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CONTENTS

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Programme Chair
Professor Mark Sherlock (*Dublin*)

Strands, Convenors and Facilitators

Disorders of the hypothalamus and pituitary	Convenor: Professor William Drake (*London*) Facilitator: Dr Niamh Martin (*London*) Facilitator: Dr John Ayuk (*Birmingham*)
Disorders of growth and development	Convenor: Dr Talat Mushtaq (*Leeds*) Facilitator: Dr Neil Wright (*Sheffield*)
Disorders of the thyroid gland	Convenor: Professor Simon Pearce (*Newcastle upon Tyne*) Facilitator: Dr Carla Moran (*Dublin*) Facilitator: Dr Salman Razvi (*Newcastle*)
Disorders of the adrenal gland	Convenor: Professor Michael O'Reilly (*Dublin*) Facilitator: Professor Mark Sherlock (*Dublin*)
Disorders of the gonads	Convenor: Dr Richard Quinton (*Newcastle*) Facilitator: Dr Channa Jayasena (*London*)
Disorders of the parathyroid glands, calcium metabolism and bone	Convenor: Dr Rachel Crowley (*Dublin*) Facilitator: Dr Jennifer Walsh (*Sheffield*) Facilitator: Dr Marian Schini (*Sheffield*)
Disorders of appetite and weight	Convenor: Professor Jeremy Tomlinson (*Oxford*) Facilitator: Professor Barbara McGowan (*London*) Facilitator: Dr Karl Neff (*Dublin*)
Miscellaneous endocrine and metabolic disorders	Convenor: Professor Maralyn Druce (*London*) Facilitator: Dr Miles Levy (*Leicester*) Facilitator: Professor Mark Sherlock (*Dublin*)

CONTENTS

Workshop A: Disorders of the hypothalamus and pituitary

WA1

Yet another case of Diabetes Insipidus!ÿ

Valmiki Salema & Anand Velusamy
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26year old Human rights activist being evaluated for left hip and thigh pain over the preceding 7 months, was referred to our services in November 2015 with headache, secondary amenorrhoea and raised prolactin levels. The headache which was mainly frontal started a few months ago and coincided with the amenorrhoea. She did not report visual disturbances or lactation. She also described the feeling of increased thirst and increased urinary frequency over this period. Apart from being investigated for the Left lower limb pain, she had no other past medical history. She attained menarche at the age of 12years. She had fairly regular periods initially, till she started taking oral contraceptives. The contraceptives were stopped due to the headache, but she remained amenorrhoeic. On Examination, her vitals were stable. She was not clinically dehydrated. She did not have any visual field defects. There was no milk expression or breast tenderness. Her blood tests at this clinic appointment showed raised prolactin levels (794mIU/l), secondary hypogonadism (Estradiol <92 pmol/l, FSH: 5.4 IU/l, LH: 5.4 IU/l), raised sodium levels (Na: 146 mmol/l) with correspondingly raised serum osmolality of 295mosm/l. The rest of her pituitary functions including IGF1, Thyroid and Cortisol were normal. Given her symptoms and test results, she went on to have a cannulated prolactin and a water deprivation test. These confirmed the raised prolactin and the presence of Cranial Diabetes Insipidus. Her MRI pituitary demonstrated the loss of the posterior pituitary bright spot, and thickening of the pituitary stalk. An inflammatory condition like Langerhans Histiocytosis was suggested. She was managed with Desmopressin and was referred for a full body FDG PET. This revealed the presence of heterogeneously increased tracer uptake around the proximal left femur, the bony cortex appearing thickened, irregular and moth-eaten. There was subtle tracer uptake in the pituitary. She then had a Left femoral tissue biopsy which confirmed the diagnosis of Langerhans cell Histiocytosis. She was reviewed in the haem-oncology MDM. Low dose femoral radiotherapy was suggested, which she underwent in February 2016. She then had pituitary radiotherapy in January 2017. Her femoral and pituitary lesions responded well to the Radiotherapy. She is currently being managed with hormonal replacement, Cabergoline and Desmopressin. She continues to be followed by our endocrine and haemato-oncology teams. Langerhans cell Histiocytosis is a rare infiltrative condition with unknown aetiology. Some genetic association with the BRAF and MAP2K genes have been identified.

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WA2

Lymphocytic hypophysitis in pregnancyÿ

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A 33-year-old woman who was 38-weeks pregnant was referred to our Endocrine team for bilateral temporal hemianopia. Her past medical history includes juvenile myoclonic epilepsy, for which she takes lamotrigine 275mg BD. She was reviewed by the Endocrinologist in 2018 for polyuria and nocturia which were attributed to the introduction of antiepileptics (normal pituitary biochemistry and MR pituitary). Her symptoms subsequently improved. Current symptoms started with acute retroorbital headache followed by blurring of her peripheral vision. Her headaches improved with hydration but her visual symptoms persisted. She did not reveal any symptoms related to anterior pituitary hormone abnormalities. She reports nocturia (3 times overnight) since the beginning of third trimester however, no polydipsia. Clinical examination showed bitemporal hemianopia. Fundoscopy showed normal optic discs. Pituitary blood tests:
ACTH: 9 ng/l, cortisol: 70 nmol/l (at 3.50 pm)
IGF-1: 162 microgram/l
fT4: 5.6 pmol/l, TSH: 1.19 mU/l
Prolactin: 1,754 mU/l
Urine osmolality: 365 mmol/kg, serum osmolality: 277 mmol/kg, serum sodium: 135 mmol/l.
An urgent MR brain and pituitary showed significant enlargement of her pituitary gland, and an upwards extension and compression of the optic chiasm. Neuro-ophthalmology assessment revealed bilateral enlarged blind spots with an early bitemporal hemianopia with marginally reduced visual acuity in the right eye and slight reduction in colour vision in both eyes. Retinal OCT findings were unremarkable. The working diagnosis was a non-functioning pituitary macro-adenoma or lymphocytic hypophysitis. We commenced dexamethasone 6mg OD and bromocriptine 2.5mg OD to reduce the size of the lesion. Levothyroxine 50 mg was also started. Repeat neuro-ophthalmology assessment after 48 hours revealed no improvement. As such, she had an emergency c-section (baby safely delivered) to enable us to plan for urgent surgical decompression. Bromocriptine was stopped at this point. A repeat MR pituitary with contrast post-delivery did not reveal any improvement and her visual symptoms persisted. Her dexamethasone was stopped after 5 days, and she was commenced on hydrocortisone (10 mg/5 mg/5 mg). She was referred for urgent transsphenoidal surgery. The appearances of the pituitary were in keeping with hypophysitis so only biopsy was taken. Her hydrocortisone was changed to prednisolone 30 mg. Her biopsy results confirmed lymphocytic hypophysitis. Since starting prednisolone, she has developed diabetes insipidus. Her vision improved, and her visual fields are normal to red pin confrontation. Central scotoma has also normalised. This case demonstrates the diagnostic challenges of lymphocytic hypophysitis in pregnancy and the importance of early diagnosis and management. Early initiation of high-dose steroids could result in favourable neuro-ophthalmic outcome.

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WA3

A case of pituitary apoplexy in a macroprolactinomaÿ

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A 32-year-old man was urgently referred to the endocrinology and neurosurgical teams by the neuro-ophthalmologist. He gave a 3 week history of sudden onset of left-sided visual impairment, with further visual deterioration a week previously. Urgent review in the eye clinic had revealed that the visual acuity in his left eye was reduced to finger counting only, with a pale left optic disc and a relative afferent pupillary defect on examination. Visual field testing demonstrated a temporal hemianopia in the right eye, with residual vision only in the upper nasal quadrant in the left eye. He reported a left-sided headache and some nausea at the time of onset of the acute visual loss. He had experienced intermittent headaches and reduced libido over the previous 1-2 years, with lethargy and occasional non-specific visual symptoms over previous months. An urgent MRI brain revealed a 38x30x27mm pituitary mass extending into the suprasellar cistern, with stretching of the optic chiasm and compression of the left side. There was evidence of haemorrhage within the lesion. His pituitary profile showed:- prolactin 16,341 (normal <324) mU/l, LH 3.1 IU/l, FSH 3.7 IU/l, testosterone 6.7 (normal 7.6-31) nmol/l, IGF-1 35 (normal 11-29) nmol/l, random cortisol 233 nmol/l, TSH 1.31mU/l, FT4 11 (normal 11-23) pmol/l. A diagnosis of pituitary apoplexy within a macroprolactinoma was made. The patient underwent urgent transsphenoidal surgery following pituitary MDT discussion in an attempt to improve/preserve his vision. He was also started on cabergoline. He reported a rapid and significant visual improvement post-operatively. He has been advised to continue on cabergoline.
Discussion

1. First line treatment for a macroprolactinoma is dopamine agonist therapy. In our case, surgery was offered in view of the acute visual deterioration, felt most likely be secondary to pituitary apoplexy causing a sudden enlargement of the pituitary lesion. The good post-operative visual outcome supported the presence of neuropraxia to his optic nerve from apoplexy.
2. This case highlighted the importance of detailed discussion of the benefits and risks of management options both within the pituitary MDT and with the patient. Urgent surgery was offered to improve/preserve vision, although this outcome could not be guaranteed. Hypopituitarism was a risk; he had no children, and future fertility could be affected.

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WA4

Non-functioning pituitary adenoma with high Ki 67 10%ÿ

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A 54 year old gentleman presented to the eye services with reduced vision on the right attributed to a cataract. Following cataract surgery there was no improvement and his vision declined further with reducing vision also on the left. He was reviewed in Neuro-ophthalmology clinic 29/10/21 and clinical suspicion of a pituitary lesion based on binasal retinal ganglion cell layer loss and bilateral optic atrophy prompted urgent imaging. His right eye visual acuity was

to hand movements only with a relative afferent pupil defect and left 6/9. Visual fields were grossly restricted on the right and showed a temporal hemianopia and reduced nasal sensitivity in the left. An urgent MRI orbit on 02/11/21 showed a homogeneous enhancing mass within the sella with bi-lobulated suprasellar extension elevating the optic chiasm and with marked compression of the right pre-chiasmatic optic nerve. He was referred urgently to neurosurgery and endocrinology. His co-morbidities include CKD3, obstructive sleep apnoea, hypertensive heart failure, bronchiectasis, and rheumatoid arthritis for which he was taking prednisolone 12.5 mg daily. Pre-surgical bloods on 08/11/21showed TSH 1. /l, T4 10.6 pmol/l, Testosterone 2.1 nmol/l, IGF-1 17.7 nmol/l and peak GH and cortisol levels during a GST of 0.2 mg/l and 248 nmol/l respectively. He underwent elective endoscopic endonasal trans-sphenoidal debulking of pituitary tumour on 16/11/21 with an uneventful post-operative course without evidence of hypo/hypernatraemia, polydipsia or polyuria. He continued a double dose of prednisolone for three days. Ophthalmology review showed mild improvement. Both eyes continued to show optic atrophy. Visual acuity improved to 6/36 and 6/9 in the right and left eye respectively. Post-operative bloods on 10/12/21 revealed a peak cortisol 248 nmol/l and peak growth hormone of 0.2 mg/l on repeat GST; Testosterone 3.8 nmol/l, LH 4.3 iu/l, FSH 0.2 iu/l, TSH 2.0 miu/l, Free T4 10.4 pmol/l, IGF1 17.7 (6.3-27.2) nmol/l. Histopathology confirmed a null cell pituitary adenoma positive for synaptophysin with a high proliferative index (Ki67 10%) and P53 in sparse cells suggesting possible future aggressive biological behaviour. Post surgically he developed hypopituitarism (GH, LH/FSH and ACTH deficiencies). He has been tired and lethargic. He is to be initiated on testosterone replacement and we will consider levothyroxine replacement in view of his low Free T4. He is currently on hydrocortisone 10 mg/5 mg/5 mg following reduction of his prednisolone dose to 5 mg OD.

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WA5

A case of recurring prolactinoma in pregnancyÿ

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Background
Prolactinomas are the most common functioning pituitary tumours, accounting for 40% of all pituitary adenomas. Prolactinomas may enlarge in pregnancy, the management of which may prove challenging.
Case Presentation
A 23 year old lady was referred to the endocrine clinic with secondary amenorrhoea and bifrontal headaches in 2012. Biochemical tests on referral revealed: FT4- 5.8 pmol/l, TSH-1.1 mU/l, Prolactin-4432 mIU/l, LH- 4.8 IU/l, FSH- 4.6IU/l. CT head was suggestive of pituitary macroadenoma, with MRI (July 2012) confirming a cystic lesion in the pituitary (22x15 mm) with suprasellar extension, abutting the optic chiasm. Visual field testing was normal. She was commenced on cabergoline 250 mg twice weekly, which resulted in resolution of the adenoma and normalisation of serum prolactin levels (May 2013). A month later, she became pregnant and cabergoline was stopped. However, she had recurrence of headaches and self-reported left sided hemianopia. MR pituitary was hence repeated. This showed recurrence of pituitary macroadenoma measuring 14x12x14 mm protruding into the right sphenoid sinus. Repeat visual field was normal. She was re-started on cabergoline 250 mg twice weekly at 14 weeks of gestation. At 22 weeks of gestation, repeat MR pituitary showed further increase in size of the adenoma (16x13x15 mm), now abutting the optic chiasm. The dose of cabergoline was hence increased and an urgent neurosurgery advice was sought. As per neurosurgical advice, monthly MR scans and visual field testing were performed and no further increase in the size of the adenoma was noted. Following a normal full term delivery in 2014, she was continued on cabergoline. Serum prolactin again normalised (210 mIU/l) with resolution of the adenoma (August 2015). In 2016, she became pregnant again. Patient discontinued cabergoline and had recurrence of the pituitary macroadenoma (14x16x19 mm). Cabergoline was hence restarted and she was closely monitored with monthly visual field tests and MR scans. There was further enlargement of the adenoma (18x15x25 mm), displacing the optic chiasm superiorly at 33 weeks gestation. This was managed with increased dose of cabergoline in view of normal visual field assessments. Following delivery, her MR pituitary again showed shrinkage of the prolactinoma. She remains on cabergoline and under regular endocrine follow up.
Discussion
Pregnancy can cause recurrence of prolactinomas. Enlarging symptomatic prolactinomas are managed with dopamine agonists. Trans-sphenoidal surgery may be indicated in sight threatening macroprolactinomas, even in pregnancy.

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WA6

Pituitary function tests – Partial empty sella syndrome with panhypopituitarismÿ

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Case history
66 year old male referred with a thyrotoxic biochemistry. History was in favour of a subacute thyroiditis with a painful neck and short-term elevation of fT3 and fT4 which have improved to lower limits of normal without any treatment at the time of first clinic visit. He was monitored for thyroiditis and the biochemistry gradually changed and patient started to complain of tiredness.
Investigations and treatment

	Sep 2019	Oct 2019	Nov 2019	Jan 2020	Nov 2020	June 2021
TSH (mUnit/l)	<0.01	0.25	5.19	4.64	4.87	2.37
fT3 (pmol/l)	-	3.9	4.1	4.6	4.6	-
fT4 (pmol/l)	40.6	11.9	10.4	12.2	12.4	3.6

Morning Pituitary profile in June 2021

	June 2021
TSH (mUnit/l)	2.4
fT3 (pmol/l)	2
fT4 (pmol/l)	3.8
LH (IU/l)	2.5
FSH (IU/l)	2
Testosterone (nmol/l)	2
Prolactin (mUnit/l)	58
Cortisol (nmol/l)	304
ACTH (ng/l)	15

Levothyroxine commenced and dose gradually up titrated.
SST Sep 2021:
Cortisol 279 ->567
MRI pituitary: Very little tissue is seen within the pituitary fossa. This measures 3 mm in height and enhances. Suggestive of partial empty sella. Hypogonadism persisted on bloods and Testosterone replacement commenced.
DEXA:
Lumbar spine t score -0.1
Mean right NOF -2.5
Mean left NOF -2.4
Ensured Levothyroxine adequately replaced prior to ITT. (fT4 16.1)
ITT Jan 2022:

	Glucose	Cortisol	Growth hormone
0 min	5.0	147	0.09
30 min	1.7	169	0.06
60 min	4.5	282	0.38
90 min	6.7	235	0.32
120 min	8.3	170	0.13

Diagnosis of hypopituitarism confirmed and patient commenced on Prednisolone 4 mg OD.
Conclusion and points for discussion
Empty sella syndrome is a condition in which the pituitary gland is shrunk or flattened on MRI. If some of the pituitary gland is still visible on MRI it is called a partial empty sella syndrome. In majority of patients and empty sella is an incidental finding and does not need treatment. However, some may present with hypopituitarism requiring hormonal replacement. He showed an adequate response on SST even though he failed the ITT. Therefore, is SST a good alternative to look for secondary hypoadrenalism due to pituitary hypofunction? Hypothyroidism must be adequately replaced with Levothyroxine prior to ITT as this can impair the growth hormone and cortisol response.

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WA7

Non-functioning granulomatous pituitary adenoma: Common pathology in an unlikely siteÿ

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Background
Tuberculosis (TB) is an important cause of mortality and morbidity globally. Only a small proportion cases of systemic TB present with lesions spreading to meninges, sella, or ventricles. Cases of intra-sellar pituitary adenoma secondary to TB have been rarely identified, often with uncertainty on medical management as opposed to more aggressive surgical therapy. We report an interesting case of pituitary adenoma presenting with pan-hypopituitarism and posterior pituitary dysfunction and discuss the clinical conundrums of medical management.
Case Presentation
A 42-year old South Asian gentleman initially presented with low libido and erectile dysfunction, found to have secondary hypogonadism. He subsequently described features of headaches, lethargy, and excessive tiredness, but was apyrexial, and did not report weight loss or night sweats. Pituitary magnetic resonance imaging (MRI) demonstrated enlarged bulky pituitary with stalk pushed posteriorly, initially managed as a non-functioning pituitary adenoma.
Investigations
Dynamic pituitary function testing confirmed growth hormone deficiencies, secondary adrenal insufficiency, secondary hypothyroidism. Insulin tolerance test was performed with a peak cortisol of 103 nmol/l and peak GH of 0.36 microgram/l. Prolactin 360 mU/l. IGF1 14. Testosterone 6.4 nmol/l; LH 1.2 U/l, FSH 2.2 U/l. Hypertonic saline infusion test also confirmed cranial diabetes insipidus.
Progress in medical management
Treatment for pan-hypopituitarism was initiated accordingly. The patient was managed under joint care with infectious diseases and neurosurgical team due to clinical suspicion of intra-sellar TB. Due to lack of constitutional features of systemic TB, and presence of cranial diabetes insipidus, a trans-sphenoidal pituitary biopsy was organised. Pituitary histology demonstrated evidence of granulomatous adenoma, but negative for AAFB. After 8 months of anti-TB treatment, there was radiological evidence of reduction in size of pituitary lesion and improvement in symptoms of headache. In this rare case presentation, we discuss the consideration of trial of anti-tuberculous therapy and our experience in managing this scenario with follow-up radiological imaging, before considering pituitary surgery.

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WA8

Rapid enlargement of non-functioning pituitary adenoma during pregnancy and its spontaneous regression postpartumÿ

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33-year-old female presented at 35 weeks of pregnancy with black spots in the peripheral vision and headaches to Ophthalmology department. No other relevant clinical symptoms of note and no past medical history. On examination she had bitemporal hemianopia confirmed on perimetry hence was referred to Endocrine department. The MRI showed pituitary macroadenoma (1.8 cm x 2 cm x 1.2 cm), with extension into suprasellar and parasellar regions and displacement of the optic chiasm. Biochemical profile showed a Prolactin of 2420 ng/ml, secondary hypothyroidism - TSH (0.04 mU/l), T4 (9.1 mg/dl) and 9AM cortisol (164 mg/dl). Discussions with Oxford MDT advised early C-section and Trans-sphenoidal surgery following delivery with weekly visual field monitoring. She was delivered successfully 3 weeks after presentation with no post op complications. She was started on steroid replacement peri-operatively as empirical therapy, followed by levothyroxine. Post-delivery her SST was normal and hence she was weaned off steroids gradually (as she remained on them for 12 weeks post-partum due to nonattendance at some appointments). Following delivery, her vision improved and so did her visual fields. Her MRI post-partum showed reduction in size of the pituitary lesion (reduced from 1.8 to 1.0 cm in maximal craniocaudal diameter and no longer compressing optic chiasm). She was re-discussed at Oxford Pituitary MDT. Given that her visual fields normalised and she desired to have more children, it was felt Trans-sphenoidal surgery would have a risk of infertility hence they recommended 6 month follow up scans and debulking surgery only if a significant adenoma was still present prior to next pregnancy. Her latest pituitary MRI shows further spontaneous reduction in size of pituitary tumour from 1 cm to 0.7 cm in craniocaudal dimension. She is keeping well with no clinical symptoms and normal visual fields; she is breastfeeding, and her cycles restarted postpartum. She managed to conceive second time, 8 months after delivery but had a miscarriage unfortunately.
Discussion
- How to investigate a young pregnant female with late presentation and vision threatening pathology with no baseline hormone profile or brain scans. MDT and patient involvement in decisions remains crucial centre point.
- Interpreting pituitary biochemical profile in pregnancy. Safety of serial contrast MRIs during pregnancy.
- Management options – Surgery vs conservative approach in 3rd trimester with patient being on board with risks of each.
- Changes in pituitary tumours (functioning and non-functioning) during and after pregnancy.

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WA9

Usefulness of desmopressin stimulation test in ACTH dependent Cushing's syndrome in a young patient with no obvious pituitary lesionÿ

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A 41 year-old male was referred urgently from secondary care with high suspicion of Cushing's syndrome. His past medical history included psychosis and bipolar disorder, previous low impact foot fractures, rib fractures on coughing and spinal wedge fractures on X-ray, all within the last 5 years. He was taking quetiapine 300 mg modified-release and amitriptyline 10 mg daily, and tramadol 50 mg as needed. The patient reported decreasing mobility with increasing back pain, easy bruising, a change in facial appearance and one stone in weight gain over the last 5 years. He was a non-smoker and rarely consumes alcohol. On examination, he exhibited florid cushingoid appearance with moon face, facial plethora, thin skin, multiple new purple striae, central adiposity, a very large interscapular fat pad and severe proximal myopathy. There were no visual field defects on confrontational bedside testing. Initial biochemical investigations revealed unsuppressed cortisol (576 nmol/l) on 1 mg overnight dexamethasone suppression test (ONDST). 24 hours urine cortisol concentration was raised at 683 nmol/day (NR<132). Confirmatory testing with 48 hours low dose dexamethasone suppression test (LDDST) demonstrated failure to suppress serum cortisol level at 588 nmol/l. A diagnosis of Cushing's syndrome was made. His unsuppressed random ACTH (adrenocorticotropic hormone) level at 53 ng/l (NR 7.2-63 ng/l) pointed towards ACTH-dependent Cushing's syndrome. Other pituitary hormonal profile revealed central hypogonadism (low testosterone level at 4.6 nmol/l (NR 8.6-29 nmol/l) with unstimulated gonadotrophins) and intact thyroidal axis. His bone density scan confirmed osteoporosis at the level of hip and lumbar spine. MR imaging of his pituitary gland did not identify any lesion within the fossa. Given that the pre-test probability for Cushing's disease was high, we proceeded with a peripheral desmopressin (DDAVP) stimulation test using 10 mg intravenous desmopressin. The results showed a 100% rise in serum cortisol level and more than 100% rise in ACTH concentrations within 30 minutes of DDAVP injection, thus strongly suggesting Cushing's disease. The patient is awaiting Inferior Petrosal Sinus Sampling (IPSS) before proceeding with trans-sphenoidal pituitary exploration by our dedicated neurosurgeon.
Conclusion
Diagnosis of Cushing's disease requires a meticulous and systematic assessment along with clinical correlation and pre-test probability. No single test offers robust diagnostic performance but rather a combination of clinical assessment, biochemical investigations and specialised imaging is needed to guide multi-disciplinary approach to management.

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WA10

A case of Pituitary macroadenoma co-secreting TSH and GH complicated with pituitary apoplexyÿ

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Background
The plurihormonal pituitary adenomas represent 10-15% of all functioning pituitary adenoma. Mixed Growth hormone and prolactin secreting adenomas are

the commonest one, approximately 5% of surgically removed adenoma. Other hormonal mixture of adenoma may occur, but very rare. We present a rare case of co-secreting TSH and GH adenoma.

Clinical Case

A 45 year old gentleman, generally fit and well, presented with 3 years history of blurred vision in the right eye and generally decline in energy and low libido recently in April 2017. He was found on formal perimetry to have upper temporal visual field deficit in the right eye and visual acuity was N5 bilaterally. He denied headache and change in physical appearance. The patient was of tall stature with a Body mass index of 35.02 kg/m^2. There was no clinical features suggestive of acromegaly. The MRI pituitary demonstrated a 3.6 cm pituitary lesion compatible with a macroadenoma, with suprasellar extension, compressing the optic chiasma. He had biochemically evidence excess of TSH and GH level (Table[1]) with nadir GH 1.27 ug/l on OGTT. Subsequently, he became thyrotoxic and commenced on carbimazole to control thyroid excess prior to definitive management alongside with testosterone replacement.

Table 1 Pituitary profile (Presentation and Post-operative)

	Initial	Post-op
TSH (0.35-5.50 mUl/l)	5.1	0.74
T4 (10-20 pmol/l)	40.1	15.1
Testosterone (8.4-28.7 nmol/l)	6.6	4
LH (2-9 U/l)	0.1	1.3
FSH (1-18U/l)	0.3	1.9
Cortisol (200-500 nmol/l)	591	504
ACTH (90-46 ng/l)	26	29.4
GH	1	0.8
IGF-1 (74-196 ng/ml)	514	436
Prolactin (45-375 mUl/l)	311	132

In July 2017, the patient had flu like symptoms with sudden onset of headache and significant visual deterioration in his right eye. An urgent MRI pituitary revealed a significant increase in tumor size with small foci of infarct, suggestive of pituitary apoplexy. Hydrocortisone was started as a precaution to address cortisol deficiency and edema due to chiasm compression. Afterwards, patient successfully had transphenoidal surgery and histology showed plurihormonal adenoma with GH and TSH excess, Ki67>10%. His visual field was significantly improved with stable anterior remnant without chiasma compromise on MRI pituitary. Post-operative pituitary profile was repeated (Table[1]). Thereafter, the carbimazole was stopped. After reassurance of GST, hydrocortisone was weaned off. However, the testosterone treatment was continued for secondary hypogonadism.

Discussion

This is a rare case of TSH and GH co-secreting pituitary macroadenoma, with mass affect and hyperthyroid symptoms without clinical features of acromegaly.

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WA11

A case of lymphocytic hypophysitis presenting with diabetes insipidusÿ

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Introduction

Lymphocytic hypophysitis(LH) is a rare autoimmune endocrinopathy that causes pituitary gland inflammation, resulting in hypopituitarism. Headache is the most common presenting symptom; however, diabetes insipidus (DI) may be the first feature in some patients. Here we report one such case.

Case

a 36-year-old female was referred to the Endocrine clinic with sudden onset of polydipsia, polyuria and nocturia. She also reported amenorrhoea but no galactorrhoea. There was no history of any significant headaches or visual disturbances. Past medical history included autism with anxiety. Fluoxetine and Gabapentin were discontinued by primary care with no improvement in her symptoms. No obvious endocrinopathy was found on clinical examination. The pituitary profile showed hypogonadotropic hypogonadism (FSH 5.8U/l and LH 4.6U/l, oestradiol <92 pmol/l) with slightly elevated prolactin (531 mU/l; NR=102-496). Biochemistry was suggestive of DI with a urine osmolality of 82 mosm/kg and serum osmolality of 298 mosm/kg. Her serum sodium was 142 mmol/l. Desmopressin (DDVAP) 300 mg/day was commenced. A subsequent Pituitary MRI illustrated pituitary stalk thickening and enhancement, suggestive of an inflammatory process. A right-sided 3.5mm pituitary microadenoma was also noted. A water deprivation test confirmed the DI. She was also started on HRT. A screen for causes of pituitary stalk infiltration was performed including CT neck, thorax, abdomen and pelvis; IgG4, serum ACE, AFP, Anti-neutrophil Cytoplasmic antibody (ANCA), and Beta -2 microglobulin. All of which were normal. She was reviewed again after six months. DI was well controlled on DDVAP 200 mg/day. A follow-up pituitary scan revealed a significant reduction in the pituitary stalk thickening. The pituitary microadenoma had not changed. However, she had developed new vertex headaches. Repeat pituitary profile showed a rise in prolactin to 896 miu/l, raising the clinical conundrum as to whether this hyperprolactinaemia is due to the stalk effect caused by LH, or does she have a co-incidental microprolactinoma?

Discussion

LH is an autoimmune condition that involves infiltration of the pituitary gland with T and B lymphocytes. It may also be caused by infiltrative diseases like sarcoidosis, amyloidosis and haemochromatosis. Although confirmation of the diagnosis requires a pituitary biopsy, it is practically not feasible. Hence, diagnosis is based on symptoms, biochemical and radiological findings. In our patient, LH caused the sudden onset of DI and hypogonadism. She has responded well to treatment but should a dopamine agonist trial be considered since she has now developed hyperprolactinaemia in association with new headaches?

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WA12

Pituitary functions and Hypothalamic Pituitary Axis Assessment Post Pituitary Surgeryÿ

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47 year old gentleman referred to Neurosurgery Department with incidental findings of pituitary macroadenoma with chiasmal compression and cavernous sinus involvement, whilst getting investigated for tinnitus. His past medical history included chronic migraines only. He has been experiencing increased frequency of migraines along with lethargy, decreased libido and loss of morning erections for some time prior to presentation. His formal visual fields showed a slight inferior temporal defect in right eye while left eye had a slight superior temporal defect. His 9am pituitary profile showed cortisol 286 mmol/l, TSH 1.76 mIU/l, T4 8.8 pmol/l, FSH 1.6 IU/l, LH 1.3 IU/l, IGF1 16.2 nmol/l, Testosterone 3.2 nmol/l, Prolactin 534 mIU/l. He was started on hydrocortisone, levothyroxine and testosterone gel. He underwent Transphenoidal Surgery soon after the diagnosis of pituitary macroadenoma. Histology showed gonadotroph adenoma with Ki 67<3%. Post-operative day two, 9 am pituitary profile showed cortisol 166 mmol/l, TSH 0.20 mIU/l, T4 11.0 pmol/l, FSH 1.6 IU/l, LH 0.8 IU/l, IGF1 nmol/l 15.1, testosterone 0.4 nmol/l, prolactin 141 mIU/l. He has experienced epigastric pain after starting hydrocortisone prior to surgery and was not keen to continue hydrocortisone postoperatively due to gastric side-effects. He was adviced hydrocortisone with PPI cover along with levothyroxine postoperatively. Awaiting his insulin tolerance test (ITT) to assess is hypothalamic pituitary axis post-surgery; he self-ceased his hydrocortisone amidst of pandemic. He was asked to restart on a reduced dose of 10 mg +5mg with lansoprazole considering his 9am cortisol was 163 mmol/l. After the pandemic, he underwent ITT (more than 1 year after surgery) that demonstrated a good cortisol response of 498 mmol/l but inadequate growth hormone response. He was asked to stop his hydrocortisone.

Conclusion

Sellar and parasellar masses are a common finding, and most of them are treated via trans-sphenoidal surgery. Hypopituitarism is one of the most frequent sequelae, with central adrenal insufficiency being the deficit that requires a timely diagnosis and treatment. The peri-operative management of adrenal insufficiency is influenced by the preoperative status of the hypothalamic–pituitary–adrenal axis. ITT is considered the gold standard for assessment of GH and ACTH reserve in patients with pituitary disease following pituitary surgery. It has been evidenced that recovery in pituitary function is seen during the late-postoperative follow-up. ACTH is known to recover most frequently however GH is shown to be least likely to recover.

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Workshop B: Disorders of growth and development

WB1

Delayed growth and puberty due to pituitary iron deposition from Ćbeta-thalassaemia majorÿ

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Introduction
The predominant management of beta-thalassemia major is repeated blood transfusions but this runs the risk of haemosiderosis leading to multiple endocrinopathies. Iron chelation therapy can reduce this risk, however universal access is poor.
Case Presentation
An 18 year old male with "type 1 diabetes" was referred to Young Adult Diabetes Clinic having arrived to the UK from Syria 10 days previously. The only past medical history of note was transfusion dependent beta-thalassaemia major and consequent splenectomy. He was a non-smoker and no family history of diabetes. The initial clinician noticed his biological age did not match his chronological age owing to minimal signs of pubertal changes including hair growth. Pubertal assessment: axillary hair stage 1, pubic hair stage 2, genitals stage 2 to 3 with 3 ml testes on both sides. Height: 150.5 cm (<0.4 Centile), weight 46 kg (<0.4 Centile). Bone age was 14-15 on x-ray. He also had frontal bossing suggesting extramedullary haematopoesis and bronze skin pigmentation. His diabetes was actually secondary to pancreatic iron deposition.ĆInitial InvestigationsĆA

Investigations:	Results:	Normal range:
Serum Ferritin	10212	23-540 mg/l
Testosterone	0.4	9.4-37.0 mmol/l
Follicle stimulating hormone	0.6	1.0-10.0iu/l
Luteinising hormone	0.5	1-9iu/l
Sex hormone binding globulin	130	15-40 nmol/l
IGF1	66	105-346 mg/l
Prolactin	44	50-400miu/l
Cortisol	188 Ćrepeat - 742	138-620 nmol/l
TSH	2.3	0.3-5 miu/l
fT4	15	9-25 pmol/l
HbA1c	79	<42 mmol/mol
ALT	155	2-53 iu/l
ALP	230	30-130 iu/l

GHRH-arginine test showed growth hormone deficiency. He also had hypogonadotrophic hypogonadism. MRI identified iron overload in the heart and liver; MRI pituitary showed loss of signal intensity in anterior pituitary suggestive of hypopituitarism secondary to iron overload.ĆProgressĆHe was started on growth hormone initially 1.2 mg/day and then testosterone starting at 75 mg a month titrating to 250 mg. He gained 19 cm over four years with final height of 169 cm (15th centile). Testes grew to 10mm bilaterally with axillary, pubic and facial hair development. Iron chelation lowered ferritin to the reference range. Now aged 22 continues on growth hormone and testosterone replacement therapy.ĆConclusionĆDelayed puberty may present later in patients with limited access to healthcare. Replacement of the underlying hormonal deficits can help achieve adult height and development of secondary sexual characteristics. Late treatment even into the early 20s may help achieve close to predicted adult height. Iron chelation will help prevent further deterioration in soft tissue damage but will not reverse damage to the pituitary.

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WB2

The many sequelae of sub-optimal control of CAH during adolescenceÿ

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Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency can have multiple effects on growth, sexual development, fertility and overall health. Sub-optimal adherence to treatment regimens during adolescence and puberty can have lifelong consequences. We present the case of 20-year-old male who was diagnosed at birth. His parents are first cousins, and his two siblings also have CAH. Initial treatment comprised hydrocortisone and fludrocortisone and administration was by his parents. Growth was normal until age 10 when his height was noted to have augmented along with increased skin pigmentation. Biochemical evaluation showed elevated 17-hydroxyprogesterone >100 nmol/l (0-6) despite adequate doses by body weight. Poor compliance was suggested as a possible cause. Prednisolone was suggested to improve compliance. Despite this, bone age was that of a 19-year-old when he was chronologically 16 and growth ceased at 153 cm. Within a year of growth completion, he developed bilateral testicular adrenal rest tumors (TART). Care was further complicated by the development of type 1 diabetes age 18. On recent assessment he acknowledges poor compliance but has recently restarted taking prednisolone as he is motivated to improve his overall health, including diabetes control. Biochemistry reflects recent adherence (17-OHP 27.9 nmol/l) but long-term sequelae of sub-optimal control during adolescence remain. He has developed hypogonadotropic hypogonadism secondary to excess adrenal androgens (LH 0.5, FSH <0.3, Testosterone 1.1 nmol/l). Recent ultrasound shows increased TART size, and he has been counselled on the effects this may have on future fertility.
Conclusion
Compliance with medications in CAH is one of the most important factors in management. During adolescence it is often difficult to comprehend the lifelong consequences of certain actions. Poor compliance can lead to delayed puberty, short stature, hypertension, low testosterone and development of Testicular Adrenal rest tumor (TART). There are many ways to improve compliance including optimising medication regimes, motivational interviewing, education, shared decision making. Recognizing signs of poor adherence prior to the development of complications is key and requires careful history taking and biochemical evaluation. We use this case to highlight some of the pitfalls and potential solutions.

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WB3

Giant prolactinoma in a prepubertal girl- challenges in the managementÿ

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We report a case of a peripubertal 11 yr old girl with a diagnosis of macroprolactinoma. She was diagnosed 1,5 years before her presentation in our clinic in the context of headache. At the diagnostic, the MRI described a moderate enhancing homogenous mass- of 27/16/14 mm -centred on the diaphragm sellae –extended laterally in the right cavernous sinus in contact with the left optic nerve, anterior in the posterior segment of the olfactory sulcus and inferior to the Meckel cave. The provisional radiological diagnostic of meningioma was changed after finding a prolactin level of 67585 mUI/l. After three months of 1 mg Cabergoline weekly treatment, the serum prolactin level falls 10%. She lost from follow up while continuing treatment. August 2021- due to increased headaches, she addressed to the endocrinology and a new assessment was done with progressive tumour dimension on MRI to 35/24/27 mm.
Clinical: normal visual field, 1500 mL urinary output, BP 100/60 mmHg, height-146 cm (+0 SD, MPH=166 cm +/- 8.5 cm), Tanner Stage I- prepubertal.
Investigations planned:

Hormonal evaluation (Aug 2021) on 1 mg CBG weekly

	normal range	value	CBG total Ćdose
prolactin mUI/l	<210	184879 Ć (80% recovery Ćafter PEG);	110 mg
IGF1	123-427	515.5	
GH ng/mL	0.12-8.05	2.16	
FSH	0.9-8.9	0.4	
LH	<3.1	<0.3	
estradiol pmoL/l	18.4-250	42	
cortisol nmol/l	357	171-536	
ACTH	24.38	7.2-63	
TSH mUI/l	0.5-4.3	2.04	
freeT4 pmoL/l	12-21	14.1	
PTH pg/mL	15-65	21.3	
Calcium	8.8-10.8	10.5	

*CBG, Cabergoline total dose since diagnostic

SST, GH suppression test, Genetics
Principals and considerations of the treatment:
- a gradual increase of the Cabergoline to a dose of 3,5 mg/week – was obtained with good tolerance
- a decrease of 20% of the serum prolactin level in a month was registered after achieving the dose of 3 mg Cabergoline weekly - peripubertal age of the patient achieves normal serum prolactin the condition for a spontaneous course of the puberty

The first intention treatment in prolactinoma is dopamine agonists. Prolactinoma larger than 4 centimetres with prolactin levels above 21000 UI/l is considered a giant prolactinoma. Irrespective of the size, they are very responsive to medical treatment. Resistant prolactinoma is defined as failure to normalize prolactin levels or inability to achieve 50% volume shrinkage. Surgery is reserved in apoplexy, progressive neuro-ophthalmic syndrome, optical chiasm herniation, or leak cerebrospinal fluid while tumour shrinkage.

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WB4

Activating mutation of the Calcium sensing receptor as a cause of hypocalcemiaÿ

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Introduction
Calcium sensing receptor (CaSR) plays a role in calciotropic processes by regulating parathyroid hormone secretion and urinary calcium excretion. Activating mutation of the CaSR, with heterozygous gain in function, causes autosomal dominant hypocalcaemia 1 (ADH1), a rare disorder with a prevalence of 3.9 per 100,000. Aggressive treatment to normalise serum calcium causes nephrocalcinosis and hypercalcaemia. We present a case of a 27-year-old female with CaSR mutation who developed nephrocalcinosis and brain calcifications.
Case Presentation
Our patient presented aged 11 years with severe hypocalcaemia and undetectable parathyroid hormone (PTH). Genetic testing confirmed the presence of CaSR mutation. She was treated with 2.5 mg alfacalcidol and 500mg calcium supplements daily with calcium levels in the reference range. Nephrocalcinosis was diagnosed a year later. The calcium level was set at a lower range between 1.70-2.10 mmol/l until age 17. A multidisciplinary team meeting was held following transfer to adult endocrine services, and it was decided to use urinary calcium levels as the guide for replacement. At 26 years of age, her urinary calcium showed a rise (see chart) and an Ultrasound of her kidneys showed recurrence of nephrocalcinosis. Bone mineral density was normal. Our patient was using the oral contraceptive pill since menarche aged 12 and developed post-pill amenorrhea aged 26 with a diagnosis of premature ovarian insufficiency (POI) biochemically treated with HRT. At the end of the same year, the patient developed a generalised tonic-clonic seizure treated with anticonvulsant, Imaging showed marked calcification in subcortical white matter, basal ganglia, thalamus, and cerebellum. Her hypocalcaemia is currently managed on alfacalcidol and calcium, monitored by urine calcium.
Conclusion
This is a rare case of a patient with CaSR mutation developing complications such as nephrocalcinosis, seizures and calcification in several areas of the brain. It is not clear if POI is linked to this condition. We are currently considering firstly non-conventional therapies such as diuretics or recombinant parathyroid hormone to prevent complications and secondly best measure to monitor calcium load.

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Year	Calci(mmol/l)	Adj (mol/l)	Phosphate (mmol/l)	[illegible]	Creatinine (umol/l)	Potassium (mmol/l)	eGFR
2016	1.75	1.78	1.85	6	60	4.5	>90
2018	1.67	1.70	1.43	2.4	69	4.0	>90
2021	2.32	2.24	1.91	8.5	75	4.6	84

WB5

A rare case of Turner's syndromeÿ

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Introduction
Primary amenorrhea is usually caused by either gonadal or anatomical abnormalities. Turner's syndrome (TS) is the result of partial or complete absence of X chromosome in females with an incidence of 1 in 2500 live female births. Mullerian agenesis due to Mayer-Rokitansky-Hauser syndrome (M-R-K-H syndrome; embryonic underdevelopment of the vagina with variable uterine development) has an incidence of 1 in 5000 females and can be mistakenly diagnosed in patients with no prior exposure to oestrogen. We report a rare case of primary amenorrhea and absent Mullerian structures on index imaging.
Case Summary
A 17 year old girl presented to the endocrine team with primary amenorrhea. She was born without pregnancy complications and had a healthy childhood. She had short stature compared to her family members. Her mother and sister attained menarche at age of 16 and 14 respectively. Phenotypically, she was female, tanner stage 2 breast development, female genitalia, and sparse pubic hair. There were no typical features of TS. Body mass index was 30.3 kg/m^2. The rest of her physical examination was unremarkable. Biochemically, there was hypergonadotropic hypogonadism (Table[1]). Radiologically, there was absence of uterus and Mullerian structures on transabdominal pelvic ultrasound. MRI abdomen and pelvic demonstrated normal kidneys, and absence of uterus, cervix, and ovaries with underdeveloped vagina. The cytogenetics analysis showed a mosaic karyotype with 45X 17%, normal female karyotype with 46XX 83%, consistent with mosaic Turner's syndrome. Coeliac, Cardiology and audiological screening were unremarkable.
The patient was commenced on unopposed transdermal oestrogen supplementation for pubertal induction. The patient experienced withdrawal bleeding approximately 2 years after commencement of oestrogen and has since started progestin supplementation. A pelvic MRI will be repeated upon completion of pubertal induction to assess uterine development.

Table 1: Initial Investigations

LH (2-13 U/l)	32.9
FSH (3-10 U/l)	119.5
Serum estradiol (72-529 pmol/l)	100
Androstenedione (0.0-6 nmol/l)	2.3
SHBG(18-144 nmol/l)	15
Testosterone (<1.6 nmol/l)	0.5
Free androgen index (<4.6)	3.3
TSH (0.35-5.50 mU/l)	1.5
Free T4 (10-20 pmol/l)	12.9
Prolactin (59-619 mU/l)	123
IGF-1(190-429 ng/mL)	220
Serum cortisol (200-500) nmol/l	397

Conclusion
This is a rare case of TS presenting with radiological features of gonadal and Mullerian dysgenesis. M-R-K-H syndrome can be prematurely diagnosed in these patients. Uterine development can occur following exposure to oestrogen. Patient counselling is of importance the implication for fertility and possibility of conception at appropriate interval.

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WB6

Functional Hypogonadotropic Hypogonadism presenting with delayed puberty and primary amenorrhoeaÿ

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18 year old student was referred by the Gynaecology team with primary amenorrhoea, delayed puberty, and minimum breast development.
History
The patient was born by an emergency caesarean section with a birth weight of eight pounds and four ounces. She had a normal development during infancy and childhood and there was no reported developmental delay in the family. She had adrenarche at the age of ten with a normal appearance of axillary and pubic hair. Unfortunately, she developed severe anorexia nervosa at the age of eleven and needed admission to the hospital. Since after that she has had very minimum physical development. Her mother is 168 centimetres and her father is 178 centimetres respectively.
Examination
Her body weight was 48 kilograms with a height of 151 centimeters with a BMI of 19. She had a pre-pubertal body shape with Tanner stage II breast and Tanner stage III pubic hair.
Investigations
Karyotype: 46 XX X-ray Hand & Wrist: Chronological age - 18 years 9 months, Bone age - 15 years Transabdominal USS: Anteverted Uterus with 55 x 19 x 33 mm with 3mm endometrium thickness. Unremarkable ovaries. MRI pituitary: No pituitary or hypothalamic abnormality.
Treatment
According to patient preference, induction of puberty by using 1 mg oestradiol validate tablets with starting dose of 0.25 mg for six months followed by 0.25 mg increment every six months until achieving 1 mg dose. She was reassessed ten

Prolactin (57-56.1)	111 mu/l
IGF-1 (13.7-45.0)	19.2 nmol/l
Cortisol	268 nmol/l
TSH (0.34-5.6)	22.2 mu/l
FT4 (7.9-13.6)	7.8 pmol/l
FSH	9.4 iu/l
LH	2.7 iu/l
Oestradiol	121 pmol/l
DHEA (1.7-8.4)	6.10 umol/l
Androstenedione (1.6-7.5)	3.0 nmol/l

months following the treatment.

Oestradiol was increased to 1 mg with the introduction of Utrogestan 200 mg twelve days for every one to three months for six months. As she had a withdrawal bleed with achieving normal BMI with the recovery of the Hypothalamo-pituitary-gonadal axis and reasonable breast development, the replacement therapy was discontinued after 14 months of treatment.

	Before puberty Induction	After puberty Induction
Height (Centimetres)	151	156.5
Weight (Kilogram)	48	62
BMI	21.1	25.5
Pelvis USS	55x19x33 mm uterus with 3 mm endometrium	86x46x44 mm uterus with 5 mm endometirum
Bone Age (Years)	15	16.5
Pubertal stage: Breast	Tanner II	Tanner IV
: Pubic hair	Tanner III	Tanner IV
: Menstruation	Amenorrhoea	1x menstrual bleed

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Workshop C: Disorders of the thyroid gland

WC1

Subclinical hyperthyroidism and its many facets; a presentation with severe thyroid eye diseaseÿ

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Case History

A 70-year-old man of Chinese origin presents with a two-month history of worsening visual acuity and double vision. He denied systemic symptoms apart from marginal weight loss. Other medical history includes stable asthma, treated with inhalers. He has a niece and nephew with thyroid disease. He is an ex-smoker, retired accountant, and drinks occasional alcohol. On examination, he was normotensive with a body mass index of 22 kg/m^2 however was found to have new-onset atrial fibrillation. There was no upper limb tremor nor thyroid goitre present. There was eyelid swelling, gaze-evoked orbital pain, constant bilateral vertical diplopia, limited elevation of both eyes, and restricted adduction particularly severe in the right eye. A follow-up review described right-sided esotropia and deteriorating visual acuity (6/12) compared to the left (6/6). There was no conjunctival redness or chemosis and pupil reactions were normal.

Investigations

Thyroid-stimulating hormone (TSH) was undetectable <0.02 mU/l (0.27- 4.2), free thyroxine 22.5 pmol/l (10.8- 25.5) and free triiodothyronine 6.3 pmol/l (3.1-6.8). TSH receptor antibodies were positive 4.6 IU/l. Magnetic resonance imaging described marked swelling and oedema with signal alteration of orbital rectal muscles affecting the inferior and medial recti and homogenous enhancement of all the orbital rectus muscles with inflammatory stranding of the intraconal fat. Intraocular pressures were raised in each eye: 32 and 28 mmHg (12-22). An ultrasound reported both lobes of the thyroid to be normal in size. A benign solitary right 4mm hyperechoic nodule was noted. The great vessels were normal. There was no lymphadenopathy.

Outcome

The patient was started on Carbimazole 5mg once a day, Selenium 100 mg twice a day, lubricating eye drops, and high dose steroid therapy. He received 5 doses of intravenous methylprednisolone 500mg and then was switched to oral prednisolone 70mg titrating down by 5mg weekly. He has been anticoagulated and initiated on bisphosphonate therapy.

Conclusion with points for discussion

This gentleman presents with severe active grave"s ophthalmopathy (GO) without overt thyrotoxicosis or a diffuse goitre. The raised intraocular pressures are likely due to congestion of the intraocular muscles. The unilateral severity of ocular signs prompted diagnostic confirmation with orbital imaging. It is possible his presentation with GO proceeded impending thyrotoxicosis. Early multi-disciplinary team involvement was vital due to the high clinical activity score which has improved since steroid therapy. It was important to also address other complications including cardiovascular risks and reduced bone mineral density.

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WC2

Thyroid function tests - Thyroid hormone resistanceÿ

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Case history

61 year old female with a history of inherited dilated cardiomyopathy was referred with abnormal thyroid functions not improving with Levothyroxine. She has been on Levothyroxine 100 mg which she has discontinued 5 months prior to the review but her thyroid function abnormality persisted. She had no family history of thyroid abnormalities.

Investigations

	TSH (mUnit/l)	fT4 (pmol/l)	fT3 (pmol/l)
Aug 2019	3	35	-
Nov 2019	2.68	49	-
Jan 2020	5.22	41.6	-
March 2020	4.93	37.9	9.3
June 2020	11.8	29	11.2
August 2020	5.79	30.6	7.6
May 2021	6.47	32	8.4

Negative TSH receptor antibodies.

Negative TSH receptor antibodies.ĆTreatment and follow up:

Above thyroid function results raised 2 main clinical suspicions which are Thyroid hormone resistance and a TSHoma. She was further investigated with a MRI pituitary which was normal.

No assay interference confirmed on Delfia blood test at Cambridge lab.

Prolactin (mUnits/L)	260
Cortisol (nmol/L)	281
SHBG (nmol/L)	14

Genetic testing: Heterozygous for THRB-related thyroid hormone resistance

Delfia assay		Centaur assay
TSH (mUnit/l)	3.2	
fT4 (pmol/l)	31.9	26.5
Calculated fT4 (based on total T4 and TBG)	24	
fT3 (pmol/l)	-	6.82
TBG	18.6	

Conclusion and points for discussion

- In the presence of a raised fT4 with an unsuppressed TSH; a TSH secreting adenoma and thyroid hormone resistance should be the main differential diagnosis.
- There are two types of thyroid hormone resistance;
  1. Generalised resistance to thyroid hormone (GRTH)
     - Most present with a goitre or incidentally found abnormal thyroid functions
     - Also, may present with mild hyperthyroidism, deaf mutism or delayed bone maturation
     - Usually does not need treatment
  2. Selective pituitary resistance to thyroid hormone (PRTH)
     - Patients exhibit definite clinical manifestations of thyrotoxicosis
     - Need a chronic suppression of TSH secretion with D T4, tri-iodothyroacetic acid, Octrotide or Bromocriptine.
     - If medical management is ineffective, they would need thyroid ablation with radioiodine or surgery.
- 85% of thyroid hormone resistance results from gene encoding TRbeta, and its identification confirms the diagnosis. Normally the affected individuals will be heterozygous with an autosomal dominant inheritance pattern.

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WC3

Familial dysalbuminaemic hyperthyroxinaemia as a cause of discordant thyroid function testsÿ

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Introduction

Discordant thyroid function tests are frequently identified in clinical practice and should raise suspicions about laboratory analytical interference.

Case report

A 59 year old male was referred to Endocrine services for abnormal thyroid function tests following his recent Emergency department presentation with palpitations. His TFT (Roche) showed FT4 level was raised at 27.1 pmol/l (6.5 - 17.0), and his TSH normal at 2.57 uIU/ml (0.34 - 5.60) indicating a discordant TFT pattern. Clinically he was euthyroid. An incidental discovery of possible left-sided pituitary microadenoma was reported during a previous MRI brain scan done for TIA. Subsequently MRI scan of the pituitary was performed and reported an area of signal intensity that was not typical for a microadenoma. In view of discordant TFT results, further serum samples were sent to external laboratory (Delfia) to rule out assay interference. With the results of TSH 2.42 mU/l (0.40-4.00), FT4 17.6 pmol/l (9.0-20.0), total T4 216.8 nmol/l (69.0-141.0), TBG 26.2 ug/ml (14.0-31.0), it was confirmed that discordant pattern of thyroid function could be due to assay interference. Subsequently genetic testing was undertaken which confirmed Familial dysalbuminaemic hyperthyroxinaemia (FDH) in which a mutant (R218H), circulating albumin protein caused falsely elevated thyroid hormone (FT4, FT3) results in some measurement methods.

Conclusions

Familial dysalbuminaemic hyperthyroxinaemia is an inherited condition caused by mutations in the ALB gene, which encodes circulating albumin protein (Larsen et al., 2008). FDH may be more frequent than previously thought, despite the fact that its prevalence is unknown. The mutant albumin has an increased affinity for T4 resulting in discordant thyroid function tests (TFTs). The biochemical profile demonstrates increased serum T4 concentrations with normal FT4, total serum T3, and TSH levels. Biochemical tests and albumin genotyping can be used as a

means to confirm the diagnosis of FDH. Because all of the mutations linked to FDH so far have involved residue in the albumin molecule, molecular genetic testing is rather easy and yields a clear result (Cartwright et al., 2009).

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WC4

A grave interference: TSH interference due to macro-TSH Ćpost-thyroidectomy for graves" diseaseÿ

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A 26 year old gentleman presented to his GP in July 2018 with a one month history of thyrotoxic symptoms, including palpitations and weight loss. His initial thyroid function tests (TFTs) showed a hyperthyroid picture, including a FT4 of >100pmol/l (RR 12-22). His TSH receptor antibody was 11.1 IU/l (RR <1.75). He had no evidence of thyroid eye disease, and no goitre or thyroid nodules on exam. His Graves" disease was initially managed medically with carbimazole. He subsequently developed a goitre with compressive symptoms, so underwent a total thyroidectomy in January 2019. He was started on thyroxine immediately in the post-operative period, and had no post-operative hypoparathyroidism. Despite uptitration of his levothyroxine to 125 mg OD, his TSH remained persistently high (TSH 13.4mU/l, RR 0.27-4.2; FT4 19.2pmol/l, RR 10.5-22). He was taking the levothyroxine correctly, and was on an appropriate dose for his weight (60 kg). He was clinically euthyroid on levothyroxine, had no neck lumps or evidence of thyroid eye disease on exam. Given the difficulty achieving normal TFTs post-op, this patient was referred to a Speciality Thyroid Service in December 2020. His TFTs were assessed for assay interference, and results are shown in the table below.

There was abnormal TSH recovery after precipitation with polyethylene glycol (22%), demonstrating TSH interference. His estimated true TSH was only slightly above the normal range. Due to assay interference, TSH is not a reliable indicator of thyroid status in his case. Clinical symptoms and FT4 level are used as a guide for levothyroxine dosing. He was maintained successfully on 125 mg of levothyroxine. Macro-TSH is a rare finding, caused by binding of TSH to other plasma proteins, most often immunoglobulins, resulting in falsely elevated TSH measurement (1). Failure to identify macro-TSH can result in inappropriately high levothyroxine doses. Assay interference should be considered in patients with isolated raised TSH, particularly in the absence of thyroid dysfunction. If assay interference had been excluded, the differential diagnoses include resistance thyroid hormone beta and TSHoma.

1. Larsen, Camilla Bøgelund, et al. "Macro-TSH: a diagnostic challenge." European Thyroid Journal 10.1 (2021): 93-97.

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	Roche	Abbott	Centaur	DEFLIA
TSH (mU/l)	9.76	9.1	10.21	9.9
RR	0.27-4.2	0.35-4.94	0.35-5.5	0.4-4.0
FT4 (pmol/l)	20.1	14.9	18.4	18.2
RR	12-22	9-20	10.5-21	9-20
FT3 (pmol/l)			4.59	
RR			3.5-6.5	
TT4 (nmol/l)				134
RR				69-141

WC5

Two case reports of suspected thyroid assay interferenceÿ

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Case 1

A 17-year-old female was referred to the endocrinology outpatients due to abnormal thyroid function tests (TFTs) (as below) detected on routine monitoring for Thyroxine replacement therapy. Following exclusion of pregnancy, possibilities of assay interference due to heterophilic antibodies as well as thyroid hormone resistance were considered. Repeat analysis was arranged at two laboratories using different methods. Results were concordant, excluding assay interference. The above results were explained by intermittent non-compliance with replacement therapy which is a common cause for erratic TFTs due to different half-lives of thyroid hormones as well as exogenous Thyroxine. Intermittent Thyroxine intake can result in normal or elevated thyroid hormone levels which fail to normalise the TSH levels.

Case 2

An 87-year-old woman with recently diagnosed "hypothyroidism" was referred to the endocrine outpatients due to discrepant TFTs. Historic results confirmed a persistently raised TSH for two years with free T4 levels at the lower end of normal range. Recent initiation of Thyroxine replacement therapy had led to thyrotoxicosis symptoms without any change in TSH levels. A spuriously elevated TSH was suspected. Repeat TFTs (as below) check with a 9 a.m. anterior pituitary hormone profile (normal) was undertaken. A trial off Thyroxine for 3 months resulted in the following TFTs: Given above TFTs, Thyroxine replacement therapy was resumed with repeat testing as follows: The patient was investigated for macro TSH using polyethylene glycol (PEG) precipitation method revealing a "biologically active" TSH of approximately 3 mU/l, which was within the reference interval. MacroTSH is an uncommon cause for interference which can lead to spuriously elevated results. Going forward for this patient, free T4 should be used to assess for adequacy of replacement therapy.

Test	Result	Reference interval
TSH	23.55 mU/l	0.35-3.50
Free T4	13.5 pmol/l	7.5-21.5
Free T3	4.7 pmol/l	3.8-6.0
Anti-TPO Ab	>600 kU/l	0.0-34.0

Test	Result	Reference interval
TSH (Abbott)	17.12 mU/L	0.35-3.50
Free T4 (Abbott)	13.1 pmol/L	7.5-21.1

Test	Result	Reference interval
TSH	13.71 mU/L	0.35-3.50
Free T4	33 pmol/L	7.5-21.5
Free T3	6.3	3.8-6.0

Test	Result	Reference interval
TSH	46.20 mU/L	0.35-3.50
Free T4	5 pmol/L	7.5-21.5

Test	Result	Reference interval
TSH	23.9 mU/L	0.35-3.50
Free T4	5.0 pmol/L	7.5-21.5
Free T3	1.6 pmol/L	3.8-6.0

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Workshop D: Disorders of the adrenal gland

WD1

Iatrogenic Cushing's syndrome with secondary adrenal insufficiency due to concomitant use of chronic intranasal steroids and fluconazole - a dangerous combinationÿ

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Background
Intranasal steroids are commonly used for allergic rhinitis, rhinosinusitis and nasal polyps as they are considered safe in terms of long-term adverse effects profile due to favourable pharmacokinetic characteristics as compared to other oral and inhaled steroids. Some are also available over the counter without prescription.
Case
We report a patient with iatrogenic Cushing"s syndrome and secondary adrenal insufficiency due to chronic intranasal steroid use. A 42-year-old lady was referred to endocrinology with a recent history of tiredness, proximal muscle weakness and low 9 AM morning cortisol levels (7 nmol/l [RR: 172-497 nmol/l]). She was feeling tired and had non-specific pain all over her body. She had a history of chronic allergic rhinitis for which she was prescribed regular intranasal beclomethasone and fluticasone for many years. Further history revealed that she was regularly prescribed fluconazole 50mg OD for 15 days a month for the last 1 year before this presentation. On examination, she had purple abdominal striae, proximal myopathy, supraclavicular and subscapular fat deposition. Further investigations showed 9 am cortisol of 36 nmol/l with no response to Short Synacthen (Post Synacthen cortisol levels: 30 mins - 116 nmol/l, 60 min - 156 nmol/l), and ACTH levels of <3 ng/l. The rest of the Pituitary profile was normal.
Progress
She was started on hydrocortisone 10mg/5mg/5mg and she was referred to the ENT team for assessment and advice regarding suitable non-steroidal treatment for her chronic rhinitis. Despite physiological steroid replacement, she continued to feel pain and myalgia. She was asked to double the dose of hydrocortisone replacement. After this change, she felt much better and remains under follow up with the endocrine team to supervise gradual weaning to a lower physiological replacement dose.
Discussion
This patient demonstrates that though intranasal steroids are considered safe for the treatment of allergic rhinitis, treating physicians and general practitioners should use it with caution especially when using with other medications. The concomitant use of enzyme inhibitors can significantly increase bioavailability of some intranasal steroids especially fluticasone and budesonide which can lead to adverse effects like iatrogenic Cushing"s syndrome and secondary adrenal insufficiency. Moreover, Fluconazole can also downregulate steroidogenesis and its concurrent use with nasal steroids can also precipitate adrenal suppression.
Questions for discussion
1. Bioavailability of commonly used inhaled/intra-nasal steroids and effect of enzyme inhibitors on it2ĆHow to wean these patients off steroids safely and effectively.

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WD2

Addison"s disease in individual living with HIV: is Covid-19 the culprit?ÿ

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Introduction
There are emerging reports showing the relationship between human immunodeficiency virus (HIV), Covid-19 and adrenal insufficiency. This was attributed to thrombotic events and necrosis, leading to hypoadrenalism. The HIV virus can also lead to Addison"s disease due to destruction of adrenal gland. Prevalence of adrenal infarction with COVID-19 was found to be 23% and 88% this was shown to be affecting both adrenal glands.
Case report
A 46-year female with HIV presented with fever, hyponatraemia of 129 mmol/l and was subsequently diagnosed with Pneumonia. She recovered well with antibiotics. Four months prior to her presentation, she tested positive for COVID-19 and experienced gradual weight loss of 15 kg with tiredness all the time. Further investigations for hyponatraemia showed low cortisol level of 21 nmol/l and repeat of 29 nmol/l with ACTH below 3ng/l (7.2-63.3ng/l) and screening for adrenal antibodies was negative for adrenocortical antibodies. Tuberculosis was excluded using Elispot, sputum and BAL culture and cytology. Magnetic resonance imaging of the pituitary, autoimmune, hormonal, and biochemical screenings were all normal. Importantly, the pituitary production of all other hormones was in the normal range. In the view of negative findings, she was deemed to have isolated ACTH deficiency with resulting in Addison"s disease associated with COVID-19. She was started on intravenous hydrocortisone and in few days her sodium improved to 143 mmol/l which was later converted to hydrocortisone tablets. Since taking Hydrocortisone, she has stopped vomiting and her weight is steadily increasing. To our knowledge, there are potentially increased risk of Addison"s disease in individuals living with HIV through isolated ACTH deficiency following COVID-19 infections.
Conclusion
This case demonstrates association of COVID-19 with Addison"s disease in HIV. Previous cases and studies showed adrenal insufficiency associated HIV and COVID-19 likely linked to destruction of adrenal glands. There is possibility of direct insult to adrenal glands by Coronavirus by causing haemorrhage, necrosis or venous thromboembolism which can lead to consequence of hypoadrenalism. Such thrombotic events in adrenal glands can lead to impaired function of pituitary adrenal axis. Our case shows that COVID-19 in individuals living with HIV may also decrease the pituitary production of ACTH. Therefore, further research is needed to understand why the ACTH pituitary production is more vulnerable to the impact of COVID-19 in comparison with other hormones produced by the pituitary gland.

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WD3

A rare case of hypocortisolism in hypercoagulable stateÿ

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We report a case of 39-year-old woman presenting with sudden severe abdominal pain and vomiting. She had a past medical history of anti-phospholipid antibody syndrome (APLS) diagnosed in the United States (US) 20 years ago. She had multiple episodes of vomiting over the last 10 years and was diagnosed with cyclical vomiting as investigations including CT abdomen and endoscopy did not reveal a structural cause. She was taking warfarin for APLS. She was haemodynamically stable and clinical examination was unremarkable. Investigations showed normal electrolytes, subtherapeutic international normalised ratio (INR), raised cardiolipin antibody and raised activated partial thromboplastin time (APTT). CT abdomen showed enlarged bilateral adrenal glands with heterogenous parenchyma suggestive of adrenal haemorrhage and warfarin was stopped. A morning cortisol level was 171 nmol/l and short synacthen test showed inadequate cortisol response rising from 166 mmol/l only to 179 nmol/l at 30 minutes confirming the diagnosis of primary adrenal insufficiency. She was commenced on oral hydrocortisone. Subsequent MRI adrenals confirmed stable bilateral adrenal haemorrhage with cystic area of peripheral methaemoglobin and central haemosiderin. As the adrenal haemorrhage was non-progressive, anticoagulation was restarted due to high risk of thrombosis in the future. She is being followed up in the endocrine clinic with full adrenal work up including renin and aldosterone awaited. Adrenal infarction or haemorrhage is a rare complication of APLS, and hypercoagulable state may lead to adrenal vein thrombosis with haemorrhagic transformation of adrenal glands. The presenting features of adrenal thrombosis and haemorrhage include localised pain and / or adrenal insufficiency but often such patients do not have any symptoms. Patients with APLS and adrenal insufficiency may not present with hypotension as patients with APLS are commonly hypertensive, therefore masking hypotension. Unless promptly treated with intravenous glucocorticoids, complete adrenal insufficiency associated with vascular phenomenon of APLS can potentially be fatal. Therefore, physicians should have a high index of suspicion in such cases. Decision about anticoagulation should be individualised but most patients need anticoagulation as they remain at high risk of thrombotic phenomenon elsewhere.

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WD4

An Atypical Presentation of Addison"s Diseaseÿ

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History
A 52-year-old woman was referred by her GP for colonoscopy in view of 7 months" history of unexplained weight loss of nearly 2.5 stones, constipation and recently detected normocytic anaemia. Her past medical history was unremarkable except for bronchial asthma that was managed with albuterol. However, on the day of the scheduled colonoscopy, she was noted to be hypotensive (BP- 63/38 mm Hg, heart rate 93 bpm) and was hence admitted for fluid resuscitation. Following admission (day 1), she received 3 L of Hartmann"s solution intravenously for hypotension and severe dehydration. On day 2, the patient was found to be delirious and noted to have a random blood glucose of 1.6 mmol/l, which was treated with intravenous 10% dextrose. Serum electrolytes were normal (Na 135 mmol/l; K+ 4.2 mmol/l). Unfortunately, attempts to restore the BP failed despite adequate fluid resuscitation with 1 L of normal saline and 1 L of Hartmann"s solution (BP 96/40). Subsequently, on day 3, she was detected to have hyponatremia (Na 124 mmol/l) which was treated with 1 L of normal saline. However, over the next 4 days, her serum sodium level dropped further to 117 mmol/l in spite of daily fluid resuscitation with normal saline and Hartmann"s solution. Hyponatraemia-related work-up showed plasma osmolality-246 mOsm/kg, urine osmolality-341 mOsm/kg and urinary Na-45 mmol/l. She was hence referred to the endocrinologist. As her clinical profile was suggestive of hypocortisolism (hypoglycaemia, hyponatremia and hypotension), a random cortisol was carried out, which was found to be very low (26 nmol/l). Subsequently, a short Synacthen test (SST) revealed suboptimal response with baseline serum cortisol of 21 nmol/l and 88 nmol/l at 30 minutes. A diagnosis of Addison"s disease was made. CT adrenals revealed a normal study.
Treatment
She was treated with IV hydrocortisone 200 mg stat followed by 100 mg QDS, along with 100 mg of fludrocortisone daily. Saline infusions were continued. With the above treatment, hypotension and hyponatraemia resolved. At discharge, the patient was switched to oral maintenance therapy with hydrocortisone (10mg at 08:00, 10 mg at 12:00 and 5 mg at 17:00) and fludrocortisone 100 mg daily. She remains under endocrine follow up and has regained her weight.
Discussion
Atypical presentations of Addison" s disease as above mandate a high index of suspicion to ensure early diagnosis and prompt treatment.

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WD5

Optimising the biochemical control in a young patient with classical Congenital Adrenal Hyperplasia (CAH) and history of azoospermia, resulted in spermatogenesisÿ

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A male with classical salt-wasting congenital adrenal hyperplasia (CAH; 21-hydroxylase deficiency) who was diagnosed in infancy and had normal pubertal growth and development attended the endocrine department for routine follow up in June 2019 (age 26). His current daily medications are hydrocortisone 10 mg on waking, 5 mg at 4 pm and fludrocortisone 200 mg once daily. He also has injectable hydrocortisone sodium phosphate 100mg for emergency use. Over recent years, he reports good energy levels and his weight has been stable. He reports occasional mild postural dizziness. He complained of a pea-sized lump in the left testicle which he had noted 6 months prior and this was confirmed on examination. Blood tests confirmed suboptimal biochemical control of his CAH with raised ACTH (387 ng/l range 0-47), androstenedione (>35 nmol/l range 1.4-9.1) and 17OHP (212.7 nmol/l target range 6.3 to 20 nmol/l) levels, undectable LH (<0.5 iu/l range 1.7-8.6) and FSH (<0.5 iu/l range 1.5-12.4) and a mildly low total and free testosterone levels (7.7 nmol/l range 8.6-29 and 144 pmol/l range 198-669, respectively). Testicular cancer tumour markers were negative. A scrotal ultrasound showed bilateral testicular masses consistent with testicular adrenal rest tissue (TART) and a 0.5 cm left epididymal cyst. Semenalysis at this point demonstrated azoospermia. To improve his CAH biochemical control, for the management of TART and as the patient and his partner expressed a desire to start a family in the coming years, his steroid regimen was adjusted and prednisolone 1mg at night was added. Over coming months, the couple were referred for genetic partner testing and the patients" prednisolone dose was gradually increased up to 3mg to achieve better biochemical control. Further blood tests 5 months later (November 2020) demonstrated a marked improvement in adrenal androgen levels. His LH and FSH levels became detectable and there was a modest improvement in serum testosterone levels. Repeat semenalysis demonstrated a sperm count of 6 million/ml. Serial scrotal ultrasound scans demonstrated no change in the size of the TARTs despite optimisation of CAH control.
Conclusion
Classical CAH is associated with subfertility in men and this is multifactorial. In this case, improving the biochemical control of CAH with escalating glucocorticoid doses has resulted in spermatogenesis and a measurable improvement in his sperm count in just a few months, despite there being no change in the TARTs present on ultrasound.

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WD6

Acute presentations of 4 patients with spontaneous adrenal haemorrhageÿ

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We report on 4 patients who acutely presented to our unit and diagnosed with adrenal haemorrhage.
Case 1
A 72 year old man presented with generalised abdominal pain, fever and raised CRP a week after hip replacement surgery. CT abdomen showed non-enhancing bilateral adrenal lesions consistent with adrenal haemorrhage. He was taking Apixaban for DVT following hip replacement. SST was performed which confirmed suboptimal cortisol response. Hence, Treated as Adrenal insufficiency secondary to Waterhouse Friedrichsen syndrome.
Case 2
A 63 man has hypertension presented with acute severe left flank pain. CT renal and CT angiogram showed a large left adrenal and perinephric haemorrhage. This was treated with coil embolization of the left suprarenal artery. Initial biochemistry showed mildly raised plasma normetanephines which subsequently normalised. ONDST and aldosterone/plasma renin activity were normal. Serial CT scan showed gradual resolution of the adrenal haemorrhage with no underlying adrenal lesion.
Case 3
A 56 year old man presented with a 3 day history of epigastric and left sided abdominal pain with nausea and fever. CT scan of the abdomen revealed a 5 cm adrenal haemorrhage which was contained within the gland. Adrenal biochemistry were normal. Serial scans showed resolution of the adrenal haemorrhage and a residual adrenal nodule.
Case 4
A 19 year old primigravida, 35 weeks gestation, presented with acute severe right flank pain and vomiting. MRCP was performed. This revealed a right adrenal gland haemorrhage. Adrenal biochemistry were normal. She was delivered by Caesarian Section at term with 100 mg IV hydrocortisone cover and with no complications to either mother or baby. CT adrenals performed 8 weeks postpartum was entirely normal with no evidence of residual haemorrhage or adrenal mass.
Conclusion
We report on 4 patients who were found to have unilateral or bilateral adrenal haemorrhage. The common presenting symptom was abdominal pain. Adrenal function was essentially normal in all patients apart from the patient with bilateral adrenal haemorrhage (case 1) who had **adrenal insufficiency secondary to Waterhouse Friedrichsen Syndrome**. In last 3 cases adrenal haemorrhage resolved or decreased in size on subsequent scans. Anticoagulants were being used in one patient otherwise no risk factors identified in the remaining cases. One patient required coil embolization to stop the bleeding. Adrenal haemorrhage though rare, should be included in the differential diagnosis of acute abdominal pain as if missed diagnosed could be complicated with life threatening adrenal insufficiency.

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WD7

A rare endocrine complication of immunotherapy in lung cancerÿ

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Lung cancer is the second most common cancer in the world with the leading position as a cause of oncological fatality. The immunotherapy is applied as the second line of chemotherapy, and seems a breakthrough therapy, promising a

better quality of life to patients in the late stages of cancer. Pembrolizumab (also, known as MK-3475 or Keyruda) is a humanised antibody PD-1 receptor or antibody to programmed death ligand one. Side effects considered as acceptable and mostly presented with fatigue, pruritus, and decreased appetite. Primary adrenal insufficiency was reported in less than in one per cent of patients treated with Pembrolizumab. Nevertheless, this is rare but still seen presentation, which could lead to the development of adrenal crisis - a medical emergency. Misdiagnosis of a life-threatening condition might lead to an enormous physical and emotional impact with an already compromised quality of life. We report a case of a 72-year- old female patient, who developed acute adrenal insufficiency following a course of immunotherapy with Pembrolizumab for advanced lung cancer. The patient presented with nausea, vomiting, loose stools, dizziness, two weeks after her fourth cycle with Pembrolizumab, which initially was seen as usual complains followed a session of chemotherapy. On the other hand, the examination on the admission revealed significant hypotension in a patient known for long-term hypertension. She was dehydrated with mild tachycardia. In the Emergency Department, she was noted to have a severely low cortisol level on 33 mmol/l from an earlier investigation, and intravenous hydrocortisone was started. Oral hydrocortisone was continued on discharge to ensure metabolic and hemodynamic stability. This case report demonstrates the rare but possible endocrine complications of the immunotherapy that raised the possibility of the required differential diagnosis with possible development of life-treating Hypophysitis and raised the awareness of the potential development of the acute adrenal inefficiency in patients on immunotherapy for advanced cancer.
Discussion
This case illustrates the prompt and accurate diagnosis of acute adrenal insufficiency leading to optimal patient outcome.

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WD8

Atypical late presentation of congenital adrenal hyperplasia with adrenal myelolipomasÿ

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64 y/o male was being investigated for raised PSA. Following an MRI and biopsy, he was diagnosed with high grade prostatic intraepithelial neoplasia requiring close PSA surveillance. Incidentally, he was found to have bilateral adrenal lesions, measuring 6.4 cm on the left and 4 cm on the right. Prior to review in endocrine clinic, adrenal workup and CT adrenals were performed. CT showed both adrenal masses contain fat and calcification and are thought to be bilateral adrenal myelolipomas. Interestingly, adrenal workup, showed significantly raised l 17OH-progesterone (17OHP) at >300 nmol/l (1.2-5), raised renin level at 175.6mU/l (5.4-30), and ACTH of 140ng/l (0.0-5.0). From the history, he has been married twice though has never had any children, mainly due to personal circumstances rather than the inability to father a child. He has always been sexually active. He is totally asymptomatic from endocrine point of view and he is not on any medication. On examination he had normal secondary sexual characteristics. His right testis was significantly enlarged and apparently this has always been the case. It is non-tender. Short synacthen test revealed exaggerated 17OHP response (364 nmol/l at 0min and 718 nmol/l at 30min) with blunted cortisol response (110 nmol/l at 0 min and 104 nmol/l at 30 mins), confirming congenital adrenal hyperplasia (CAH) with glucocorticoid deficiency. Repeat renin level remains significantly elevated at 213.5mU/l suggesting mineralocorticoid deficiency. USS testes showed large lobulated right testes with an irregular complex calcific mass (31 x 38 x 38mm) with smaller lobulated left testes with diffusely heterogenous echotexture at the lower pole raising suspicion of whether these are testicular adrenal test tumors (TART). He has been commenced on glucocorticoid and mineralocorticoid replacements. Multidisciplinary team decided on conservative management for the adrenal myelolipomas, with yearly CT surveillance. In summary, this is an interesting case of middle-age male who was incidentally found to have large bilateral adrenal myelolipomas, a rare benign adrenal tumor. The association of adrenal myelolipomas with late-diagnosed and poorly managed CAH has been documented in number of studies and case reports. Despite being asymptomatic, biochemical work-up confirmed diagnosis of CAH with glucocorticoid and mineralocorticoid deficiency necessitating treatment which is uncommonly seen in non-classical CAH, as most of them does not require treatment. The US findings also raised suspicion of TART, which rarely reported in non-classical type.

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WD9

Journey with classical adrenal hyperplasia. Expectations and reality of treatmentÿ

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27-year-old male presented to the outpatient adult Endocrine team with Classical Salt wasting CAH due to 21 -Hydroxylase Deficiency. He has 659 A/C G splice mutation. There was no prior family history of CAH. The diagnosis was made at birth and he was commenced on hydrocortisone and Fludrocortisone. Further confirmatory tests were done at the age of one month. He was regularly followed up in the pediatric endocrine clinic. There have always been issues with compliance. He had a few presentations with adrenal crisis. He attained a height of 170.6 cm and weight of 65 kg. His height was not far off from parental targets. He was athletic and keen from the beginning to do Medicine Degree. He is currently studying medicine. He was referred to our local services at the age of 24 due to relocation. Initially, he was well maintained on 15mg of hydrocortisone in two divided and 150 mg of fludrocortisone. He noticed his shaving frequency is every 3 days and reduced hair growth all over his body. He has not noticed any lumps in the testicles. He has normal libido and denied any erectile dysfunction. Examination revealed normal testis bilaterally with normal secondary sexual development. We performed: cortisol and 17 hydroxy-progesterone day curve with zero-hour renin. 0 h renin 5.5 with normal electrolytes and renal profile. We also performed baseline Androstenedione 18.3 nmol/l, Testosterone 7.2 nmol/l and DHEAs 2.0Umol/l. FSH/lH was low. Bone scan and US testis (Surveillance of TARTs) were organized. US testis showed three lesions 0.6, 0.7 and 0.8 cm lesions bilaterally. Patient was advised to delay the evening dose of hydrocortisone to suppress morning peaks of 17-OH progesterone and Androstenedione levels. We also discussed that dose needs to be increased. He admits missing the evening doses and complaints of difficulty sleeping at night if takes steroids too late. He is also concerned increasing the corticosteroid dose gives him cushingoid appearance. The goals of treatment are adequate steroid therapy (mineralocorticoid and corticosteroid) to suppress CRH and ACTH without causing overtreatment. Avoid Salt wasting/Adrenal crisis. Dose titration to prevent suppression of FSH/lH and treatment of TARTs. Regular follow up of TARTs to avoid permanent Infertility and testicular atrophy. Discussions regarding fertility and genetic counselling for future family planning and inheritance. Avoidance of overtreatment of Steroid therapy.

	0hr	+2 hrs	+4hours	+6hours	+8hours
Plasma 17-OH Ćprogester-one (nmol/l)	>300	292	86	55	51
Cortisol	48	584	387	347	188

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WD10

Cushing"s crises arising from a neuroendocrine tumour treated with etomidate infusionÿ

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Introduction
Ectopic ACTH syndrome is rare but is frequently severe condition because of the intensity of the hypercortisolism that may be dissociated from the tumoral condition. It should often be considered as an endocrine emergency requiring an emergency response both in terms of diagnostic procedures and therapeutic interventions. Patient management is complex and necessitates dual skills, in the diagnosis and treatment (1). Etomidate, an imidazole-derivative anesthetic agent, blocks 11-beta-hydroxylase. It is used intravenously at 0.3 mg/kg/h. Its use is limited by the requirement for administration by the intravenous route. However, it rapidly decreases cortisol concentration and may be used as an adjunct to be impending surgical procedure (2). We are presenting case of Cushing crisis presented with severe hypercortisolism treated with etomidate infusion, secondary to neuroendocrine tumor.
Case summary
43-year-old lady with previous 47 mm right adrenal incidentaloma for which underwent right adrenalectomy in November 2020, histology reported as Adrenal oncocytoma. In September 2021 developed symptoms of lethargy and weight gain, seen in December 2021 found to be in florid Cushing, failed to suppress on low dose dexamethasone suppression test with ACTH of 583 ng/l (7.2-63.3), 9am Cortisol of 1484 nmol/l and 24-hour Urinary Free Cortisol of 14945 unit nmol (0-

125 Unit nmol/24hr) with severe hypokalemia K 2.9mmol and high blood pressure. Started on Metyrapone 250mg BD titrated to 1g TDS and Spironolactone 100 mg OD and intravenous potassium. Cortisol persistently remained>1000 nmol/l for which started Etomidate infusion (0.04-0.05 mg/kg/hr) to control Hypercortisolism. a full endogenous blockade of achieved cortisol<300 nmol/l, started on block and replace regimen with Hydrocortisone. Cortisol measured 6 hourly whiles on etomidate infusion rate adjusted based on serial cortisol levels. Further images obtained PET CT scan revealed multiple liver lesions, normal pituitary MRI. CT Pancreas showed 24 mm soft tissue nodule at the lateral pancreatic head and bilobed 18 mm nodule at the medial aspect of the uncinate process. Liver biopsy showed well differentiated neuroendocrine tumor, appearance and immunohistochemical profile do not fit with metastatic spread of the previous adrenal tumor. Pancreatic endoscopic US guided biopsy showed well differentiated neuroendocrine tumor of intermediate grade (NET G2,2019 WHO). Discussed at the NET MDT decision of Adrenalectomy has been made. Elective Robotic left adrenalectomy in January 2022, good postoperative recovery, discharged home on Hydrocortisone replacement with plans to be seen in Oncology outpatient clinic to start chemotherapy treatment.

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WD11

Gabapentin induced low cortisolÿ

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A 56 year old man with history of Hypertension, "Pre-diabetes" and Osteoarthritis was noted to have a low morning Cortisol of 31 nmol/l at 0912 hrs and <28 nmol/l at 0741 hrs on the first and 4th postoperative days respectively following a left total knee replacement. His regular medications were Amlodipine 5mg OD, Ramipril 5mg OD, Bisoprolol 3.75mg OD, Atorvastatin 20mg HS, Gabapentin 100mg TDS. Post operatively he was also given Zomorph 10mg BD with Oramorph PRN for pain control and Low Molecular Weight Heparin for Venous Thromboembolism prophylaxis. The patient did not receive any steroids peri operatively. Intra operatively blood pressure was consistently around 120/70 mmHg. Apart from an intra articular steroid injection 2 years before, he was not taking any steroid in any form. He reported no sickness/vomiting/dizziness. His postoperative pain was under control with opioids. On examination pulse was 63/mt, regular, BP 125/70mmHg (receiving his usual anti hypertension medications), Temperature 36.7 C, no altered pigmentation noted, capillary blood glucose was 5.8 mmol/l. Laboratory investigations showed Sodium 135 mmol/l (133-146), Potassium 4.4 mmol/l (3.5-5.3), Urea 5 mmol/l (1.7-7.1), Creatinine 74 umol/l (59-104). Without any steroid replacement, a stimulation test with Tetracosactide 250 microgram (Short Synacthen Test) was done on 5th postoperative day (in the evening) which showed normal adrenal response– 0 minute Cortisol 30 nmol/l, 30 minutes (post Tetracosactide) Cortisol 465 nmol/l. Adrenocorticotropic Hormone(ACTH) level was 6 ng/l (normal <47). Though a very low 9 am Cortisol would suggest hypocortisolism (in those not taking any steroids) and warrant immediate steroid replacement, the fact that the patient had an uneventful major surgery made us to look for another explanation. The normal adrenal response to the stimulation with Tetracosactide reassured us that we were not dealing with hypocortisolism. Most probably the Gabapentin was suppressing the stress response in our patient. Significant reduction in the plasma cortisol level have been noted in patients given Gabapentin one hour before surgery[1]. The likely explanation why the first morning Cortisol checked is that it was probably incorrectly requested or tested (The Cortisol printed just above the Full Blood Count in the Blood Sciences paper request form in our Trust, now replaced with electronic requests). The patient was reassured and discharged. ReferenceĆ1. Gabapentin-induced changes of plasma cortisol level and immune status in hysterectomized women; December 2014; International Immunopharmacology 23(2):530-6

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WD12

A danger of treating hypothyroidismÿ

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This 46 year old lady with no significant past medical history was referred urgently to the Endocrine Investigation Unit with a 9 month history of increasing lethargy and gradual weight loss of around 5 kg. Two months prior, she had been diagnosed with subclinical hypothyroidism and after commencing Levothyroxine, quickly lost another 5 kg in weight over a period of 6 weeks and had postural dizziness with systolic BP readings between 80 and 90 mmHg. She was having a normal menstrual cycle. She works as a Vet. Her father has Type 1 Diabetes and Coeliac Disease. On examination, she felt that her skin was more tanned than she would expect for the winter. Her dentist had commented on slight gum pigmentation. There were no pigmented scars. Blood tests in primary care showed sodium 129 mmol/l, potassium 4.9 mmol/l, fasting glucose 5.1 mmol/l and an undetectable 9am cortisol at <28 nmol/l. Thyroid function two months prior showed TSH 10.25mU/l (0.35-4.94 mU/l) and free T4 8.1pmol/l (8-19.1pmol/l). After commencing Hydrocortisone 10mg on waking and 10mg at 5pm, her energy levels and dizziness improved dramatically. ACTH (on Hydrocortisone) was 84ng/l (7-56ng/l) and adrenal antibodies were positive. She was informed of her diagnosis of primary adrenal insufficiency, Addison"s disease. She was provided with information on the condition and understands the steroid sick day rules. She was commenced on Fludrocortisone 50 mg daily and her Hydrocortisone dose was adjusted to 10mg on waking and 5mg at 5pm, with the suggestion that she may require an additional 5mg on more stressful or active days. She received preliminary steroid education with the Endocrine Specialist Nurse.

Discussion

This case illustrates some important learning points 1: Elevated thyroid stimulating hormone without signs of primary hypothyroidism can be a feature of adrenal insufficiency and may improve after glucocorticoid replacement. She had weight loss, where weight gain is more classically associated with hypothyroidism. 2: Although adrenal insufficiency was not considered in her case initially - it is important that it is confirmed or ruled out if suspected, before treatment of hypothyroidism, to reduce risk of precipitating an adrenal crisis. Her symptoms were likely exacerbated after commencing Levothyroxine due to increased cortisol clearance and increased metabolic rate. 3: The presence of related autoimmune conditions should be considered and in this lady"s case it will be important to reassess thyroid antibody status and need for continued thyroid replacement once her adrenal insufficiency has been addressed.

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WD13

Male infertility in CAH – a balance of risk?ÿ

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26 year old gentleman with classic salt-wasting CAH due to 21-hydroxylase deficiency was maintained on hydrocortisone 7.5mg+7.5mg+5mg along with fludrocortisone 100 mg OD. Due to inadequate biochemical control, his hydrocortisone was increased to 10mg+10mg+5mg initially, which was subsequently switched to prednisolone 5mg+2.5mg. His 17-OH progesterone continued to remain high (300-400 nmol/l) with suppressed gonadotrophins and a high normal testosterone suggestive of mostly adrenal origin of his testosterone (as shown in Table below). His testicular ultrasound demonstrated bilateral adrenal rests which were observed to be increasing in size on subsequent scans. His prednisolone was further increased to 5 mg+ 2.5 mg+ 2.5 mg. During this time, he has continued to gain weight and currently having a BMI of 32 Kg/m2. Given concerns regarding potential fertility, he was advised to have semen analysis with a plan for subsequent cryopreservation. Compliance with medication was potentially an issue. He was very concerned about his weight. Initial semen analysis demonstrated azoospermia. His biochemical markers are tabulated below along with changes in his glucocorticoid doses.

Conclusion

Biochemical Ćmarkers	2016	2017	2018	2019	2020	2021
FSH (IU/l)	0.1	0.1	0.3	0.3	0.3	0.3
LH (IU/l)	0.1	0.1	0.3	0.3	0.3	0.3
Testosterone Ć (nmol/l)	15.1	21.1	29.9	16.3	27.4	33.2
Androstenedione (nmol/l)	35		35		35	64
17-OH Ćproges-terone Ć(nmol/l)	647	305	458	143	363	494
HbA1c Ć(mmol/mol)	36	35	34		38	
Glucocorticoids	HC 7.5mgĆ +7.5-5mgĆ +5mg	HC 10mgĆ +10mgĆ +5mg	Pred Ć 2.5m-gĆ TDS	Pred 5mgĆ +2.5-5mg	Pred 5mgĆ +2.5-5mgĆ +2.5-5mg	Pred 5mgĆ +5mg

The occurrence of testicular adrenal rest tumors (TARTs) along with suppression of the hypothalamic-pituitary-gonadal axis are causes for reduced fertility. Treatment options of for TARTs are principally intensification of glucocorticoid therapy, leading to a reduction in the size of the TARTs by suppression of the ACTH secretion. In can be difficult to adequately suppress excess androgens without causing hypercortisolism. Further intensifications of glucocorticoid therapy might not be favourable option for our patient. Other options would include use of sustained release preparations of steroid, gonadotrophin therapy or future use of CRF antagonists, which are currently on trial along with surgical interventions such as mTESE.

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WD14

Adrenal insufficiency after unilateral adrenalectomy for Cushing"s Syndromeÿ

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We present a 38-year-old patient who had adrenal insufficiency following laparoscopic removal of 3.2 cm cortisol-secreting right adrenal tumour. His biopsy showed adrenocortical adenoma in keeping with Cushing's syndrome. He had a history of hypertension with suboptimal control despite being on 3 anti-hypertensives. His early morning cortisol (by GP to investigate secondary causes) were elevated and this prompted Endocrine referral. Clinical history and examination were suggestive of Cushing"s hence we performed midnight cortisol, 24hour urinary-free cortisol and cortisol day-curve which confirmed increased cortisol production. His CT adrenals showed a 3.2 cm enhancing lesion in right adrenal gland (absolute washout of 40%). His plasma metanephrines and paired renin and aldosterone were unremarkable. The working diagnosis at this point was a functioning atypical adrenocortical adenoma vs low-grade adrenocortical carcinoma so was planned for urgent surgery. He had 6mg dexamethasone during induction pre-surgery followed by 100mg IM QDS hydrocortisone post-operatively. Once he was able to eat and drink, his IM hydrocortisone was converted to oral 20mg/10mg/10mg and down to 10mg/5mg/5mg within 3 days of surgery. Steroid education was provided pre-discharge. We felt that he was metabolising the hydrocortisone too quickly, so we incremented his hydrocortisone to 10mg/10mg/5mg/2.5mg. We noted reduced absorption and rapid metabolism of the hydrocortisone, and this coincided with him reporting extreme tiredness. We switched his hydrocortisone to prednisolone 5mg. His cortisol pre-prednisolone at 12 months was 312 nmol/l and ACTH of 71 ng/l suggesting axis recovery. The cortisol and ACTH prior to this were showing inadequate axis recovery. We reduced his prednisolone by 1 mg every 2 weeks and when he was on 2 mg, his afternoon cortisol was 252 nmol/l suggesting a full recovery. We reduced it further to 1 mg and then stopped. Postoperative cortisol insufficiency following unilateral adrenalectomy for hypercortisolism is inevitable. It is mandatory to treat patients with glucocorticoid therapy intra-and post operatively. The duration of cortisol replacement is variable, and a longer follow-up is required to look into the recovery of the contralateral adrenal gland.

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Hydrocortisone day curve 1-month post-operation

Time (minute)	Cortisol nmol/l
0	18
30	106
60	467
120	234
180	117
300	50
420	206
540	84
570	94
600	95
660	140

Hydrocortisone day curve 4 weeks post dose adjustment

Time (minute)	Cortisol nmol/l	ACTH ng/l
0	17	7
30	44	
60	199	
120	329	<3
180	158	
240	91	
360	324	
480	124	
540	175	
570	301	

WD15

ACTH secreting Pancreatic NET - an unusual presentation – A Case reportÿ

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Neuroendocrine tumours are heterogenous group of diseases that can originate from any part of the gastrointestinal tract, bronchi, Thyroid and Pancreas. Tumours that arise from the endocrine Pancreas, on the islet of Pancreas, are called Pancreatic NET. Pancreatic NETs have an incidence of < 0.1 % per one million person and can lead to secretion of ectopic ACTH (1). Ectopic ACTH secretion accounts for 5-10 % of all patients presenting with ACTH dependent hypercortisolism: Small cell carcinoma of lung (SCLL) and Neuroendocrine tumours (NETs) accounts for majority of such cases (6). True CS can either be ACTH dependent or ACTH independent. ACTH dependent CS is uncommon with 1-2 cases/million of population/per year reported in the literature, with primary adenoma being source of ACTH in two-thirds of such patients. (7) Here we present a case of a 62-year-old female, who presented to Emergency department with two months history of personality changes, severe euphoria, polydipsia, dry mouth and severe peripheral oedema. Her family were quite concerned as she became very euphoric and suffered with more insomnia lately. She had walked 100000 steps in the 3 days prior to her admission. Her Euphoria rapidly progressed to a delusional state prior the admission. Our patient was even reviewed by the psychiatry team for her delusional state. Laboratory and imaging investigations revealed hypokalaemia, hyperglycaemia, ACTH dependant hypercortisolaemia. She was later diagnosed as Steroid induced psychosis by the psychiatry team. Our patient had minimal features of the typical Cushing"s syndrome at her initial present. Her Gallium PET scan detected a well differentiated 2.5 cm lesion in the pancreatic body/tail. The patient underwent a successful open distal pancreatectomy.

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WD16

Non-classic congenital adrenal hyperplasia (NCCAH)ÿ

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Case history
30-year-old female presented with subfertility for a year. She has had menarche at the age of 13 and regular periods for 2 years prior to commencing on hormonal contraception (initially COCP and then implant). Off contraception her menstrual cycles resumed after 6 weeks with a regular cycle length of 24 days. She has also suffered from generalised excessive body hair since young.
Investigations
Treatment and follow up: Following the diagnosis of NCCAH, she was commenced on Prednisolone 5mg once daily. She has been having positive ovulation tests with LH surges mid cycle. Patient and her husband had genetic testing and counselling.Ć• She carried 2 pathogenic variants in CYP21A2 gene confirming NCCAH Ć• Husband did not carry any pathogenic variant in the gene Ć• Low risk of conceiving a child with classic CAH (congenital adrenal hyperplasia). USS pelvis at the end of menstrual cycle showed an endometrial thickness of 4.6mm. Therefore, in order to improve her chances in fertility prednisolone was increased to 2.5mg three times daily. The plan is to reduce her prednisolone to 5mg once daily when she successfully conceives, and to continue during the pregnancy. She would require IV hydrocortisone during the delivery.
Conclusions and points for discussion
CAH is a group of autosomal recessive conditions, which has varying degrees of enzyme deficiency in the steroid synthesis pathway. CAH is characterised by increased plasma 17-hydroxyprogesterone levels. Patients with NCCAH normally present with hirsutism or subfertility in adolescence or adulthood, in comparison to classic CAH patients who present with salt wasting and virilisation in the neonatal period. NCCAH is treated with corticosteroid replacement while achieving an adequate balance between androgen suppression and the effects of excess glucocorticoid replacement. Patient education on medication compliance, risk of addisonian crisis and sick day rules are important in the management of

these patients. Treatment of affected women with corticosteroids reduce the degree of infant virilisation at birth on a female foetus. In NCCAH genetic testing (diagnostic on patient and screening on partner) is vital to identify their risk of conceiving a child with classic CAH. We did not do a synacthen test with 17-OHP levels as her levels were 76.9 nmol/l.

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	Initial investigations	Investigations post treatment
17-OHP	41.8 -> 76.9	10.5
Testosterone	2.5	0.7
SHBG	108	
Oestradiol	278	229
Progesterone	37	
LH	6.4	5.5
FSH	4.8	4.9
Cortisol	405	
Androstenidione	13.4	
DHEAS	6.7	
ACTH	22	
Prolactin	396	
TSH	3.29	
Free T4	14.2	

WD17

Cushing syndrome during pregnancy: A case presentationÿ

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A 26 year old 22 weeks pregnant woman was referred to the Endocrine team after she presented with high blood pressure without evidence of proteinuria. She had no past medical history and was newly diagnosed with gestational diabetes. On clinical examination, she had some clinical features consistent with hypercortisolism such as very prominent large purplish striae over her abdomen, bad facial acne, multiple superficial ecchymoses due to easy skin bruisability and excessive weight gain.She had abnormally high 24-hour urinary cortisol (3510nmol/24 - hour), undetectable serum ACTH level (<3ng/l) with loss of diurnal variability on cortisol day curve. Her early morning cortisol was inappropriately raised following both a 2mg and 8mg overnight dexamethasone suppression test being above 1000 nmol/l on both instances. Radiologically, she was found to have a left 3.8 x 3.1 x 3.8 cm lesion within the left adrenal gland on an MRI adrenals. She agreed for laparoscopic adrenalectomy at 26/40 gestational week. Histology confirmed adrenal cortical adenoma. She improved clinically after the procedure and was maintained on hydrocortisone replacement therapy until delivery. She gave birth to a healthy baby girl at 34 weeks and was progressively weaned off the hydrocortisone. The initial short Synacthen test post surgery showed inadequate response but improved on subsequent testing. Her hydrocortisone was eventually stopped after 8 months of slow weaning. This case highlights the difficulty in diagnosing Cushing's syndrome during pregnancy due to overlap of clinical features. Additionally, biochemical results are confounded by changes in the hypothalamic-pituitary-adrenal axis in normal pregnancy requiring careful interpretation of biochemical investigations.

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Workshop E: Disorders of the gonads

WE1

How to solve the Rubik's cube? A case of functional hypothalamic amenorrhoea in a low BMI female

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32 year old female presented to her GP following a first trimester miscarriage which consequently resulted in her experiencing secondary amenorrhoea for more than 9 months. Secondary amenorrhoea is defined as cessation of regular menses for 3-6 months or the cessation of irregular menses for 6-12 months. Her main concern was around her subfertility and dry skin. She started menarche at the age of 10 with regular monthly menses until her copper coil insertion 4 years ago. She had conceived spontaneously 2 months after removal of her copper coil. Her BMI has always ranged been 17-19 kg/m2 since the age of 16. She visits the gym regularly and eats <1500 calories per day. She is not on any medications or supplements. Blood test in clinic (Table 1): An MRI scan was performed and discussed in our MDM which confirmed no pituitary defect. DEXA bone scan showed bone mineral density to lie in normal range for age of patient. Despite improving her BMI (19.5 kg/m2) clinically she remained unchanged. There are multifactorial causes linked to secondary amenorrhoea. Functional hypothalamic amenorrhoea is a diagnosis of exclusion and accounts for 30% of cases. Current guidance focuses on nutrition and hormone replacement. During nutritional recovery the luteal phase is short with prolonged follicular phase resulting in longer menstrual cycles; this correlates with abnormal folliculogenesis. Interestingly when females modify intense activity and/or improve caloric intake they can also show a triad of symptoms described as "female athlete triad" (low energy, low bone density and menstrual dysfunction). Among those keen to conceive first line therapy involves pulsatile gonadotrophin-releasing hormone followed by gonadotrophin therapy and induction of ovulation. The choice of oestrogen substrate is unclear. To reduce foetal complications fertility services should only be offered when BMI is >18.5 kg/m2 and nutritional improvement is made. Evidence on cognitive behavioural therapy remains limited. The long-term risk to bone, cardiac function and fertility remains unknown.

Table 1: Blood results

		Normal range
FSH	4.3 IU/l	Follicular stage 2.4-12.6 Luteal stage 1.0-11.4
LH	1.9 IU/l	Follicular stage 3.5-12.5 Luteal stage 1.7-7.7
Oestradiol	<92 pmol/l	
Testosterone	<0.5 nmol/l	
DHEAS	6.2 mol/l	
Prolactin	349 mIU/l	
TSH	1.32 mIU/l	
T4	9.9 pmol/l	
T3	2.6 pmol/l	
9 am cortisol	409 nmol/l	
17 hydroxyprogesterone	<0.8 nmol/l	
IGF-1	23.4 nmol/l	10.2-40.7 nmol/l
Anti Mullerian hormone	17.2 pmol/l	
Beta HCG	<1 IU/l	

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WE2

47, XYY syndrome: hypogonadism and osteoporosis

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A male, born in 1957, with history of familial spinocerebellar ataxia, Type 2 diabetes (diagnosed in 1999), asthma, learning difficulties, chronic pancreatitis, recurrent falls, multiple low trauma fractures and osteoporosis was referred to Endocrinology Department in 2019. He sustained a right radial fracture at the age of 34 (1992), followed by comminuted right distal radius and Ulna styloid process fracture in 2002, Left and right Neck of Femur fractures in 2013 and 2014 respectively. DEXA scan in 2015 revealed Lumbar spine T score of -3.3 and one third forearm T-score of -4.1. He was started on oral bisphosphonates, calcium and vitamin D supplement. Unfortunately, he was intolerant to oral bisphosphonates. A repeat DEXA scan in 2018 showed a further 3.3% loss of bone density at lumbar spine. He subsequently sustained a left tibial plateau fracture in October 2018 which prompted a Rheumatologist review who suspected Klinefelter"s syndrome and referred to the Endocrinologists. He was on Fluoxetine, Gliclazide and Metformin. On examination his height was 182 cm, BMI 29.7, he had bilateral gynecomastia, sparse axillary and pubic hair, and hypoplastic small testes bilaterally. Laboratory investigations showed Hb125 g/l (normal 130-170), l MCV 90.1 fL (83-101), TSH 0.87 mU/l (0.35-3.50) FT4 11 pmol/l (8-21), negative coeliac screen, adjusted calcium 2.41 mmol/l (2.20-2.60), HbA1c 58 mmol/mol Vitamin D 19 nmol/l (50-120), 9 am testosterone 1.2 nmol/ (normal 6.7-25.6), FSH 38.1 IU/l(normal 1.0-12.0) and LH 15.8 IU/l (normal 0.6-12.1). His karyotype revealed 47 XYY. He is now on testosterone replacement, yearly intravenous Zoledronic acid along with calcium and Vitamin D supplement. 47 XYY, a disorder with extra Y chromosome, which occurs 1 out of 1000 males, is often undiagnosed due to nonspecific clinical features. The chromosomal anomaly is due to nondisjunction in meiosis II. Phenotypically the male could exhibit tall stature, macrocephaly, macroorchidism, hypoplastic scrotum, hypotonia, hyperteliorism, tremors, learning disability, behavioural problems, delayed speech and language development, infertility due to spermatogenesis impairment. Testosterone levels are usually normal, rarely low. ĆFurther reading Ć1. 47,XYY Syndrome: Clinical Phenotype and timing of ascertainment: Martha Z Bardskey et al; *J Paediat* 2013:163(4):1085-1094. Ć2. 47,XYY Syndrome and Male Infertility; Ina W. Kim et al: *Rev Urol* 2013(4): 188-196

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WE3

Polycythaemia related to exogenous testosterone administration

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This 60-year-old male was reviewed remotely for follow up in the general endocrine outpatient clinic having originally been referred for erectile dysfunction and low libido. He had a past medical history of hypertension and dyslipidaemia and was prescribed amlodipine and atorvastatin. On previous clinical assessments, he had increased muscle bulk, normal secondary sexual characteristics with testes measuring 15mls and 12mls. There had been no evidence of gynaecomastia. He worked as a gym instructor. The patient reported a long history of using testosterone, other anabolic steroids and tamoxifen for athletic performance enhancement, but described stopping these several years earlier. Serum testosterone concentration was low on serial measurements (1.0-7.2 nmol/l) with sex hormone binding globulin (SHBG) below the reference range. Gonadotrophins were consistently low (LH <0.1 IU/l – 0.9 IU/l, FSH <0.1 IU/l – 1.2 IU/l). Pituitary profile was otherwise within normal limits. The patient had undergone a CT head (due to contraindication to MRI) which demonstrated no evidence of pituitary pathology. Polycythaemia had been noted on serial testing with no genetic cause or other secondary causes identified following haematology specialty review. At a previous review, testosterone replacement was felt be to inappropriate due to the risk of cardiovascular and thromboembolic disease given the presence of polycythaemia (Haemoglobin 173-195g/l; Haematocrit 0.54-0.60L/l). However, testosterone replacement with a long-acting injected preparation had been subsequently initiated on a 14-weekly basis which the patient was receiving in the community. Up to date pathology results demonstrated polycythaemia (Haemoglobin 188g/l; Haematocrit 0.56L/l) and elevated serum testosterone (58.7 nmol/l). It was recommended that prescribed testosterone replacement was stopped and the rationale for discontinuation explained. The patient was concerned about deterioration in sexual function. Urgent haematological advice was sought, and venesection subsequently arranged. Testosterone stimulates erythrocytosis and replacement therapy can lead to polycythaemia. Increasing haematocrit concentrations can usually be managed by reducing the dose of testosterone replacement, increasing the interval between injections of long-acting testosterone preparations, or converting to a transdermal preparation. In cases where haematocrit is markedly elevated, haematological advice should be sought and, rarely, venesection may be required.

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WE4

Secondary Amenorrhea: Hypothalamic Amenorrhea an important cause to consider

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Hypothalamic amenorrhea is a diagnosis of exclusion. It accounts for 30% of cases of secondary amenorrhoea in women of reproductive age. It is caused by

abnormal signalling between the hypothalamus and the pituitary gland due to deficient pulsatile secretion of GnRH. This reduced secretion of GnRH leads to levels of LH and FSH that are insufficient to maintain full folliculogenesis and normal ovulatory ovarian function, with consequent oestrogen deficiency. There are many causes, including poor nutrition, stress, medications or excessive exercise. 22-year-old lady with history of low BMI was referred by her GP with secondary amenorrhea. History was significant for weight loss over the past 2 years although she had made efforts to improve this recently (BMI 16 kg/m2 initially, improved to 18 kg/m2). She also described weightlifting four times per week with lengthy sessions and cardiovascular exercise in-between. She was non-smoker and denied any drug abuse. Initial evaluation showed BMI of 18 kg/m2, normal prolactin (248 mu/l) but undetectable oestradiol level <92 pmol/l alongside inappropriately low gonadotropins (LH 3 IU/l FSH 6 IU/l). Thyroid function and anterior pituitary hormone profile were otherwise normal. There were no clinical manifestations of hyperandrogenism, and biochemical androgen levels were normal. Ultrasound showed normal appearances of female reproductive organs with no signs to suggest polycystic ovarian syndrome. On review by the endocrine team, we discussed the importance of achieving healthy weight gain, reasonable fat mass compared with lean body mass and adequate BMI as best management for hypothalamic amenorrhea and directed her towards psychological services via GP. Interval laboratory evaluation showed oestradiol 239 pmol/l, testosterone 1 nmol/l, Serum prolactin 303 mU/l, LH 8 IU/l, FSH 7 mU/l. Patient had resolution of her periods with appropriate diet and weight gain and was later discharged from further follow up.

Conclusion

It is important to thoroughly exclude organic and anatomic causes of amenorrhea before establishing the diagnosis of hypothalamic amenorrhea. Optimising weight and reducing excessive exercise can be challenging and may often require co-ordinated input from psychological services, endocrinology, primary care and wider family members. Hormone replacement therapy has a role when HA is prolonged, or the underlying cause cannot be addressed.

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WE5

A challenging case of hypogonadismÿ

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Gonadal dysgenesis with *DAX1* duplication as the cause of XY disorder of sexual development is a rare condition. Duplication of this causes male to female sex reversal while mutation or deletion can cause adrenal hypoplasia congenita with hypogonadotropic hypogonadism. We present a case of 37-year-old lady who was referred to endocrine clinic with ongoing symptoms of fatigue. She was diagnosed with 46 XY gonadal dysgenesis when she presented with groin swelling at the age of 1 year and had bilateral gonadectomy which showed prepubertal testis at one side and short fallopian tube containing a streak gonad on the other side. She had a normal uterus and plasma testosterone response to hCG stimulation test indicated the presence of testicular tissue. She had a reduction surgery for clitoromegaly at the age of 12 years and puberty was induced with exogenous oestrogen. She has been on hormone replacement therapy since puberty. Chromosomal microarray test was performed to look for the cause of XY DSD and she was found to have *DAX1* duplication (NROB1) gene and chromosome 46 XY inversion 9 (p11q21). Her symptoms of fatigue have been ongoing with marked exhaustion even in daily activities. She had surgery for repair of incarcerated left femoral hernia 2 years ago which showed part of uterus and fallopian tube in the hernia sac. She has been on different preparations of oestrogen replacement therapy with no significant improvement in her symptoms. She was also recently given the possible diagnosis of ME/CFS. Recently, she has been in touch with Daisy Network and found the support helpful emotionally. She is a non-smoker, takes minimal alcohol and her current BMI is 37.5 kg/m2. She is euthyroid, euadrenal and her current blood test showed FSH 13.5, LH 8.6, oestradiol 127. She is currently on oestrogel 6 pumps daily (increased by another department) and utrogestan 200 mg at night for 2 weeks every month. This case describes the challenging management of rare condition of hypogonadism in which ongoing symptoms of fatigue are present despite high dose of hormone replacement therapy. Whether the symptoms of fatigue are due to hormone deficiency related to *DAX1* duplication or simply related to ME/CFS is unclear. The case also highlights the need for multi-disciplinary approach including medical and psychological support.

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WE6

Role of sonography in the diagnosis of primary amenorrhea - benefits vs pitfallsÿ

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A 17 year-old female was referred to Endocrinology with primary amenorrhoea and arrested puberty (B4 PH4 AH2). She reported breast development in line with her peer group and had experienced a single "show" of vaginal spotting aged 15 years. Although guidelines recommend baseline pelvic USS in the investigation of primary amenorrhoea, it generally only adds value in females with high LH +FSH and abnormal karyotype; indeed, it may raise undue concerns of uterine (Mullerian) agenesis when the prepubertal uterus is too small to be visualised[1], and a recent review has explicitly discouraged this practice[2]. However, in this case, baseline USS was useful in guiding us to the diagnosis of 46XX gonadal dysgenesis, whereas the history and Tanner staging had initially led us to consider premature ovarian insufficiency instead. Given her breast development was satisfactory, the usual target of classical pubertal induction through incremental Estradiol therapy could be set aside; instead, the aim was to optimise uterine development to maximise her chances of successful egg-donation-parenthood in later life. Over a period of 4 years, her Estradiol dose was progressively increased from 0.5 mg alternate days to 3 mg daily, with serum oestradiol rising accordingly. As of the latest visit, she is close to fulfilling our criteria for the introduction of a progestogen, in that she has full breast development, her uterus has a mature configuration, with dimensions close to the median for nulliparous emgonadal females and thickening endometrium, along with a satisfactory oestradiol level. She has not yet experienced any bleeding and the endometrium is not excessively thickened so we plan to continue Estradiol monotherapy until this occurs, or there is no further increment in uterine dimensions on USS.

Results		Normal Range
FSH	53.2 IU/l	1-10
LH	22.5 IU/l	1-12
Oestradiol (MS)	32 pmol/l	
adjusted Calcium	2.49 mmol/l	2.20 – 2.60
SHBG	40 nmol/l	14-110
Testosterone	1.7 nmol/l	<2.8
TSH	1.93 mU/l	0.3 – 4.7
TPO-Ab	10 kU/l	<34
Ovarian & GPC Abs	negative	
Karyotype	46XX	

USS: prepubertal uterus (40mm length x 7mm AP x 19mm transverse diameter), with a thin endometrial stripe; ovaries not visualised.

E2 dose/day mg	0.5	1.0	1.5	2.0	3.0
FSH IU/l	47.0	46.8	34.1	25.7	17.4
E2 pmol/l	112	216	238	282	344
Uterus mm		64 x 22 x 30	64 x 26 x 40		64 x 32 x 45
Endometrium mm		"normal"	8.2		6.2
DEXA Ćz-score				-1,6	

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WE7

Isolated Hypogonadotropic Hypogonadismÿ

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17 year old male was referred by GP with short stature and delayed development of secondary sex characteristics.

History

He was born at full term with a bodyweight of eight pounds and normal development till adolescence. He is the second out of three children and as his parents and siblings entered puberty at expected ages and he has not suffered from the chronic illness make constitutional delay of puberty or functional hypothalamic hypogonadism less likely. He is working as a chef and reported no problem with a sense of smell.

Examination

On examination, his body weight was 73.6 kilograms with a height of 159.3 centimeters with a BMI of 29. The baseline pubertal staging was Stage 3 Tanner 2

with four milliliters testes, five centimeters penis, minimal coarse hair at the base of the penis, and no evidence of hair growth in other parts of the body.
Investigations
ACTH (0-46) :25 ng/l TSH (0.34-5.6) :1.55 mu/l T4 (7.9-13.6) :12.3 pmol/l FSH :1.2 iu/l LH. :0.6 iu/l Testosterone. :1.8 nmol/l IGF-1 :26.5 nmol/l Prolactin :127 mu/l Cortisol :378 nmol/l HCG :<0.5 17-OH :<0.2 Bone age on radial X-ray: Chronological age - 17 years and 6 months, Bone age -15 years. MRI pituitary: small anterior pituitary gland, no adenoma. Genetic testing: Kallmann syndrome 5 genes panel - no mutation.
Treatment
Puberty induction was started with intramuscular testosterone (Sustanon) injection of 50 mg for four months followed by 75 mg for four months followed by 150 mg for four months until the full dose of 250 mg. He was aware that family planning involves discontinuation of testosterone injection and spermatogenesis stimulation with HCG/FSH injections or TESE (Testicular sperm extraction). There was an improvement in testicular volume (8 milliliters), penis size, and density of pubic hair (Tanner stage IV) approximately twelve months of treatment, and a trial of discontinuing the testosterone was made to access reversibility of hypogonadism. Unfortunately, the patient missed appointments and was reviewed twelve months later. The repeat blood tests after stopping the treatment showed testosterone of 1.6 with FSH 0.9 iu/l and LH of 0.8 iu/l. Diagnosis of permanent hypogonadotropic hypogonadism (likely congenital) was made and intramuscular testosterone (Sustanon) was restarted. The treatment was changed to twelve weekly testosterone undecanoate (Nebido) injections when there was a good level of testosterone.

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WE8

Central hypogonadism in a man with a Rathke's cleft cystÿ

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A 57 year old man presented with a 2 year history of erectile dysfunction and loss of libido. He was able to achieve erections but could not maintain them for intercourse. This was causing considerable strain on his marital life. He also complained of lethargy and general fatigue. His past medical history included diet-controlled type 2 diabetes and hypertension. He was an ex-smoker with a 40 pack year history and drank socially. He was an office worker. He had 3 grown up children. There was no history of illicit drug, opiate, steroid or over the counter medication use. Serum testosterone checked at his GP was 5.3 nmol/l, which prompted endocrinology referral. On examination, his BP and CBG were normal. He was overweight (BMI 28) with central obesity. He had a post-pubertal voice, a full beard and normal male pattern hair development. There was no gynaecomastia, goitre, or other peripheral stigmata of endocrinopathy. He had a normal adult-sized penis. Both testes were palpated in the scrotum and testicular volume was 15 ml bilaterally. Baseline bloods showed a normocytic anaemia with Hb 121, normal PSA, renal and liver function, and HbA1c 51 mmol/mol. Endocrine blood panel done at 9 am and in a fasting state showed a low serum testosterone of 5.7 nmol/l, with normal SHBG and inappropriately normal gonadotrophins (LH 8.3 IU/l and FSH 9.0 IU/l). The rest of the pituitary profile was normal. A biochemical diagnosis of central hypogonadism was secured. MRI pituitary was the next logical step and showed a non-enhancing T1 hyperintense focus in the anterior pituitary gland on sagittal sequence, consistent with an intrasellar Rathke's cleft cyst with proteinaceous content. The diagnosis was therefore central hypogonadism due to Rathke's cleft cyst. Pituitary MDT recommended an observational approach with serial pituitary imaging. Testosterone replacement therapy in the form of transdermal gel was opted by the patient. Tostran 2% gel 20 mg once daily was started and the dose gradually uptitrated every 3 weeks, aiming for testosterone in the mid normal range. Symptomatic benefit and target testosterone level were achieved with a Tostran 2% gel dose of 50 mg OD. PSA and haematocrit monitored every 3-6 months initially remained normal. Investigation for anaemia showed iron deficiency, which was treated with iron supplements. At the 1 year follow up, the patient was fully satisfied with his sexual function, energy levels, vitality and mental well being.

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WE9

Primary female hypogonadismÿ

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Female with primary hypogonadism have inadequate function of the ovaries, with impaired production of germ cells (eggs) and sex hormones (oestrogen and progesterone). We recently came across a 22-year old female with short stature in childhood and adulthood she received growth hormone treatment (due to arrested puberty) between 3-5 years of age and further treatment at age of 10 years. She had history of IUGR, primary amenorrhoea, sensorineural deafness, congenitally missing teeth, anxiety, depression, severe vitamin D deficiency & secondary hyperparathyroidism. Examination shows height was 142.1 cm (4ft 7in) and weight 37.8 kg. Breast development was good (Tanner stage 4/5). Very mobile fingers and toes noted. Investigations showed significantly low oestradiol <60 pmol/l, and the LH was 28.6IU/l, FSH 52.6IU/l. The AMH level was low at 0.7 nmol/l. Ovarian antibody was negative, TFTs were normal. In past she had chromosomal analysis which showed normal karyotype. Imaging suggested her bone age was corresponding to 17 years and the USS uterus did not show any major abnormality (except slightly small uterus) It's quite like she has Perrault syndrome, though this need to be confirmed by genetic analysis, which is awaited. She was started on evorel (oestrogen) patch 25 mg and plan is to optimise the dose until she gets period and then she could be on the HRT. She was also started on vit D due to significantly low level 13 nmol/l. She remains under the follow up of endocrine team. Perrault syndrome is an inherited autosomal recessive condition characterized by sensorineural hearing loss and abnormalities of the ovaries. Neurological problems may also occur. The condition has several genetic causes.

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WE10

A rare case of male hypogonadismÿ

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A 29 year old gentleman presented to Urology with scrotal pain. He had renal calculi but examination also revealed small testicles for which he was referred to Endocrinology. He achieved normal developmental milestones. He had no history of mumps or testicular torsion or surgery. He had no history of hypospadias or undescended testicles. He was not on any regular medication and denied anabolic steroids use. He reported a normal sense of smell. His body weight was 72 Kg with height 1.75 m and BMI 23.5. Blood pressure was normal. He had full male secondary sexual characteristics with stage IV Tanner pubic hair and normal external genitalia. Testicular volume was 3-4 ml bilaterally. There was no evidence of gynaecomastia. He scored 1/10 on ADAM questionnaire. Blood results showed raised LH (16 IU/l~ reference range: 0.6-1.2) and FSH (43 IU/l ~ reference range: 1-12.1) with low Testosterone (8.8 nmol/l~ reference range: 7.0-27.0) and normal SHBG at 34 nmol/l (reference range:13.5-71.4). Prolactin was 161 mU/l (reference range 73-407) and oestradiol was 118 (reference range : 40-162). Thyroid function was normal. Semen analysis revealed azoospermia. His Haemoglobin, liver and renal functions were normal. Interestingly Karyotype analysis revealed SRY positive,46 XX Testicular disorder of sexual development (DSD). After appropriate counselling, he was offered Testosterone gel replacement and referred to a Clinical Geneticist. SRY positive 46 XX testicular DSD is seen with frequency of 1: 20,000 in male population and usually arises from paternal meiotic recombination event leading to translocation. The presence of SRY gene and absence of major regions of Y chromosome still leads to the expectance of completely masculinised phenotype. Patients often only present in adulthood with infertility but may also exhibit hypogonadism or gynaecomastia. This case highlights the role of karyotyping in patients with primary hypogonadism and azoospermia.

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WE11

Anabolic steroid induced hypogonadism: Challenge to endocrinologists with expanding anabolic steroid users' websitesÿ

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40year old bodybuilder was re-referred to clinic with low mood, reduced libido, poor morning erections and fatigue. His past medical history included hypogonadal hypogonadism secondary to anabolic androgen abuse, mental health disease and personality disorders. He had undergone breast reconstruction surgery for bilateral gynaecomastia secondary to anabolic steroid use despite taking precautionary tamoxifen injections as per peer groups' advice. Previously, he was lost for clinic follow up after two months of treatment with testosterone

enanthate injections after diagnosis in 2011. He continued on illegal testosterone supplements and had multiple hospital admissions later with cocaine induced cardiac vasospasm and seizures. His mental health worsened and was started on antipsychotics and subsequently, he discontinued anabolic steroids completely for last 2 years. Mood, libido, and energy levels did not recover and hence re-attended endocrine clinic after 11 years through GP referral.ĆInvestigations: HCt-0.463 LH-1 IU/l (1.5-9.3) FSH- 0.9 IU/l (1.4-18.4) Tetosterone-1.8 nmol/l(9-34.7) SHBG-9 nmol/l (17-66) Prolactin-1865 mIU/l (50-400) TSH-1.2 nmol/l (0.5-4.5) Cortisol- 467 PSA-0.17 mg/l Bone profie, U&E and LFT- Normal. Testogel was started on agreement of total avoidance of anabolic steroid use and regular monitoring for adverse effects. ĆLearning Points: Ć1. Anabolic abuse is now common among general population for physical aesthetic improvement with increased lean mass and reduced body fat. Ć2. Anabolic steroids induce feedback suppression of the hypothalamic-pituitary-gonadal axis resulting in inhibition of pulsatile gonadotropin-releasing hormone release and decrease in luteinizing hormone and follicle-stimulating hormone Ć3. Researchers has classified 4 types of anabolic steroid misusers: (1) the Expert type; (2) the YOLO (You Live Only Once) type; (3) the Athlete type; and (4) the Wellbeing type. Ć4. Knowledge on various regime of anabolic steroid use would help the endocrinologists to gain the trust and to improve the patient engagement in the treatment. Ć5. Information available on anabolic steroid users' websites provides the users with advice on possible adverse effects and medications to minimize those. Ć6. Anabolic steroids cause testicular atrophy, infertility, gynaecomastia, and low endogenous testosterone which are self-managed by use of hCG, SERM and AI. Ć7. Aromatase inhibitors and SERMs potentiate pituitary gonadotropin secretion and therefore increases endogenous testosterone release by inhibiting oestrogenic negative feedback. Ć8. hCG binds to LH receptor resulting in increased endogenous testosterone production. Ć9. Topical testosterone should be preferred for initiation of treatment, whereas gonadotrophin therapy is only recommended when fertility is desired in men with secondary hypogonadism

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WE12

"Is there a right time to stop hormone replacement therapy?"ÿ

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A 59-year-old woman with 46XY complete androgen insensitivity syndrome was referred back to our service. She also has history of hypertension and migraines. She was gonadectomised at the age of 15 years and treated with Ethinylestradiol. She married and was able to have enjoyable sex without the need for vaginoplasty or dilators. However, at 54 years she was firmly advised to stop Ethinylestradiol due to satisfactory bone density and "risks of HRT outweighing benefits", and so her treatment was progressively reduced to zero over the course of a year and she was discharged from follow-up. She immediately developed pronounced severe vasomotor symptoms (sweating and flushing) that did not abate over time, along with other adverse clinical features, including scalp hair loss, palpitations, arthralgia, urinary frequency, fatigue, and vaginal dryness that almost immediately ended her sex life. Overall, her quality of life went from "good" to "poor". A repeat DEXA scan showed osteopenia at the hip with normal density at spine (T score of -1.7 and -0.7 respectively). It was explained to her that the landmark WHI study (2002) found no excess risk of breast cancer in women lacking a uterus on oestrogen-only HRT. Moreover, whereas the synthetic oestrogen Ethinylestradiol is associated with increased risks of hypertension, migraine and venous thromboembolism, these risks are far lower with native 17, beta Estradiol (E2), particularly if given transdermally. She was therefor started on Estradiol patches along with supplementary vaginal oestrogen for vulvovaginal atrophy, and also referred to community gynaecology to assess whether resumption of penetrative intercourse might be feasible. In Endocrinology, it is common practice to consider withdrawal of HRT for hypogonadal women in their mid-50s. However, it is crucial to deliver the right message, which is "We really wanted you to continue taking HRT until now, but from this point onwards, the choice is yours based upon your current risk benefit profile and quality of life issues", rather than "You"re 54 years" old and so it's definitely time for you to stop HRT.

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WE13

Reversible hypopituitarism in a young male athleteÿ

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Negative caloric balance and low body weight can impair pituitary function. This syndrome is well recognised in women, but it is less often diagnosed or considered in men. We present the case of a 16-year-old male who presented with increasing tiredness, bloating and inability to focus over a period of 3 months. He had been involved in regular sporting activities over last few years recently increased the physical activity focusing on fitness with a calorie deficit diet leading to significant weight loss over a period of 3 to 4 months. He had a normal childhood and satisfactorily achieved all his developmental milestones. He entered puberty at approximately 12 years of age and developed normal male secondary sexual characteristics with normal sexual functions. He was 180 cm tall and 55.25 kg initially with a Body Mass Index at the 6th centile for his age. On examination, he had Tanner stage 5 sexual development, fully descended testicles bilaterally which were soft, 15ml in volume. He shaved regularly and noticed no change in his body or facial hair volume. His had normal sense of smell. His initial pituitary profile showed pituitary dysfunction and is summarised in table 1. His pituitary MRI was normal and baseline investigations ruled out chronic illness. His DEXA scan showed normal bone density and Vitamin D levels were satisfactory. He was given advice to reduce his exercise down to maximum 150 to 200min moderate physical activity per week and increase his caloric intake with the assistance of a dietician. He also commenced 50 micrograms of levothyroxine. His weight was carefully monitored, and this has improved gradually up to 76 kg over the next 8 months with recovery of pituitary function. The pituitary profile changes are summarised in table 1. This case highlights how hypopituitarism should be considered as a cause of fatigue in male athletes and recovery of hypothalamic pituitary axis following appropriate dietary and lifestyle modifications.

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Table 1 Pituitary Function Test Results

Test	Before Treatment	After Treatment	Reference Range
FSH (IU/l)	2.0	1.5	1.4 - 18.1
LH (IU/l)	<0.5	4.0	1.5 - 9.3
Total Testosterone (nmol/l)	1.8	19.7	7.9 - 24.7
TSH (mIU/l)	1.06	1.87	0.48 - 4.17
Free T4 (pmol/l)	7.8	13.0	10 - 20
Free T3 (pmol/l)	3.2	4.8	4.7 - 7.2
IGF-1 (nmol/l)	27.1	42.7	23.0 - 70.0 (age adjusted)
Prolactin (72 mIU/l)	72	183	45 - 375
Cortisol (nmol/l)	568	N/A	

WE14

ABSTRACT WITHDRAWNÿ

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

WF1

Osteoporosis secondary to recurrent hyperparathyroidismÿ

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A 72 year old lady presented to Endocrinology in 2001 with primary hyperparathyroidism and had a parathyroid adenoma resected, resulting in normocalcaemia. In 2006, she developed mild hypercalcaemia (2.61-2.71 mmol/l) and underwent extensive investigations for recurrent PHPT. Parathyroid localization studies, including FDG PET, failed to identify any adenoma. The patient declined bilateral neck exploration and she was managed conservatively. A DEXA scan showed evidence of osteoporosis at the spine (T score -2.9) and normal bone mineral density (BMD, T score -1.0) at the hip. She was treated with annual IV zoledronic acid for five years. During this time, her serum calcium normalized, and she was discharged to primary care in 2011. In 2021, she was re-referred to secondary care with persistent hypercalcaemia (~2.67 mmol/l). A renal tract ultrasound showed no evidence of nephrocalcinosis. There was no history of fragility fracture. A repeat DEXA scan showed a T-score of -1.9 at the spine, -1.3 at the hip and -4.2 at the left radius. Her FRAX score revealed a 10-year probability of a major osteoporotic fracture at 16% and that of a hip fracture at 3.6%. With regards to other risk factors for osteoporosis, she stopped smoking 2 years ago, after having been a lifelong smoker. She has a BMI of 23.67 kg/m2. She was recently diagnosed with seropositive rheumatoid arthritis (RA) and is on treatment with methotrexate. She is awaiting knee replacement surgery for osteoarthritis (OA). She also has a known background of upper lobe lung fibrosis secondary to previous pneumonia. Her regular medications include methotrexate, folic acid, sulfasalazine and morphine sulphate. She receives regular intra-articular glucocorticoid injections for OA. Due to frequent flares of RA requiring courses of oral glucocorticoids, treatment with biologics is being consider-edĆQuestions:

1. A T-score of -4.2 at the radius in the context of PHPT is an indication for parathyroidectomy. Other risk factors for low wrist BMD could be RA and GC use. Is there a need for surgery if previous investigations failed to localize any adenoma and the patient is not keen on neck exploration?
2. As per the FRAX score, treatment for osteoporosis is not indicated as per NOGG 3. In patients with PHPT with osteoporosis who do not undergo surgery, denosumab is considered. However, our patient is not a candidate because of i) lung fibrosis and ii) biologics therapy for RA. Denosumab is also unlikely to reverse low radius BMD

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WF2

Secondary osteoporosisÿ

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Osteoporosis is estimated to effect more than 3 million people in UK and secondary osteoporosis accounts for about 30% of women and 55% of men with vertebral fractures. There are many causes of secondary osteoporosis, such as endocrine, gastrointestinal disorders, steroid use, as well as immobility, obesity, bulimia and anorexia nervosa. We present a case of Osteoporosis secondary to anorexia nervosa.77 year"s old lady initially referred to bone clinic at the age of 46 with vertebral fractures with evidence of osteoporosis on DXA scan. Initially managed with IV pamidronate, vertebroplasty and lidocaine injections at painful sites. With no significant improvement in bone DXA scan, she was commenced on trial for teriparatide with some improvement but with considerable side effects (nausea) which was eventually stopped after 18 months. With further decline in bone density, she was initiated on Strontium Ranelate and raloxifene, IV zoledronic acid and eventually currently on subcutaneous denosumab. During this time, she also sustained variable vertebral fractures and limited mobility due to back pain. Most recent DXA Scan showed a T score in the spine of -5.2 and a Z score of -3.4, this is a loss of 4% bone density since her last scan in August 2017, there was a T score in the hip of -3.3 and a Z score of -1.7, this is an increase of 2.4% since her last scan. She has previously been supported with dietician and psychological support with regards to her anorexia nervosa, but she is still struggling with maintaining healthy weight of 36 kg.

Conclusion

Secondary osteoporosis due to Anorexia nervosa can prove to both challenging with treatment options and the individuals needs of the patient. There are limited resources such as the eating disorder service, the patients have a poor body image due to the height loss, which in turn leads to feeling full easily as the organs are restricted. Difficulty in carrying out daily household tasks and the guilt associated with it being self-inflicted.

Low oestrogen in anorexia nervosa secondary to hypothalamic dysfunction can lead to bone loss. Healthy weight gain is the most important aspect of management with multidisciplinary approach involving psychologist, dietician and endocrine team.

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WF3

Bisphosphonate treatment failure in a lady with osteoporosisÿ

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A 72 year old lady was referred after recurrence of fragility fractures, despite being on bisphosphonate therapy for 10 years. She had 2 low-impact falls in 2020 and 2021, which resulted in hip and right distal femur fractures respectively. She had been compliant on alendronic acid 70mg once weekly since 2012, when she was diagnosed with osteoporosis at the age of 62, after sustaining 2 fragility fractures of the distal radius and elbow after separate low-impact falls. DXA scan at the time showed a left femur total T score of -3.5 On review, she confirmed adherence to alendronic acid. She did not feel she was losing height. Her appetite was unremarkable and she did not have any pain or constitutional symptoms. She was an ex-smoker with a 50 pack year smoking history. She drank alcohol occasionally. She had 2 children and did not report any menstrual issues pre-menopause. Her menopause was at the age of 48. There was no parental history of hip fracture or osteoporosis. She was mobile with a frame Her past medical history included polio as a child, COPD (diagnosed in 2016), and hypertension. She had been on an inhaled steroid since her COPD diagnosis and has had at least one 5-day course of oral prednisolone for COPD exacerbation per year On examination, her weight was 70 kg, height 1.67 m, and BMI 25 kg/m^2. There was no kyphosis or vertebral tenderness on palpation Baseline bloods showed a normal full blood count, renal, liver and thyroid function. Bone profile was normal and she was vitamin D replete. ALP was mildly raised at 134. Coeliac screen was negative. There was no paraprotein on myeloma screen. Bone turnover marker, CTX was within normal limits A repeat DXA scan showed a left hip bone density in the osteoporotic range with a T score of -3.5. Vertebral fracture assessment (VFA) from L5 to T4 did not reveal any definite fractures A diagnosis of bisphosphonate treatment failure was therefore made She was referred to the metabolic bone MDT for initiation of second line osteoporosis medication Potential drugs that would be considered include denosumab and teriparatide.

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Workshop G: Disorders of appetite and weight

WG1

GLP1RA therapy in Bardet-Biedl syndromeÿ

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Background
Bardet-Biedl syndrome (BBS) is a rare genetic condition characterised by ciliary protein dysfunction leading to multi-organ damage. Patients with BBS can suffer from hyperphagia and severe obesity from childhood and associated weight-related comorbid diseases such as type 2 diabetes and hypertension. However, the optimal weight management strategy and response to weight loss pharmacotherapy is unknown.
Case presentation
We present a case of a woman aged 28 who attended our weight management service with a history of hyperphagia and obesity since early childhood. Her body mass index (BMI) was 37.9 kg/m2 on presentation. She also had a history of type 2 diabetes, hypothyroidism, acanthosis nigricans, hypertension, polycystic ovarian syndrome, and retinitis pigmentosa. A clinical diagnosis of Bardet-Biedl syndrome (BBS) was suspected, and genetic testing by Sanger sequencing confirmed homozygous c. 1599_1602del p. (Thr53411efs*21) in the BBS10 gene (12q21.2). Management was focused on weight reduction with dietitian input. A trial of canagliflozin achieved initial weight reduction followed by rapid weight regain. Canagliflozin was stopped and Liraglutide was subsequently initiated. Liraglutide resulted in significant weight loss over a five-month period with reduction in BMI to 33.5 kg/m2. Following patient preference, Liraglutide was switched to Semaglutide for the convenience of once weekly injections. Following 19 months of treatment with Semaglutide, there was further weight loss, achieving a BMI of 24.3 kg/m2.
Discussion
GLP1RA therapy in our patient with BBS led to a significant total weight reduction of 33% within 30 months of treatment. Long-term weight maintenance and metabolic benefits of continued GLP1RA therapy remain to be seen.
Conclusion
We report significant weight reduction utilising GLP1RA therapy in a patient with genetic obesity due to BBS. Liraglutide and Semaglutide were associated with substantial reduction in body weight. This provides a novel therapeutic approach for obesity management in patients with rare genetic disorders such as BBS.

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WG2

Bariatric surgery in lady living with HIV: Safe and effective operation?
ÿ

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Introduction
Bariatric surgery was shown to treat obesity and decrease cardiovascular risk such as metabolic syndrome, diabetes, and hypertension. In individuals living with HIV, bariatric surgery can alter oral bioavailability of anti-viral therapy through its impact on the intestinal pH, intestinal transit time and first pass mechanism. This can have adverse impact on CD4 count and viral load (VL). Nevertheless, numerous studies highlight that bariatric surgery does not have any short-term complications on individuals receiving ART and one study showed that showed that 70% of patients had undetectable VL with correct ART kinetic parameters six months after the operation.
Case report
A case of 49-year-old African female with HIV with excellent compliance to antiretrovirals. She is known to have Type 2 diabetes mellitus controlled with tablets, liver cirrhosis, hypertension, and endometriosis. Unfortunately, over the years, she developed gross obesity with body mass index (BMI) of 52.08 kg/m2 and weight of 148 kg. Prior to bariatric surgery, she had poor glycaemic control with HbA1c of 8.4%. Her HIV was controlled well with Raltegavir and Trurada and her CD4 count was >200 with undetectable VL. She underwent sleeve gastrectomy and did not experience any post-operative complication. 4 months post-operation, she lost 28 kg, lowering her BMI to 38.62 kg/m2. Her diabetes control improved with HbA1c of 5.5% with glycated haemoglobin of 37% and no longer required diabetic medications. Despite bariatric surgery, her VL remained undetectable with HIV RNA below 1.30 and maintained CD4 count above 200.
Conclusion
Despite the risk associated with bariatric surgery, our case report clearly showed that bariatric surgery can be safe and effective in individuals living with HIV. Further research is needed to establish (i) whether there is ethnic variation in relation to the outcome (ii) if certain antiretroviral medication is well absorbed with bariatric surgery (iii) and whether genetic variation may have role. Nevertheless, such patients will require close monitoring to ensure adequate viral control.

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Workshop H: Miscellaneous endocrine and metabolic disorders

WH1

A rare cause of hyponatremia uncovered slowly in the coldÿ

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Introduction
Hyponatraemia is a common electrolyte abnormality seen among hospitalised patients. We describe below, an inpatient seen with severe hyponatraemia.
Case description
71yr old gentleman with no co-morbidities, admitted with acute confusion and slurred speech. Physical examination: Observations: Temperature 35C, heart rate 53/min, otherwise stable. GCS 15/15, no focal neurology except slurred speech and broad-based gait. Investigations: ECG: Sinus bradycardia, 47/min with PR-313ms, CXR-unremarkable CT head-nil acute. Hb 119g/l, WCC 3.0x10^9/l, platelet 120x 10^9/l, CRP 10mg/l Na 109 mmol/l with other electrolytes, renal and liver function tests within normal limits. Stroke team review- Treated with thrombolysis for left MCA stroke. Further investigations- MRI brain and carotid Doppler excluded stroke. During ward round, he was examined and noted to be euvolemic and so fluid restricted to <1.5L/day and further test related to hyponatraemia requested. Cardiologist also reviewed for bradycardia and advised he may need a pacemaker if PR prolongation persisted. Haematological investigations for pancytopenia were unremarkable.
Results
Serum cortisol 549 nmol/l; Na 112 mmol/l; osmolality 235mOsm/kg Urine osmolality 481mOsm/kg; sodium 30 mmol/l TSH 45mu/l, FT4 4pmol/l Next day, his BP dropped to 68/46mmHg with minimal response to fluid challenge, blood sugars remained normal, sodium had improved to from 109 mmol/l to 112 mmol/l, and was also given stat dose of Hydrocortisone(100mg) intravenously but no significant improvement in his BP noted. He was then commenced on 0.9%NaCl 8-hourly with electrolytes monitored daily. He was started on Levothyroxine 50micrograms a day after discussing with endocrinology team. Patient remained stable but with confusion and no improvement. On 7th day, TSH worsened (54.4mu/l and FT4-5.8pmol/l). Levothyroxine was increased to 75micrograms a day and, sodium continued to increase gradually (109—112—115—116—117—119—118). On the dawn of 8th day, crash call was put out as patient became unresponsive, GCS 3/15, with compromised airway, BP-68mmHg (systolic), hypothermic (30.3C), bradycardic (36/min), normal blood glucose. His airway was secured, resuscitated with intravenous fluids, Hydrocortisone 200mg stat, and transferred to ITU for intubation and vasopressor support. He was started on intravenous Liothyronine 20 mg TDS, and then switched to oral levothyroxine after one week. His TFTs improved gradually (45–54.4–95.4–12.8–9.8).
Questions/Discussion
Was this Myxoedema coma? Why did it happen after one week of being on Levothyroxine? Does hypertonic saline have any role in hypothyroidism related hyponatraemia? MRI head done 2weeks into admission was reported as central pontine myelinosis. Why did this happen in spite of gradual increase in sodium levels?

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WH2

Postpartum Hyponatremiaÿ

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Background
Severe hyponatremia can be associated with oxytocin infusion. The incidence of hyponatraemia after oxytocin is around 5%. There are reported cases of serious neurological complications including seizures, coma and maternal death.
Case report
A 37-year-old female with known partial central diabetes insipidus following a head injury was established on Desmopressin nasal spray 10 mg twice a day. She had an uneventful pregnancy on the same dose. For delivery, she was commenced on Oxytocin infusion and eventually underwent a caesarean section and delivered a healthy baby. Eleven days post-partum, she presented with a 1-day history of frontal and parietal headache with no other associated symptoms. It did not improve with paracetamol or Ibuprofen. Her blood test showed sodium of 119 mmol/l. She was admitted under the medical team in a Gynaecology ward. The medical team reviewed her in the evening. Her examination showed euvolemic status and Brisk reflexes. Other biochemistry showed serum osmolality 246mOsmol/kg, urine sodium 6 mmol/l and urine osmolality 445mOsmol/kg in keeping with SIADH. The endocrine team was consulted and advised to hold Desmopressin, replace serum sodium slowly by less than 8 mmol/24 hours with an IV infusion of 125 ml/hour normal saline, repeat the serum sodium after 6 hours, check for 9 am cortisol and TFT, request an urgent pituitary MRI, and keep a strict input/output fluid chart. The Sodium level after 6 hours showed Na of 126 mmo/l. Unfortunately, the fluid was stopped later and VBG after 6 hours reported Sodium of 136 mmol/l while the serum sodium level was 139 mmol/l. The Urine output was noted to be 8 L in 12 hours. The patient was given 500ml of Dextrose 5% over 1 hour and prescribed her usual Desmopressin dose. The ITU team was called and an urgent Head & Pituitary MRI was done with no abnormality. Cortisol & TFT were normal. The patient was observed for 2 days and discharged later.
Conclusion
The antidiuretic effect of oxytocin can result in water intoxication and hyponatremia that may lead to serious neurological sequelae and maternal death. Early suspicion could prevent these complications. Rapid correction of sodium should be avoided as it can result in osmotic demyelination syndrome which can cause profound neurological damage. Our patient had oxytocin for delivery 11 days prior to her presentation and was also exclusively breastfeeding. The postulated theory for her profound hyponatraemia was secondary to synthetic oxytocin as well as oxytocin produced from exclusively breastfeeding.

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WH3

Rhabdomyolysis due to rapid correction of sodium in a patient with hyponatremia secondary to water intoxicationÿ

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Hyponatremia due to water intoxication is often associated with mental disorders like schizophrenia and psychosis. Patients usually present with headaches, seizures and altered consciousness. The mainstay treatment in these cases is fluid restriction. A 31-year-old man was brought to the hospital following a fall and disorientation. He had a history of Schizophrenia which had been well controlled on risperidone. A few weeks before this presentation, he drank about 20 litres of water a day. The CT scan of head was unremarkable. On examination, he was euvolemic. Blood results showed severe hypotonic hyponatremia with low urine osmolality and low urinary sodium. (Serum Sodium: 111 mmol/l [RR: 135-145 mmol/l], Serum Osmolality 229 mosmol/kg [RR: 275-295 mosmol/kg], Urine Osmolality 55 mmol/l, Urine Sodium <20 mmol/l) with normal TFT (TSH: 0.4 mu/l [RR: 0.3-4.2 mu/l]) and random cortisol levels (602 nmol/l [RR: 172-497 nmol/l]), and slightly raised Creatinine Kinase levels of 3356 iu/l. He was diagnosed with hyponatremia secondary to psychogenic polydipsia and fluid restriction was commenced. His sodium got corrected rapidly following fluid restriction, at the same time his Creatinine Kinase (CK) levels rose significantly (See Table 1). Though rhabdomyolysis is an under-recognised complication of water intoxication, it is usually mild. However, rapid correction of sodium can lead to significant deterioration in rhabdomyolysis. This patient demonstrates that rapid correction of sodium levels in patients with water intoxication can cause rhabdomyolysis. Therefore, sodium levels and strict fluid intake/output should be monitored closely in the early phase of treatment to prevent rhabdomyolysis. 5% dextrose solution with matched urine output can be used to prevent rapid correction of sodium in these patients as fluid restriction alone can be dangerous. Though the exact mechanism for this is still controversial, it is thought to be due to rapid shift in electrolytes and osmolality during rapid correction of sodium.

Table 1 Serum sodium and CK levels.

Date and time of blood test	Serum Sodium levels	Serum CK levels (RR: 39-308 iu/l)
09/10/2021, 12:32	111 mmol/l	3356 iu/l
10/10/2021, 00:55	128 mmol/l	-
10/10/2021, 13:09	130 mmol/l	-
11/10/2021, 07:36	130 mmol/l	-
12/10/2021, 15:33	133 mmol/l	131072 iu/l
13/10/2021, 09:58	137 mmol/l	103334 iu/l
14/10/2021, 10:34	136 mmol/l	55339 iu/l
15/10/2021, 11:13	137 mmol/l	19617 iu/l
18/10/2021, 12:14	138 mmol/l	1669 iu/l

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WH4

Severe hyponatraemia related to ACTH deficiency and SIADH from lymphocytic hypophysitisÿ

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A fit and well 41-year-old lady who was 10-days post-partum was referred to our Endocrine team for hyponatraemia (serum sodium 117 mmol/l). She had a spontaneous vaginal delivery but had 1.5L blood loss due to difficulty with placenta removal. Her baby is well with no medical issues. During pregnancy, she was started on aspirin due to maternal age and had diet-controlled gestational diabetes. She presented to hospital with extreme lethargy. She also reported lightheadedness and occipital headaches. Her headaches have been present since her delivery which did not resolve with simple analgesia. She had no previous headaches during her pregnancy. She was concerned about the lack of breastmilk production. She reported no other endocrine symptoms including visual abnormalities. She did conceive naturally. No examination findings of endocrinopathies were detected and clinically she was euvolaemic. There was no postural drop in her blood pressure and her visual fields were intact to red pin. Investigation findings
Sodium: 117 mmol/l (sodium immediately post-partum: 129 mmol/l) Potassium: 4.6 mmol/l Urea: 3.0 mmol/l Creatinine: 41umol/l eGFR: >90 ml/minute Our impression at this point was hyponatraemia related to presumed lymphocytic hypophysitis. We commenced her on hydrocortisone replacement (10mg/5mg/5mg) whilst waiting for her pituitary panel, and domperidone 10mg TDS to help with her milk supply. Pituitary blood tests: fT4 : 8.9pmol/l, TSH: 1.20mU/l Cortisol: 44 nmol/l (5pm) Prolactin level: 424mU/l IGF-1: 59microgram/l Following this, we commenced additional levothyroxine 75 mg OD. She was keen go home so we organised a 48-hour review. Unfortunately, she returned the next day feeling more lethargic and this time, with nausea and some tingling sensation in her fingers with persisting headaches. Similarly, her clinical examination revealed euvolaemia. Her repeat serum sodium was 113 mmol/l. Her serum osmolality was 236 mmol/kg, urine osmolality 661 mmol/kg and urine sodium 86 mmol/l. With the working diagnosis of SIADH secondary to lymphocytic hypophysitis, we recommended absolute fluid restriction. We monitored her urine output and serum sodium very closely with an aim to achieve 1L negative balance accompanied by safe level of serum sodium rise. Her serum sodium beautifully rose within the next few days with gradual easing of fluid restriction. The Radiology MDT discussion of her MR pituitary concluded changes in keeping with lymphocytic hypophysitis. Lymphocytic hypophysitis is a very rare cause of hyponatraemia. Our case highlights the importance of having an open clinical suspicion and the need for accurate chronological history to clinch the diagnosis and safely manage these patients.

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WH5

Hyponatraemia: A real life scenarioÿ

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Hyponatraemia is the most common electrolyte abnormality encountered in clinical practice and second most common endocrine referral. Acute severe hyponatremia is potentially life-threatening and must be treated promptly and aggressively. SIADH, Cortisol deficiency, Liver Disease, Heart disease, certain medications and excess alcohol intake can frequently lead to hyponatremia. We present a case of 41 year old male known to have alcoholic liver disease and depression who presented to Emergency department with hematemesis, epistaxis and drowsiness. Clinical history suggested increased alcohol intake, decreased oral fluid intake and recently increased dose of risperidone. On assessment, vital signs were normal with Fluctuating GCS, ascites on abdominal examination and clinically dehydrated with decreased urine output and dry mucous membrane. Investigations revealed low serum sodium of 99 mmol/l, normal potassium: 4.2 mmol/l, hemaglobulin: 89g/l, creatinine: 38, Albumin: 24g/dl, normal thyroid function test and blood glucose. Serum and urine osmolality"s and cortisol were not available in acute setting. Initially patient was fluid restricted to 750 ml/day in view of ascites on clinical examination. ICU and Endocrine review was also sought. Endocrine team deemed hyponatraemia multifactorial with decompensated liver disease, excess alcohol intake, dehydration and antidepressant as contributing causes and considering hypovolemia status advised albumin infusion with careful fluid replacement with 0.9% normal saline and close monitoring of serum sodium and withholding hypertonic saline with the review of reassessing after fluid replacement. Serum sodium improve to 113 mmol/l in 24 hours. Serum and urine osmolality"s done on 7th day of admission reveal serum 283mOsm/kg, urine osmolality: 315mOsm/kg, urine sodium<20mEq/l with serum sodium of 137 mmol/kg. Patient managed as decompensated liver disease under gastroenterology team. While commonly encountered metabolic abnormality, it can sometimes prove difficult to manage especially in acute settings when investigations are not available immediately. Although Current guidelines would support hypertonic saline in in the context of fluctuating GCS it"s usually not straightforward and whilst normal saline worked in this case, Central pontine demyelination risk is much higher particularly in patient with excess alcohol intake. Fluid assessment, treating underlying cause with careful fluid administration remains the mainstay of management.

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CONTENTS

Oral Communications

OC1

Genetic analysis of patients with undiagnosed short stature identified novel dominant negative GH receptor variants which provide important insights into GHR physiology

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Case history
Two unrelated male patients were referred for evaluation of short stature. The first patient aged 16.5 years, had a birth weight of 2.6 kg at term (BWSDS -2.4), height 153 cm (HSDS -3.2) at referral and normal BMI SDS of 0.6. He had early postnatal hypoglycemia, which was conservatively managed, but no other significant clinical history. He had relative macrocephaly and disproportionate short stature. His mother was also short with a similar phenotype (height 147.6 cm, HSDS -2.4). The second patient aged 14.6 years, had a normal BW of 3.7 kg at term (BWSDS 0.2), height at referral was 155 cm (SDS -2.7) and BMI SDS was -1.5. There were no dysmorphic features.
Investigations
Baseline serum analyses were unremarkable for both patients. A skeletal survey of the first patient showed borderline mesomelic shortening in the upper limbs, no evidence of Madelung deformity and a slight hyperlordosis. His IGF-I was 501ng/ml (SDS +2.15), and GH binding protein (GHBP) was 467pM (NR 154-1073pM). The second patient had a high peak GH level (57.5μg/l), low IGF-I (< 25ng/ml; -3.0 SDS) and elevated GHBP of 3366pM (NR 154-1073pM).
Results and treatment
Genetic analysis performed using our custom short stature whole genome panel identified two novel heterozygous *GHR* variants (c.876-15T>G (MUT1) and c.902T>G (MUT2)). Segregation studies confirmed MUT1 was maternally inherited and MUT2 arose de-novo. *In vitro* splicing assays confirmed both GHR variants activate the same alternative splice acceptor site resulting in abnormal splicing and exclusion of 26 base pairs of *GHR* exon 9. Western blotting confirmed both variants produced truncated GHR proteins which exerted a dominant negative (DN) effect with blunted GHR signalling. Comprehensive *in vitro* characterisation using NanoBiT complementation assays revealed both mutant GHR dimers exhibited increased cell surface expression and GHBP production compared to wildtype (WT) GHR. This resulted in GH sequestration and reduction in its availability to bind/signal via WT GHRs leading to short stature. RhIGF-1 treatment could not be initiated in these patients due to their advanced bone age at the time of diagnosis.
Conclusions and Discussion points
We identified two novel DN *GHR* variants which expand the GHI spectrum. Heterozygous defects in the intracellular domain of GHR should be considered in cases with a mild-moderate (non-classical) GHI phenotype. Patients with non-classical GHI have a varied phenotype which makes clinical assessment challenging. Early incorporation of genetic analysis in the assessment of short stature enhances diagnosis and enables timely access to treatment.

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OC2

A case of multiple paragangliomas in a chronic hypoxic patient with congenital heart disease

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A 50-year-old female with complex chronic hypoxic congenital heart disease was incidentally identified with a 2 cm extra-vesicular nodule of the bladder during a surveillance ultrasound scan. Suspicious of a bladder carcinoma she uneventfully underwent open partial cystectomy. Histology confirmed a bladder paraganglioma with local lymph node invasion. Post-operative biochemical work-up disclosed raised plasma metanephrine"s: normetadrenaline 7073 pmol/l (120-1180 pmol/l), metadrenaline 485 pmol/l (80-510 pmol/l), 3-methoxythyramine < 120 pmol/l and normal range chromogranin A and B. She was also polycythaemic and had an extensive background of multiple cardiac surgeries. Her symptoms were minimal with infrequent sweating and mood changes. Our Patient was started on doxazosin. Previously she was on bisoprolol and her blood pressure remained systolic <130 mmHg. Further whole body MRI imaging detected multiple nodes in the neck and mediastinum. Eleven-gene panel did not identify genetic mutations. There was no family history of paragangliomas. A 68Ga-DOTATATE PET CT was arranged which showed avidity to multiple mediastinal nodules; largest 3 cm and bilateral sub-centimetre carotid paragangliomas. Additionally somatic testing was arranged. In view of her complex cardiac anatomy and previous sternotomies a conservative management plan was adopted. We started our patient on somatostatin analogue Lanreotide to medically treat her multiple paraganglioma"s. Repeat 68Ga-DOTATATE PET CT scan on Lanreotide showed nil changes. Plan is to continue surveillance scans and yearly plasma metanephrine"s. Hypoxia results in tumorigenesis and has been linked to paragangliomas/phaechromocytomas through activation of hypoxia-inducible-factor (HIF) proteins. Congenital heart disease and paragangliomas/phaechromocytomas can cause polycythaemia. There is an increased occurrence of head and neck paragangliomas in chronic hypoxia. Germline mutations are present in 40% of paragangliomas/phaechromocytomas cases; amongst these SDHx and VHL gene mutations are associated with pseudohypoxia-related-cluster-1 driven paragangliomas. Other HIF's have been linked to development of paragangliomas/phaechromocytomas such as EGLN1 and EPAS1. Although we have not been able to identify an inherited cause of paragangliomas it is possible that there could be a change in later samples. Somatic testing is new to UK and allows us to further develop knowledge and management strategies. Storing sample is advocated. This case highlights a unique complex case of multiple paragangliomas in a chronic hypoxic individual. We believe a chronic hypoxic state has contributed to her disease burden and her management is dependent on her baseline functionality. Pharmacological treatments are limited, understanding of hypoxia pathways may help in future developments of HIF inhibitors.

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OC3

Doege-Potter Syndrome: A rare case of confusion

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Case History
A 51 year old man was brought in by ambulance with new confusion was found to have hypoglycaemia with a blood glucose of 1.8. He was treated by paramedics. His PMHx included a recent diagnosis of solitary pleural fibrous tumour, recent diagnosis of epilepsy. The patient had been admitted to hospital 10 weeks ago with recurrent confusions. Collateral history unveiled visual hallucinations. He had recently lost unintentional weight. Random blood glucose at first presentation was in range. During his work up on the very first presentation showed right sided pleural based mass. A CT scan of the thorax, abdomen and pelvis showed an unusual large mass in the right hemithorax. Histopathology showed a benign solitary pleural based fibrous tumour. Lung MDT concluded that surgical resection should be the mainstay of treatment. For his confusion neurologist review was sought which resulted in a diagnosis of possible epilepsy and arranged for a battery of investigations and MRI scan which were all normal. He was commenced on anti-epileptics, however despite increasing the dose of multiple anti-epileptics his episodes of confusion was becoming more severe and more frequent. As he was found to have hypoglycaemia for the first time on this latest admission. We investigated him for Insulinoma and paraneoplastic IGF-2 driven hypoglycemia from pleural fibroma. Investigations confirmed IGF-2 driven hypoglycemia and he was cured after surgical resection. He has not had any hypoglycaemia since surgery.
Investigation
Plasma Blood Glucose 2.3 mmol/l (3.6-6.1) Insulin levels at the time of hypoglycaemia: <1pmol/l C-peptide at the time of hypoglycaemia: <103 pool/l Oral Hypoglycemic screening at the time of hypoglycaemia Negative Beta-hydroxybutyrate at the time of hypoglycaemia 0.2 mmol/l Insulin antibodies Negative IGF-I 6.6 nmol/l (13.4-62.1) IGF-II 136.6 nmol/l IGF I: IGF II ratio 20.7 (<10) Cortisol 334 mol/l, TSH 3.46 NMDA receptor Ab negative VGKC Ab negative Anti-GAD Ab negative. CT-TAP showed pleural based tumour with no other abnormality MRI head normal.
Results and Treatment
The results confirmed that he had IGF-II driven hypoglycemia from the pleural fibroma (Doege Potter Syndrome). He underwent surgical resection of the tumour. After surgery he has not had any hypoglycemia. Post-surgery he has recovered well and has come anti-epileptic medications.
Conclusion
- Thorough and systematic work-up of non-diabetes related hypoglycaemia is essential.
- In patients with a background of a known tumour presenting with neurological symptoms considering paraneoplastic syndromes is important.

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OC4

Barakat syndrome: A rare cause of primary hypoparathyroidism

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Case history
A 54-year-old lady was diagnosed with primary hypoparathyroidism in 2006, after being referred by her Rheumatologist as her father and brother had familial hypoparathyroidism and sensorineural deafness. She was followed up in endocrine clinic for management of primary hypoparathyroidism. Her hypocalcaemia is well managed with calcium supplementation, with no specific symptoms of hypocalcaemia. She has recurrent urinary tract infections with known borderline chronic kidney disease. Other notable past medical history includes familial sensorineural deafness from childhood and psoriatic arthritis with enthesitis. After discussion on an internet hypoparathyroidism support group in 2015, she questioned the possibility of her having "Barakat syndrome".
Investigations
In 2005, adjusted calcium level was 2.12 (normal range 2.2-2.6 nmol/l) and PTH level was 21 (normal 7-53 range pg/ml). With treatment, adjusted calcium and phosphate levels remain within normal limits. Known chronic mild anaemia. Twenty-four-hour urinary calcium output performed in February 2022 was < 2.548 mmol/24h (2.7-7.5 mmol/24hr) in 3185ml urine. Urea 5.7 (normal range 3-7.6 mmol/l), creatinine 99 (normal range 55-87 mmol/l) and eGFR 56 ml/min. Sequencing GATA3 analysis for this patient in 2015 showed heterozygous mutations of c.291 303delins6p(Asp98fs). An MRI brain in 2019 was negative for basal ganglia calcification, excluding Fahr"s syndrome. Renal USS 2020 showed slightly atrophic right kidney measuring 8.5 cm, normal left kidney. Microalbuminuria was confirmed in 2021, with urinary microalbumin of 140mg/l (normal range < 30mg/l).
Management
Barakat syndrome was diagnosed in this patient due to the classical triad of diagnoses, confirmed by genetic analysis showing heterozygous GATA3 mutation. Her hypocalcaemia is well managed with 250nanograms 1-alfacalcidiol three times daily. Her seronegative arthritis is managed with analgesia and anti-rheumatic agents. Her chronic anaemia is managed by iron and blood transfusions as required.
Conclusions and discussion
Barakat syndrome is an autosomal dominant genetic disorder caused by haploinsufficiency of GATA binding protein 3 (GATA3) gene. There are currently no formal guidelines for diagnosis. In this case, the patient presented with classical triad of renal disease, sensorineural deafness, and hypoparathyroidism, with diagnosis being confirmed via genetic analysis. From those with Barakat syndrome confirmed on genetic testing, 60% have all three classical manifestations, with 27% not having renal disease. The most common individual phenotypic presentation was deafness (93%), then hypoparathyroidism (87%), with least common being renal disease (61%). Therefore, Barakat syndrome should be considered in those presenting with any of sensorineural deafness, hypoparathyroidism or renal disease. Genetic testing could be used as a means for earlier diagnosis.

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OC5

Unusual cause of acromegaly in a young patient

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Case History
A 35-year-old was referred to surgery with a confirmed diagnosis of symptomatic acromegaly. Her GH failed to suppress during an oral glucose tolerance test (OGTT), her IGF-1 and prolactin was high. The histology and immunocytochemistry suggested pituitary hyperplasia. We started to look for conditions associated with pituitary hyperplasia resulting in GHRH production, including the genetic tests for inherited conditions. A solitary nodule was noted in her neck during an examination.
Investigations
She had an ultrasound scan guided fine needle aspiration of the thyroid nodule, and cytology was Thy3f nodule. Her calcitonin level was normal. She had an NMGa68DOTATATE whole body PET CT and this showed a large DOTATATE avid mass from the right adrenal gland compatible with Pheochromocytoma. Her 24 hours total urinary metadrenaline and normetadrenaline was high. Her genetic test for MEN1, CDKN1B, and MEN2 are negative. Her GHRH was markedly high.
Treatment
She had adrenalectomy for pheochromocytoma and remains very well.
Conclusions and points for discussion
Acromegaly is rarely due to an excess of the GH-releasing hormone (GHRH). Ectopic GHRH secretion accounts for <1% of cases of Acromegaly. It is most commonly secondary to gastropancreatic neuroendocrine tumours and bronchial carcinoid tumours. Dynamic pituitary tests are not helpful in distinguishing acromegalic patients with pituitary tumours from those harbouring extra pituitary tumours. When a GHRH secreting tumour is not identified, then the possibility of an underlying genetic syndrome such as MEN1/MEN4, Carney Complex, McCune Albright and X-linked acrogigantism syndrome should be considered. The distinction of pituitary vs extrapituitary Acromegaly is important in planning management. Surgical resection of the tumour secreting ectopic GHRH if possible is the treatment of choice in a patient with the ectopic GHRH syndrome Ectopic GHRH acromegaly should be suspected in a patient with biochemical/-clinical features of acromegaly in the presence of co-existing neuroendocrine tumours, or if there is resolution of acromegaly after the surgical resection of the primary neuroendocrine tumour when there is diffuse pituitary enlargement on imaging and persistent acromegaly after surgery if there is histological evidence of somatotroph hyperplasia. Plasma GHRH levels are usually elevated in patients with peripheral GHRH-secreting tumours and are normal or low in patients with pituitary acromegaly

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OC6

Treatment with Selective RET inhibitors in Medullary Thyroid Cancer – A Case series

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Case history
A 54-year-old lady was diagnosed with primary hypoparathyroidism in 2005, after being referred by her Rheumatologist as her father and brother had familial hypoparathyroidism and sensorineural deafness. She was followed up in endocrine clinic for management of primary hypoparathyroidism. Her hypocalcaemia is well managed with calcium supplementation, with no specific symptoms of hypocalcaemia. She has recurrent urinary tract infections with known borderline chronic kidney disease. Other notable past medical history includes familial sensorineural deafness from childhood and psoriatic arthritis with enthesitis. After discussion on an internet hypoparathyroidism support group in 2015, she questioned the possibility of her having 'Barakat syndrome'.
Investigations
In 2005, adjusted calcium level was 2.12 (normal range 2.2-2.6nmol/l) and PTH level was 21 (normal 7-53 range pg/ml). With treatment, adjusted calcium and phosphate levels remain within normal limits. Known chronic mild anaemia. Twenty-four-hour urinary calcium output performed in February 2022 was < 2.548 mmol/24hr (2.7-7.5 mmol/24hr) in 3185ml urine. Urea 5.7 (normal range 3-7.6mmol/l), creatinine 99 (normal range 55-87mmol/l) and eGFR 56ml/min. Sequencing GATA3 analysis for this patient in 2015 showed heterozygous mutations of c.291 303delins6p(Asp98fs). An MRI brain in 2019 was negative for basal ganglia calcification, excluding Fahr's syndrome. Renal USS 2020 showed slightly atrophic right kidney measuring 8.5cm, normal left kidney. Microalbuminuria was confirmed in 2021, with urinary microalbumin of 140mg/l (normal range '30mg/l).
Management
Barakat syndrome was diagnosed in this patient due to the classical triad of diagnoses, confirmed by genetic analysis showing heterozygous GATA3 mutation. Her hypocalcaemia is well managed with 250nanograms 1-alfacalcidiol three times daily. Her seronegative arthritis is managed with analgesia and anti-rheumatic agents. Her chronic anaemia is managed by iron and blood transfusions as required.
Conclusions and discussion
Barakat syndrome is an autosomal dominant genetic disorder caused by haploinsufficiency of GATA binding protein 3 (GATA3) gene. There are currently no formal guidelines for diagnosis. In this case, the patient presented with classical triad of renal disease, sensorineural deafness, and hypoparathyroidism, with diagnosis being confirmed via genetic analysis.
From those with Barakat syndrome confirmed on genetic testing, 65% have all three classical manifestations. The most common individual phenotypic presentation was deafness (96%), then hypoparathyroidism (93%), with the least common being renal disease (72%).

Therefore, Barakat syndrome should be considered in those presenting with any of sensorineural deafness, hypoparathyroidism or renal disease. Genetic testing could be used as a means for earlier diagnosis.

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OC7

Paseriotide keeping Nelson"s syndrome at bay

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Case history
Our patient is a 64 year old lady who had bilateral adrenalectomy in 1978 for Cushing"s disease. This was followed by radiotherapy in late 1978. To get further reduction of the ACTH producing pituitary adenoma she had transsphenoidal surgery in 1979 and then transfrontal craniotomy in 1982. This was followed by further radiotherapy in 1985. It left her with panhypopituitarism and she was on full hormone replacement. She presented to our hospital in late 2008 complaining of hyperpigmentation.
Investigations
Her ACTH was 5019ng/l (normalvalue 10-50) in 2005. In 2009 her ACTH had increased to 12468ng/l. Her MRI pituitary then showed bilateral parasellar lesions arising from the floor of the pituitary fossa and soft tissue lesions in both cavernous sinuses. In 2010 her ACTH levels were 34000-38000 and her hyperpigmentation was worse. In December 2010, she developed severe headache and MRI showed pituitary apoplexy.
Results and treatment
She was started somatostatin analogues and later established on Paseriotide 60 mg IM monthly. Further MRIs showed haemorrhagic component had resolved and in Dec 2012, there was some regression of the parasellar masses in the MRI of 2012. Her ACTH had dropped down to 5000ng/l. Presently her ACTH levels are 1398ng/l. Her pigmentation is much less and MRIs are showing stable masses. As a side effect of Paseriotide, she developed diabetes mellitus, which is well controlled on Metformin.
Conclusions and points for discussion
Nelson"s syndrome is a condition where there is enlargement of an ACTH producing tumour after bilateral adrenalectomy for the management of Cushing"s disease. The tumour continues to produce ACTH causing hyperpigmentation. We present a follow up case of a patient where long term treatment of over 10 years with Paseriotide has given good quality of life for a patient with Nelson"s syndrome. Pasireotide is a novel pituitary-directed somatostatin analogue with a high binding affinity to almost all somatostatin receptors.

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OC8

Familial dysalbuminaemic hyperthyroxinaemia, a rare cause of discordant TFTs

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Section 1: Case history
A 61-year-old lady was referred by her GP to our endocrine clinic with abnormal thyroid function tests (TFTs) incidentally identified in routine blood tests. She had no symptoms suggestive of thyrotoxicosis apart from occasional palpitations when using inhalers for asthma. She had no family history of endocrine significance. She was on salbutamol, salmeterol, fluticasone inhalers and laxatives. Physical examination was unremarkable with no goitre.
Section 2: Investigations
Initial TFTs showed a free T4- 23.8 pmol/l (NR- 11-22) and TSH- 6.41 miU/l (NR- 0.3-5). Thyroid receptor antibodies and anti TPO antibodies were negative. Subsequent TFTs in next clinic visits showed persistent mildly elevated free T4 ranging between 21.4-29.8 pmol/l. Free T3 was normal. TSH measurements after the initial visit were normal. Pituitary function tests showed normal prolactin, growth hormone and IGF-1 measurements with post-menopausal pattern gonadotrophins along with a normal alpha-subunit. Her short synacthen test was normal. Pituitary MRI showed no pituitary adenoma.
Section 3: Results and treatment
She subsequently underwent genetic testing. She was found to be heterozygous for the c.725G>A p.(Arg242His) albumin gene variant which confirmed the diagnosis of familial dysalbuminaemic hyperthyroxinemia (FDH). She was not given any antithyroid medications at any point. Patient was discharged back to the GP with reassurance as FDH does not need any treatment. Her family members were advised to check TFTs to avoid unnecessary investigations in the future.
Section 4: Conclusions and points for discussion
FDH is an autosomal dominant disorder characterized by mutations in the human serum albumin causing increased affinity of thyroxine to albumin. Prevalence is about 0.2 percent in Hispanics and 0.01 percent in Caucasian population. Affected individuals have high total T4 +/- free T4 but normal T3 and TSH and are clinically euthyroid. Serum albumin is quantitively normal. Although in theory, free T4 measurements should be normal in FDH, many T4 assays are adversely affected by changes in albumin concentration and give spuriously high values. Free T4 assays used in our hospital were not sensitive enough to correct albumin changes seen in FDH, they are better at correcting for thyroid binding globulin alterations. FDH cases can be confused with hyperthyroidism, thyroid hormone resistance or TSH-oma and may cause unnecessary treatment with antithyroid medications. Knowledge about FDH will allow clinicians to avoid complicated laboratory testings and inappropriate treatment.

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OC9

A case of ChAdOx1 vaccine-induced thrombocytopenia and thrombosis syndrome leading to bilateral adrenal haemorrhage and adrenal insufficiency

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Case History
We report the case of a 23-year-old woman who developed adrenal insufficiency secondary to bilateral adrenal haemorrhage in the context of vaccine-induced thrombosis and thrombocytopenia (VITT). She presented with breathlessness and chest pain eight days after receiving her first dose of the adenoviral vector-based ChAdOx1 vaccine. Over the course of a week, she developed fulminant VITT. Her only comorbidity was obesity, with BMI of 35 kg/m2.
Investigations
Investigations showed low platelet count of 43 x109/l and raised D-Dimers > 100,000 ng/ml. CT pulmonary angiogram showed multiple lobar and segmental pulmonary emboli, requiring anticoagulation. Additional cross-sectional imaging performed sixteen days post-vaccination due to acute clinical deterioration with refractory hypotension, revealed bilateral adrenal haemorrhage, non-occlusive splenic vein thrombosis and right ventricular thrombosis. Cortisol level was <25 nmol/l, confirming adrenal insufficiency. Anti-platelet factor 4 antibodies were detected confirming definite VITT in accordance with the UK diagnostic criteria.
Results and treatment
The patient received intravenous hydrocortisone replacement and was aggressively resuscitated with intravenous fluids promptly. Furthermore, she required anticoagulation, plasmapheresis and immunosuppression. After 4 weeks in hospital, she recovered fully and was discharged on warfarin, hydrocortisone and fludrocortisone replacement. Short synacthen tests (SST) at 3 and 9 months after presentation demonstrated a flat response (0" cortisol 37 nmol/l and 30" cortisol 43 nmol/l; at 9 months 0" 41 nmol/l and 30" 53 nmol/l) demonstrating ongoing adrenal insufficiency. Magnetic-resonance-imaging of the adrenal glands showed resolving adrenal haemorrhage. She is still receiving hydrocortisone 10/5/5 mg and fludrocortisone 50 mg daily
Conclusions and points for discussions
Adrenal insufficiency secondary to bilateral adrenal haemorrhage should be suspected in patients with VITT and treated promptly. Adrenal vein haemorrhage can occur as the initial presentation of VITT or even days to weeks later after the development of thrombosis in other more classic sites. Completion of vaccination schedule against SARS-CoV-2 using an mRNA-based vaccine should be recommended to patients post-VITT, as mRNA-based vaccines have not been associated with VITT, but confer protection against SARS-CoV-2. There is

paucity of data regarding the potential for recovery of adrenal function after bilateral adrenal haemorrhage in the context of VITT and thus more studies are needed to inform clinical practice. Finally, this case highlights the need for disease registries for rare conditions, such as VITT. This is crucial as direct cooperation and sharing of information by clinicians might enable quicker identification of disease patterns than would have been possible via established reporting tools of adverse events.

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OC10

Not your usual barn door Hyponatremia- A twist in the tale of a common Electrolyte abnormality

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Case History

We report the case of a 25-year-old Asian male who presented to our hospital with recurrent episodes of abdominal pain complicated by significant Hyponatremia. Initial admission was in November 2021 followed by March, 2022 with similar symptoms. He remained under surgical care during both admissions. For his severe hyponatremia, an urgent Endocrine input was sought. The patient was not on any medications that could be implicated in his biochemical picture and his past medical history was unremarkable except for appendicectomy. During his stay, he also had recurrent episodes of fluctuating confusion associated with severe hypertension.

Investigations

Biochemistry during both admissions revealed severe Hyponatremia with nadir sodium 103 mmol/l. Hyponatremia work up was consistent with SIADH without any obvious cause. Extended biochemistry confirmed normal Lipid profile, Thyroid functions, and re-assuring Cortisol levels. Computerised Tomography (CT) imaging on both occasions ruled out any evidence of obvious surgical pathology. Due to lack of any obvious explanation to his symptoms, Porphyria screen was requested to exclude Acute Intermittent Porphyria (AIP).

Results and treatment

During the first admission, his symptoms were managed by analgesia and anti-emetics. He required exploratory laparotomy for suspected intestinal obstruction, given his previous history of appendicectomy. His sodium levels improved well with Fluid restriction and Urea tablets. To ensure strict electrolyte monitoring, he was transferred to the High Dependency Unit on both occasions. His stay in HDU was complicated by recurrent episodes confusion and severe hypertension consistent with sympathetic overactivity. Following discharge after his first admission, he was due to be followed up in the Endocrine outpatient clinic, however, unfortunately did not attend respective appointments. During the second admission of a similar nature, given lack of obvious explanation to his symptoms, Porphyria screen was requested as one of the rarer medical causes of abdominal pain and severe hyponatremia. This revealed significantly elevated random PBG excretion - 91(high) and total porphyrin levels PBG- 310(high). He has now been referred to the regional Tertiary Porphyria Centre for management.

Conclusions and points for discussion

AIP is one of several disorders that arise from enzymatic derangements in the biosynthetic pathway of the heme molecule. AIP is the most common of the acute porphyrias worldwide, with an estimated prevalence of approximately 5 per 100,000 people This case highlights the importance of considering the diagnosis of AIP in patients presenting with recurrent abdominal pain and Hyponatremia, where in surgical causes have been excluded.

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Poster Presentations

P1

Pseudohypoparathyroidism presenting with extensive bone lytic lesion histology proven Brown tumours

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Summary
59-year-old female diagnosed at the age of 41 in 2004 with pseudohypoparathyroidism (PHP) initially presenting with raised PTH 152 pmol/l (1.6-6.9), Phosphate 1.91 mmol/l (0.87-1.45), adjusted calcium 1.90 mmol/l (2.20-2.60), raised ALP 600 units/l (0-129) and low vitamin D 29 nmol/l. Since diagnosis started on alfacalcidol 1 mg daily and Calcichew-D3. Investigations by hepatology team in the view of persistently raised ALP showed normal liver ultrasound, Fibroscan and non-invasive liver screen, In June 2019 presented to the hospital with fall. A Trauma CT head & neck showed multiple skull lytic lesions with possibility of myeloma raised on the CT report, was referred to haematology team. Myeloma screen came back negative, low dose skeletal CT showed multiple lytic expansile lesions throughout the axial skeleton, which also confirmed on FDG PET CT. Bone biopsy histopathology reported as Brown tumour of secondary hyperparathyroidism. As PTH remined massively elevated over the last two years between 194 to 272 pmol/l, she started on Cinacalcet 30 mg twice/day in addition to alfacalcidol 1.75 mg and Calcichew four tablets daily. One week after Cinacalcet, biochemical improvement noted with PTH level improved from 193.3 to 172 pmol/l, ALP from 868 to 772 units/l. She currently undergoing a slow titration in Cinacalcet with regular blood checks in clinic.
Discussion
The unique features of this case:
1. The massive elevation of PTH due PTH resistance (PHP 1b).
2. The formation of extensive brown tumours due to chronic activation of osteoclastic activity by the elevated PTH in spite of the PTH resistance.

Brown tumour, also known as osteitis fibrosa cystica and rarely as osteoclastoma, is one of the manifestations of hyperparathyroidism. It represents a reparative cellular process, rather than a neoplastic process. Increased PTH levels stimulates osteoclastic activity resulting in cortical bone resorption and marrow fibrosis. Brown tumours have been described in small series of patients with pseudohypoparathyroidism. Despite PTH resistance in this condition, there is activation of osteoclastic activity. Cinacalcet is proposed to exert calcimimetic action through allosteric modulation of the calcium-sensing receptor (CaR) on the parathyroid cell surface. The primary role of the CaR is control of PTH secretion in response to extracellular calcium concentration. Cinacalcet acts to reduce circulating PTH concentration through activation of the CaR by increasing its sensitivity to extracellular calcium. We present early evidence that this treatment may act to suppress PTH secretion in PHP 1b.

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P2

A curious case of hypokalaemia causing VF cardiac arrest in a young adult male

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History
The patient is a 30 year old man who was admitted by ambulance following a witnessed collapse. He had arrived from out of state to visit family and they had spent most of the day house hunting and afterwards, gone out for drinks. It was here that he collapsed and became unconscious, with immediate bystander CPR given, until arrival of the crew who carried out a 25 minute resuscitation with six shocks given. He was intubated and transported to the hospital into the intensive care unit. His medical history was of mild asthma for which he took salbutamol inhalers infrequently, with no acute exacerbations requiring hospital admission. No other medications of note. His blood pressure on arrival was 142/84mmHg having received metaraminol for hypotension and heart rate 136b/m.
Investigations and Results
Electrogardiogram was normal sinus rhythm. Initial mixed acidosis on venous blood gas with PH 7.23, anion gap 25.2, bicarbonate 19.9, PCO2 7.28 likely due to the arrest and resuscitation. This however reverted to a persistent metabolic alkalosis by the second day of admission: PH 7.52, bicarbonate 29.6, anion gap 6.5. Serum potassium was 2.1 mmol/l (3.5 -5.3), magnesium 0.88 mmol/l (0.7 - 1.07), chloride 92 mmol/l, sodium 138 mmol/l, calcium 2.14 mmol/l (2.20 - 2.6). Urine biochemistry on day 2 showed high urine potassium of 106 mmol/l in the presence of hypokalaemia, urine sodium 46 mmol/l, with normal urine calcium and magnesium. Serum renin and aldosterone were elevated. Our working diagnosis: salt-wasting nephropathy (Gitelman's vs Bartter's syndrome) to exclude long QT syndromes.
Treatment
He required vasopressor support in ITU, nutrition management and electrolyte replacement therapy often needing multiple doses of intravenous potassium, magnesium and phosphate to maintain normal levels. He underwent cardiology work-up including coronary angiogram, cardiac MRI and Ajmaline testing which were all negative. However a decision was made to insert an implantable defibrillator to minimise future recurrence of cardiac arrest. A genetic analysis revealed that he is heterozygous for the SLC12A3 pathogenic variant consistent with Gitelman's syndrome.
Conclusion and points for discussion
As this is a rare presentation of Gitelman's syndrome, it is worth highlighting this as a frontline consideration in severe hypokalaemia in a fit young adult especially when presenting acutely like this. Historically, Gitelman's syndrome is considered a mild chronic disease, with many patients remaining asymptomatic. Many patients may not exhibit the classic features initially, but a high index of suspicion should be maintained at all times.

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P3

Rare Cause of hypopituitarism –A diagnostic dilemma! Beyond hormones

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Case history
We report an interesting case of a rare cause of hypopituitarism where our patient presented to the hospital with acute onset headache, vomiting, and feeling generally unwell.
Investigations/Results
On routine bloods, he was found to have hyponatremia. On further workup of hyponatremia, he had low morning cortisol which was confirmed as secondary adrenal insufficiency on dynamic function testing. He was also deficient in gonadotrophins alongside secondary hypothyroidism with low TSH, fT4, LH, FSH, and testosterone levels. He was started on appropriate hormone replacement therapy. Initial imaging was unremarkable including a normal brain CT and MRI showing pituitary within normal size limits to age but slightly bulky.
Clinical course/diagnosis
He re-presented to the hospital with disabling headaches, new worsening of vision, and 6th cranial nerve palsy. Given bulky appearing MRI On the previous scan, suspicion of apoplexy was raised but MRI Pituitary ruled this out. He continued to present to a local hospital with disabling headaches without any cause and was subsequently referred to Specialist Neurology Services at Tertiary care hospital. Repeat imaging on this occasion showed profusely enhanced smooth pachymeninges raising the suspicion of infective or inflammatory etiology which were ruled out on further testing. He was diagnosed to have idiopathic hypertrophic pachymeningitis (IHPM) after a thorough assessment.
Treatment
He was started on high-dose steroids with a good clinical response with improvement in his headaches, vision, cranial nerve palsies, and resolution of diplopia. He continues to show clinical improvement.
Conclusion
Hypopituitarism is known to occur due to various well-known causes, but rare causes of it described in literature if remain undiagnosed can cause significant clinical deterioration despite adequate hormonal replacement; therefore, it"s crucial to think out of the box and look for rare causes if the presentation is not classical to ensure appropriate maangement.
Points of discussion
Infective and inflammatory causes need to be excluded before the diagnosis of IHPM can be made. Suspect IHPM with the worsening clinical condition even after hormone replacement therapy for hypopituitarism. MRI brain is a valuable resource in addition to the biochemical profile performed for hormonal irregularities and should be used as a problem-solving tool. The initial imaging review could be within normal limits. Particular attention should be paid to the pachymeninges to identify any thickening or abnormal enhancement.

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P4

Late presentation of a rare cause of Primary Amenorrhoea

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Case History
A 20-year-old lady was referred by GP to the endocrine clinic with frequent and gradually worsening non-specific headaches and primary amenorrhoea. She denied cyclical pelvic pain, acne, hirsutism or anosmia. She consulted her GP for delay in menarche when she was 16 years old but was advised to wait until the age of 18 years but unfortunately it was the middle of the Covid-19 pandemic and hence the delay in the referral. There was past medical history of migraine, Depression, asthma and behavioural problems. At the age of 2 years, she was diagnosed with cystic kidney which became non-functional later. Her medications included sumatriptan, steroid inhalers and SSRIs. There is no significant family history. On examination breast development, axillary and pubic hair development were normal indicating Tanner stage 5, BMI 24.5 with height (166 cm) and weight (63 kg) and no virilisation. She had normal peripheral visual fields.
Investigations
Her initial investigations showed elevated prolactin and serum testosterone with normal gonadotropins. Initially diagnostic focus was to rule out anatomical abnormalities and PCOS. SSRIs were stopped. Transvaginal and Transabdominal Ultrasound and showed no endometrium with normal ovaries with likely diagnosis of Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome. Subsequent MRI demonstrated that vaginal vault was partly missing and confirmed Type A MRKH syndrome. On follow up assessment prolactin was normal and headache improved following psychological therapy and she was referred to gynaecology.
Conclusions and points for discussion
MRKH syndrome, also referred to as Mullerian aplasia, is a congenital disorder characterized by aplasia of the uterus and upper part of vagina with normal secondary sexual characteristics and a normal female karyotype (46, XX). Diagnosis is often made during adolescence and it has an estimated prevalence of 1 in 5000 live female births. A good history and examination can narrow down the differentials significantly. In our case, the diagnosis was significantly delayed due to the factors described leading to increased stress and anxiety. The psychosexual impact of this syndrome should never be underestimated. A multi-disciplinary approach with vaginal agenesis therapy and therapeutic counselling and education with non-invasive vaginal dilations are recommended as first-line therapy and surgery as the last option.

	08/02/22	08/12/21	09/07/19
Cortisol 0900	402		
Free Testosterone	89		
FSH	6.0	13.3	6.9
LH	9.3	80.3	12.9
Prolactin	423	768	130
Oestradial	267	1343	209
SHBG	38		
FT4	11.8	12.3	
Testosterone	3.8	3.6	1.6
TSH	1.68	1.08	

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P5

Noninsulinoma pancreatogenous hypoglycemia syndrome (NIPHS)- a therapeutic challenge

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Case History
39-year- old female presented to Endocrine services in 2002 with recurrent symptomatic fasting and post-prandial hypoglycaemia. No other medical history of significance noted.
Investigations
Short synacthen test, oral glucose tolerance test (OGTT), several supervised 72-hour fasts. Imaging (anatomic and function) included CT A-P, EBUS, Octreotide scan and MRI Pancreas.
Results
Short Synacthen test: Basal Cortisol 258 nmol/l, 30 min cortisol 673 nmol/l
OGTT: Fasting plasma glucose 4.0 mmol/l, post glucose load 3.8 mmol/l. Initial 72-Hour fast: plasma glucose 2.8 mmol/l, insulin 19.7 mU/l (0-16) and C-Peptide 851 pmol/l (140-1390). Repeat 72-hour fast several months later: plasma glucose 2.0 mmol/l with concomitant insulin level of 10.3 mU/l and C-Peptide >4000 pmol/l. Hydroxybutyric acid 0.80 mmol/l. All imaging studies were negative and failed to identify an underlying lesion and she was eventually diagnosed with NIPHS.
Treatment
Patient commenced on diazoxide with dietary advice regarding frequent low glycaemic index carbohydrate meals. She had progressive weight gain and later also developed renal impairment which led to discontinuation of diazoxide. A trial of Octreotide and later acarbose were prescribed but discontinued due to side effects. She was reluctant to try calcium channel blockers and continued to suffer from frequent daily post-prandial hypoglycaemic episodes which led to further weight gain. Our patient, subsequently sought advice from a weight loss specialist privately and was commenced on liraglutide 1.8mg OD which not only was beneficial with weight loss but importantly terminated her hypoglycaemia. She remains hypoglycaemia free on a maintenance dose of liraglutide 0.6mg OD which she continues to self-fund.
Conclusion
Noninsulinoma pancreatogenous hypoglycemia syndrome (NIPHS) is extremely rare in adults and typically causes post prandial hypoglycaemia. It results from an increase in the size and number of pancreatic beta cells islets with focal or diffuse hypertrophy and hyperfunction, also known as nesidioblastosis. Treatment can be challenging and includes pancreatectomy, calcium channel antagonists and diazoxide. Treatment with GLP-1 analogues in this cohort of patients has not been described. However, there are a few case reports in literature, describing use of GLP-1 analogues in the management of postprandial hypoglycaemia after Roux-en-Y gastric bypass. It is postulated that GLP-1 analogues not only slow the gut motility but in low glucose conditions, they induce a downregulation of insulin secretion and upregulation of the glucagon level with consequent glucose stabilizing effect.

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P6

Endocrinopathy behind the facemask

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Case history
A 44-year-old gentleman presented to A&E with a 2-week history of fevers and rigors. He gave a background history of hypertension. He was noted to have new onset atrial fibrillation with rapid ventricular response, and a new diagnosis of hypertrophic obstructive cardiomyopathy (HOCM) was made on echocardiography. A vegetation identified on the mitral valve led to an unexpected diagnosis of infective endocarditis. Antibiotic treatment for infective endocarditis (Streptococcus oralis) was unsuccessful and he was subsequently transferred to a specialist centre for mitral valve replacement surgery. During the admission, a history of chronic headaches was investigated. MRI pituitary revealed a 3.8 x1.9 cm pituitary macroadenoma with suprasellar extension and right cavernous sinus invasion. He was further evaluated in an endocrine clinic setting. On removing his facemask, typical acromegalic features with supraorbital ridge prominence, significant underbite and macroglossia were noted. Visual fields were normal to confrontation testing; no organomegaly was present on bedside examination.
Investigations
Urgent endocrine investigations including baseline pituitary function testing were performed. IGF-1 was significantly elevated at 140.3 nmol/l (range 8.5-31.0), 9am cortisol 352 nmol/l (range 200-750), prolactin 1119mU/l (range 60-300), TSH 1.98mU/l (range 0.34-5.60), FSH <0.1 U/l (range 1.7-8.0) and testosterone 8.7 (range 10.0-30.0). Acromegaly was confirmed with an oral glucose tolerance test showing a paradoxical rise in growth hormone. Glucose levels remained normal throughout the OGTT.
Treatment
The patient was commenced on monthly Lanreotide injections and referred onto a specialist neuro-endocrine clinic. Unfortunately, this gentleman"s endocrine and medical management was further complicated by a second episode of infective endocarditis on his mechanical mitral valve. This has responded to antibiotic therapy. Although the size of the suprasellar mass has reduced, there was continued invasion of the right cavernous sinus whilst IGF-1 levels remained elevated; Cabergoline has been added. The safety of pituitary surgery, which is now planned, remains a concern due to his ongoing requirement for anti-coagulation.
Conclusions and points for discussion
This case highlights the requirement for early diagnosis and treatment to prevent further complications and the need for individualisation of complex treatment

decisions within a multidisciplinary setting. Cardiovascular complications including HOCM, arrhythmias, arterial hypertension and valvulopathy, as well as colonic benign neoplasms such as polyposis, are common complications of acromegaly. For patients presenting with "idiopathic" HOCM, IGF-1 assay may be considered to screen for acromegaly. Finally, the requirements for facemasks and virtual telephone consultations during the Covid-19 pandemic have likely compounded potential delays in diagnosis.

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P7

Widespread skin hypopigmentation caused by finasteride when used for female hirsutism

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Case history
A 39 year old lady was referred to endocrinology with hirsutism. In the clinic, the pattern of hair growth was confirmed as androgenic, she had cliteromegaly and family members had commented on her voice deepening. She underwent menarche at 13 years old, has menorrhagia and has had hirsutism her entire adult life that had recently worsened. Her biochemistry confirmed hyperandrogenism with non-suppressed LH/FSH. At her second appointment after serious pathology had been excluded she disclosed exogenous testosterone use. After cessation of her supplements her testosterone normalised but her hirsutism persisted and she was commenced on finasteride. This was well tolerated for 18 months with good improvement in symptoms. However, she began to develop loss of skin pigmentation over her entire body. Her mother was Afro-Caribbean and her father was Caucasian and pre-finasteride had dark skin which had clearly lightened considerably causing gross anxiety to the patient. The loss of pigmentation persisted despite sun-bed use and was confirmed by clinicians more familiar with the patient and by using the patient's own photographs. At the time of case submission she has stopped finasteride with the hope that the changes are reversible.
Investigations Initial tests
Testosterone 38.2 nmol/l (NR:0.3-1.7) confirmed on mass spectrometry and minimal suppression after dexamethasone LH/FSH 5.7/9.2iu DHEAS 6.7umol/l (NR:0.7-11.5) CT: no adrenal or ovarian lesions
After cessation of exogenous testosterone
Testosterone 0.8 nmol/l
Results and treatment
Testosterone normalised with cessation of exogenous supplements and her hirsutism has significantly improved on finasteride. We have now withdrawn the treatment due to the profound skin changes. We are asking dermatology for a review with regards a skin biopsy assess melanocyte activity. We are also in conversation with laboratories who have experience in melanogenesis as there have been laboratory reports of the phenomenon *in vitro* but only vitiligo reported in male subjects previously.
Conclusions and points for discussion
1. If the biochemistry and clinical picture indicate likely exogenous use, this should be fully explored with the patient without prejudice whilst serious underlying pathology is excluded
2. Finasteride (a 5-alpha-reductase inhibitor) has been observed in the laboratory to significantly decrease tyrosinase activity which is the rate-limiting enzyme of melanogenesis. This suggests an explanatory mechanism for the phenomenon observed in our patient
3. This may be a side-effect to council patients on before commencement of treatment

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P8

Cushing's or not Cushing's!

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Case History
A 71-year-old man with well controlled hypertension and left eye blindness due to congenital toxoplasma chorioretinitis presented to his GP with worsening headache. Initial CT head revealed a massive left parasellar lesion (32*25*36 mm) with suprasellar extension. Gadolinium-enhanced MRI revealed large cystic sellar mass, marked chiasmal compression and total encasement of Left carotid artery. 48 hours after MRI he was admitted acute severe right abdominal pain. CT abdomen showed right adrenal haemorrhage with possible underlying adrenal mass and diffuse right retroperitoneal hematoma. Clinical assessment did not reveal a Cushingoid phenotype. He had complete visual loss on the left eye (old) with complete oculomotor palsy (sub-acute). Formal ophthalmic assessment confirmed left optic nerve (ON) damage, chorioretinal scarring and mild right ON involvement.
Investigations
Biochemical investigations showed significant ACTH-dependent hypercortisolaemia (9am cortisol >1750 nmol/l, ACTH 1213 ng/l, 24h UFC >1422 nmol/24h) and profound central hypogonadism. The rest of the anterior pituitary profile was normal. Owing to the severity of hypercortisolaemia that persisted over a week, Metyrapone was commenced. There was rapid reduction of cortisol to 563 nmol/l. Metyrapone was stopped within four days of commencement. Cortisol biochemistry improved but did not normalise at four weeks post adrenal haemorrhage; 24h UFC 116nmol/24h (<120), post ODST cortisol 280 nmol/l and ongoing loss of diurnal rhythm.
Treatment
Trans-sphenoidal surgery was undertaken following regional MDT discussion with the primary aim of preserving vision in the right eye. Surgery was uneventful. Histology showed an ACTH staining, densely granulated corticotroph adenoma with Ki67 index of 5%. He had severe biochemical hypercortisolaemia in the early postoperative period (Cortisol >1600 nmol/l and ACTH 376 ng/l) that improved spontaneously 2 weeks later to 601 nmol/l and 253ng/l respectively. Two months later, right adrenal haemorrhage has completely resolved and underlying indeterminate 1.5*1.9 cm mass revealed (HU; precontrast 39, portal 59 and delayed phase 55). He awaited further follow up with close biochemical monitoring and consideration of a stage procedure to achieve further clearance.
Discussion
- This pituitary adenoma appears to represent a whispering/smouldering corticotroph adenoma leading to an exuberant cortisol response to stress.
- The size and anatomical extent of the lesion make clearance a difficult undertaking with significant associated risk.
- Despite the severe derangement in biochemistry there is no clinical evidence of end organ effects of chronic hypercortisolaemia.

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P9

Late local recurrence of an adrenal tumour presenting with Cushing's disease

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Section 1: Case history
A 68 year old lady presented with a 2 week history of pedal swelling, with large blisters appearing on her feet. Her past medical history included adrenal Cushing"s treated with a right laparoscopic adrenalectomy on a 4.7x5.2 cm lipid poor adenoma 12 years previously; she had been discharged 7 years ago after repeated normal overnight dexamethasone suppression tests. Over the last year she had gained 12 kg in weight and been diagnosed with type 2 diabetes. She also reported hair loss and proximal myopathy. She was treated with furosemide although her BNP was only 28ng/l. An ultrasound suggested a right renal mass. She was referred to the Endocrine service.
Section 2: Investigations
On review in clinic, she was noted to be clinically Cushingoid. Her random cortisol was 638 nmol/l at 5pm and she failed to supress in an overnight dexamethasone suppression test with a cortisol of 584 nmol/l at 9am after 1mg of dexamethasone. A CT abdomen demonstrated a large heterogenous mass in the right suprarenal region, suspicious for malignancy in keeping with likely adrenocortical cancer with near complete effacement of the IVC.
Section 3: Results and treatment
Her case was discussed in the adrenal MDT. The initial histology from the previous adrenalectomy was suggestive of an adenoma, but a breach of the capsule was noted. It was not possible to determine if this was an intraoperative breach. A surgical resection was recommended, and she was commenced on metyrapone to control her cortisol prior to surgery. She was unable to tolerate this due to nausea, so was switched to fluconazole which allowed adequate cortisol control. The patient subsequently underwent resection of the adrenal bed mass with right nephrectomy. The histology demonstrated adrenocortical carcinoma with a high Weiss score of 5, scoring for high nuclear grade, confluent tumour necrosis, increased mitotic activity, and atypical mitotic figures. Post operatively

she has been started on adjuvant mitotane with concomitant hydrocortisone.
Section 4: Conclusions and points for discussion
This is a case of a patient who had originally presented with adrenal Cushing"s due to what was thought to be a benign adenoma, representing after a significant period of time as an adrenocortical cancer. This highlights the challenges of predicting behaviour of adrenal tumours, particularly in larger adrenal masses, and also raises the question of how long it is appropriate to follow up patients with adrenal Cushing"s disease following surgical resection.

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P10

Familial hypocalciuric hypercalcaemia or multiple endocrine neoplasia 1? – when assay interference challenges the diagnosis

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Case history
An asymptomatic 26-year-old female was found to have hypercalcaemia with an associated normal PTH and vitamin D deficiency on blood tests in primary care. She was referred to the endocrinology clinic for further assessment. There was no history of renal calculi, constipation or fractures. The patient was taking the combined oral contraceptive pill only. There was a family history of hypercalcaemia, with an uncle affected in his 50s and a first cousin in his 20s. Therefore the differential diagnosis included Familial Hypocalciuric Hypercalcaemia (FHH), and Primary Hyperparathyroidism due to Multiple Endocrine Neoplasia type 1 (MEN1).
Investigations
The patient underwent repeat blood tests and 24 hour urinary calcium collection. Due to the possibility of MEN1, fasting gut hormones were also measured.
Results and treatment
Repeat bloods showed a corrected calcium of 2.65 mmol/l, PTH 5.2 pmol/l, phosphate 1.00 mmol/l and a vitamin D 35 nmol/l. Once vitamin D replete, the urinary calcium creatinine clearance ratio was 0.09 supporting a diagnosis of FHH. Fasting gut hormones, at the time of initial assessment showed an isolated raised Chromogranin A of 326 pmol/l which remained raised at 607pmol/l when repeated. Genetic testing identified a mutation in the calcium sensing receptor confirming the diagnosis of FHH. No MEN1 mutation was identified. Despite the confirmed diagnosis of FHH, the Chromogranin A levels remained persistently raised. The patient was referred for a CT abdomen and DOTOTATE scan; both were normal. More detailed testing of Chromogranin A was arranged via Clinical Chemistry. Repeat analysis of serial dilutions on the assay showed that Chromogranin A did not fall linearly with dilution, suggesting assay interference. Furthermore, Chromogranin A levels were normal when repeated on a different assay. No treatment was required for the patient with a confirmed diagnosis of FHH only.
Conclusions and points for discussion
Individuals presenting with hypercalcaemia and elevated gut hormones are often considered to have MEN1, or if no mutation is found, to have a MEN1 phenocopy. Here we present a case with an alternative explanation, removing the need for ongoing follow up. This case also highlights the importance of confirming the diagnosis of primary hyperparathyroidism prior to further investigations for MEN1. Also that assay interference should be considered when results are not in keeping with the clinical picture. Close liaison with Clinical Biochemistry Colleagues can facilitate correct testing with serial dilution assays.

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P11

A bronchogenic cyst presenting as an adrenal cyst

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Case history
A 26-year-old female presented with acute left-sided loin pain. There was a preceding dull ache for two months. She had no dysuria or haematuria. Her past medical history was unremarkable except for rhinosinusitis.
Investigations
Abdominal CT revealed oval shaped lesion adjacent to the upper pole of the left kidney. The left adrenal gland could not be separately visualized. The lesion had mass effect on the fundus of the stomach. Adrenal MRI confirmed presence of a 6 X 5.5 X 4.5 cm fluid-containing lesion centred in the left adrenal gland, in keeping with an adrenal cyst. The patient had normal aldosterone-renin ratio, overnight dexamethasone suppression test and 24-hour urine metanephrines.
Results and treatment
Due to the size of the mass and the associated symptoms, laparoscopic left adrenalectomy was performed. The cyst ruptured intraoperatively, and mucinous content was noted. Histopathology showed cystic lesion separate to the adrenal gland. It had ciliated lining and an island of cartilage within the wall of the cyst. These findings were consisting with bronchogenic cyst (BC).
Conclusions and points for discussion
Adrenal cysts are uncommon, they represent 1% of adrenal lesions identified incidentally on CT scans. They are usually unilateral and asymptomatic. Abdominal or flank pain, abdominal mass, spontaneous haemorrhage and rupture have been reported. Adrenal cysts are categorized into four subtypes: endothelial, epithelial, pseudocyst, and parasitic. One of the conditions that can mimic an adrenal cyst is a sub-diaphragmatic bronchogenic cyst. BCs are developmental anomalies, usually located in the mediastinum or lung parenchyma. In some cases, they may detach and migrate to the abdomen and can be found anywhere in the abdominal cavity. BCs in the retroperitoneum are extremely rare and tend to occur on the left side (82% of cases), in the pancreas or the left adrenal gland. Frequently, BCs can be identified only post-operatively as definitive diagnosis required histopathological examination. Cystic endocrine active adrenal lesions have been described, and consequently functional status should be evaluated for all cysts. Risk of malignancy was reported to be 7% in one series. There is no general agreement on management of adrenal cysts. Many authors recommend surgical management for:
- Symptomatic or functional cysts.
- Cysts with features suggestive of malignancy
- Cysts larger than 5 cm in diameter.

Sometimes due to cyst size or location, adrenalectomy is required. Asymptomatic, small lesions can be conservatively followed with imaging, although no surveillance protocol has been described.

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P12

ABSTRACT WITHDRAWN

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P13

A rare case of Adrenal Incidentaloma

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A usually fit 41-Year-old female was incidentally found to have a 9 cm left-sided adrenal mass during radiological investigations prior to an appendicectomy for acute appendicitis. She did not demonstrate any clinical features of adrenal hormone hyper- or hypofunction.
Investigation
Further investigations were carried out to determine the nature of the mass and biochemically assess adrenal function. These revaled normal metanephrines: plasma metanephrines 151 pmol/l [0.0-510.0], normetanephrine 346.7 pmol/l [0-1180] and 3-Methoxytyramine $<$75.0 pmol/l [0.0-180]. She had appropriate suppression of cortisol ($<$50 nmol/l) after a 1 mg overnight dexamethasone suppression test along with a normal 24-hour urinary free cortisol excretion (42 nmol/24h). Serum dehydroepiandrosterone-Sulphate (1.4 umol/l), 17-hydroxy-progesterone (4.8 nmol/l) and testosterone (1.2 nmol/l) were all within normal limits. Radiologically, on dedicated adrenal imaging the large mass was deemed of undeterminate nature and the key differential diagnoses were adrenocortical carcinoma, phaeochromocytoma (the pattern of enhancement suggested this more likely!) and GIST. Further imaging revealed intense localised tracer uptake during an 18-fluorodeoxyglucose positive emission topography (FDG-PET) scan but without uptake on an Meta-Iodo-Benzyl-Guanidine scan (MIBG). 24 hour urinary steroid metabolites screening did not show any abnormalities.
Treatment
She underwent robot assisted laparoscopic left adrenalectomy after multi-disciplinary team discussion. Histologically, the tumour demonstrated features

consistent with schwannoma. The specimen stained diffusely positive for S100 and SOX 10, with associated patchy expression of GFAP and focal coexpression of AE1/3. All this confirmed the diagnosis of Schwannoma. During the follow-up patient she recovered well from the surgery was empirically treated with hydrocortisone and discharged after a 2-day stay in hospital. A short synacthen test one week later was normal and the patient was weaned off hydrocortisone and fared well since.

Discussion

Adrenal schwannoma is a rare site for a schwannoma to develop. There are no radiological features to suggest schwannoma and hence they should be approached as any other adrenal incidentaloma. The diagnosis is however benign, and surgery is curative with no case report showing any recurrence after prolonged follow-up.

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P14

A functioning pancreatic neuroendocrine tumour presenting as diarrhoea with hypokalaemic acidosis

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Case history

58 year old man presented with collapse secondary to profuse water diarrhoea. He had severe AKI, hypokalaemia, metabolic acidosis, hyponatraemia and hypercalcaemia. He had fluid and electrolyte replacement he in ICU, but profuse diarrhoea persisted and with it, was in hypotension and delerium. He had been having progressive diarrhoea and weight loss for 2 years while he was in South Africa.

Investigations

Upper and lower GI endoscopies had been negative. CT abdomen showed a lesion in the pancreas with liver and lung metastasis. His liver biopsy was suggestive of G2 Neuroendocrine tumour (NET). His blood tests showed Na 116 mmol/l, K 2.9 mmol/l, Ca 3.4 mmol/l, Creatinine 395 micromol/l, pH 7.01, and bicarbonate 3 mmol/l. His chromogranin A was 6104(0-59pmol/l) and chromogranin B was 1122 (0-149 pmol/l), VIP 118(0-30pmol/l), somatostatin 7116pmol/l (0-150pmol/l). His FDG PET CT showed uptake in the pancreatic, liver and lung lesions, but the lesions were not very avid on Gallium Dotatate PET CT.

Results and treatment

In ICU, he was given an octreotide infusion at 200 mg/ hour, with creon and loperamide. Diarrhoea improved, but calcium increased to 3.9 mmol/l inspite of aggressive hydration. So he had bisphosphonates and 3 days of ultrafiltration after which AKI and hypercalcaemia resolved. Octreotide was reduced to 6 hourly and he had a staging CT to consider chemotherapy and radiofrequency ablation of liver lesions. Unfortunately his functional status was PS3/4, so couldn"t have systemic chemotherapy or ablation. He had 120 mg s/c Lanreotide which is a long acting somatostatin analogue.

Conclusions and points for discussion

We present here a patient who had a functioning pancreatic NET with VIPoma and somatostatinoma features. It also illustrates the catastrophic metabolic derangements such conditions can present with. Octreotide infusion can help reduce the severity of the diarrhoea by binding to the somatostatin receptors and reducing the output of the functioning peptides.

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P15

ABSTRACT WITHDRAWN

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P16

Just another pituitary lesion

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Case history

37F presented with 4 years history of amenorrhea. In addition, she had fatigue, low mood and joint pains. She also had history of polyuria and nocturia.

Investigations

Her investigations revealed FSH 2.4 IU/l, LH 1.1 IU/l, Oestradiol $<$ 92 pmol/l, T4 $<$5 pmol/l, TSH 1.5 mIU/l, IGF-1 13.3 nmol/l (8.5- 30.07), Cortisol 65 nmol/l, Prolactin 68 mIU/l. She was started on Hydrocortisone and levothyroxine. Pituitary MRI revealed a 15 mm lesion not impinging on the chiasm. Heterogeneous enhancement was in keeping with an inflammatory process. Osmolarities were consistent with a diagnosis of DI.

Results and treatment

Interval imaging at 4 months did not show change in size. However, to obtain a histological diagnosis she underwent a TSS. Histology revealed pus like material and chronic inflammatory infiltrate. Extended microbiology screen including TB was negative. She was started on PO Co-amoxiclav for 4- 6 weeks with aim to repeat MRI afterwards. Interval scan at 2 months post TSS showed peripherally enhancing lobulated lesion, which appeared larger than (1st) post-operative imaging, with slight chiasm contact and minimal displacement. She was offered a second TSS and this time the plan is for her to remain on IV antibiotics for 6 weeks.

Conclusion and points for discussion

Pituitary abscess is a rare finding. The clinical presentation and radiological appearance is similar to many other pituitary lesions. On review of literature, patient can present with fever and non-specific signs and symptoms in addition to pituitary dysfunction. The mainstay of diagnosis remains on histopathology. Most of these lesions resolve after IV antibiotics.

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P17

Brown tumour of the palate heralding a diagnosis of severe primary hyperparathyroidism in a young male

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Case history

An 18 year old male student presented to the dentist with an eight week history of left-sided facial pain and swelling. He was subsequently referred to the maxillofacial team. His only previous medical encounter was for a traumatic right humerus fracture following a roller-skating injury. He took no regular medication. His father died of an unknown malignant process several years previous and family history was otherwise unremarkable. On questioning, the patient described symptoms of thirst, polyuria, lethargy, constipation and frequent headaches. Examination of the hard palate revealed a left-sided, firm 3x3 cm ulcerated mass with palatal expansion. Soft tissues were normal.

Investigations

Blood tests showed an elevated adjusted calcium 3.30 mmol/l (2.20-2.60), a low phosphate 0.50 mmol/l (0.80-1.50), and an elevated alkaline phosphatase of 799U/l (30-130). Renal and liver function were normal. Parathyroid hormone was markedly elevated at 126.56pmol/l (1.48-7.63), with a slightly low 25-hydroxyvitamin D3 30.1 nmol/l. Twenty-four hour urine collection (volume 5.3L) showed an elevated urinary calcium of 17.89 mmol/24h (2.50-7.50). Cross-sectional imaging (CT) of the facial bones revealed an expansile lytic lesion in the left maxilla with generalised osteosclerosis and multiple further small lytic lesions in the imaged bones. A 34mm nodule posterior to the right lobe of the thyroid was noted. Histology obtained from a biopsy of the palatal mass revealed features of a benign giant cell lesion with the histological differential diagnosis being between a giant cell granuloma and a hyperparathyroidism-related brown tumour.

Results and treatment

Blood tests and histology are in keeping with a diagnosis of primary hyperparathyroidism and in light of symptoms and significant hypercalcemia, Cinalcalcet was started along with vitamin D supplementation. Radiological appearances suggest multiple brown tumours with a nodule in keeping with a parathyroid adenoma. Histology supports the biochemical and radiological findings. Given his age, consent was obtained for genetic testing for Familial Primary Hyperparathyroidism. An important differential diagnosis to be considered is parathyroid carcinoma given the parathyroid hormone level.

Conclusions and points for discussion

This young male has severe symptomatic primary hyperparathyroidism with significant bone involvement. Brown tumours are now a rare presentation of hyperparathyroidism, in part due to increased frequency of blood tests undertaken in the general population and earlier diagnosis of primary hyperparathyroidism. It is important to screen all young people presenting with primary hyperparathyroidism for genetic causes which has potential implications for further screening of

both the individual and family members. Genetic testing can also inform the surgical approach.

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P18

A case of Severe and Chronic Vitamin D Toxicity: when all treatment options are exhausted

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Case History
A 68-year-old gentleman was admitted to the hospital following a history of weight loss, lethargy, tiredness for about 6 months. His past history includes hiatus hernia, esophagitis and kidney stones. He reported taking over the counter vitamin D (60,000 IU daily) for more than 2 years. He was not on any other regular medications.
Investigations
His initial investigations showed acute kidney injury with severe PTH independent hypercalcaemia due to vitamin D toxicity [Creatinine: 467 umol/l (59-107 umol/l), Adjusted Calcium 3.26 mmol/l (2.2-2.6 mmol/l), PTH: 0.7 pmol/l (1.3-9.3pmol/l)]. His Total Vitamin D >525 nmol/l. CT TAP didn"t show any abnormalities.
Results and treatment
Initially, he was treated with fluid resuscitation with slight initial improvement in his calcium levels and renal function. Subsequently, he was given one dose of IV Pamidronate 30mg after discussion with the renal team and due to limited treatment options for severe hypercalcaemia. He was then treated with increase in fluid intake with a trial of prednisolone 30mg once a day for a period of 1-2 weeks but due to side effects (fluid retention and ankle oedema), they were stopped. He then had a trial of ketoconazole 200mg once a day which resulted in significant improvement of calcium levels. Ketoconazole had to be stopped due to transaminitis. Subsequently, he was followed up regularly on ultra-low calcium diet and increase in fluid intake with intermittent IV fluid resuscitation with gradual improvement in vitamin D and calcium levels. Although, his calcium levels have now normalised, vitamin D levels have remained in toxic range for 17 months since initial presentation (Results in the table).
Conclusion and points for discussion
Vitamin D supplements are readily available over the counter without any restrictions. Due to its pharmacokinetic properties, it is stored in the body for long term once ingested. We hereby discuss calcium fall in our patient over a period of time with the different interventions, evidence and their mechanism of action. We will also discuss various other treatment options for vitamin D toxicity.

Date	Adjusted Calcium level	Vitamin D	Creatinine levels
13/08/2020	3.26 mmol/l	>525 nmol/l	419 umol/l
08/10/2020	2.85 mmol/l	>525 nmol/l	306 umol/l
09/12/2020	2.67 mmol/l	>525 nmol/l	249 umol/l
22/03/2021	2.51 mmol/l	470 nmol/l	232 umol/l
21/01/2022	2.60 mmol/l	285 nmol/l	184 umol/l

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P19

Amiodarone-induced thyroiditis, complicated by a thyroid storm in a man with Becker Muscular Dystrophy

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Section 1: Case history
A 46 year old man with Becker Muscular Dystrophy (BMD), was admitted with palpitations and shortness of breath. He had a past medial history of severe left ventricular dysfunction (LVSD) and cardiac arrhythmias, including atrial fibrillation (AF) treated with amiodarone, and an implantable cardiac defibrillator (ICD) for non-sustained ventricular tachycardia (VT). He had been treated with 3 months of prednisolone for suspected type 2 amiodarone induced thyroiditis. His baseline mobility had declined in recent years, but he mobilised at home with a stick and outside with a mobility scooter.
Section 2: Investigations
Cardiac monitoring revealed short non-sustained VT and interrogation of the ICD showed AF with fast ventricular response for which 18 shocks from the ICD had been delivered. Chest radiograph showed acute pulmonary oedema and echocardiogram confirmed severe LVSD. The cardiac arrhythmias and cardiac decompensation were driven by severely deranged thyroid function with T4 of 89 pmol/l (acutely rising from 30pmol/l) and TSH <0.01. He scored over 45 on the Burch Wartofsky scale, confirming an acute thyroid storm.
Section 3: Results and treatment
The acute pulmonary oedema resolved with intravenous (IV) glyceryl trinitrate, IV furosemide and continuous positive pressure ventilation (CPAP). The AF/VT storm failed to resolve with IV amiodarone, bisoprolol, ivabradine, overdrive pacing, and direct current cardioversion (DCCV). He subsequently had 3 short episodes of pulseless VT requiring cardiopulmonary resuscitation and shocks. VT ablation was deemed too high risk and the cardiothoracic multidisciplinary deemed him unsuitable for cardiac transplantation. The thyroid storm failed to resolve with carbimazole followed by maximal endocrine therapy comprising propylthiouracil, lithium and cholestyramine, and the thyrotoxicosis had deteriorated despite 3 months of high-dose prednisolone. Total thyroidectomy was deemed the only definitive solution to resolve the thyrotoxicosis, and facilitate ongoing use of amiodarone for the cardiac arrhythmias, but definitive cardiac stabilisation was necessary beforehand. AV node ablation with CRTD was therefore successfully completed. An open total thyroidectomy was performed with no immediate or acute complications. He received peri- and post-operative hydrocortisone for adrenal suppression, which was optimised post-operatively due to hypotension. He was discharged home at his functional baseline.
Section 4: Conclusions and points for discussion
This case depicts exemplary multidisciplinary team working with the endocrinologists, cardiologists, and surgeons, to perform a total thyroidectomy with an excellent post-operative outcome, in a high-risk surgical candidate. Life expectancy in BMD is 40-50 years, highlighting the remarkable outcome achieved in this case.

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P20

Adrenocortical carcinoma in two young patients

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The first case is a 19-year-old male who presented to his GP with lumbar pain, scrotal bruising, and weight loss. Abdominal CT showed a left 6.4 cm x 12 cm suprarenal mass; the right adrenal gland was atrophic. Plasma metanephrines and MIBG were normal. Urinary steroid profile (USP) showed raised 11-deoxycortisol, consistent with adrenocortical carcinoma (ACC). He underwent a left nephrectomy and adrenalectomy. Histology confirmed ACC. The lesion was encapsulated with negative margins; Modified-Weiss score 7, Ki67 43.2%; ENSAT staging 2 and pT2N0. Post-operative CT showed non-specific nodules in the surgical bed and normal ACC markers. He proceeded with Carboplatin-Etoposide chemotherapy after sperm banking and Mitotane. He was reviewed in the clinic, remained active, and referred for genetics. The second case is a 20-year-old female with one month of abdominal pain. She had an ultrasound which showed a left suprarenal mass. CT adrenal showed a 10.5 cm soft tissue within the left adrenal, with no evidence of invasion and normal right adrenal. The examination was unremarkable. There was no weight loss; periods were regular. There was no family history. Plasma metanephrines were normal. USP showed increased metabolites of steroid-precursors consistent with ACC. She had left adrenalectomy. The histology confirmed ACC, Modified-Weiss score 3, Ki67 2.6%, pT2 N0, ENSAT stage 2. Post-operative imaging showed no recurrence or metastases. USP showed no evidence of recurrence. She had TP53 gene testing. Both cases demonstrate rare cancer presenting in a younger age group with different trajectories. The presentation can include non-specific symptoms. There was no evidence of functionality in both patients; the size of the tumour was similar; however, Ki67 differed significantly. In ACC, the 5-year survival is 20-35%. Recurrence is 23-85% after complete surgical removal. A Ki67 of $\leq 10\%$ is a good prognostic factor. The ADIUVO-2 Trial will provide data on low-risk patients, comparing observation against Mitotane treatment. It has shown 5-year recurrence-free survival is approximately 75%. A careful follow-up period should be established in this group. As in our second patient, where there is no clear pathway for post-operative management, subjecting them to Mitotane treatment could be more harmful to health. An MDT approach is required for meticulous management of the patient. Further studies looking into the recurrence-free patient groups are necessary. As endocrinologists, we must emphasise the uncertainty of this condition and provide holistic management, including

addressing fertility and genetic screening. Management of ACC should be addressed with a personalised approach and tailored care.

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P21

Phaeochromocytoma in a patient with end stage renal disease on haemodialysis: diagnostic and management challenges

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Case History

A 61 year old woman on haemodialysis with end stage renal failure secondary to immune-complex mediated diffuse proliferative glomerulonephritis was admitted with accelerated hypertension presenting with acute right microvascular 6th nerve palsy and left optic nerve ischaemic atrophy. Her BP had been well controlled over the last 10 years but since the end of 2020 systolic BP readings were frequently recorded above 200mmHg. Multiple antihypertensive classes were commenced during admission. She was discharged on maximum doses of doxazosin, bisoprolol, nifedipine, hydralazine and isosorbide mononitrate. Phenoxybenzamine, labetalol and GTN patch were later added. Admission was complicated by severe faecal impaction requiring emergency laparotomy and subtotal colectomy with end-ileostomy.

Investigations

24 hour urine metadrenalines were within reference range, albeit with a low urine volume 323mL; normetadrenaline:0.64umol/d(0 - 3.3), metadrenaline:0.08umol/d(0 - 1.2), methoxytyramine:0.05umol/d(0 - 2.5). Plasma catecholamines showed elevated noradrenaline; noradrenaline:43.49 nmol/l(0 – 5), adrenaline: 1.28 nmol/l(0 – 8). Aldosterone/Renin ratio: 84.1. Overnight Dexamethasone Suppression Test; Serum cortisol 40 nmol/l showing adequate suppression. CT Abdomen and pelvis with contrast demonstrated haemorrhage into a 4.5 x 4.5 cm supra-renal soft tissue density mass, with resolution of haemorrhage at interval scanning. NM Tc99m HYNIC-TOC WB SPECT CT (Tektrotyd) demonstrated a high-grade somatostatin receptor positive right adrenal mass suggestive of functioning somatostatin avid lesion and focal uptake posterior to right lobe of thyroid.

Treatment

She had two further admissions due to severe uncontrolled hypertension. Despite multiple anti-hypertensive agents her BP remained poorly controlled. She was referred to tertiary care in London for management of uncontrolled hypertension and surgery for phaeochromocytoma. She was started there on GTN infusion. Subcutaneous octreotide injections were tried to slow gastric motility and improve absorption of anti-hypertensive medications due to concerns of poor absorption in view of previous GI surgery. GTN was switched from infusion to patch. She was also started on clonidine patch. Management options were discussed which included alpha and beta blockade, surgery and external beam radiotherapy. Anaesthetic assessment concluded there were significant surgical risks, and she therefore is being managed conservatively with alpha and beta blockade. Her systolic BP readings now range between 125-170mmHg.

Conclusion

Diagnosis of phaeochromocytoma can be challenging in patients with end stage renal disease on haemodialysis. Phaeochromocytomas overexpress somatostatin receptors. This can be utilised in somatostatin receptor scintigraphy using Tc99m HYNIC-TOC. Somatostatin receptor analogs are also being used in treatment of phaeochromocytomas. Addition of clonidine can be useful in those with challenging hypertension.

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P22

Neurosarcoidosis – an uncommon but important cause of hypopituitarism

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Sarcoidosis is a granulomatous multi-systemdisorder of unknown ethology. It has a higher prevalence in Northern Europe and the UK. Neurosarcoidosis is a relatively less common, but serious complication of sarcoidosis. CASE: A 48 year old man presented to the hospital with intermittent fever, and neck pain and stiffness, of six weeksduration. This was associated with excessive tiredness, loss of libido, decreased appetite, and unintentional weight loss of two stone over a period of three months. Past history of firm painless cervical lymphadenopathy three years prior for which he wasreferred to haematology. CT of thorax, abdomen and pelvis at the time showed bilateral hilar, axillary and cervicallymphadenopathy. He was diagnosed with sarcoidosis as lymph node biopsy showed epithelioid granulomas, elevated serum angiotensin converting enzyme (ACE) levels, and negative cultures and serology. Since no major organs were involved, he was not commenced on any treatment. On examination this time, hewas hypotensive, with palpablebilateral, firm, non-tender cervical lymph nodes, and nuchalrigidity. There were no other significant clinical findings on examination. On investigation, routine blood tests showed he was anemic with leukopenia (lymphopenia). Blood culture was negative. He underwent a CT thorax, abdomen and pelvis to rule out malignancy. It showed similar, but more extensive lymph node involvement than before. He also had a MRI head with contrast due to associated visual disturbances, which showed multifocal leptomeningeal disease involving cranial nerves, ventricular system and pituitary stalk. CSF examination showed elevated protein (1.23 g/l) and lymphocytes (15), but was sterile, with normal ACE levels. Pituitary function tests were suggestive of hypopituitarism, involving gonadal and thyroid axes, which explained his presenting complaints. His paired osmolalities and electrolytes levels were normal suggesting no evidence of diabetes insipidus. Cervical lymph node biopsy reported presence of non-necrotising epithelioid granulomas. He was commenced on high dose Prednisolone initially, followed by Azathioprine, for neurosarcoidosis alongside hormone replacement, with which he improved. Subsequent MRI scans showed resolution of the lesions in the pituitary and other involved structures, along with improvement in symptoms.

Conclusion

Neurosarcoidosis is an uncommon presentation of sarcoidosis and it may often be sub-clinical. Since it can manifest if various ways, it can be a challenge to diagnose it early. Although it can affect any part of the nervous system, the pituitary gland, hypothalamus and cranial nerves are most commonly involved. Therefore, patients with sarcoidosis, especially those with inactive disease and vague systemic symptoms, should be evaluated for related hypopituitarism.

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P23

A rare case of co-occurrence of autoimmune thyroid disease and Myasthenia gravis

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Introduction

Grave"s disease (GD) is a common cause of thyrotoxicosis, Myasthenia Gravis (MG) is less common (incidence of 3-30cases per million). Between 5-10% of patients with MG also have thyroid disease. However, only 0.14% of patients with GD having MG. Both are autoimmune diseases sharing pathophysiological mechanisms. Co-existence, although rare, is well established. MG may mimic the neuromuscular signs of GD especially if these are subtle. We report a case of a 32year old female with ptosis who was later found to have GD and MG coexistence.

Case

A patient with no past medical history was referred to Ophthalmology with a partial left ptosis. Physical examination revealed fatigable ptosis of her left upper eyelid and a lid lag with possible right eyelid retraction. She had a good levator palpebrae superioris muscle function, and her visual acuity was 6/4 in both eyes. She did not report diplopia, and there was no proptosis. Although symptoms of thyrotoxicosis were absent, her presentation raised the possibility of Grave"s ophthalmopathy (GO) - but ptosis with fatigability is not common in GO. Hence, investigations were arranged to check thyroid function (TFT), autoimmune thyroid screen and autoantibodies against the acetylcholine receptor (AChR) and muscle-specific tyrosine kinase (MuSK). Initial TFT showed a suppressed TSH (<0.01;N$=0.27$-4.20miu/l) and marginally elevated FT4 (22.5;N$=$12-22pmol/l)and FT3 (8.3;N$=3.1$-6.8pmol/l). However, a month later, further results showed a significant deterioration, FT4 46.6pmol/l and FT3 26.9pmol/l. Carbimazole 30mg once daily was commenced with subsequent biochemical improvement. Coeliac screen was negative. Both TSH receptor and Ach Receptor antibodies were positive, establishing dual autoimmune pathologies. She is waiting for an Electromyography.

Discussion

GD and MG are autoimmune diseases mediated by autoantibodies targeting membrane receptors- thyroid stimulating hormone receptors and postsynaptic

neuromuscular junction respectively. Although coexistence may occur, and ocular symptoms and muscle weakness may be a presenting clinical feature of both conditions ptosis is not a common feature of GO; hence its presence may indicate MG. Furthermore, the co-association of GD and MG can pose a treatment challenge for the clinicians. Carbimazole for GD may increase the risk of myasthenic crises. Additionally, should definitive surgical management be considered for GD there is evidence of poorer outcomes when MG is also present. This case highlights the need for clinicians to be aware of the fact that both GD and MG may co-exist and the impact dual pathology may have on treatment outcomes.

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P24

A tricky situation: hypercalcaemia in pregnancy

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Section 1: Case history
A 39-year-old Asian lady at 18 weeks of gestation, after in *vitro* fertilisation pregnancy, was found to have an adjusted calcium level of 3.08 (range 2.20-2.60 mmol/l) on routine blood tests. She was asymptomatic. Her Parathyroid hormone (PTH) was 14.1 (1.1-6.9pmol/l) and 25 hydroxy vitamin D 16 (15-174 nmol/l). She had insulin treated diabetes following an episode of pancreatitis for which no cause was identified. She was treated as an inpatient with intravenous fluids and furosemide which improved the calcium to 2.67; however, calcium would increase to >3 after cessation of IV fluids.
Section 2: Investigations
24-hour urinary calcium and creatinine excretion results are inconclusive in pregnancy. A genetic analysis Hyperparathyroidism gene panel excluded Familial hypocalciuric hypercalcaemia (FHH). USS parathyroid did not identify an adenoma. Following multi-disciplinary team discussion, a CT neck scan was performed, and it did not localise an adenoma.
Section 3: Results and treatment
A clinical diagnosis of primary hyperparathyroidism (PHPT) was then made. Patient was reviewed by Obstetricians and Endocrine surgeons. In view of persistent hypercalcaemia, she was initiated on Cinacalcet 30mg twice daily which maintained her calcium level between 2.69 and 3.21. She had a parathyroidectomy at 31 weeks of gestation where a right inferior parathyroid adenoma was removed. Post-operative calcium level was 2.58 and PTH 3. She had a caesarean section at 36 weeks and successfully delivered a baby girl. The new-born"s calcium and PTH were normal, however; phosphate was high. Phosphate levels were monitored and normalised after 2 weeks. Cinacalcet has been reported to be associated with neonatal hyperphosphatemia.
Section 4: Conclusions and points for discussion
Hypercalcaemia in pregnancy is uncommon but has potential maternal and foetal complications, making a compelling argument for routine antenatal and calcium screening. The use of high-dose Cinacalcet in pregnancy as in this case, can help to manage resistant hypercalcaemia. This case highlights the beneficial role of joint management and timely surgical interventions for severe primary hyperparathyroidism in pregnancy to ensure the best possible maternal and foetal outcomes.

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P25

An exception to the rule: transformation of an adrenocortical lesion with benign radiological characteristics

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Section 1: Case history
A 69 year old man with chronic obstructive pulmonary disease was admitted with acute onset shortness of breath. A CT pulmonary angiogram revealed no focal lung abnormality but identified an incidental 40 x 32 mm left-sided adrenal lesion. An unenhanced CT, undertaken to characterise the lesion, showed a homogeneous, well-circumscribed appearance with a radiodensity of 4 Hounsfield units. Prior to involvement of the Endocrinology team, a dedicated MRI was also undertaken, which demonstrated signal dropout. Review of historical imaging showed the lesion to be present on a study 12 years earlier, measuring 30mm. Despite the patient"s co-morbidities of type 2 diabetes mellitus, obesity and hypertension – biochemical work-up was not suggestive of an adrenal hypersecretory syndrome. No significant change in size was observed on a repeat adrenal MRI two years later, and chemical shift analysis was again reassuring. Twelve months later, another acute respiratory exacerbation prompted further cross-sectional imaging of the chest. Unexpectedly, multiple scattered pulmonary nodules were seen in both lungs in addition to enlarged thoracic nodes suspicious for metastases. A staging CT showed the adrenal lesion to have enlarged to 50mm and to have changed in morphological appearance.
Section 2: Investigations
Urinary steroid profiling demonstrated a relative increase in progesterone, pregnenediol and 17-hydroxyprogesterone metabolites, suggestive of a malignant adrenocortical tumour. Molecular imaging showed the pulmonary nodules and thoracic nodes to be both FDG and metomidate avid, in-keeping with metastatic adrenocortical carcinoma (ACC).
Section 3: Results and treatment
Given disseminated disease with a poor functional status, a symptom-control approach was adopted following careful MDT discussion.
Section 4: Conclusions and points for discussion
We report the apparent transformation of a benign, non-functioning adrenocortical lesion into a malignancy - 14 years after it was initially imaged. To our knowledge, only two other such cases have been reported in the literature. In order to avoid excessive investigation, and the associated cost, current *European Society of Endocrinology* Guidelines suggest that non-functioning adrenal incidentalomas with benign features on initial imaging do not require further radiological surveillance. A recent large multi-centre study reported 0 of 98 ACCs to have unenhanced HU <10 or the presence of chemical shift. The only radiological feature of concern for the lesion in our case was size. We suggest that urinary steroid metabolite profiling be considered for all adrenal masses >4 cm, even when they meet other radiological criteria for characterisation as lipid-rich adenomata.

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P26

An unusual cardiovascular manifestation of hyperthyroidism

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Case History
41-year-old female presented with a 3-day history of fever, cough, and breathlessness. She had palpitations, diarrhoea and weight loss of 4-5 kg over 1 month. Graves" disease had been diagnosed 5 years prior to this episode and she had been treated with carbimazole but was not in remission. On this occasion, she was febrile and had atrial fibrillation. She also had right pleural effusion and bilateral pedal oedema.
Investigations
Blood tests confirmed Graves" thyrotoxicosis (T4 100pmol/l, T3 40.2pmol/l, TSH <0.03mU/l and high TSH receptor antibody 17U/l). She had high BNP 1141ng/l and deranged liver function tests. Chest X-ray and a CT chest confirmed a large right-sided pleural effusion causing near complete collapse of the right lung. Echocardiography showed an enlarged right ventricle (RV) with severe tricuspid regurgitation and raised pulmonary artery pressure (PAP 43-48mmHg).
Treatment
Diagnosis of Graves" thyrotoxicosis with impending thyroid storm was made. She was treated on ITU with carbimazole 60mg, prednisolone 40mg a day and beta-blockers. A chest drain was inserted to reduce the right-sided effusion. She had radioactive iodine 500MBq but was still requiring carbimazole 20mg to control thyroid function 7 months later (T4 18.9pmol/l, T3 5.8pmol/l, TSH <0.02mU/l). Repeat echocardiography showed resolution of pulmonary hypertension (PAP 20-25mmHg) and normal RV.
Discussion
Left ventricular failure is known to be associated with thyrotoxicosis, whereas RV dysfunction and pulmonary hypertension are not well-recognised complications. Several case reports describe an association between thyrotoxicosis and RV failure mostly seen in female patients with newly diagnosed Graves" disease. Signs of RV failure and pulmonary hypertension resolve when euthyroidism is achieved. RV dysfunction is predominantly driven by increased cardiac output and pulmonary vascular resistance. The condition may be under-diagnosed due to the non-specific symptoms of breathlessness and fatigue. Signs and symptoms of

RV dysfunction should be sought in all patients with newly diagnosed thyrotoxicosis. In patients with unexplained RV failure or pulmonary hypertension thyroid dysfunction should be checked as it may improve with restoration of euthyroidism.

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P27

A rare case of recurrent insulinoma

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Section 1: Case History
A 45-year-old gentleman attended the emergency department in December 2016 with an episode of stupor, confusion and lethargy with blood glucose of 1.8 mmol/l. He recovered after administration of IV glucose. He had 'funny spells' for a year prior to the event. He had a history of childhood asthma and was not on any regular medications. There were no significant findings in the clinical examination and no relevant family history.
Section 2: Investigations
A 72 hour fasting test was arranging. After 3 hours, the patient developed symptoms of hypoglycemia. Serum glucose levels from this time were 2.8 mmol/l, Insulin 25.4pmol/l and C-peptide 3.25 nmol/l, suggestive of hyperinsulinemia hypoglycemia. The sulphonylurea screening was negative. The urea and electrolytes, thyroid, pituitary, adrenal and fasting gut hormone levels were within normal limits. His HbA1C was 28 (26-41 mmol/mol). An MRI of pancreas demonstrated that there was a 3.5 cm x 2.6 cm exophytic lesion arising from the tail of the pancreas, with some local lymphadenopathy.
Section 3: Results and treatment
The patient was managed well with dietary adjustment and glucose tablets. He was referred to Hepatobiliary MDT and had Gallium Dotate PET CT revealed that there was an uptake with the tail of pancreatic lesion without evidence of metastases. Subsequently, he successfully underwent Laparoscopic resection of a distal pancreatic insulinoma in June 2017. Histology showed a well differentiated grade 1 neuroendocrine tumour with an MiB1 of 1% pT2N0. The biochemical and genetic MEN1 screening was negative. There were no further hypoglycemic episodes until April 2021 where he had a hypoglycemic episode (Blood glucose 1.1 mmol/l) requiring an ambulance assistance. The paired serum glucose 2.9 mmol/l, Insulin 385pmol/l, proinsulin 535pmol/ and C-peptide 349pmol/l were suggestive of recurrent insulinoma. No new enhancing pancreatic lesion in repeated MRI pancreas was identified. The repeated fasting gut hormones were within normal limits. A HbA1C was 26 mmol/mol. He had been referred to Hepatobiliary MDT due to concern of recurrent insulinoma.
Section 4: Conclusions and points of discussions
This is a rare case of insulinoma. The risk of recurrence was 5 to 7 percent without MEN1 and occurred between 4 to 18.5 years after initial operation. There is a likelihood of risk of recurrence in this case clinically and biochemically. Therefore, the further repeating MRI pancreas, EUS to look for residual tissue and a 72 hours fasting test is indicated.

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P28

Waterhouse Friedrichsen syndrome-A Complex Case

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Introduction
Waterhouse Friedrichsen syndrome-Severe adrenal insufficiency is a rare but life-threatening condition secondary to bilateral adrenal haemorrhages. In many cases, it is caused by fulminant meningococcaemia, but there are numerous other aetiologies, it can also be caused by use of medications that promote blood clotting, reduce platelet count, primary antiphospholipid syndrome, renal vein thrombosis or steroid use and has been associated with splenectomy as well. It is characterised by fever, rash and septic shock.
Case History
We present a convoluted case of 32 years old lady who presented with pleuritic chest pain and shortness of breath after long flight. Her past medical history included ocular surface disorder and Sjogren"s syndrome. A CT Pulmonary Angiogram confirmed a pulmonary embolism and consolidation. She was discharged on Apixaban and antibiotic. She presented a week later with worsening shortness of breath, headache, nausea and vomiting. Meningitis ruled out with normal lumbar puncture. With persistent and worsening inflammatory markers, CT thorax abdomen and pelvis was performed which suggested oedematous adrenal glands bilaterally consistent with adrenal haemorrhage and wedge-shaped, pleural-based regions of consolidation in lower lobes of both lungs. Random Cortisol levels were profoundly low at 14 nmol/l and Short Synacthen test confirmed adrenal insufficiency. She was replaced with hydrocortisone. Her Pituitary profile was normal apart from slightly raised prolactin at 1158 mU/l. In view of her ongoing headache and low cortisol, she underwent an MRI head that ruled out Pituitary Apoplexy but showed incidental finding of occluded superior sinus likely secondary to thrombus. Further CT Venogram confirmed multifocal cerebral Dural venous sinus thrombosis within the superior sagittal sinus and right sigmoid sinus/proximal right Internal Jugular Vein. Biochemical testing for thrombosis revealed isolated rise in lupus anticoagulant, which was deemed to be of minimal significance in absence of raised CLIP and Beta2 glycoproteins. Antiphospholipid was ruled out by Rheumatologist on clinical assessment.
Conclusion
Waterhouse-Friedrichsen syndrome is associated with high mortality. Management comprises of treating underlying condition and supportive care. It is important to suspect and investigate adrenal insufficiency as steroid replacement is crucial for good outcome. A good education regarding regular steroid replacement including sick day rules when commencing steroid replacement is paramount. A meticulous follow up plan in an Endocrine clinic is essential to monitor steroid replacement and progression of adrenal haemorrhages.

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P29

COVID-19 induced hypoparathyroidism

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Case history
A 55-year-old man presented to the Emergency Department with worsening breathlessness 11 days after testing positive for severe acute respiratory syndrome coronavirus 2 (SARS CoV 2). He reported ongoing diarrhoea, starting 1 week prior to the SARS CoV 2 infection. He was previously fit and well, on no regular medication. On examination he was alert, with all clinical observations within normal limits and there were no significant findings in the chest and abdomen.
Investigations, results and treatment
Day 1 Sodium 127 mmol/l (133-146) Potassium 3 mmol/l (3.5-5.3) eGFR 58 ml/min CRP 41 mg/l (0-10) Serum osmolality 267 mosmol/Kg (280-300) Provisional Diagnosis: Hypovolaemic hyponatraemia and hypokalaemia secondary to diarrhoea. Treatment: Intravenous fluids. **Day 2** Adjusted Calcium 0.98 mmol/l (2.2-2.6) Phosphate 1.01 mmol/l (0.74-1.62) ALP 78 U/l (40-150) PTH 5 ng/l (15-68) Magnesium 0.52 mmol/l (0.7-1.0) Vitamin D 34 nmol/l (50-200) Stool culture – Campylobacter sp. ECG – Prolonged QTc Provisional Diagnosis: Profound hypocalcaemia secondary to hypomagnesaemia due to campylobacter diarrhoea. Treatment: Intravenous fluids replacement of calcium and magnesium, and oral loading dose cholecalciferol. **Day 11 (discharged from hospital)** Adjusted Calcium 1.96 mmol/l (2.2-2.6) PTH 4 ng/l (15-68) Magnesium 0.92 mmol/l (0.7-1.0) Sodium 137 mmol/l (133-146) Potassium 4.8 mmol/l (3.5-5.3) eGFR >90 ml/min Provisional Diagnosis: Resolving hypocalcaemia and other electrolyte disturbances secondary to campylobacter diarrhoea. Treatment: Cholecalciferol 20,000 units once weekly for 6 weeks, Adcal-D3 4 tablets daily and Alfacalcidol 0.5 micrograms once weekly. **3 Months Later** Parathyroid antibodies - Negative Adjusted Calcium 2.08 mmol/l (2.2-2.6) Phosphate 1.4 mmol/l (0.74-1.62) PTH 6 ng/l (15-68) Magnesium 0.82 mmol/l (0.7-1.0) Final Diagnosis: SARS CoV 2 infection-induced hypoparathyroidism, complicated by campylobacter diarrhoea (resolved). Treatment: Adcal-D3 2 tablets daily and Alfacalcidol 1 microgram daily.
Conclusions and points for discussion
Hypocalcemia is a prevalent symptom of SARS CoV 2 infection, and appears to be a predictor of severe infection but is largely self-resolving. Several reports have shown SARS CoV 2 infection leading to autoimmune diseases but rarely involve the parathyroid gland. Hypoparathyroidism is typically caused by injury to the parathyroid gland from surgery, autoimmune disease, genetic causes, or infiltrative diseases. Three case studies have described SARS CoV 2 infection-induced hypoparathyroidism, but none with as profound hypocalcaemia requiring ongoing active vitamin D therapy.

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P30

Lansoprazole induced hyperprolactinemia: Uncommon side effect of a common drug

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Hyperprolactinemia is known to have a wide differential with multiple causes including physiological, pathological and pharmacological. Drug induced causes of hyperprolactinemia are myriad however these become significant when prolactin levels rise to proportions that lead to clinical manifestations. We present a case of a 40 years old lady who was referred to endocrinology for an irregular menstrual cycle. Initial investigations revealed a prolactin level of 5767 mIU/l (range 102-496 mIU/l). Prior to the past 1 year, she had regular menstrual cycles after a menarche at the age of 13. No hirsutism was reported. Over the last 1 year she reported menstrual cycles occurring in gaps of 2 and a half months. She further reported galactorrhea for 6 months. Her past medical history only included gastro-esophageal reflux for which she was being followed up by gastroenterology and had been on lansoprazole since the past 1 year. On examination, she had a weight of 70.15 kg, height 152 cm with a BMI of 30 kg/m2. Her BP was 113/73mmHg. Visual fields were normal to confrontation. Palpation of neck revealed no palpable goitre and she was clinically euthyroid. Bloods revealed negative serum HCG, FSH 11 IU/l, Estradiol 494 pmol/l, LH 23.1 IU/l, testosterone 1 nmol/l (range 0-2.8 nmol/l), IGF 1 15.6 nmol/l (range 10.0-38 nmol/l). Pelvic Ultrasound revealed no evidence of polycystic ovaries. MRI Pituitary was reported as normal. Initially recommended a course of cabergoline in view of symptoms, patient had spontaneous resumption of menses following stopping lansoprazole. Prolactin was noted to fall to 117 mIU/l, two months post stopping lansoprazole. Lansoprazole is a commonly prescribed medication; this case report is unique as clinically significant hyperprolactinemia with such high levels of prolactin have not been reported before. Multi-disciplinary management of such cases is essential particularly with a wide variety of non-endocrine specialties prescribing these medications.

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P31

Complications of phaeochromocytoma: a case of catecholamine-induced cardiomyopathy

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Case History

We present a case of a 33-year-old woman who attended with heart failure whilst awaiting a surgical resection of phaeochromocytoma. She presented hours after an intravenous iron transfusion to treat her known iron-deficiency anaemia secondary to menorrhagia from massive uterine fibroids, for which she under the care of the gynaecology team. She was known to have a right-sided phaeochromocytoma, which was found incidentally on MRI in 2021, and was taking phenoxybenzamine in preparation for surgical resection. The massive uterine fibroids were felt to complicate the surgical approach for a resection of her phaeochromocytoma, and as such a myomectomy was deemed necessary to facilitate the adrenalectomy. The combination of procedure complexity and frequent bouts of symptomatic anaemia requiring transfusions, resulted in a delay in her planned joint procedure. She had no other significant past medical history and as part of a pre-operative assessment in November 2021, she had had a transthoracic echocardiogram (TTE) which was normal. Her presenting symptoms included progressive breathlessness, dry cough, severe fatigue, and in contrast to her previous presentations with breathlessness from anaemia, she exhibited clinical features in keeping with fluid overload.

Investigations

Chest x-ray revealed bilateral perihilar shadowing and prominent pulmonary vasculature ECG showed sinus tachycardia. TTE revealed global left systolic dysfunction with an estimated ejection fraction $<35\%$, left atrial and ventricular dilatation and high probability of pulmonary hypertension.

Results and Treatment

In view of the results above, a diagnosis of catecholamine-induced cardiomyopathy was made, and urgent endocrinology and cardiology reviews were sought. Initial medical management consisted of furosemide, bisoprolol and supplemental oxygen therapy. She was transferred to a rhythm-monitored area due to the risk of cardiac arrhythmias. Symptomatic improvement was observed, and a joint adrenalectomy and myomectomy was expedited.

Conclusions

This case highlights the importance of recognising this uncommon complication of phaeochromocytoma. It also emphasises the importance of comprehensive clinical assessment, including the physical examination, when patients present repeatedly. This patient had multiple attendances with breathlessness from her symptomatic anaemia and was treated appropriately with red blood cell and iron transfusions. However, on this occasion there were new features on examination to suggest a different aetiology that could have resulted in misdiagnosis if missed.

Table 1

NT-proBNP (<400 pg/ml)	596
CRP (<5 mg/l)	6
Hb (115-165 g/dL)	93
MCV (80-100 fL)	68
Troponin (<15 ng/ml)	24

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P32

Pituitary Apoplexy presenting with acute hyponatraemia

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Case history

48-years old man, with no comorbidities, presented to A&E due to global headache of 20 days duration, with associated intermittent vomiting, but no photophobia, cranial nerve impairment, neck pain or visual disturbance. The first head-scan (CT, computed tomography) was unremarkable, hence was discharged with safety advises. One week later, he represented to A&E with similar complaints. On enquiries, he mentioned to be reviewed by an optician 6 months ago, and was advised to use glasses. Detailed clinical assessment highlighted features of acromegaly, with acral enlargement, prognathism, fleshy nose, macroglossia and prominent eyebrows.

Investigations

The routine biochemistry showed profound hyponatremia 115 mmol/l (normal 135-145), from a baseline of 137 mmol/l previously. Further biochemistry showed serum osmolality 242 mOsm/Kg (normal 275-295), Urine Osmolality 476 mOsm/Kg (normal 50-1400); Urine Na 106 mmol/l. Hormone results were as follows: random early morning cortisol of 65 nmol/l, FT4 15.5 pmol/l (normal 12.0-22.0), TSH 0.13 munit/l (normal 0.3 – 4.2). A repeat head-CT revealed no pathology.

Results and treatment

Given the results, he was started on intravenous hydrocortisone replacement. He received IV Hydrocortisone of 100mg STAT followed by 50 mg QDS. Hypertonic saline as per trust"s protocol was co-administered. A total of 5 doses of 150 ml 2.7% NaCl boluses was given in ITU, with minor improvement of Na to 117 mmol/l. Subsequently, he received 30% NaCl infusion at 5 ml/hour with close hourly monitoring of serum sodium. After achieving a level of 125 mmol/l of serum sodium, he was stepped down to medical ward. His 9AM Pituitary profile showed ACTH < 1.5ng/l (normal 2.7 – 63.3); Prolactin 375nU/l (normal 86-324); FSH 5.3 IU/l (1.5-12.4), LH 3.2 (1.7-8.6); Testosterone 3.9 nmol/l (8.6-29.0) with IGF-1 of 47.3 nmol/l (8.5-31) and GH 3.43 mg/l. Urgent MRI Pituitary was done, which showed pituitary macroadenoma, with supra-sellar extension and hyperintense signal keeping with possible haemorrhage. Formal visual field assessment showed bilateral temporal field defects. Glucocorticoid replacement resulted in normalization of electrolytes. The case was discussed in the pituitary MDT and was deemed suitable for routine surgery. He was discharged with plan of outpatient oral glucose tolerance test for formal assessment of GH.

Conclusions

The spectrum of clinical presentation of pituitary apoplexy can be highly variable. Acute hyponatremia is an unusual presentation, especially in context of absent ocular manifestations. Severe glucocorticoid deficiency should be considered as differential in acute hyponatremia.

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P33

Post-operative impending thyroid storm

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Case history

A 32 year old female was admitted for an elective gynaecological procedure LLETZ (large loop excision of the transformation zone) under general anaesthesia as per patient"s request. An uncomplicated LLETZ procedure was performed. Post operatively, patient was found to be tachycardiac and had severe palpitations with nausea. She then reported that she had recently lost a significant amount of weight, had

been suffering with anxiety, palpitations, and tremors prior to the operation. She had not disclosed any of her symptoms to a healthcare professional at any point prior to undergoing surgery. On examination, she was apyrexial, tachycardic, had a diffuse goitre with a thyroid bruit and evidence of exophthalmos. There was no evidence of heart failure and no cardiac murmurs. An urgent endocrinology review was sought, and the patient was also reviewed by the critical care outreach nurse and intensive care consultant before deciding to admit the patient overnight on a medical ward for observation.
Investigations
Urgent thyroid function tests were sent post operatively which showed T4 >100 and suppressed TSH of <0.01. The rest of the routine blood profile was unremarkable, including a septic screen. ECG showed sinus tachycardia. TSI was positive confirming Graves' disease.
Results and treatment
She was commenced on propranolol and carbimazole for management of her thyrotoxicosis, as well as symptom control with anxiolytics and antiemetics. The patient complained of symptoms relating to pressure from her goitre and therefore a CT neck was performed which did not show any acute compromise. She was monitored under the endocrinology team until her symptoms settled and discharged with follow up.
Conclusions and points for discussion
Stress from surgery and general anaesthesia are known to precipitate thyrotoxicosis, and it is common practice to ensure patients are euthyroid before undergoing surgery. In addition to thyrotoxic crisis, further complications can arise from surgery in untreated hyperthyroidism. These complications can include intubation difficulties due to goitre and changes in metabolism of anaesthetic drugs. Pre-operative planning is vital to ensure any thyroid problems are investigated and treated prior to surgery. History and clinical examination are important aspects of the pre-operative planning process to aid in diagnosis of thyroid conditions which have potential to be exacerbated during surgery

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P34

Adrenocortical carcinoma as a cause of Cushing's syndrome

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Section 1: Case history
A 55 year old female patient sought review from her GP due to ongoing fatigue, muscle weakness, scalp hair thinning, weight gain and fluid retention. This had been ongoing for a few months and she was started on HRT. Initially she saw an improvement however her relief from symptoms was short lived. 5 months later she noticed a rash which was described as purpuric. A relative described her as having a "moon face" which prompted further review from the GP.
Section 2: Investigations
As an outpatient, 2 urinary cortisol levels were 810nmol/24h and 1657 nmol/24h. A dexamethasone suppression test showed inadequate suppression of cortisol (876 nmol/l). A urinary tract ultrasound revealed an irregular, heterogenous mass from the left kidney and hyperechoic lesions throughout the liver suspicious for metastases. Dedicated CT imaging showed a large 14 cm left sided renal mass concerning for an underlying renal cell carcinoma (RCC). She was admitted to hospital after having a collapsing episode – it was determined this was likely a vasovagal from the history but she was found to be hypokalaemic with a metabolic alkalosis, raising the suspicion of a cortisol/ACTH secreting tumour. This prompted further inpatient testing.
Section 3: Results and treatment
Further tests were performed, with an androstenedione level of 9.7 mol/l and DHEAS 64.0 mol/l. Conclusive diagnosis was gained from a renal biopsy specimen, which revealed this was actually an adrenal cortical carcinoma (ACC) rather than an RCC. Inhibin, Melan A, SF1 positive (negative for pancytokeratins, cytokeratin 7, RCC marker, PAX 8, c-kit, CD10, synaptophysin, chromogranin, S100, PLAP, Oct 3/4, Calretinin, oestrogen receptor and hepatocyte specific antigen. Patchy staining for EMA and Gata 3. Unfortunately, given the metastatic disease this patient"s prognosis is very poor. She has been started on metyrapone however is for best supportive care.
Section 4: Conclusions and points for discussion
Patients with ACC will usually present in one of three ways. In approximately 10% of patients, an adrenal mass is found as an incidentaloma. Around 30% patients present with symptoms of a mass prompting further investigations without clinical findings of hypersecretion. Most commonly (~60%) there are clinical symptoms suggesting hypersecretion from the adrenal gland. Aldosterone secretion which results in hypertension and hypokalemia is rare in ACC. It is more likely that the mineralocorticoid effects are being caused by high cortisol levels or steroid precursors such as 11-deoxycorticosteroine.

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P35

A rare case of potential Carbimazole-induced lymphopenia

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Case history
Carbimazole, a widely used medication to treat hyperthyroidism, is associated with several well-established side effects. Carbimazole-induced lymphopenia is however rarely reported in the literature. This case focuses on a 57-year-old lady diagnosed with Graves' Disease (GD) in 2015. She was started on Carbimazole which eventually stabilised her thyroid function; her severe thyroid eye disease precluded definitive treatment with radioiodine however she was reluctant to consider thyroidectomy as definitive therapy due to personal reasons and opted for ongoing medical thyroid management. Soon after commencing Carbimazole treatment, she developed a resistant lymphopenia which could not be explained by other haematological or immune disorders.
Investigations
Initial Thyroid function tests confirmed significant hyperthyroidism (TSH $<$ 0.014 [0.35-4.94 miu/l], T3 41.2 [2.9-4.9 pmol/l], Free T4 >100 [9-19 pmol/l]) with positive Anti-TSH receptor antibody (44.05 IU/l [0-2 IU/l]). Both the history and examination were consistent with Graves thyrotoxicosis. She was monitored regularly with blood tests including thyroid function and full blood count.
Results
Upon confirming a diagnosis of GD, the patient was started on Carbimazole with the usual precautions taken against agranulocytosis. One year after initiating Carbimazole treatment, she had developed lymphopenia which did not recover after a brief period of discontinuation of Carbimazole while the rest of the haematological indices were all normal. Patient did not receive any treatment for lymphopenia since she was asymptomatic.
Discussion
Neutropenia is a rare but well-known side effect of Carbimazole, on the other hand, lymphopenia is not an often-associated feature consequently there is very limited relevant literature. It is not unusual for thyrotoxicosis to be associated with neutropenia; it frequently precedes Carbimazole initiation and mostly settles after treatment. The mechanism behind Carbimazole-induced lymphopenia has not been confirmed; however, the literature suggests that Carbimazole can lead to the production of antibodies and autoantibodies which can lead to cell lineage-specific cytopenia. In conclusion, we present the case of a patient with GD where lymphopenia appears to have a temporal relationship with commencement of Carbimazole. The cause of this rare phenomenon in this context is probably due to a combination of Carbimazole effects and the condition itself, however the effect of this combination cannot be precisely established. We present this case to raise awareness among clinicians and to attract comments from our specialist colleagues based on their extensive collective clinical and research experience.

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P36

Kallman Syndrome: A unique presentation

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70yrs male was referred to endocrinology due to an abnormal blood test showing hypogonadotropic hypogonadism. Initial investigations were done due to bilateral gynecomastia worsening over 20 years, by the breast team. He did not go through puberty as a child and was given a testosterone injection at the age of 12yrs for a year. This was discontinued due to sexual arousal since then he did not have any further endocrine follow-ups. He had symptoms of tiredness, reduce libido, and erectile dysfunction. He had no sense of smell. There was no facial, axillary, or pubic hair growth. Tanner stage 1 testicles were noted with a very small penis. He underwent a mastectomy for gynecomastia. He has a background history of COPD, hypothyroidism, and BPH. His usual medications include thyroxine, Omeprazole, finasteride, and tramadol. No significant family history of endocrine problems. No history or evidence of anabolic steroids.
Investigation and Results
FBCs, renal, and liver profiles are Unremarkable. FSH <1.0 (1-10 unit/litre), LH <1, prolactin 150microunit per litre, Estradiol <37pmol/l, Testosterone $<$ 0.5(6.7-25.8 nmol/l), random Cortisol adequate, IGF-1 normal, HbA1c 37, PSA <0.050, TSH ranging between upper end of normal up to 10mu/l. MRI head/pituitary; normal pituitary gland. Further high-resolution images showed the absence of the olfactory bulb and olfactory sulci. Bone scan was organized for him but didn't attend. Xray pelvis for lower back pain reported as markedly osteopenic bone.

Treatment
Investigations and MRI findings suggestive of Kallman syndrome. Testosterone were low all his life. He was offered testosterone therapy in the form of tostran gel 2% 2 squirts/day. Treatment will help with generalized tiredness and sexual symptoms along with osteoporosis. He was informed that his gynecomastia can get worse on this replacement ad given the diagnosis of BPH we need to monitor FBC and PSA. He was further referred to a geneticist for genetic testing for Kallman syndrome.
Conclusion and discussion
Patient was unhappy with testosterone. Not much difference noted in general well-being but he experienced erections on and off which he felt embarrassed about. He also noticed an increased breast size. He had discontinued the treatment on his own and declined any further testing including genetic workup. Case was unusual due to age of presentation. It was further complicated due to BPH diagnosis with negligible testosterone and very low PSA. Offered treatment has more implications than just improving secondary sexual characteristics. Subphysiological doses were causing significant side effects.

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P37

Pancreatic encephalopathy secondary to DKA induced pancreatitis

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Background
We would like to present a case of pancreatic encephalopathy induced by DKA induced hypertriglyceridemia. The triad of acute pancreatitis, hypertriglyceridemia and diabetes is a rare occurrence. Through our case we aim to highlight the importance of making an early diagnosis as a delay in diagnosis can worsen outcomes.
Case history
We present the case of a 51 year old Type 2 Diabetic non compliant with her medications who was admitted to the emergency department with abdominal pain and generally feeling unwell. She was diagnosed as having Diabetic Ketoacidosis based on her venous blood gases and capillary ketones and started on appropriate treatment. The patient started to become more drowsy and hence had to be admitted to the intensive care unit for investigating the cause of her drowsiness and to support her airway.
Investigations and Treatment
Bloods done revealed evidence of increased Triglycerides and high lipase. She had a CT head done which showed no evidence of acute abnormalities. CT abdomen revealed evidence of peripancreatic free fluid suggesting pancreatitis. Subsequently she had a Lumbar puncture done to rule out evidence of CNS infection which was normal. The patient improved during her stay in the ICU with closed monitoring and had a full recovery.
Conclusion
Hypertriglyceridemia is associated with more complications and poor outcomes. Acute pancreatitis can be induced by diabetic ketoacidosis (DKA), complicated by hypertriglyceridemia. However, and to the best of our knowledge, the association of this triad of pancreatitis, hypertriglyceridemia, and diabetic ketoacidosis and its treatment has not been widely discussed in the literature. Rapid diagnosis is difficult due to overlapping signs, but it is crucial for adequate management.

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P38

Polycythaemia secondary to transdermal testosterone replacement therapy (TRT)

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Introduction
With increasing prevalence of hypogonadism, testosterone replacement therapy (TRT) remains the mainstay of treatment for male hypogonadism. Polycythaemia, the commonest reported side effect of TRT is often claimed to be less with transdermal preparations than intramuscular.
Case history
A 48 years gentleman, initially presented in primary care with reduced libido, erectile dysfunction(ED), low energy levels. Early morning testosterone levels (T-levels) were 10.9 nmol/l and 9.7 nmol/l (10.0-30.0 nmol/l) on two separate occasions for which he was started on transdermal TRT at 50mg/5g without any further evaluation to identify the etiology or free testosterone check or calculation. His pretreatment haemoglobin, haematocrit, thyroid, renal, lipid and bone profile, HbA1c, prostate specific antigen and liver function tests were normal but no gonadotrophins check. Within 8 weeks of TRT, his haemoglobin crept up from 167g/l to 194g/l (130-170g/l) and haematocrit from 0.50L/l to 0.58L/l (0.40-0.52L/l) when he was referred to secondary care. On review in secondary care his energy levels had improved but no improvement in libido and ED. Additionally he complained of facial flushing and generalized body itching worse after warm bath. His past medical history included well controlled primary hypothyroidism and hypertension. Examination showed extreme plethora, central obesity with BMI 39.6 kg/m2 and blood pressure of 150/80mmHg.
Investigations
Repeat blood tests confirmed polycythaemia, testosterone 6.7 nmol/l (10.0–30.0 nmol/l) and inappropriately normal follicle stimulating hormone 8.2U/l (1.3-19.3U/l), luteinizing hormone 3.7U/l (1.2-8.6U/l), normal prolactin and iron profile thus a likely diagnosis of functional hypogonadotropic hypogonadism secondary to obesity. Retrospective free testosterone calculation using formula of pretreatment T-levels revealed both normal free testosterone (0.391 nmol/l) and bioavailable (1.35 nmol/l) testosterone which indicates TRT wasn"t required in the first place.
Results and treatment
Given symptomatic polycythaemia, his TRT was immediately stopped and as per advice of haematology urgent venesection was done, prophylactic antiplatelet for 6-8 weeks and outpatient haematology follow up for secondary workup of polycythaemia which completely resolved after stopping TRT with haemoglobin of 175g/l and hematocrit 0.52L/l.
Conclusions and points for discussion
1. Polycythaemia remains the commonest side effect of TRT even with transdermal preparations.
2. In borderline or lower normal total testosterone or obesity, free testosterone should be checked using equilibrium dialysis or estimated using standard formula.
3. Once hypogonadism is confirmed, further workup to establish the cause should be considered specially gonadotrophins prior to TRT initiation.
4. Consideration of venesection and/or antiplatelet for 4-6 weeks to reduce vaso-occlusive events in severe symptomatic polycythaemia.

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P39

An interesting case of Myxoedema Coma in a patient, who presented with an unwitnessed fall, hypothermia, hyponatraemia and reduced consciousness

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Case History
We report a case of 81-year-old female of white background who was admitted after a fall with long lie and confusion. On arrival, she was found to be hypotensive BP-85/46 mmHg, Hypothermic-temp-20.9 and bradycardic HR-46 beats/min, GCS was 13/15 with low normal CBG-4.0 mmol/l. She has a history of chronic hyponatraemia, thyroidectomy 9 years prior to this presentation and a previous admission with fall leading to pelvic fractures. During that admission she was started on 25 mg levothyroxine but she later declined levothyroxine therapy due to her concerns about its side effects.
Investigations
Serum Sodium-122 mmol/litre (low), paired osmolalities- Serum osmolality-255mosm/KgH2O, urine osmolality-291 mosm/KgH2O, urine sodium-89.
Other biochemistry
CPK-2890U/l (25-200)), Random Cortisol-793 nmol/l, TSH > 48.10mIU/l (0.30-4.80), Free T4- < 3.2pmol/l (7.7-20.6), Hi Sens CRP 99.7mg/l (0.0-5.0) CBG-4.0 mmol/l initially, improved later to 6.4 mmol/l. CXR-unremarkable, Urinalysis-NAD CT Head showed no acute brain injury.
Management
As the available thyroid hormone level was deranged along with her clinical presentation, we suspected myxoedema coma, for which she was treated with intravenous Liothyronine T3-20 mg followed by levothyroxine via a nasogastric tube, starting at a dose of 50 mg and 2.7% hypertonic saline infusion as she had confusion and had altered sensorium. Her sodium level improved from 122 mmol/l to 136 mmol/l over 10 days and her symptoms completely resolved. She was discharged on Levothyroxine 150 mg. She was also treated empirically with antibiotics due to an elevated C-reactive protein.

Conclusion
This is an interesting case as this post-menopausal lady had suffered from falls and chronic hyponatraemia presented with myxoedema crisis precipitated by an unspecified infection and the fact the she had declined thyroid replacement therapy. Her sodium levels improved and symptoms resolved after hormone replacement was initiated. She is being discharged back to the care of her GP with thyroid function test monitoring in 4-6 weeks' time.

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P40

Incidentally found Acromegaly after a Road Traffic Accident

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Section 1: Case history
A 19-year-old Caucasian female presented to the A&E department with a head injury following a road traffic accident. A CT head done to exclude head injury was normal but incidentally showed a significant pituitary macroadenoma and she was referred to endocrinology as out-patient urgently. This was delayed by 4 months due to face-to-face clinics being suspended in the first wave of the pandemic. Virtual consultation revealed a history of headaches for 3-4 months on the left side with no sinister features. No change in ring size or shoe size was noted. Her past medical history was significant for well-controlled asthma and no significant family history. Clinical examination was delayed for 6 months since referral, however, there were no acromegalic features noted, weight was 16.5 stone, height 5ft 8in, and BMI 34.7.
Section 2: Investigations
Investigations were requested virtually- 1) MRI Pituitary confirmed a significant pituitary macroadenoma with no signs of compression of optic tract. 2) A complete pituitary profile including short syncathen test - unremarkable except for an IGF-1 of 127.1 nmol/l 3) Formal visual fields- normal, 4) Oral Glucose Tolerance test with GH suppression- fasting glucose 15.4 and GH 4.44 mg/l. 5) HbA1c 73 6) Gene analysis for AIP, CDC73, CDKN18, and MEN1(RET) – all negative.
Section 3: Results and treatment
She was discussed in pituitary MDT and referred to Neurosurgery. She was started on Octreotide LA while awaiting surgery and metformin for diabetes. She underwent TSS resection successfully.
Section 4: Conclusions and Points for Discussion
Post-surgery she developed transient DI and hypoadrenalism. This resolved 2 months post-surgery and she is now completely well and off all medication including metformin. She is now regularly followed up with radiological surveillance.
- Acromegaly is a rare, chronic disease, associated with increased mortality.
- Suspicion of diagnosis typically arises with classic phenotypic features and raised IGF-1 levels, confirmed by failed suppression of GH levels.
- Usually patients with acromegaly are identfied once the clinical features and associated complications of bowel polyps, nasal tract, diabetes and cardiovascular system have set in.
- Incidental diagnosis prior to the manifestation of any clinical signs and symptoms is rare.
- This has a significant impact on morbidity and mortality of the patients.
- In a world where over-investigation with radiology is often criticized due to benign incidental findings, this case makes a strong point for the benefit of continuing the same.

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P41

An interesting cause of Hypertensive Crisis: Phaeochromocytoma

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Case History
A 46 year old lady presented to A&E with a 4 day history of headache, vomiting, abdominal pain and fever. On further questioning, she admitted to having had experienced occasional episodes of palpitations, hot flushes and headaches over the past few months. She had history of appendectomy when she was young and acoustic neuroma removal few years ago. She wasn't on any regular medications. On clinical examination, she looked visibly unwell and was hypoxic requiring 8L of oxygen to maintain SpO2 above 94%. Her BP was raised at 177/103. She had bi-basal crackles on lung auscultation, otherwise her heart sounds were normal with no murmurs, though she was tachycardic. Abdominal examination revealed generalised mild tenderness on palpation with no guarding or rigidity.
Investigations
A Full Blood Count was as follows: Hb: 166 g/l, WCC: 31.7, Neutrophil: 28.3, PLT:332. Renal Profile: Na: 144, K:3.7, Urea: 10.2, Creatinine: 174, eGFR 30, Amylase: 556, Troponin: 1433 Arterial Blood Gas: pH 7.22, Pa02 10.5, PCO2 6.97, Lactate: 5.8, HCO3 14.9 CXR was reported as "Patchy areas of opacification in bilateral lower zones" CT Head: Previous Right temporal bone craniectomy CT Thorax Abdomen Pelvis: A large left heterogeneously enhancing solid ADRENAL mass with apparent cystic components measuring 7.5 cm in diameter suspicious for a phaeochromocytoma was noted with extensive bilateral pulmonary infiltrates Plasma Metanephrine: 1730 ng/l (Normal range 0-99), Plasma Normetanephrine: >3500 ng/l (Normal range: 0-169) 24 h Urine Metanephrine: 191.18 umol (Normal range: 0-1.2)
Results & Treatment
The patient was moved to ITU where she was commenced on intravenous antibiotics, fluids and oxygen & was catheterised. Over the next 5 days, there was a marked improvement in her biochemical profile & her oxygen requirement went down. An endocrine input was sought. She was started on Phennoxybenzamine 10mg BD which was gradually increased to 60mg TDS. Following MDT Discussion, she was listed for left Sided Adrenalectomy after 2 weeks. Post surgery, she was commenced on Hydrocortisone 20/10/10mg TDS & further Endocrine follow up was organized. Histology report eventually confirmed Phaeochromocytoma PASS 3
Conclusions and points for discussion
Screening for secondary hypertension should always be considered in relatively young patients without risk factors, those with resistant hypertension, individuals with sudden deterioration in BP control, hypertensive urgency and emergency & those presenting with high probability of secondary hypertension based on strong clinical clues. Relevant investigations should then be requested based on history and clinical examination.

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Author Index