T4 18.3 pmol/L, and negative thyroid peroxidase antibody. She had no clinical features of hyperthyroidism and reported no visual symptoms. Of note, she had a family history of type 1 diabetes and had been previously investigated under the endocrine team for reactive hypoglycaemia. Her symptoms were eventually successfully controlled with dietary interventions.

She was initially started on 5mg Carbimazole for subclinical thyrotoxicosis, which was gradually up-titrated to 30mg Carbimazole within 12 months, according to serial thyroid function tests. Although initially reluctant, she agreed to subsequently change to a “block-and-replace” regimen after further consultation to account for fluctuations in thyroid function tests

Conclusion: Alemtuzumab, a monoclonal antibody binding the CD52 antigen, is a treatment for active multiple sclerosis. However, autoimmunity is an adverse side effect, with thyroid autoimmune disease affecting up to 33% of patients established on the therapy[1]. Autoimmune thyroid disease following a course of Alemtuzumab is a common adverse side effect. Regular thyroid function monitoring is required, with subsequent tailored treatment according to thyroid status.

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A012 and OC6

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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Abstract: Ritonavir is an HIV protease inhibitor 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 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 secondary adrenal insufficiency (SAI) which occurs due to ACTH suppression by excess non-metabolised exogenous steroids.

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 3 and 6 months prior. She complained of generalised weakness and lethargy. She was diagnosed with HIV infection in 2001 and was taking darunavir, dolutegravir and ritonavir. She had a past medical history of asthma and fibromyalgia. Her asthma was treated with inhaled beclomethasone and formoterol twice daily. She had been treated with inhaled fluticasone prior to this and had been taking daily inhaled steroids for over five years. On examination in the clinic she was noted to be Cushingoid in appearance. 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. A short synacthen test showed an undetectable cortisol level at baseline (RR 160-550nmol/L), 167nmol/L 30mins after administering tetracosactide (RR >450nmol/L) and 244nmol/L after 60minutes (RR >600nmol/L). She was therefore diagnosed with iatrogenic Cushing's disease and secondary adrenal insufficiency. She commenced 4mg prednisolone once daily. Ritonavir was stopped immediately and darunavir was switched to triumeq, which is associated with less potent CYP450 inhibition, aiming to facilitate hepatic clearance of triamcinolone.

Patients on CYP3A4 inhibitors 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 symptomatic patients. This is particularly crucial for those who have had depot injections, where the exogenous steroid cannot be withdrawn.

A013 and OC3

Idiopathic Diabetes Insipidus – a diagnosis of exclusion

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Abstract: This 34 year old previously fit and well woman underwent a biopsy and curettage of a cystic femoral neck lesion in October 2017.

She then presented to her GP in March 2019 with polyuria and polydipsia. She was referred to the local Endocrine team and a formal water deprivation test confirmed cranial diabetes insipidus. She was commenced on regular desmopressin with the remainder of her pituitary profile intact and with a normal MRI of her pituitary gland. With no knowledge of the previous bone histology, the Endocrine team felt the aetiology of the DI was most likely to be idiopathic and subsequent annual follow-up was unremarkable.

She became pregnant with her second child in February 2020 and was seen in the Joint Antenatal Endocrine Clinic. On close review of the history, her hip problem was felt to be unusual in such a young woman, so we sought the histology from her previous trust. This revealed features in keeping with Langerhan's cell histiocytosis (LCH) and hence the unifying diagnosis. She was referred to the local specialist Haematology centre who has discussed her regularly at the National LCH Panel.

She is now in her second trimester of pregnancy and has required gradually increasing doses of desmopressin. Regular biochemical assessment has revealed no evidence of progressive pituitary disease and her pregnancy is otherwise uncomplicated.

There is little evidence for how best to manage LCH patients in pregnancy, particularly in those with multi-system involvement. The usual staging investigations and systemic treatments carry significant risks in pregnancy and have to be carefully balanced against the possibility of disease progression whilst waiting until the post-partum period. It is vital to involve multi-disciplinary colleagues from a range of specialties (Endocrinology, Haematology, Obstetrics, Radiology, Neurosurgery and Orthopaedics) in order that we ensure optimal care for each woman in these complex cases.

A014 and OC7

A case of adrenal tuberculosis mimicking non-functioning adrenal incidentaloma

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Abstract: A 77 year old gentleman was referred to the endocrinology team following the incidental finding of an adrenal nodule on computer tomography (CT) colonography. Following this, dedicated CT of the adrenal showed a 4cm nodule with an attenuation of 30 Hounsfield Units. Biochemical investigation found no evidence of adrenal insufficiency or functional hormone production. Subsequent imaging by magnetic resonance imaging (MRI) and further CT showed stable appearances in size of the lesion, however concern remained regarding the risk of malignancy. Fluorodeoxyglucose-positron emission tomography was then performed, and this found moderate to intense activity in the area. The patient underwent adrenalectomy.

Histopathology of the adrenal mass showed necrotising granulomatous inflammation, raising suspicion of adrenal tuberculosis (TB) and although acid-fast bacilli were not isolated on culture, TB ELISpot was positive. Differential diagnoses included sarcoid and granulomatosis with polyangiitis. The latter was considered unlikely given the clinical history and serum angiotensin-converting enzyme levels were not elevated. Multidisciplinary discussion decided against systemic anti-TB treatment because the patient had multiple co-morbidities and imaging studies did not show evidence of tuberculosis at other sites.

Less than 2% of adrenal incidentalomas are due to isolated adrenal TB¹. TB is the most common cause of primary adrenocortical insufficiency caused by infection². Adrenal tuberculosis is thought to rarely mimic non-functioning adrenal incidentaloma. Future development of imaging techniques and frequency of imaging will likely increase detection of non-functioning incidentalomas. This case suggests the importance of considering TB as a differential diagnosis whilst investigating non-functioning adrenal incidentalomas.

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A015 and OC5

Dual pathology leading to hypercalcaemia: the issue with confirmation bias

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Abstract: Mr AM, a 69 year old Caucasian gentleman, presented with chronic fatigue, right knee pain and thigh pain. He was found to have hypercalcaemia (3.55 mmol/L) and was admitted in September 2020. He had a past medical history of hypertension and congenital bilateral retinal detachment causing total blindness in his right eye and 50 % vision loss in his left eye. He had a significant family history of acromegaly in his brother, treated with trans-sphenoidal surgery, and metastatic breast cancer in his mother. Initial investigations included PTH, elevated at 16.22 pmol/L, a myeloma screen which was negative, vitamin D, normal at 96.2 nmol/L and normal TFT. He was given a provisional diagnosis of primary hyperparathyroidism, treated with intravenous fluids, and discharged after two days with a calcium level 2.79 mmol/L. There was a plan for further biochemical testing, parathyroid imaging and outpatient endocrine follow up.

10 days later, Mr AM represented with backpain. He had noticed the development of a painless, hard, lump in the right lower back. The mass was visible on his chest x-ray, and the radiologist advised further characterisation by ultrasound. On this occasion, his calcium was elevated at 3.91 mmol/L. He was admitted to the endocrine ward and had further investigations. A repeat myeloma screen was negative, the urine calcium creatinine clearance ratio was 0.0348, serum ACE was < 10 U/L. Imaging was requested including an ultrasound and sestamibi parathyroid, USS renal and a DEXA. He had the sestamibi during the admission which showed a focus of retained tracer on the left upper lobe consistent with a parathyroid adenoma. He was treated with intravenous fluids and cinacalcet and discharged home with a plan for the USS chest and parathyroid as an outpatient and endocrine follow up.

He was readmitted after a further 10 days with nausea and vomiting and hypercalcaemia. On this occasion, a history of significant weight loss, 9 kg within 6-months, was noted by the admitting physician and a CT chest, abdomen and pelvis was organised. This revealed multiple necrotic liver lesions, multiple lytic axial lesions, deposit in T9 vertebra, destruction of L2 vertebra and right femoral lesser trochanteric destruction. A tissue biopsy noted neuroendocrine malignancy morphology with the presence of high positivity of synaptophysin and CD 56. Chromogranin, CK20, CD 45 and melanin A were negative. Further questioning revealed that he sometimes experienced episodes of palpitation, sweating and flushing. He also had an episode of loss of consciousness three years previously. He denied headache and diarrhoea. Urine metanephrines were sent (result awaited). Genetic testing is also awaited. He was referred to the Royal Free Hospital NET department and the MDT outcome was for platinum-based chemotherapy.

Discussion: This case report highlights the issues with confirmation bias. The diagnosis of primary hyperparathyroidism was presumed on the first visit and all subsequent investigations were in line with this. As a result, the significant history of weight loss, palpitation, flushing was not noted or investigated thoroughly. The hypercalcaemia in this case is possibly due to dual pathology, primary hyperparathyroidism and the clinically dominant NET with bone metastases.

A016

A Case of Funny Thyroid Function Tests

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Abstract: The preferred treatment for hypothyroidism is oral levothyroxine (LT4) ingestion, in doses that ensure a sustained state of hormonal balance. Yet, despite physician's best effort at dose titration, up to 20-50% of patients fail to achieve optimal thyroid function test. There are various factors, which influence the absorption of LT4, including: eating habits, medications and different functional as well as organic pathologies of the gastro-intestinal tract. Impaired absorption of levothyroxine through the gastrointestinal tract is one of the major causes of not achieving adequate thyroid function control. Approximately 62–82% of levothyroxine is absorbed after oral administration. This absorption occurs within the first 3 h of ingestion and is localised mainly in the jejunum and ileum. T4 is absorbed mainly from the small intestine, which explains the higher dose requirements in malabsorption. T4 and T3 conjugates are excreted in bile and partially deconjugated in the intestine, with the release of small amounts of T4 and T3 for reabsorption. Interference with enterohepatic circulation of thyroid hormone leads to deranged thyroid hormone absorption. Gastrointestinal conditions such as bile acid malabsorption syndrome can play an integral role in reducing levothyroxine absorption. Hypothyroidism that persists despite escalation of levothyroxine dose should prompt investigation into underlying gastrointestinal malabsorption or medication interference.

We present the case of labile thyroid function tests secondary to bile acid malabsorption syndrome.

A 49 year old Caucasian woman was referred to the Endocrinology Team with 24 years history of primary hypothyroidism. Other co-morbidities included premature ovarian failure, depression, anxiety and recent changes in bowel habit. To optimise her TFTs, primary care physician have altered her Levothyroxine dose several times over the past few years. However patient was left with ongoing symptoms of hypothyroidism, mild-moderate diarrhoea, and multiple vitamin deficiencies. She reported full compliance, no dietary changes or overt interacting medications. Malabsorption syndrome was suspected and further investigations were arranged by the gastroenterology team, including faecal elastase, Hydrogen Breath Test for lactose intolerance, and Radionuclide SeHCAT bile study. Patient's SeHCAT bile study at 7-days showed an uptake of 2.7% which is significantly lower than the normal range of above 15%. Bile acid malabsorption syndrome was confirmed and this was thought to be the cause of her inadequate thyroid function control. Since starting a bile acid sequesterant (cholestyramine), her gastrointestinal signs and symptoms have settled and this was associated with a significant clinical and biochemical improvement in her thyroid function tests. Her recent TFTs have completely normalised.

Conclusion: These findings suggest that pre-existing malabsorption can reduce the bioavailability of levothyroxine. The need to use high LT4 doses in the substitutional treatment of hypothyroidism is often the very first sign of one of the pathologies that are connected with malabsorption syndrome, which might have been asymptomatic and undiagnosed previously.

A017

Hypothyroidism causing Hypercholesterolemia

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Introduction: Hypothyroidism is one of the main causes of high cholesterol and it should not be missed on initial assessment of hypercholesterolemia. The treatment for high cholesterol may be delayed to wait until the thyroid treatment is optimal, as this often brings the cholesterol levels down on its own and so removes the need for statins.

Abstract: We describe the case of a 60 year old female who was referred to the Endocrinology clinic with complaints of increasing tiredness, lethargy and weight gain (about three stones over one year) and hypercholesterolemia on blood tests. She was on Atorvastatin 20 mg for 8 months but had persistent hypercholesterolemia.

Investigations: Total cholesterol- 7.8 mmol/L, Triglyceride- 2.5 mmol/L, HDL-1.7 mmol/L, LDL-5.0 mmol/L and Total: HDL cholesterol ratio of 4.6. HbA1c was slightly high at 45 mmol/mol, primary hypothyroidism with TSH 18.3 mU/L and free T4 5.7 pmol/L.

Management: Levothyroxine was added to the treatment and follow up blood tests were requested. Following commencement of treatment with Levothyroxine, her cholesterol levels came within normal range as reflected on repeat blood tests.

Investigations:

Test Name	Results prior to Levothyroxine	Results after Levothyroxine
Total Cholesterol (mmol/L)	7.8	3.8
Triglyceride (mmol/L)	2.5	1.7
HDL (mmol/L)	1.7	1.1
LDL (mmol/L)	5.0	1.9
Total: HDL cholesterol ratio	4.6	3.5
TSH (mU/L)	18.3	2.1
Free T4 (pmol/L)	5.7	15.8

She has been having repeat blood tests for thyroid profile and cholesterol and with Levothyroxine 100mcg and Atorvastatin 20mg, her Cholesterol and Thyroid function tests both are in normal range.

Key learning:

Hypercholesterolemia in a patient can point towards underlying hypothyroidism as thyroid hormones, especially T3, play an essential role in helping the liver process and remove any excess cholesterol from the body. When the body does not produce enough thyroid hormones, the liver cannot process as much cholesterol as it should, hence resulting in hypercholesterolemia.

An underactive thyroid leads to a decrease in metabolism and cessation in the breakdown and removal of LDL. As a result, the bloodstream will have an increase in LDL and total cholesterol which can start to build up. Even mildly low thyroid hormone levels (subclinical hypothyroidism) can lead to high cholesterol.

The resulting hypercholesterolemia can then lead to more complications, like atherosclerosis, heart diseases or stroke, if not managed timely.

Because of the clear thyroid and cholesterol connection, it is very important to prevent complications like cardiovascular disease especially when suffering from hypothyroidism.

A018

Hypothyroidism causing prolonged QTc

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Introduction: Hypothyroidism can cause electrocardiographic abnormalities like- Bradycardia, ST segment depression, QT interval prolongation and flattening or inversion of T wave.

In an ECG, the QT duration represents the total time for de- and repolarization. Prolonged QT duration predisposes to life-threatening ventricular arrhythmias and therefore QT duration must always be assessed in an ECG.

Prolonged QT duration may either be congenital or acquired. One of the main causes of QT prolongation is Hypothyroidism.

Abstract: We describe the case of an 84 year lady who was admitted to the hospital after having a collapse outside the hospital. Blood tests done on presentation in A&E suggested severe Hypothyroidism (TSH > 100 and T4 <1 with TPO antibody level 174) and her ECG showed prolonged QTc. These findings were not known in the past.

All other blood tests, CT Head and Chest X ray showed normal findings.

Investigations: July 2020: TSH > 100, T4 <1 with TPO antibody level 174

Management: Whilst in the hospital she was started on Levothyroxine 100 mcg and Cardiology review was sought in view of the new ECG findings.

After review by the Cardiology team it was established that she needed no further treatment from the Cardiology point of view for the QTc prolongation as Hypothyroidism itself can prolong the QTc and once it is corrected, the QTc will get back to normal.

Her TFTs were monitored over time and the TSH levels are 1.6 after the commencement of treatment with Levothyroxine.

She was recently admitted to the hospital again with pneumonia and her ECG showed normal QTc.

Findings before and after starting treatment with Levothyroxine:

Test Name	Before Levothyroxine	After Levothyroxine
TSH	>100	1.6
QTc	Prolonged	Normal

Key learning: Normally an electrical impulse starts in the sinus node and then travels down to the ventricles, causing contraction of the ventricles' muscle cells. This contraction causes the blood to flow out of the heart and the heart muscle cells then relax. During this relaxation phase, the electrical charges of the cells need to recover. The recovery time is known as the QT interval.

The QT interval lasts just a fraction of a second but in people with prolonged QT interval, it lasts longer than it should, and this delay makes the heart more likely to develop arrhythmias.

QT duration is inversely related to heart rate; QT duration increases at low heart rate and vice versa. Therefore, one must adjust the QT duration for the heart rate, which yield corrected QT duration (QTc). Bazett's formula is used to calculate the corrected QT duration. The formula follows (all variables in seconds):

$$QTc = \frac{QT \text{ duration}}{\sqrt{RR \text{ interval}}}$$

ECG interpretation always includes assessment of the QT (QTc) duration. Increased QT interval dispersion (QTd) is a parameter shown to be associated with ventricular arrhythmias and death, so QT dispersion corrected for heart rate (QTc) is an important predictor of cardiac death.

In some cases, a prolonged QTc doesn't even need any extra treatment other than correction of hypothyroidism.

Hence it is very important to timely manage the patients with hypothyroidism as they may have prolonged QTc in ECG and if left untreated, these patients can have life threatening complications, like malignant ventricular arrhythmias and death.

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A019

An interesting case of autoimmune hypopituitarism associated with myasthenia

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A 46 year old man, previously well and healthy until he presented with vague symptoms of extreme fatigue, arm and leg weakness, loss of libido, anorexia, double vision and nocturia. He was initially referred to the neurologists owing to the limb weakness and diplopia. Few weeks later, he was referred to the endocrine team with fatigue and polyuria. Initial physical and biochemical assessment confirmed that he had pan-hypopituitarism (Glucocorticoid, Gonadotropins, Thyrotropin and ADH axes dysfunction) with no visual field deficits, headache, compressive symptoms, olfactory problems or a relevant family history. He presented in March during the lockdown, so he was admitted in a COVID19-free ward under endocrine-neurology co-management to expedite the investigations and start high dose prednisolone to control the myasthenic symptoms.

Hormonal workup: FBC and routine biochemistry are all normal, sodium is 141 mmol/L, 9 am cortisol 13 nmol/L, FSH and LH are 1.4 and 0.5 u/L, Testosterone <0.5 nmol/L, TSH 0.2 mu/L, Free T4 4.2 pmol/L, Prolactin <50 miu/L, Plasma Osm 3.5 mOs/KG, Urine Osm 183 mOs/KG (increased to 244 after an overnight fast), IGF-1 10.6 nmol/L and IGFBP-3 4.7 mg/dL.

Immunological workup: Myasthenia screen is positive for AChR-Abs. TRAB, TPO-Ab are both negative. Full autoimmune and paraneoplastic screen is negative. Anti-GAD Abs is strongly positive. Serum IgG4 levels are normal.

Imaging: MRI head revealed a normal study apart from loss of the normal posterior pituitary high signal. CT Chest, abdomen and pelvis showed no evidence of malignancy. There is some fat stranding in the anterior mediastinum that may suggest thymic hyperplasia but no solid evidence of thymoma. NCS/EMG: Findings suggest a neuro-muscular junction disorder and are consistent with myasthenia gravis. He responded very well and was discharged on high dose prednisolone 60 mg OD (to be stepped down gradually till 3-5 mg OD), thyroxine 75-100 mics on alternate days, testosterone isocaproate 250 mg IM monthly, desmopressin 100 mics PO ON and pyridostigmine 300 mg divided over 4 doses daily.

Conclusion: Hypopituitarism is most commonly caused by pituitary-hypothalamic tumors, cysts, vascular events, trauma, infiltrative disorders and radiation. Hypophysitis is a less commonly encountered cause of hypopituitarism. Hypophysitis is either caused by a systemic disease or certain drugs; immune checkpoint inhibitors. Primary hypophysitis can be histologically sub-classified to lymphocytic (autoimmune), granulomatous, xanthomatous, necrotizing and IgG4-related hypophysitis. Autoimmune hypophysitis is usually associated with other autoimmune diseases e.g. Hashimoto thyroiditis, pernicious anemia, myasthenia, rheumatoid arthritis, SLE, Sjogren syndrome, multiple sclerosis and type 1 DM. Hormonal deficiencies could be isolated or combined. **Question for the audience:** What is the role of anti-PIT-1 and other novel antibodies in the pathogenesis and diagnosis of lymphocytic (autoimmune hypophysitis)?

A020

Case study of aggressive MEN-1, complicated by non-adherence to routine follow-up

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Introduction: Multiple endocrine neoplasia type 1 is an autosomal dominant genetic condition in which there is a predisposition to developing tumours of the pituitary, pancreas and parathyroid glands. It is a rare condition that can be inherited or can arise de-novo from a spontaneous mutation. The prognosis for untreated MEN-1 is poor with a 50% mortality by age 50. Prompt diagnosis is crucial for identification of patients and affected relatives in order to monitor for early occurrence of complications which can be treated promptly.

Case report: A 30-year-old gentleman was referred to Hammersmith Hospital Endocrinology with bilateral adrenal nodules on CT KUB. He complained of an 18-month history of watery diarrhoea (up to five times a day) and intermittent nausea and vomiting without obvious relation to food.

He had MEN-1, diagnosed at a young age in Australia following episodes of hyperinsulinaemic hypoglycaemia. Genetic analysis showed this to be a sporadic mutation. He had known primary hyperparathyroidism, macroprolactinoma and multiple pancreatic tumours requiring 2 resections. His second operation was complicated by the development of a pancreatic pseudocyst that required drainage. He had intermittent hypoglycaemias thought secondary to residual insulinoma but this was managed with diet. He had been under regular follow up by his local endocrinology service but he discontinued his regular monitoring and did not seek medical attention from 2012 to 2019.

An MR pituitary showed a macroprolactinoma of 16mm, previously 7 x7mm in 2011. His prolactin was elevated at 78,316 with resultant suppression of LH & FSH and testosterone. An MR pancreas and abdomen showed multiple pancreatic neuro-endocrine tumours and bilateral adrenal lesions. His gut hormone profile showed elevated gastrin, pancreatic polypeptide and glucagon. Plasma metanephrines were normal. CT thorax showed a 12mm lesion in the right lung base. A Ga-68 DOTATATE scan showed a range of avidity in the pancreatic lesions and no evidence of increased uptake in the adrenal lesions, ruling out functional pheochromocytoma.

Due to his multi-site disease, he was managed by multiple specialties.

1. In regards to his macroprolactinoma and hyperprolactinaemia, he was started on cabergoline by his endocrinology team with resultant suppression of prolactin from 78,316 to 16,000.
2. He was referred to the respiratory and cardiothoracic team for assessment and management of the right lower lobe lesion. He underwent a VATS guided wedge resection of the lesion which confirmed a neuroendocrine tumour but it was not possible to distinguish between a primary bronchial NET or a metastasis.

3. He was referred to hepatobiliary surgery for total pancreatectomy, right adrenalectomy and splenectomy.

Unfortunately, following hepatobiliary surgery, he died postoperatively from pulmonary embolism.

Discussion: This case shows the importance of regular monitoring of patients with diagnosed MEN-1. These neoplasms are unpredictable in their frequency for occurrence and their malignant potential. Patients diagnosed at a young age may struggle with their diagnosis and the significant medical treatment and follow-up required and so may choose to disengage with healthcare until disease becomes complex and severe; at which point treatment options may either be limited or carry significant risk. If complications are identified at an earlier stage, the risk of morbidity and mortality can be significantly reduced.