Society for Endocrinology: Endocrine Update 2018

EDITORS
The abstracts submitted were marked by the Abstract Marking panel selected by the Programme Committee. With special thanks to those involved in the Society for Endocrinology events:

National Clinical Cases

Clinical Update Convenors

Dr James Ahlquist, Essex
Dr Peter Taylor, Cardiff

Abstract Markers

Dr Amir Sam, London
Dr Daniel Morganstein, London
Dr Miles Levy, Leicester
Dr Nicola Zammitt, Edinburgh
Dr Simon Aylwin, London
Dr Simon Howell, Lancashire
Dr Robert Semple, Cambridge
Dr Peter Taylor, Cardiff
CONTENTS

Society for Endocrinology: Endocrine Update 2018

NATIONAL CLINICAL CASES

Oral Communications ................................................................. OC1–OC10
Poster Presentations ................................................................. P01–P43

CLINICAL UPDATE

Workshop A: Disorders of the hypothalamus and pituitary (I)
  Diabetes insipidus ........................................................................ WA1–WA13
Workshop B: Disorders of the hypothalamus and pituitary (II)
  Management of acromegaly ........................................................ WB1–WB3
Workshop C: Disorders of the thyroid gland (I)
  Goitre and thyroid nodules .......................................................... WC1–WC4
Workshop D: Disorders of the thyroid gland (II)
  Thyroid cancer .............................................................................. WD1–WD7
Workshop E: Disorders of the adrenal gland
  Mineralocorticoid hypertension & Phaeochromocytoma ................. WE1–WE17
Workshop F: Disorders of the gonads
  Gynaecomastia and sex steroid & Sex steroid replacement in females WF1–WF4
Workshop G: Disorders of the parathyroid glands, calcium metabolism and bone
  Hypocalcaemia including vitamin D deficiency ............................. WG1–WG5
Workshop H: Miscellaneous endocrine and metabolic disorders
  Hypoglycaemia & Neuroendocrine tumours .................................. WH1–WH11
Additional Cases ............................................................................ CB1–CB16

INDEX OF AUTHORS
National Clinical Cases
OC1
Testosterone secreting clear cell ovarian tumor in a patient with Von Hippel Lindau (VHL) disease
Tehjmal Rehman, Ali Hameed, Katie Snape, Shirley Hodgson & Gul Bano St George’s University Hospitals NHS Trust, London, UK.

The VHL gene is a tumor suppressor gene located on chromosome 3p25.3. Mutations in this gene prevent production of the VHL protein and as a result, cells grow and divide uncontrollably to form the tumors and cysts. Germline VHL gene mutations predispose to a variety of tumors, most commonly retinal and cerebellar haemangioblastomas, renal cell carcinoma and pheochromocytoma. Papillary cystadenomas of the epididymis are seen in 10–20% of men are rarely in broad ligament of the uterus. Mutations in the VHL gene are inherited in an autosomal dominant pattern. A 26 years old female with a known mutation in VHL gene was under surveillance in genetic endocrine clinic. In the last 5 years she has undergone three surgeries for cerebellar haemangioblastomas. She had retinal angiomias and a cervical haemangioblastoma at C2/3. She was known to have a cyst in the right ovary measuring 4.9 cm. This had not changed in size in 4 years and her tumor markers were negative. She presented with 6 month history of feeling tired, amenorrhea and deepening of voice. Her pelvic ultrasound scan showed an increase in the size of right ovarian cyst. It measured 6.8 cm with a lobulated appearance. She had LH of 1.1 IU/l (1–9), FSH 2.3 IU/l (1–10) and testosterone of 22.1 nmol/l (0.5–2). She had a diagnostic laparoscopy and the right ovarian cyst was removed. Her periods started after 11 months of amenorrhea. Her postoperative testosterone was 1.5 nmol/l. Histology of the ovarian cyst showed it to be a clear cell carcinoma. In view of VHL mutation this was thought to be a metastasis from a renal cell carcinoma. This patient had no evidence of Renal cell carcinoma. The most likely diagnosis was testosterone producing clear cell carcinoma of the ovary. The ovarian cyst was documented on ultrasound scan 4 years ago and was non functioning before changing to a metastasis.

OS2
Episodic primary aldosteronism associated with a novel gain-of-function mutation in a cell adhesion molecule
Xilin Wu1,2, Sumedha Garg3 & Morris Brown1 1Queen Mary University of London, London, UK; 2Barts Health, London, UK; 3University of Cambridge, Cambridge, UK.

Case history
A 46-year-old headmaster with a 10-year history of hypertension presented with a BP of 164/116 mmHg on four antihypertensive drugs. He had occasional headaches, chest aches, and described one syncopal episode after an ‘exhausting rowing session’. A random cortisol was 115 nmol/l, but a repeat pre-and post-dexamethasone 1 mg at 8 p.m. cortisol was 7:1. He successfully underwent a right adrenalectomy. H&E plus immunohistochemistry (right:left).

OS3
Hyperprolactinaemia resistant to dopamine agonist due to an ectopic source of prolactin arising from a Uterine Tumour Resembling Ovarian Sex Cord Tumours (UTROSCT)
Mohamed Bakhti1, Sobia Arshad2, John Bidmead3, Masud Haq1, Dylan Lewis1, Salvador Diaz-Cano1 & Simon J. B. Aylwin1 1Department of Endocrinology, King’s College Hospital, London, UK; 2Department of Gynaecology, King’s College Hospital, London, UK; 3Department of Endocrinology, Tunbridge Wells Hospital, Tunbridge Wells, UK.

Introduction
Moderate hyperprolactinaemia occurring in a patient with a normal pituitary MRI, assuming macroadenoma and stress are excluded, is generally considered to be due to a lesion below the level of detection of the MRI scanner. Most patients with mild-moderate hyperprolactinaemia and a normal MRI respond to dopamine agonist therapy. We describe a patient who had prolactin elevation typical of a prolactin-secreting macroadroma, but with a normal MRI, and in whom the prolactin rose further with dopamine agonist treatment.

Case
A 46-year-old female presented with 12 months history of secondary amenorrhoea without galactorrhoea. Prolactin was 4746 mIU/l without macroadenoma ( macroadenoma with a normal MRI scan). A paradoxical rise in the serum prolactin rose further with dopamine agonist treatment.

Points for discussion
The notable features of this case were (1) the high prolactin suggestive of a macroadenoma with a normal MRI scan (2) the paradoxical rise in the serum prolactin after initiation of dopamine agonist therapy. Out of eight previous reports of ectopic extra-cranial prolactin secretion in the published literature, there are three ovarian germ cell tumours (two teratomas, one dermoid) which had microscopic pituitary elements. UTROSCTs are very rare uterine neoplasms with mild-moderate hyperprolactinaemia and a normal MRI respond to dopamine agonist therapy. However, two other cases have been reported with uterine tumours (one “fibroid” and one “mesenchymal tumour”) which share characteristics with this case. Hyperprolactinaemia due to extra-cranial ectopic prolactin secretion is very rare. Where suspected, the majority of ectopic prolactin-secreting tumours have been located in the ovaries and uterus.

References

DOI: 10.1530/endoabs.55.OC2

OS4
Papillary cystadenomas of the epididymis are seen in 10–26% of men are rarely seen in women. These benign tumours are often asymptomatic and generally diagnosed incidentally during an investigation of infertility or as a demonstration of a palpable testicular mass. Mostly unilateral, they may be bilateral in 20% of cases.

Case report
A 43-year-old male was described a 1.5 cm, soft, non-tender palpable swelling in the left epididymis for three years. He denied any pain, fever, or weight loss. Physical examination was normal. Serum levels of testosterone, luteinising hormone, follicle stimulating hormone, follicle stimulating hormone, prolactin, and thyroid stimulating hormone were within the normal range. Transrectal ultrasound showed a 1.5 cm, hypoechoic lesion in the left epididymis, with posterior acoustic enhancement. On MRI, the lesion showed no enhancement. Histology of the lesion showed that the tissue was composed of papillary fronds of dense connective tissue, with surrounding seminiferous tubules. The patient was followed up for one year and no recurrence was noted.

Discussion
Papillary cystadenomas of the epididymis are rare benign neoplasms of unknown aetiology. They are usually found incidentally, and are often asymptomatic. Their clinical presentation is variable, ranging from a palpable mass to infertility. Diagnosis is usually made through imaging studies, and histological examination of the lesion is required for definitive diagnosis. Treatment options include observation, surgical excision or long-term follow-up, depending on the size and symptoms of the lesion. In the current case, the patient was managed conservatively, with no recurrence noted after one year.

References

DOI: 10.1530/endoabs.55.OC4
OC4
Management of massive (up to 550 mm) bilateral adrenal masses in a non-adherent patient with 21-hydroxylase deficiency congenital adrenal hyperplasia: A complex risk-benefit analysis

Jasmin Waterhouse1, Laila Parvanta2, Scott Akker2, Dan Berney2 & Victor Lawrence1
1Isle of Wight NHS Trust, Newport, UK; 2Barts Health NHS Trust, London, UK.

Case history
We report a 38-year-old Caucasian woman with classical salt wasting congenital adrenal hyperplasia (CAH) who increasingly omitted medication in adolescence and eventually spent over 10 years without any adrenal replacement therapy or adrenal crises and became lost to follow up. When seen, she complained of increasing abdominal girth, fatigue, hirsutism, having type 2 diabetes, having never had a romantic/sexual relationship and was amenorrheic. Examination revealed abdominal distension by a massive palpable mass.

Investigations
Initial blood tests showed random serum Cortisol 149 mmol/l (200–600), Renin (plasma) 751.0 mU/l (2–30), plasma ACTH 333.0 ng/l (0–40), 17-OH-progesterone >726 mmol/l and serum total Testosterone 6.4 mmol/l. CT showed massive bilateral adrenal tumours which grew substantially during 3 years follow up during which ACTH and 17-OHP were appropriately suppressed. Displacement and distortion of abdominal viscera were noted.

Results and treatment
Massive bilateral adrenal enlargement, secondary to chronic ACTH stimulation due to non-adherence with adrenal replacement therapy was diagnosed. A long process of re-engagement with the patient took place until it was felt that the risk of further non-adherence was lower than the risks of leaving such massive adrenal glands in situ. The surgical strategy was to remove the larger left adrenal gland and if straightforward, to proceed to the contralateral side. Bilateral surgery was performed. The left adrenal weighed 11,405 g and measured 550 x 310 x 230 mm. The smaller right adrenal measured 170 x 145 x 180 mm. Histology confirmed florid hyperplasia with myelolipomatous metaplasia, consistent with untreated CAH.

Conclusions and points for discussion
Bilateral adrenalectomy is a therapeutic option in CAH particularly where the GC dose required for acceptable androgen suppression causes unwanted effects. Here, bilateral adrenalectomy had the potential to create new complete adrenal insufficiency in a patient whose risk of adrenal crisis might well be augmented by established treatment non-adherence. However, this risk had to be weighed against the additional risk of such massive bilateral adrenal enlargement (including haemorrhage, torsion, rupture, infarction, neoplasia and displacement of other viscera and possible diabetogenic effects of the intra-abdominal fat) particularly as it was clear that the masses continued to grow even after appropriate treatment and apparent adherence for a total of 3 years. Although it seems likely that the process of adrenal enlargement was initially ACTH-dependent, it is clear that progressive adrenal expansion eventually became independent of ACTH.

DOI: 10.1530/endoabs.55.OC4

OC6
Management of T3-toxicosis in pregnancy

Ruth Cordiner1, David Carly1, Andrew Powell1, Fiona Mackenzie3, Avril Scott2, Janice Gibson3 & Robert Lindsay1
1Glasgow Royal Infirmary, Glasgow, UK; 2University of Glasgow, Glasgow, UK; 3Princess Royal Maternity Hospital, Glasgow, UK; 4Queen Elizabeth University Hospital, Glasgow, UK.

Case history: Pre pregnancy
A 31-year-old female with no family history of thyroid disease presented with clinical hyperthyroidism and large goitre with bruit. Graves’ Disease was confirmed: TSH <0.01 (0.35–5.0 mU/l), free T3 5.34 (9.2–21.0 pmol/l), TSH Receptor Antibodies (TRAB) 19.9 U/l; TPO 6.0 U/ml. She was on carbimazole (CBZ: 20 mg BD) and propranolol. CBZ was stopped at 27/40. MRI confirmed a foetal goitre (right lobe 1.2 cm, left lobe 95th centile) was seen from 21/40 with radiological evidence of thyrototoxicosis (central vascularization on Doppler) but normal foetal heart rate. Cordocentesis was offered but declined. In conjunction with obstetrics, CBZ was increased. Foetal goitre increased, therefore cordocentesis and foetal MRI were undertaken at 27/40. MRI confirmed a foetal goitre (right lobe 1.4 cm x 1.2 cm, left lobe 1.4 cm x 1.1 cm) with minor airway flattening. Cordocentesis suggested foetal hypothyroidism: TSH 36.45, FT4 9.8, total T3 0.3. Maternal CBZ was down-titrated to 5 mg with reduction in foetal goitre from 31/40; thyroid circumference <50th centile by 37/40. Foetal growth scans were normal throughout.

Delivery and postnatal
Maternal biochemistry at 39/40: TSH <0.01 mU/l, FT4 15.0 pmol/l, total T3 3.2 pmol/l, TRABs 3.7 U/l. Baby was delivered by uncomplicated SVD. Neonatal biochemistry was nominally euthyroid but showed neonatal thyrotoxicosis at 5 days (TSH 0.31 mU/l, FT4 40.1 pmol/l, total T3 2.7 pmol/l, TRAB 6.1 U/l).

Conclusions and points for discussion
We describe a rare case of resistant T3 toxicosis in pregnancy. A number of discussion points include 1. Pre-pregnancy planning in women with Graves’ Disease. 2. Consideration of need for T4 supplementation when levels are low in T3 toxicosis in pregnancy. 3. Foetal monitoring with role of fetal ultrasound (for size and signs of hypo-and hyperthyroidism) and cordocentesis. 4. Neonatal thyrotoxicosis.

DOI: 10.1530/endoabs.55.OC6

OC7
Prolonged response to radiolabeled Yttrium⁹⁰ DOTATATE in a patient with metastatic insulinoma – 5 years follow up
Rajv Joshi1, Yong Du2 & Daniel Morganstein2
1Department of Endocrinology, Chelsea and Westminster Hospital, London, UK; 2Department of Nuclear Medicine, Royal Marsden Hospital, London, UK.

Case history
We have previously presented the case of a 31 year lady presenting with a seizure following exercise with a blood sugar of 1.4 mmol/l on a background of an 8 month history of episodic slurred speech, blurred vision and hunger relieved by eating in 2011.

Investigations
Investigations confirmed an insulinoma and imaging, including Ga⁶⁸ DOTATATE PET CT identified a lesion in the tail of the pancreas with multiple liver metastases. MEN1 testing did not reveal any mutation.

Results and treatment
She was treated with PRRT receiving 4 cycles of radiolabeled Y⁹⁰ DOTATATE therapy between August and November 2011. This resulted in a complete resolution of symptomatic hypoglycaemia. We now present 5 year follow up data.

Conclusions and points for discussion
She remains free of hypoglycaemia. Although she has suffered episodes of anxiety, capillary blood glucose monitoring has always remained normal. She has had annual MRI scans of the liver and pancreas which have shown stable changes. In 2017 she had a 5 year follow up Ga⁶⁸ DOTATATE PET CT scan the showed no somatostatin receptor avid lesions. The remaining stable lesions seen in the liver could represent scar tissue. She continues to have clinical follow up. This case illustrates that PRRT can result in long lasting remission of hypoglycaemia even in metastatic insulinoma as 5 years after treatment, and 4 years since this case was last presented, the patient has remained symptom and somatostatin receptor avid lesion free.

DOI: 10.1530/endoabs.55.OC7

OC8
Recurrent severe hypoglycaemic episodes in the context of insulin receptor antibodies
Ruth Ronneberger1, Afizah Nobeebux1, Yuliya Manova1, Gill Rumsby1, Francis Lant1, Gary Woodward1, David Isenberg1, Michael Ehrenstein1, David Halsall2, David Church2, Robert Semple1 & Helen Simpson1
1University College London Hospital, London, UK; 2University of Cambridge, Cambridge, UK.

We present a 32-year-old woman with recurrent hypoglycaemic episodes and a history of juvenile onset SLE. Over months, she experienced severe hypoglycaemic episodes with unconsciousness, occurring mainly in the early morning resulting in several hospital admissions. The patient had to take precautions like eating snacks between meals and before going to bed, and even setting an alarm clock to eat a bowl of porridge at 0200 h. She was of normal weight, did not present with any hyperpigmentation or acanthosis nigricans and did not have a history of diabetes mellitus. The known juvenile onset SLE had been difficult to control over the years with recurrent flares. Current treatment included prednisolone, hydroxychloroquine and azathioprine. A fasting blood test revealed a blood glucose of 1.8 mmol/l with borderline insulin level of 2.3 mU/l and undetectable C-peptide, making an insulinoma unlikely. NEFA and 3-hydroxybutyrate were inappropriately low, suggestive of hyperinsulinaemia or action via the insulin receptor. Drug-induced hypoglycaemia and solfonlyurea abuse was excluded, the ongoing prednisolone treatment contributed an underlying hypoglycaemia. Insulin antibodies were found to be negative on two separate samples. A random insulin study was performed, showing hyperinsulinaemia (3.504 pmol/l), elevated C-peptide (3.240 pmol/l) and raised adiponectin concentration (27.1 µg/ml), consistent with an insulin receptor dysfunction. In fact, insulin receptor antibodies were found to be weakly positive, giving diagnosis a type B insulin resistance syndrome. In view of another flare of his SLE and the newly diagnosed type B insulin resistance, our patient was commenced on Rituximab which helped control her hypoglycaemia. After two doses, she did not have any more hypoglycaemic episodes. Type B insulin resistance with insulin receptor antibodies is a very rare condition, commonly associated with other autoimmune diseases. The history of SLE in our patient, severe fasting hyperglycaemia, hyperinsulinaemia and raised adiponectin concentration were suggestive of the underlying insulin receptor dysfunction. The most common symptom of type B insulin resistance is hyperglycaemia with extremely high insulin need while some patients seem to suffer both from hyper- and hypoglycaemic episodes, possibly due to fluctuating antibody titters. Our patient presented purely with hypoglycaemic episodes. Treatment for this condition is not yet standardised, and the production of autoantibodies may even remit spontaneously. Different therapeutic approaches in the past achieved very mixed outcomes, and although our patient showed a great improvement on Rituximab, the duration of remission and possible long term treatment remains unknown.

DOI: 10.1530/endoabs.55.OC8

OC9
Appearances can deceive - a rare presentation of paraganglioma
Lia Anguelova, Archana Dhere, Mike Tadmim, Garry Tan & Bahram Jafar-Mohamadi
OCDEM, Oxford, UK.

Case
A 36-year-old gentleman presented with two month history of severe headaches, vomiting, polyuria and polydipsia. He reported profound episodic sweating especially on exertion and gradual weight loss. He was hypertensive (220/110 mmHg) at presentation. He had no palpitations, anxiety, dizziness, flushing or pallor. He had no diaphoresis or abdominal pain. His only family history was of Type 2 diabetes mellitus.

Investigation
Biochemical investigations showed glucose (23 mmol/l), ketones (3.3 mmol/l), and mild acidosis (pH 7.32). A diagnosis of DKA was made and treatment initiated. At this point investigations for secondary hypertension demonstrated elevated urinary and plasma Norepinephrine 4786 pmol/l(120–1180). He had a normal response to overnight dexamethasone suppression test. A diagnosis of aphaechromocytoma/paraganglioma was biochemically suspected and a CT-abdomen showed a 6 cm left suprarenal necrotic lesion and NM-MIBG (123) scan was consistent with a MBG-avid left adrenal lesion.

Treatment
A laparoscopic left adrenalectomy was performed following adequate alpha and beta blockade. Histopathology demonstrated a paraganglioma (positive for chromogranin and synaptophysin, and negative for inhibin and melan-A) with a PASS score of 11/20. Genetic testing confirmed an heterozygous mutation for C689G>A.p.(Arg230His) of SDHB gene. Unfortunately on follow up scan a new Rib deposit was identified as well as a carotid body tumour. From a diabetes perspective he was started on insulin, but interestingly, when he was started on alpha and beta blockade, his glycaemic control improved: he stopped his prandial insulin and remained on a low dose of basal insulin. At presentation, his fasting C-peptide (89 pmol/l) was low with a glucose of 7.2 mmol/l supported a diagnosis of type 1 diabetes mellitus. However his anti-GAD, anti-IA2 and anti-islet cell antibodies were negative and his HbA1c was 11%. Four months after the removal of his tumour he developed hypoglycaemia and his insulin injections were stopped. His HbA1c normalised as well as his C-peptide suggesting that the initial DKA was as a result of excess catecholamines. Glycaemic indices have started to rise again now when a new likely metastatic deposit has been identified.

Conclusion
Diabetic ketoacidosis as first presentation of a paraganglioma is extremely rare. This case demonstrates the importance of evaluation of secondary causes of hypertension in young patients even in the setting of DKA. In our case, it led to early identification of a tumour with malignant propensity and possible marker for follow up.

DOI: 10.1530/endoabs.55.OC9

OC10
An unexpected VIP
Niki Margari1, Nicola Tufton1, Karunakaran Vithian2, Sampi Mehta3 & Scott Akker1
1St Bartholomew’s Hospital, London, UK; 2Colchester General Hospital, Colchester, UK; 3Southend University Hospital NHS Foundation Trust, Westcliff-on-Sea, UK.

Case history
A 69-year-old Caucasian male presented with persistent abdominal pain and was found to have a large right adrenal mass on CT. Interestingly his family history...
revealed that his daughter had been treated for Cushing’s disease. He was normotensive and denied classical symptoms of catecholamine excess. He had exertional dyspnoea in keeping with COPD. Subsequent tests were consistent with a secretory phaeochromocytoma and urine normetadrenaline 85.671 nmol/day (<4,400 nmol/day), metadrenaline 39.110 nmol/day (<2.00 nmol/day) and 3-methoxytyramine 3,154 nmol/day (<2,500 nmol/day). He was commenced on alpha- and beta-blockade. Whilst on holiday, prior to surgery, he collapsed with abdominal pain and developed severe watery diarrhoea.

Investigations

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

Results and treatment

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

Points for discussion

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

DOI: 10.1530/endoabs.55.OC10
Aldosterone is a steroid hormone that specifically binds to the mineralocorticoid receptor (MR). Production and secretion of aldosterone is triggered by changes in blood pressure (BP). Primary aldosteronism (PA) is an important cause of secondary hypertension. The effects of aldosterone have been described in renal and vascular tissue but recent studies have shown that MR is also expressed in non-epithelial cells such as those of the immune system. A 29-year-old Afro-Caribbean man was referred to clinic with treatment-resistant stage 2 hypertension and an elevated renin-aldosterone ratio. He was initially seen in cardiology clinic for palpitations, atypical chest pain and a BP 185/123 mmHg. Indapamide 2.5 mg daily was initiated. He had no history of headaches, dizziness, nausea or vomiting. Hypertension screen demonstrated an elevated aldosterone renin ratio (ARR) >1850. There were no features to suggest Cushings’s or acromegaly and no evidence of goitre although the patient complained of recent weight gain and symptoms suggestive of hypothyroidism. Thyroid function tests (TFTs) performed at his initial visit were consistent with primary thyroid disease (free thyroxine 9 pmol/l, thyroid stimulating hormone 27.52 mIU/l) necessitating treatment with levothyroxine 50 mcg twice daily. His BP control remained suboptimal and Doxazosin 2 mg twice daily was added. The patient was reviewed in 4 months at which point his BP had improved to 139/77 mmHg. A saline infusion test was suggestive of primary disease (baseline aldosterone 750 pmol/l with a 4 h aldosterone suppression result of 430 pmol/l). Magnetic resonance imaging of the adrenal glands showed no evidence of adenoma adenoma. Adrenal venous sampling indicated bilateral secretion of aldosterone. Repeat TFT’s on levothyroxine showed adequate replacement (TSH 5.37 mIU/l, free T3 5.6 pmol/l, free thyroxine 9.7 pmol/l) and very high titres of thyroid peroxidase antibodies 1579 mIU/l. The patient was started on Spironolactone 50 mg daily. Autoimmune diseases are more common in women with a more Th2- predominant immune response, whereas a Th1 response and inflammation is usually more severe in men. Chronic thyroiditis is classified as a Th1 disorder. There has been evidence to suggest that mineralocorticoids have been strongly associated with the modulation of various cells of the immune system. This is the first reported case of PA in a man exacerbating the course of autoimmune thyroid disease. For patients presenting with PA, it would be wise to consider the possibility of coexistent autoimmune disease.

DOI: 10.1530/endoabs.55.P1

P02

Abstract withdrawn.

P03

Non-functional duodenal neuroendocrine carcinoma- a rare cause of diabetes mellitus
Chad Bisambar1, Andrew Collier1 & Fraser Duthie2
1NHS Ayrshire and Arran, Ayr, UK; 2NHS Glasgow and Greater Clyde, Glasgow, UK.

Case history
We present a 40 year old female admitted with hyperglycaemia, polyuria, polydipsia and weight loss of 6 kg over a 1 month period. She had no sleep naps or change in bowel habit. There was no personal or family history of malignancy or diabetes mellitus. She denied any alcohol, cigarette or illicit drug use. She took no prescription or OTC medication. On examination, she was jaundiced with pale mucous membranes. The rest of systemic examination was normal. Capillary glucose was 23.1 mmol/l.

Investigations
FBC, LFT, U and E, HbA1c, Urinary ACR, blood film, fasting gut hormone profile, CT- chest, abdomen and pelvis, duodenoscopy and biopsy, MRI liver, Octreotide scan, Endoscopic Ultrasound and biopsy. Screen for MEN 1 syndrome.

Chronic thyroiditis is classified as a Th1 disorder. There has been evidence to suggest that mineralocorticoids have been strongly associated with the modulation of various cells of the immune system. This is the first reported case of PA in a man exacerbating the course of autoimmune thyroid disease. For patients presenting with PA, it would be wise to consider the possibility of coexistent autoimmune disease.

DOI: 10.1530/endoabs.55.P1

P04

Case report – severe metabolic acidosis secondary to starvation ketoacidosis
Suhaniya Samarasinghe, Philip Oddie, Kate Millar & Rashmi Kaushal
West Middlesex University Hospital, London, UK.

During starvation, ketone bodies acetoacetate and 3-D-hydroxybutyrate are freely soluble energy substrates made by the liver. Their major role is to supply an alternative glucose substrate for the brain under conditions of medium- and long-term energy restriction. The most common cause of pathological ketoacidosis is poorly controlled type 1 diabetic mellitus triggering uncontrolled hyperglycaemia. Other common causes are alcoholic ketoacidosis and fasting ketoacidosis. In non-diabetic patients developing significant metabolic acidosis, important differentials include salicylate poisoning, methanol or ethylene glycol poisoning, elevated serum lactate levels, uremic acidosis or malnutrition with extremely poor oral intake. Clinically, fasting is rarely a suspected cause of significant metabolic acidosis. A 46-year-old patient with a 20-year history of multiple sclerosis presented to the emergency department for the second time in a 72-hour period with intractable vomiting. Regular medications were sertraline and topiramate. She had a Glasgow coma score 14, respiratory rate 28 breaths per minute, heart rate 90 beats per minute, blood pressure 110/65 mmHg. The patient was clinically dehydrated and exhibited Kussmaul breathing. Initial venous blood gas (VBG) showed a metabolic acidosis pH 7.005, pCO2 3.55 kpa, lactate 0.96, HCO3 7.5 mmol/l (22 – 26), base excess –23.6 m Default (−2 to +2), blood glucose 5.5 mmol/l, blood ketones 4.8 mmol/l (0.6-6.0 mmol/l). Admission bloods ruled out paracetamol and salicylate poisoning, uraemia (urea 3.4 mmol/l), acute renal failure (normal urea: creatinine ratio and eGFR >90 ml/min per 1.73 m2) and tumour lysis syndrome – serum uric acid 205 micromol/l (155–357). The patient had a high anion gap metabolic acidosis 17.6 mEq/l. She was started on a fixed rate insulin infusion (FRII) as per diabetic ketoacidosis (DKA) protocol and intravenous sodium bicarbonate 1.26%. Repeat VBG showed a worsening metabolic acidosis pH 6.97, base excess –26.6 mEq/L, bicarbonate 4.3 mmol/l. She was admitted to the high dependency unit. Her ketosis resolved after 24 hours on FRII and IV sodium bicarbonate. Starvation ketoacidosis is a rare but important differential diagnosis for metabolic acidosis.

This case is unique on account of severity of ketoacidosis in a young, relatively healthy patient. An exaggerated response to fasting has been described in pregnant patients, the elderly and young infants. There are currently no set guidelines for treatment of this patient subgroup but use of FRII in conjunction with IV sodium bicarbonate has proven to be successful in reversing the metabolic acidosis.

DOI: 10.1530/endoabs.55.P4
Curious case of hypercalcemia in pregnancy
Sanesh Pillai & Ruth McCinney
Chesterfield Royal Hospital, Chesterfield, UK.

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

Case history
A 39-year-old lady first presented to our endocrine outpatient clinic in September 2014 with hypertension and oedema. She had gestational diabetes managed with diet alone. Initial calcium level was normal; it gradually increased in the next few days though this was not noted. She was diagnosed with preeclampsia and treated with steroids for foetal lung maturation. Calcium level normalized after steroids but on the day of delivery was 2.74. She had an induced vaginal delivery at 35 weeks. 6 days later she was readmitted due to high blood pressure. Calcium on admission was 3.09. This was treated with iv fluids and then, when calcium rose to 3.19, a dose of pamidronate. She felt well and her only symptom was constipation. Examination was normal except for a flow murmur. Calcium fell into the normal range 2 weeks after pamidronate and remained normal subsequently. She was on 400 units of Vitamin D supplements as per RCOG guidelines, during pregnancy.

Investigations
PTH was 12 (15–60) and 25-OH vitamin D was 113.8 reflecting supplementation. Serum ACE was normal A PTHP was undetectable, however this was taken 21 days after delivery. A low dose CT scan of chest Abdo-pelvis was done to rule out occult malignancy: this was normal except focal thickening of the gall bladder wall which ultrasound suggested was adenomyomatosis.

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

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

DOI: 10.1530/endoabs.55.P5

Abstract withdrawn.

Interesting unfolding of a case of refractory hypoglycaemia
Seong Keat Cheah1, Abraham Mathews1, John Grant2, David Halsall2, Shyam Seshadri1 & Singhan Krishnan1
1Endocrinology, Hinchingbrooke Hospital, North West Anglia NHS Foundation Trust, Huntingdon, UK; 2Pathology, Addenbrooke Hospital, Cambridge University Hospital NHS Foundation Trust, Cambridge, UK.

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

Investigations
Serum cortisol of 65 nmol/l
SST: baseline cortisol: 11 nmol/l; cortisol at 30 mins: 139 nmol/l; 60 mins: 183 nmol/l
Paired ACTH: 10 nmol/l

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

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

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

hypoglycaemia was less than 10, which was inconsistent with non-islet cell tumour induced hypoglycaemia (NICTH).

Results and treatment
In view of multiple comorbidities, a palliative approach was taken. The post-mortem confirmed a clear cell renal carcinoma of the left kidney. Unexpectedly, the liver metastases has morphology and immunoprofile consistent with proinsulin secreting neuroendocrine tumour. The immunostaining showed focal strong insulin immunoreactivity, as well as widespread CD56, synaptophysin, and chromogranin A, with negative staining for RCC.

Conclusions and points for discussion
Proinsulinomas are rare and can be missed if plasma proinsulin concentration is not measured along with insulin. Proinsulin cross-reacts variably with c-peptide and insulin assays; the effect is assay dependent. In this case the discrepancy between the insulin and c-peptide concentrations was too great to be accounted for by the faster clearance of insulin, raising the suspicion of assay interference. The DiaSorin liaison C-peptide assay used here has been shown to be 100% cross reactive with proinsulin based on spiking studies with a pro-insulin reference preparation. While reported cases of proinsulinoma are typically pancreatic in origin, this case has radiologically unremarkable pancreas despite concomitant renal and liver lesions. The unexpected radiological findings raised doubts if the hypoglycaemia was caused by the high malignancy load or NICTH. These were then confirmed to be completely separate entities immunohistohistologically: Proinsulinoma of the liver, with a renal cell carcinoma. In view of proinsulinoma’s rarity, no conclusive association had been drawn between the two to our knowledge.

DOI: 10.1530/endoabs.55.P9

P10
Multiple bone tumours in primary hyperparathyroidism – not so brown after all
Julia Calvo-Latorre1, Victor Lawrence2 & Lorena Arnez2
1Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; 2Isle of Wight NHS Trust, Newport, UK.

Case history
A 28 year-old male of British origin was referred with a one-year history of a left-sided chest mass and an abnormal chest X-ray. He was otherwise fit and well, had a past medical history of vitiligo and had no relevant family history. His physical examination revealed some hypopigmented spots on his skin, several tattoos across his back and a firm mass on his left upper chest, which was mildly tender on palpation. He had no other palpable masses.

Investigations
Laboratory investigation revealed hypercalcaemia (adjusted serum calcium 2.63 mmol/l), an elevated parathyroid hormone (PTH 8.0 pmol/l), elevated bone markers (alkaline phosphatase 479 U/L, N-terminal propeptide of type I collagen 616 mcg/l) and a low vitamin D (9.1 nmol/l). Cross sectional imaging with computed tomography and whole body magnetic resonance imaging (MRI) showed multiple heterogeneous tumorous areas involving the left superior pubic ramus, left acetabulum, left iliac bone, right clavicle as well as ribs bilaterally. The largest of these lesions was centred in the left 3rd rib and corresponded to the patient’s palpable mass. Biopsy of this larger mass showed morphological features consistent with a brown tumour of hyperparathyroidism. Parathyroid scintigraphy revealed a hot spot that was thought to represent a parathyroid adenoma.

Results and treatment
The diagnosis of brown tumour of hyperparathyroidism secondary to a parathyroid adenoma was made and the patient underwent a targeted parathyroidectomy with histological confirmation of an adenoma. Post-operative bloods showed normal adjusted calcium and PTH levels, but worsening bone markers. MRI repeated serially to 3 years after the operation showed the bone lesions were increasing in size, instead of regressing, as might have been expected of a brown tumour. The initial biopsy was subsequently reviewed and found to show fibrous dysplasia with diffuse aneurismal bone cyst-like change. The differential diagnoses included poorly differentiated thyroid cancer or a metastatic head and neck tumor. Second ultrasound scan a week later showed a marked enlargement of the mass involving the entire left lobe of thyroid extending into adjacent soft tissues and encroaching towards right side. Second FNA showed widespread lymphocytes with thick fibrous bands and infiltrates of B and T cells, suspicion of a lymphoproliferative disorder. She developed stridor and bilateral vocal cord palsy and had an urgent tracheostomy with biopsy of the neck mass. Histology showed dense fibrous tissue extending into surrounding skeletal muscles and adipose tissue with lymphocytic infiltrate and chronic inflammatory features. The lymphocytes were composed of mixed T and B cell population with plasma cells and few epithelial cells. A diagnosis of Riedel’s thyroiditis was made and the patient was started on high dose steroids. She reported a transient improvement, however the mass started to grow rapidly prompting emergency admission. A trial of Tamoxifen was given with no benefit. CT neck revealed a marked progression of the mass compressing airways, vocal cords and left internal jugular vein, extending to the level of left oropharynx. The patient had emergency tracheostomy. Rituximab was given with some benefit. On repeat core biopsy, histology revealed atypical lymphocytes diffusely positive for CD20, CD79a, CD10, Bcl-6 and Oct-2. Ki-67 proliferation index was over 95%. This confirmed the diagnosis of large diffuse B cell lymphoma. Patient was referred for chemotherapy. This case highlights the challenges in diagnosis of Riedel’s thyroiditis and differentiating Riedel’s thyroiditis from lymphoma due to overlapping histological features and limitations of medical treatment available for Riedel’s thyroiditis.

DOI: 10.1530/endoabs.55.P11

P11
A challenging case of rapidly enlarging thyroid mass
Tejmal Rehman, Ali Hameed, Dae Kim, Ruth Pettengell & Gul Bano
St George’s University Hospitals NHS Trust, London, UK.

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

DOI: 10.1530/endoabs.55.P11

P12
Idiopathic FSH deficiency
Ravikumar Ravindran1, Justyna Witzack2, Lakdasa Premawardhana1 & Mohamed Adlan1
1Ystrad Mynach Hospital, Caerphilly, UK; 2Ystrad Mynach, Caerphilly, UK.

Case history
A 24-year-old previously healthy male presented to his GP with unilateral “gynaecomastia”, prompting investigations which showed a low FSH of 0.7 (1–12 IU/l). He had normal libido, erectile function, and a normal sense of smell. He had no children. He was subsequently investigated for persistent dysuria but imaging and cystoscopy were entirely normal. He was a non-smoker who took little alcohol and worked as an insurance agent. His past medical history and family history were unremarkable. Clinical examination revealed a normally androgenized male with no gynaecomastia and normal facial, axillary and pubic hair. His testes were normal in volume and consistency.

Investigations
Unstimulated pituitary hormone tests – (a) FSH – 0.7, 0.8, 0.8 (1–12 IU/l); LH – 1.3, 3.8, 3.3 (1–9 IU/l); (b) 9 am testosterone – 13, 21, 19 (9.7–38.2 nmol/l); (c) prolactin 176, 201 (53–360 µIU/l); (d) free T4 14.8 pmol/l, TSH 1.82 µIU/l; (e) random cortisol 393 nmol/l; (f) oestradiol 87 (<160 pmol/l); (g) FSH 4.1.

Semen analysis – (a) volume 4.3 (>1.4 ml), pH 8.3 (>7.1); (b) sperm concentration 2 (>14.9 million/ml), total sperm ejaculate 8.6 (38.9 million).

Gonadotrophin releasing hormone test – Time after GnRH (minutes)

<table>
<thead>
<tr>
<th>minutes</th>
<th>FSH</th>
<th>LH</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>1.3</td>
<td>4.1</td>
</tr>
<tr>
<td>30</td>
<td>1.3</td>
<td>4.1</td>
</tr>
<tr>
<td>45</td>
<td>1.5</td>
<td>13.5</td>
</tr>
<tr>
<td>60</td>
<td>1.7</td>
<td>11.1</td>
</tr>
</tbody>
</table>

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

Results and treatment
The above results indicate that this man had isolated FSH deficiency probably of pituitary origin. This lack of FSH has led to poor spermatogenesis and reduction in sperm numbers both absolute and per ejaculate. However, this isolated FSH deficiency does not appear to be due to either a structural hypothalamo-pituitary defect or to a FSH beta gene mutation.

Conclusion and Points for Discussion
We have presented a case with probable isolated pituitary FSH deficiency. However, the following matters need to be addressed – (a) whether gonadotrophin releasing hormone “priming” have increased the FSH response to GnRH?; (b) whether GnRH testing?; (c) is there a need for testicular biopsy?

DOE: 10.1530/endoabs.55.P13

P14
Low ACTH and cortisol production following adrenalectomy for primary aldoosteronism

Emily Goodchild, Xin Wu, Jackie Salsbury, Tom Kurzawinski, Matthew Matson, Heok Cheow, Teng Teng Chung, William Drake & Morris Brown

A 52 year-old lady was seen for further assessment of primary hyperparathyroidism (PHPT). She complained of intermittent symptoms of bloating but was otherwise asymptomatic. She was menopausal on hormone replacement therapy (HRT) and had started lithium for bipolar disorder 4 years ago. She had no known history of nephrolithiasis and no history of fractures. Her past medical history included Hodgkin’s lymphoma treated with chemotherapy 14 years ago, bipolar disorder and alcohol related fatty liver disease. Her medications were HRT (consisting of estradiol gel and micronized progesterone), lithium, citalopram and tamoxifen. She did not have any known family history of calcium disorders. Biochemistry confirmed PHPT. Calcium to creatinine clearance ratio was low, as often observed with the use of lithium. Going through her past medical records, she had a biochemical picture of PHPT for at least 5 years, however, serum calcium levels 5 years ago were only borderline. Calcium to creatinine clearance ratio was low even before the initiation of lithium. Her GP was not able to provide any calcium measurements dated more than 5 years ago.

Case history
Investigations
Biochemical results: Pre-lithium: Adjusted calcium 2.6 mmol/l (2.2–2.6), Phosphate 0.84 mmol/l (0.8–1.5), ALP 68 IU/l (30–130), PTH 7.2 pmol/l (1.1–6.8), eGFR > 90 ml/min/1.73 m², 25OHD 58 nmol/l, calcium to creatinine clearance ratio 0.004. Post-lithium: Adjusted calcium 2.92 mmol/l, Phosphate 0.83 mmol/l, ALP 109 IU/l, PTH 9.5 pmol/l, eGFR 76 ml/min/1.73 m², 25OHD 99.8 mmol/l, calcium to creatinine clearance ratio 0.009, serum urate 0.76 mmol/l (0.4–1.0), Kidney ultrasound: No evidence of nephrolithiasis. DXA scan: Lumbar spine T-score: −0.6 (stable over 3 years), femoral neck T-score: −1.8 (9% bone loss over 3 years), total hip T-score: −1 (3.9% bone loss over 3 years). Sequencing of the Calcium Sensing Receptor (CaSR) gene: heterozygosity for c.164C>T p.(Pro55Leu).

Results and treatment
A diagnosis of familial hypocalciuric hypercalcaemia (FHH) was made. Lithium was considered to be the reason for the rise in the calcium levels. Currently the patient is under conservative regular follow-up.

Conclusions and points for discussion
This is the first reported case of the effects of lithium in a patient with FHH. This case illustrates that lithium can alter the CaSR set point even in the mutated patient.

DOE: 10.1530/endoabs.55.P14

P15
A surgical treatment for cardiomyopathy

Omar Kireesh, Mark Gurnell, William Drake & Teng Teng Chung

A 74-year-old gentleman with primary aldosteronism (PA) was referred for the ‘MATCH’ study – a prospective comparison of 11C-metomidate PET CT with adrenal vein sampling. He took no exogenous steroids.

Case history
A 74-year-old gentleman with primary aldosteronism (PA) was referred for the ‘MATCH’ study – a prospective comparison of 11C-metomidate PET CT with adrenal vein sampling. He took no exogenous steroids.

Investigations
Na 147 mmol/l, K 3.7 mmol/l, aldosterone 496 pmol/l, renin activity <0.17 pmol/min/ml, random cortisol 247 mmol/l and concomitant ACTH 9.3 ng/l. Two overnight dexamethasone suppression tests recorded values of 61 and 24 nmol/l (<50). CT showed a 1.5 cm nodule on the left and a smaller nodule on the right. Adrenal vein sampling (table) showed apparent non-cannulation of the right adrenal vein. Metomidate-PET CT scan demonstrated high left adrenal adenoma uptake, with a diagnostic ratio L:R of 2.43 (<1.25).

Results and treatment
Following left adrenalectomy, he was discharged on amlopidine 10 mg and hydrocortisone 10 mg. Histopathology confirmed a 9×9 mm adrenal ‘nodularity’ with a mixture of cells resembling either zona glomerulosa (ZG) or zona fasciculata (ZF). Eight weeks later, he reported severe tiredness. The 0900 cortisol was 69 nmol/l, ACTH 4 ng/l. His short synACTH test values were 41, 207 and 271 nmol/l. His symptoms resolved on steroid replacement. CT of his neck showed a 2 cm nodule on the left.

Conclusions and points for discussion
Sustained post-operative adrenal insufficiency is, unusually, associated with isolated ACTH insufficiency. His small adenoma, with mixed ZG- and ZF-like cells, does not fit the picture of contralateral adrenal suppression by a large ZF-left adrenal adenoma co-secreting cortisol and aldosterone. A positive PET scan demonstrated high left adrenal adenoma uptake in the contralateral gland, from autonomous production by the adenoma, which produced sufficient ACTH to maintain cortisol levels. Under-expression of CYP11B1 (11β-hydroxylase), due to variants in its gene promoter, is a common feature of PA (MacKenzie et al 2017). We postulate that adrenal insufficiency is an under-recognised consequence of removing half of the adrenal mass; and that administering dexamethasone at induction of general anaesthesia may convert sub-clinical to overt insufficiency by suppressing the pituitary at the critical moment of adaptation to adrenalectomy.

DOE: 10.1530/endoabs.55.P14
breathlessness and several years of markedly reduced exercise tolerance. He was intolerant of spironolactone and eplerenone. His past medical history included hypertension, obstructive sleep apnoea, Steven-Johnson syndrome secondary to allopurinol, thyrotoxicosis treated with radio-active iodine, monoclonal gammopathy, pernicious anaemia, glaucoma, carpal tunnel syndrome and previous tuberculosis exposure. He was initially referred to a cardiologist for assessment of poorly controlled hypertension and heart failure.

Investigations
His echocardiogram revealed severe concentric LVH with a normal LV ejection fraction and a large pericardial effusion. His coronary arteries were unobstructed. A presumptive diagnosis was made of cardiac amyloidosis although subsequent investigations, including a rectal biopsy, were not supportive of this. Endomyocardial biopsy revealed only myocardial hypertrophy and focal fibrosis with no evidence of lympohytic, granulomatous or amyloid infiltration. His cardiac MRI demonstrated a very unusual pattern of LVH. The patient continued to suffer from ongoing worsening of breathlessness and was treated with pericardial drainage, followed by formation of pericardial window. He was then referred to endocrinology from his local hospital for a right sided adrenal nodule and hyperaldosteronism. Four years previously, hypokalaemic hypertension with aldosterone 8,200 pmol/l (100–800) and renin 0.2 pmol/ml per l (0.5–3.1) had been noted. Primary aldosteronism was re-confirmed (serum aldosterone > 4,271 pmol/l, renin < 0.17 mmol/l per l); an adrenal CT demonstrated bilateral adrenal nodules, 3 cm on the right and 2 cm on the left. Adrenal venous sampling was not possible as his interfering medications could not be weaned without cardiac decompensation. Subsequent 11C Metomidate scan demonstrated bilateral uptake but with an obvious dominant very hot nodule to the right.

Results and treatment
The patient underwent a right laparoscopic adrenalectomy without complication. The following months post-operatively, the patient’s symptoms significantly improved with exercise capacity transforming from 5 to 10 metres to unlimited. His blood pressure and potassium normalised with a marked reduction in anti-hypertensive agents. His post-operative aldosterone normalised to 280 pmol/l with renin 0.80 mmol/l per l. More surprisingly there appeared to be significant LVH regression on his echocardiogram.

Conclusions and points for discussion
This case demonstrates the profound effect severe primary hyperaldosteronism has on myocardial function and the challenges faced with the diagnosis of lateralising disease justifying unilateral adrenalectomy. It also highlights the potential reversibility of myocardial inflammation and fibrosis when the aldosterone burden is reduced.

DOE: 10.1530/endoabs.55.P15

P17
Hypercalcaemia in a body builder
Ravikumar Ravindran, Justyna Witczak, Lakdasa Premawardhana & Mohamed Adaln
Ystrad Mynach Hospital, Caerphilly, UK.

Case history
A 53-year-old obsessive body builder, presented with severe constipation. He had used growth hormone, anabolic steroids and testosterone at variable doses for over 20 years. He had a protein intake of over 400 g/day over an extended period. He denied osmotic symptoms, joint or muscle pains, and excessive tiredness. Previously, he had benign prostatic hyperplasia and renal stone disease but was not on any prescription medication and took no over the counter ‘supplements’. He was a non-smoker and consumed no alcohol. There was no significant family history and his children were well.

Investigations
The following investigations were done at admission – i) corrected calcium – 3.66 (ref range 2.6–3.3 mmol/l); ii) phosphate – 1.39 (0.80–1.50 mmol/l); iii) creatinine – 1.15 (0.80–1.50 mmol/l); iv) uric acid – 218 (115–350 mmol/l); v) total protein – 64 (60–80 g/l); vi) albumin – 36 (35–45 g/l); vii) liver function tests – normal; viii) kidney function tests – normal; ix) C reactive protein – 1.9 (0–5.0 mg/l); x) ESR – 21 (0–20 mm/h); xi) thromboplastin time – 1.3 (1.0–2.5); xii) coagulation profile – normal; xiii) haemoglobin – 16.5 (13.0–17.5 g/dl); iv) eosinophils – 0.3% (0.5–5.0%); xiv) urinalysis – red cells and protein positive, otherwise normal.

Results and treatment
A diagnosis of possible non-PTH mediated hypercalcaemia with acute kidney injury was diagnosed. He was rapidly rehydrated with normalization in serum calcium, his creatinine levelled to 180 mmol/l and creatine kinase to around 4,000 U/l. We believe the hypercalcaemia was caused by rhabdomyolysis induced by inflammatory myositis, excessive exercise (non-traumatic exertional rhabdomyolysis) and possible ingestion of myotoxins (hitherto unsubstantiated).

Conclusions and points for discussion
This subject presented with a possible rare cause for hypercalcaemia – rhabdomyolysis induced by a combination of factors in this obsessive body builder. Rhabdomyolysis produces hypercalcaemia by several mechanisms and is thought to be present in about 9% of these subjects. Points for discussion – i) the importance of isotope renography in subjects with high muscle mass and ‘impaired’ renal function; ii) why was PTH not completely suppressed despite significantly high serum calcium levels – is there coexistent primary hyperparathyroidism?; iii) could raised vitamin A levels play a role?

DOE: 10.1530/endoabs.55.P17

P16
A case of low serum cortisol secondary to inhaled fluticasone use in a retroviral-positive patient on a protease inhibitor
Joseph Anthony, Akis Sharma & Tannaz Vakilgilani
St. Mary’s Hospital, Imperial College Healthcare NHS Trust, London, UK.

Case history
A 45-year-old male was referred to Endocrinology from the Infectious Diseases clinic for investigation of possible adrenal insufficiency. The patient had multiple co-morbidities including asthma, hepatitis B and HIV. The patient’s GP had introduced a fluticasone inhaler to control the symptoms of his asthma, however when the patient was seen in Infectious Diseases clinic as an interaction with his protease inhibitor (atazanavir) was suspected. A random cortisol test was performed, showing a cortisol of less than 20, thus the patient’s flucntasone inhaler was stopped and he was referred to Endocrinology. His history and examination showed no symptoms or signs of adrenal insufficiency.

Investigations
A short synacthen test and subsequent long synacthen test were requested when the patient had discontinued use of the fluticasone inhaler for 1 week. Thyroid function tests were normal. HIV and hepatitis B viral loads were both undetectable.

Results and treatment
SST result: 0 min cortisol 158, 30 min cortisol 289, 60 min cortisol 315. LST result: 0 min cortisol 348, 60 min cortisol 501, 240 min cortisol 584, 360 min cortisol 600, 480 min cortisol 645, 1,440 min cortisol 543 and 2,880 min cortisol 393. ACTH level 49.2. The patient was reassured that although his SST was suboptimal, his subsequent LST result was completely satisfactory. It was explained he had temporary adrenal insufficiency with the combination therapy, which had resolved over time after withdrawal of the fluticasone inhaler.

Conclusions and points for discussion
Interactions between protease inhibitors and inhaled or intranasal corticosteroids are well documented in the literature. The drug-drug interaction is secondary to the inhibition of hepatic cytochrome P450 3A4 isozyme by protease inhibitors, which is partly responsible for the metabolism of steroids. This case concerns concurrent use of a protease inhibitor and inhaled corticosteroid, leading to low cortisol levels with temporary adrenal suppression. Such interactions have become a common source of referral to endocrinology. Could this interaction be minimised by the use of an alternative steroid inhaler such as beclometasone, or the use of an alternative anti-retroviral medication?

DOE: 10.1530/endoabs.55.P16

P18
Type 1 diabetes presenting with unilateral left foot drop
Adrian P Z Li1, Jonathan Best2, Dulmini Kariyawasam3, Anna Brackenridge4, Stephen Thomas5 & Giuseppe Malteese4
1Emergency Assessment Unit, Princess Royal University Hospital, London, UK; 2National Hospital for Neurology and Neurosurgery, London, UK; 3Department of Diabetes and Endocrinology, Guy’s and St Thomas’ NHS Trust, London, UK; 4Department of Diabetes and Endocrinology, St George’s University Hospital, London, UK.

Case history
A 26-year-old lady presented with a two-week history of weakness associated with pins and needles affecting the lateral calf and dorsomedical aspect of her left leg. She had a diagnosis of diabetes mellitus (type 1) and was on insulin therapy. She denied any history of diabetic foot ulceration. Her symptoms had started about 2 weeks ago when she developed weakness of her left foot, which became progressively worse with night pain. She had normal peripheral pulses.

Investigations
A diagnosis of possible diabetic mononeuropathy was made. Her blood glucose was normal and her fasting C peptide was elevated at 3.1 nmol/l (0.6–1.9). Further investigations were pursued for possible causative factors. Her antibody tests were negative. Her MRI demonstrated an area of hypointensity in the left common peroneal nerve consistent with a plexopathy. The diagnosis of diabetic peripheral neuropathy was confirmed.

Results and treatment
The patient was referred to a neurologist for further assessment. The patient was treated symptomatically with physiotherapy.

Conclusions and points for discussion
This case highlights the importance of careful history taking and clinical examination in the diagnosis of possible mononeuropathy and the importance of prompt and accurate investigations in patients with diabetes mellitus. Diabetes is a common cause of peripheral neuropathy and the patient should be referred to a neurologist for further assessment.

DOE: 10.1530/endoabs.55.P18
A male patient presented to the Endocrine clinic age 64, with an 18-year history of long-standing erectile dysfunction and loss of libido due to hypothalamic involvement. The patient was reviewed by Oral Medicine due to a 2.5-year history of xerostomia, and Dermatology for white/pink polycyclic patches over the left upper arm. The patient had also been receiving levothyroxine for 10 years for presumed primary hypothyroidism.

Investigations

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

Results and treatment

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

Conclusions and points for discussion

Symptoms of hyperglycaemia represent the most common presentation in patients with newly diagnosed T1DM. Some subjects may present with vague complaints such as weight loss and fatigue. Cases of T1DM presenting with neurologic manifestations including cerebral infarction, extrapontine myelitis and ataxia have been described in the paediatric population but they are extremely rare in adults. Hyperglycaemia-induced hemibalismus in adults with type 2 diabetes has been previously reported. Here we describe for the first time a new onset T1DM presenting with right foot drop and no symptoms attributable to hyperglycaemia.

In our case no history of weight loss or osmotic symptoms was elicited and the identification of hyperglycaemia, thought to be responsible for the peroneal nerve conduction block, was merely incidental. Our case confirms that new onset diabetes can be associated with neurologic manifestations and reiterates the importance of including diabetes mellitus in the differential diagnosis of an otherwise healthy patient presenting with peripheral neuropathy.

DOI: 10.1530/endoabs.55.P18

P20

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

Layla Thurston, Jonathan Fox & Shelarya Qureshi

West Middlesex University Hospital, London, UK.

Case history

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

Investigations

Serum TSH was greatly elevated at 206 mIU/l and free T4 was undetectable at <3.20 pmol/l. T3 was 2.8 pmol/l. She was referred urgently to the medical team for assessment in A&E where further blood tests demonstrated a raised creatinine at 90 mmol/l with an eGFR 61 ml/min and a raised creatinine kinase (CK) at 1018 IU/l. Lipid profile was in keeping with an overt hypothyroidism. Total cholesterol was raised 6.13 mmol/l with normal triglycerides at 1.22 mmol/l, total cholesterol to HDL ratio was raised at 5.24, LDL cholesterol was raised at 4.41 mmol/l and non-LDL cholesterol was raised at 5.00 mmol/l. ALT was raised at 63 IU/l. Her ECG was abnormal with a low voltage and flattened T waves with a rate of 75 bpm. An echocardiogram showed a slightly hypokinetic basal inferior wall.

Results and treatment

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

Conclusions and discussion

It is rare for autoantibodies to bind to, but not activate, the TSH receptor thereby blocking the action of TSH causing hypothyroidism. TSH receptor blocking antibodies, when present, are generally found to be of a higher titer than TSH blocking the action of TSH causing hypothyroidism. TSH-receptor-blocking antibody (TBAb) positive hypothyroidism was reported to be associated with a high level of TBAb, however, this case is notable in showing a low level of TBAb. The clinical suspicion was high and she was commenced on levothyroxine with significant symptomatic improvement. This case report demonstrates there is a risk of transition to hyperthyroidism following treatment with thyroxine and highlights the diagnostic and therapeutic challenges associated with TBAb positive hypothyroidism.
Catastrophic antiphospholipid syndrome (CAPS) is the most severe form of APS. Conclusions and points for discussion

Investigations

Bloods on admission: Hb 111; Platelets 113; CRP 118; Prothrombin time 16.1, activated partial thromboplastin time 72. Further results: random cortisol 17; ACTH 683 (in-keeping with primary adrenal insufficiency). Negative results: ANCA, HIV PCR, anti dsDNA, C3 and C4. Significant positive results: anticardiolipin IgG (124.6 [normal range <20]); anti-beta-2-glycoprotein-1 IgG (528.7 [normal range <20]) – highly suggestive of Primary Antiphospholipid Syndrome (APS).

Results and treatment

Following discussion with the haematology and rheumatology department at Royal Hallamshire Hospital, Sheffield the patient was commenced on methylprednisolone, IV immunoglobulin and warfarin loading (with bridging enoxaparin). However, she was found in cardiac arrest the following morning and resuscitation attempts were unsuccessful. Post-mortem examination was consistent with rapidly advancing APS causing widespread vasculitis and intravascular thrombosis, resulting in vascular occlusion and infarction of multiple organs including the skin, heart, lungs, kidneys, adrenals and small bowel.

Conclusions and points for discussion

Catastrophic antiphospholipid syndrome (CAPS) is the most severe form of APS and represents <1% of APS cases. Diagnosis requires vascular thrombosis in ≥3 organs/tissues; development of symptoms simultaneously or in <1 week; evidence of small vessel thrombosis and laboratory confirmation of APS. Due to its rarity, the majority of data regarding management comes from retrospective analysis of the CAPS registry. The current consensus is combination therapy with anticoagulation, IV immunoglobulin or plasma exchange, corticosteroids and rituximab. Mortality remains high despite optimal treatment.

DOI: 10.1530/endoabs.55.P21

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

Elefstratos Stratos & Sanjeev Sharma

The Ipswich Hospital NHS Trust, Ipswich, UK.

Case history & Management

A 36-year old lady of Lithuanian descent first presented in 2011 with secondary infertility due to hyperprolactinaemia of 1554 (N=0–500). Her MRI was normal and was started on Cabergoline which was stopped 5 months later when she became pregnant. She delivered normally but was thereafter lost to follow-up. She was referred back in 2014 with galactorrhoea and hyperprolactinaemia (6856) and MRI this time showed a 0.7 mm microprolactinoma. Cabergoline was restarted and 6 months later was stopped again when she became pregnant for the third time. Following this successful pregnancy, she returned to Lithuania and was lost to follow-up. In 2016, she resurfaced as an emergency at 34 weeks of pregnancy with headaches, bitemporal visual field loss and reduced foetal growth. Prolactin level was 119.965 and MRI showed a 3.1×3.2 cm macroprolactinoma with some apoplecty. Fortunately, she delivered soon after and neurosurgical intervention was not required. Except prematurity, baby remained unaffected. Since 2016, she remains on Cabergoline with undetectable (<40) prolactin levels, visual fields have recovered fully and serial MRI surveillance demonstrating gradual reduction of tumour mass.

Conclusions and points for discussion

This unique case demonstrates in a step-wise manner, the stimulatory effects of pregnancy on pituitary lactotrophs. Our subject’s history suggests that every pregnancy led to a sequential increase in her lactotroph cell mass as characterised by initial a normal MRI and progressing to a microprolactinoma and culminating in a symptomatic macroprolactinoma. Current guidelines suggest that for hyperprolactinaemic patients with normal MRI or microprolactinoma, there is no utility of either biochemical, radiological or visual field surveillance during pregnancy. While this is applicable for the majority of such cases, this case example suggests that endocrinologists should still exercise caution and arrange for follow-up surveillance in such patients following completion of pregnancy. If future pregnancies are aspired, then it is important to have pre-pregnancy counselling to discuss potential risks including macroadenomatous transformation, growth retardation and consequences of pituitary insufficiency.

DOI: 10.1530/endoabs.55.P22

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

Aditi Sharma, Roshani Wadhwan & Vassiliki Bravis

St Marys Hospital, London, UK.

Case History

A 71-year old male, who had been on amiodarone therapy for many years, was receiving Levothyroxine therapy due to amiodarone-induced hypothyroidism. He was subsequently found to have thyrotoxicosis, which remained after levothyroxine discontinuation. He had type 2 diabetes and ischaemic cardiomyopathy and had an implanted cardiac defibrillator due to multiple VT arrests. Amiodarone therapy had contributed to stabilisation of his cardiac arrhythmias and had continued beyond his diagnosis of amiodarone-induced hypothyroidism for that reason.

Investigations

The patient complained of 10 kg unintentional weight loss and agitation and examination revealed a regular heart rate of 58 bpm, blood pressure 127/73 mmHg, euvoalaemia and resting tremor. Neck examination was unremarkable. Thyroid function confirmed thyrotoxicosis with TSH <0.01 milliunit/l, FT4 31.8 pmol/l, FT3 15.7 pmol/l. Thereafter he was successfully weaned off the prednisolone and the Gliclazide within a total period of less than 3 months. At the end of that period he was found to have thyrotoxicosis, which remained after amiodarone discontinuation. Amiodarone therapy had contributed to stabilisation of his cardiac arrhythmias and had continued beyond his diagnosis of amiodarone-induced hypothyroidism for that reason.

Results and treatment

After consultation with the Cardiologist, amiodarone was discontinued and bisoprolol was uptitrated. He was commenced on prednisolone 40mg daily for one month, along with Gliclazide for glycaemic control, and repeat blood tests showed marked improvement (TSH 0.17 milliunit/l, FT3 3.2 pmol/l, FT4 15.7 pmol/l). Thereafter he was successfully weaned off the prednisolone and the Gliclazide within a total period of less than 3 months. At the end of that period he was found to have thyrotoxicosis, which remained after amiodarone discontinuation. Amiodarone therapy had contributed to stabilisation of his cardiac arrhythmias and had continued beyond his diagnosis of amiodarone-induced hypothyroidism for that reason.

Conclusion and points for discussion

Amiodarone is a potent antiarrhythmic drug that is used to treat arrhythmias, but can precipitate thyroid dysfunction due to its iodine-rich chemical structure and long half-life. It remains unclear whether amiodarone should be continued after diagnosis of thyrotoxicosis. There have been instances of amiodarone-induced coronary vasospasm and ischaemic ventricular fibrillation related to hyperthyroidism and some studies have shown that continuation of amiodarone delays restoration of euthyroid status, and increases risk of recurrence. Risk of recurrence has been documented in the literature as being as high as 10%. However, in other cases euthyroid states are still achieved with continuation of amiodarone and treatment with steroids.

DOI: 10.1530/endoabs.55.P24

DOI: 10.1530/endoabs.55.P23

Abstract withdrawn.
P25
Detectable testosterone despite androgen deprivation therapy in prostate cancer: hunting for the source
Akaterini Theocharaki1, Yae-eun Suh2, Daniel Morganstein1 & Nicholas Van1
1Beta Cell, Chelsea and Westminster Hospital, London, UK; 2Clinical Oncology, The Royal Marsden NHS Foundation Trust, London, UK.

Background
Androgen-deprivation therapy (ADT) is commonly used in the management of advanced prostate cancer. ADT can be achieved through bilateral orchiectomy, by administration of GnRH receptor agonists, or by using the newer GnRH receptor antagonist Degarelix. The classical desired biochemical goal is to achieve a serum testosterone of <1.7 nmol/l.

Case Presentation
A man with metastatic prostate cancer on androgen deprivation therapy and serum total testosterone above the therapeutic goal (3.7 nmol/l), was referred to the Endocrine clinic. He had a previous medical history of hyperprolactinaemia and hypogonadism diagnosed 17 years prior to his presentation. In the past he had been treated with Cabergoline followed by testosterone replacement therapy with parenteral testosterone undecanoate. Previous MRI head scanning was normal. The last testosterone undecanoate injection was 13 months prior to his referral to the Endocrine clinic. Androgen deprivation consisted initially of Goserelin for four months, followed by Leuprorelin acetate for three months and subsequently Degarelix for another three months. During the time of treatment with the GnRH agonists (Goserelin followed by Leuprorelin) and the GnRH antagonist Degarelix, serum testosterone had shown little variation and was always above the therapeutic threshold. He was additionally on the androgen receptor inhibitor Enzalutamide, PSA was declining and the disease was clinically stable.

Investigations showed a raised extracted testosterone with MS/MS, undetectable gonadotropins, normoprolactinaemia and no rise in other serum androgens. Urine steroid biochemistry showed low androgens making an adrenal source for the measured testosterone unlikely, and measured testosterone did not change following a low dose dexamethasone suppression test. Review of available cross-sectional imaging showed unilaterial adrenal nodularity that was unchanged in repeated scanning. In the subsequent months, total testosterone started to decline with a lowest achieved level of 1.8 nmol/l.

Discussion
Evidence suggests that a testosterone level below the classical therapeutic target in advanced prostate cancer is associated with improved outcomes and lower progression toward castration-resistant prostate cancer. In this context serum testosterone is together with PSA an important biochemical target. Because of its mechanism of action, the GnRH antagonist Degarelix prevents testosterone microsurges that have been observed immediately following GnRH agonist administration, with potential clinical implications. We speculate that the persistently detectable testosterone levels here are likely to arise from insufficient response to treatment with GnRH agonists, with eventual decline on prolonged treatment with Degarelix. A less likely explanation is the presence of residual testosterone undecanoate depot.

DOI: 10.1530/endoabs.55.P25

P26
Normotensive hypokalemic primary aldosteronism: How is this Possible?
Andrew Tang, Janice Pasieka & Gregory Kline
University of Calgary, Calgary, Canada.

Case history
A 40-year-old woman presented with long-standing hypokalemia fluctuating between 2.3 and 2.5 mmol/l. She had episodes of right-sided weakness and was seen by Neurologists without a clear diagnosis. She had no other past medical history. Physical examination was unremarkable. Her blood pressure (BP) was 116/63.

Investigations
Plasma aldosterone was 1363 pmol/l. Plasma renin activity was 0.18 ng/ml/h. Aldosterone-renin ratio (ARR) was 7570 (normal < 550). There was inappropriate kaliuresis (173.2 mmol in 24 h). Her natriuresis was 315 mmol in 24 h, 24-hour ambulatory BP was 129/79. Her magnesium was normal at 0.88. MRI abdomen showed a 2-cm mass in the left adrenal gland. Adrenal venous sampling demonstrated lateralization to the left with an aldosterone-cortisol ratio of 36.49 in the left adrenal, 0.78 in the right adrenal, and 6.21 in the common femoral vein.

Results and treatment
She underwent a left laparoscopic adrenalectomy. Pathology revealed a 1.9 × 1.5 × 1.5 cm adrenocortical adenoma. Post-operatively, her BP was 110/70. Her ARR normalized and her potassium normalized.

Conclusions and points for discussion
38 cases of normotensive primary aldosteronism (PA) have been reported since 1972. The majority of cases are in females (28/38) from Europe (15/38) and Japan (13/38). In all cases were due to hyperplasia. There are numerous proposed mechanisms of normotensive PA. It is thought that these individuals were detected at an early stage of the disease. However, data from PA registries suggest that the development of hypokalemia is a late development in PA. As most patients are female, estrogen and progesterone may counteract the effects of hyperaldosteronism. However, it is still common to see hypertensive PA in menopausal women and in pregnancy. Partial resistance to aldosterone is an unlikely explanation as the patient had severe hypokalemia and a suppressed renin despite a normal BP. Normotensive PA has occurred patients with Cushing’s syndrome; however, this patient’s Cushing’s was normal and her hypokalemia resolved preoperatively. Perhaps this patient’s normal BP and salt-wasting was due to the natriuretic peptide system. Sodium and water retention from excess aldosterone leads to release of atrial natriuretic peptide (ANP). ANP increases systemic vasodilation. Furthermore, ANP increases glomerular filtration rate through vasodilation, promoting natriuresis and diuresis. Although there is no prospective data demonstrating long-term benefits in the diagnosis and treatment of normotensive PA, this case illustrates that PA is not confined to patients with hypertention.

DOI: 10.1530/endoabs.55.P26

P27
A case of Idiopathic Infantile Hypercalcaemia (III) persisting into adulthood, caused by compound heterozygous mutations of 1,25-dihydroxyvitamin D3 24-hydroxylase (CYP24A1)
Victoria Stokes1, Caroline M Gorvin1,2,3, Bahram Jafar-Mohammadi1, Fiona Ryan1 & Rajesh V Thakker1
1Academic Endocrinology Unit, University of Oxford, Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, UK; 2Institute of Metabolism and Systems Research (IMSR), University of Birmingham, Birmingham, UK; 3Centre for Endocrinology, Diabetes and Metabolism (CIDAM), Birmingham Health Partners, Birmingham, UK

Case history
Idiopathic Infantile Hypercalcaemia (III) classically presents in the first year of life, usually resolves by 1 year of age and is due to mutations in 1,25-dihydroxyvitamin D3 24-hydroxylase (CYP24A1) or, rarely, sodium-phosphate cotransporter-2A (SLC34A1). We report a case of III in a Caucasian female, who was born to non-consanguineous parents, with hypercalcaemia, hypercalciuria and associated complications persisting into adulthood. The proband was investigated for delayed developmental milestones and constipation at 7 months old and was found to be hypercalcaemic. Other causes of hypercalcaemia were excluded and she was diagnosed with IIIH. Nephrocalcinosis was noted at diagnosis and progressed to a symptomatic renal stone aged 12 years. A DEXA scan following a wrist and heel fracture revealed osteoporosis (SIDS −3.2 lumbar spine, −2.15 hip).

Investigations
At diagnosis, biochemistry showed an elevated serum calcium of 3.91 mmol/l (normal range (NR) 2.12–2.62), normal phosphate of 1.27 mmol/l (NR 0.80–1.45), elevated magnesium of 1.25 mmol/l (NR 0.75–1.05), normal 25(OH)D3 of 38.0 µg/ml (NR 7–50), elevated 1,25(OH)2D3 of 127 pg/ml (NR 20–50) and suppressed PTH concentration of < 0.7 pmol/l (NR 1.0–6.1). Her parents were normocalcaemic. In addition, on treatment her plasma calcium concentrations were typically at high-normal limits, and her urinary calcium:creatinine ratios are high and between 0.44 and 1.14 (hypercalciuria defined as >0.20).

Results and treatment
DNA sequence analysis of CYP24A1 revealed compound heterozygous missense mutations comprising Thr134Arg and Leu409Ser, which were inherited from her mother and father, respectively. She was treated with a low calcium and low vitamin D diet that reduced her serum calcium levels, but required pamidronate to normalise her bone mineral density, and had renal stents for nephrocalcinosis.

Conclusions and points for discussion
We report a case of III in a Caucasian child of non-consanguineous parents, caused by compound heterozygous mutations of CYP24A1. IIIH may have a wide spectrum of penetrance and may persist into adulthood and cause renal stone
A 74 year old female was treated for hyperthyroidism of uncertain aetiology by carbimazole 40 mg daily for autoimmune hyperthyroidism. Subsequent investigation of anaemia was unremarkable. Conclusion and discussion

It is presumed that the initial hyperthyroid episode 15 years earlier was autoimmune. Long-term treatment with low dose carbimazole without ever having a trial period of withdrawal was inappropriate. The rapid and severe nature of the relapse of autoimmune hyperthyroidism after such long standing treatment with low dose carbimazole is exceedingly unusual. There is limited evidence that carbimazole has an immune modulating effect, perhaps seen with high doses. It is possible that low dose carbimazole was keeping the underlying autoimmune process in remission, given the dramatic change in TRAB. An alternative hypothesis is that an intercurrent urine infection triggered an immune response that also provoked the formation of TRAB. Hyperthyroidism can also be associated with a microcytic anaemia through disruption of iron metabolism. The patient has now been rendered euthyroid with carbimazole and sinus rhythm restored. Radiiodine treatment is planned.

DOI: 10.1530/endoabs.55.P29

P28
Eponymous mischief: A syndrome within a syndrome
Nicola Tufton, Susan Cross & Scott Akker
BartsHealth NHS Trust, London, UK.

Case history
A 32 year old male diagnosed with McCune-Albright syndrome aged 18, presented with a painful left knee and difficulty in walking, limiting his usual activities. He was diagnosed with Acomegaly (IGF-1 451 ng/ml, mean GH 2.71 ug/L) aged 26 years and had multiple sites of fibrous dysplasia, causing bone pain. On examination he had tall stature and features of acromegaly with normal visual fields and palpable masses behind his left knee and upper thigh.

Investigations
ALP 657 u/l, ALT 42 u/l, bilirubin 31 mmol/l, cCa 2.3 mmol/l, PO4 0.77 mmol/l, vitamin D 69 mmol/l, FT4 15.5 pmol/l, TSH 1.95 mu/l, IGF-1 365 mcg/l (82.5–240.4 mcg/l), mean GH 2.078 ug/l, serum procollagen type 1 amino terminal peptide (P1NP) 1158 ug/l (ref range 20–70), FGFR3 160 RU/ml (ref range <100). MRI head demonstrated a normal size pituitary gland, without an obvious focal lesion, but with extensive fibrous dysplasia of the skull vault and facial bones. A whole body bone scan confirmed diffuse intense tracer uptake throughout the skeleton, which showed stability in fibrous dysplasia from a scan 3 years previously. MRI demonstrated polyostotic fibrous dysplasia and multiple lobulated intramuscular soft tissue masses, with heterogeneous enhancement, the largest of which measured 6×9×10 cm.

Treatment
Pituitary surgery was relatively contraindicated due to the extensive facial and skull bone disease making access difficult. He was therefore treated with monthly Sandostatin injections, but was not very compliant with this treatment, due to gastrointestinal side effects. He received bispaphosphate infusions for his bone disease.

Discussion
McCune-Albright syndrome is a rare condition that remains difficult to diagnose and manage, due to the multiple endocrine and bone complications. There is a rare association between McCune Albright syndrome and multiple myxomas known as Mazabraud syndrome. The first case was described in 1967, but very few cases have been reported in the literature. It is more common in women and tends to affect the larger lower limb muscle groups. Its occurrence in men is extremely rare, and myxomas tend to occur before the onset of fibrous dysplasia. There is an association between Mazabraud syndrome and an increased risk of sarcoma in the underlying bone, although the myxomas themselves do not seem to have an inherent malignancy risk. Use of new biochemical tests confirmed poor compliance with medications and high bone turnover. We will discuss the difficulties and management options posed by this case.

DOI: 10.1530/endoabs.55.P28

P29
Rapid severe relapse of autoimmune hyperthyroidism following 15 years low dose carbimazole treatment
Victoria Millson, Alison Dawson & Steve Peasey
Bradford Royal Infirmary, Bradford, UK.

Case history
A 74 year old female was treated for hyperthyroidism of uncertain aetiology by her general practitioner. Carbimazole had been continued for 15 years - current dose 5 mg daily. Following referral to endocrine outpatients, consideration was given to stopping carbimazole as this treatment was possibly no longer required, although a small risk of relapse was accepted. Prior to stopping carbimazole, Free T4 - 10.5 pmol/l (7.5–21.1), TSH - 0.61 mU/l (0.35–4.7), TRAB <1.0 (negative).

Twenty days following cessation of carbimazole the patient was admitted to hospital acutely unwell. She was breathless, mildly confused with anorexia and weight loss.

Investigations
She was in fast atrial fibrillation, had a positive TTU, microcytic anaemia: Hb - 77 g/l, MCV - 73 fl, WCC - 6.79×10^12/L, Ferritin – 40 ng/ml, CRP - 32, MSU no growth. Free T4 - 103 pmol/l (7.5–21.1), TSH <0.01mU/l (0.35–4.7), TRAB - 43.9 (>1.8 is positive). Thyroid isotope scan showed increased diffuse uptake.

Results and treatment
Treated for possible urine tract infection. Commenced on a beta-blocker and carbimazole 40 mg daily for autoimmune hyperthyroidism. Subsequent investigation of anaemia was unremarkable. Conclusion and discussion

It is presumed that the initial hyperthyroid episode 15 years earlier was autoimmune. Long-term treatment with low dose carbimazole without ever having a trial period of withdrawal was inappropriate. The rapid and severe nature of the relapse of autoimmune hyperthyroidism after such long standing treatment with low dose carbimazole is exceedingly unusual. There is limited evidence that carbimazole has an immune modulating effect, perhaps seen with high doses. It is possible that low dose carbimazole was keeping the underlying autoimmune process in remission, given the dramatic change in TRAB. An alternative hypothesis is that an intercurrent urine infection triggered an immune response that also provoked the formation of TRAB. Hyperthyroidism can also be associated with a microcytic anaemia through disruption of iron metabolism. The patient has now been rendered euthyroid with carbimazole and sinus rhythm restored. Radiiodine treatment is planned.

DOI: 10.1530/endoabs.55.P29

P30
Critical illness, adrenal insufficiency and steroid therapy
Aditi Sharma, Maria Chicco & Vassiliki Bravis
St Marys Hospital, London, UK.

A 71-year-old man was diagnosed with poorly differentiated T4N0M0 gastric adenocarcinoma. He received neoadjuvant chemotherapy, followed by elective subtotal gastrectomy. Mean arterial pressure was maintained above 70 mmHg throughout the 5-hour operation. On post-operative day 3, the patient became confused, pyrexial, hypotensive with new-onset atrial fibrillation. CT head was unremarkable and CT chest/abdomen/pelvis (CAP) showed bilateral pleural effusions with normal adrenal glands. He was treated for chest sepsis with IV antibiotics with improvement. On post-operative day 5, a repeat CT CAP, which was done to rule out gastric leak from the surgery site, due to worsening sepsis, showed new, bilateral adrenal haemorrhages. The patient had no history of tuberculous or recent travel outside the UK. Investigations

Adrenal function was interrogated with a short synacthen test (SST). Results and treatment

Baseline serum cortisol was 474 nmol/l with an ACTH of 28.6 nU/ml. The SST showed serum cortisol increment to 524 nmol/l and 599 nmol/l at 30 and 60 minutes respectively. Albumin at the time was 24 g/l (NR 35–50) and total protein 49 g/l (NR 60–80). The patient subsequently became severely septic with persistent hypotension, despite on-going antibiotic and fluid therapy, and was started on 100 mg intravenous hydrocortisone qds. His repeat SST whilst still on ITU 6 weeks later showed baseline cortisol 1416 nmol/l, cortisol 1333 nmol/l at 30 minutes and 1259 nmol/l at 60 minutes, in the context of albumin of 16 g/l. A repeat CT shows reabsorption of the previous haemorrhages and has revealed bilateral adrenal adenomas.

Conclusions and discussion

At first glance, the baseline serum cortisol was within normal reported range. However, that is for tests performed under ‘normal’ circumstances, ie not in critical illness. On the other hand, serum total cortisol levels in the presence of hypoproteinaemia, which may be present in critical illness, can be highly variable and the reported incidence of ‘adrenal insufficiency’ in sepsis and septic shock is between 30 and 70%. Furthermore, there is evidence for treating patients with septic shock and adrenal insufficiency with stress doses of steroids. The actual cortisol increment in this patient after administration of synacthen was suboptimal, both by ‘normal’ reported values (requires increment >150 nmol/l) but also in the context of critical illness (requires increment >250 nmol/l). The finding of adrenal haemorrhages further contributed to the decision for steroid therapy. Free cortisol index calculations can further assist in decisions towards steroid therapy.

DOI: 10.1530/endoabs.55.P30
P31
Hyperprolactinaemia, Cushing’s syndrome and Adrenal Insufficiency - diagnostic and management challenges with multiple co-morbidities and polypharmacy

Patrick Quinn1, Mohsin Siddiqui1, Daniel Morganstein1,1,2 & Alison Wen1,2
1Chelsea and Westminster Hospital, London, UK; 2Imperial College, London, UK.

Case history
A 51 year old lady was referred to Endocrinology with low plasma cortisol, hyperprolactinaemia and galactorrhea. Extensive past medical history included primary hypothyroidism, B12 deficiency, diaphragmatic paralysis requiring NIV, recurrent aspergillosis, sino-atrial node disease with PPM, immunodeficiency, inflammatory arthropathy and autoimmune pancreatic insufficiency. She took numerous medications:- Itraconazole 100 mg daily, Levothyroxine 75 mg daily, Creon 10 mg tds. Risendronate 35 mg 2 tds. Hydroxychloroquine 200 mg daily, Domperidone 10 mg tds, Lansoprazole 30 mg daily, Uniphyllin 200 mg bd, intermittent IVIG infusions and Prednisolone 7.5 mg daily. She was Cunninghorm, normotensive with no postural hypotension, had expressible galactorrhea and normal visual fields to confrontation.

Investigations
Serum electrolytes were normal. Prolactin was markedly elevated at 4585 mu/l (normal range 100–500). Short synacthen test showed undetectable ACTH and cortisol of <20 nmol/l at baseline, 60 nmol/l at 30 minutes and 74 nmol/l at 60 minutes. Basal pituitary function was otherwise normal. CT pituitary, performed due to MRI incompatibility, was normal with no macroadenoma or haemorrhage.

Results and treatment
Exogenous Cushing’s Syndrome with adrenal suppression secondary to interaction between Itrazconazole and chronic corticosteroids and hyperprolactinaemia secondary to interaction between Itrazconazole and Domperidone were diagnosed. Prolactin rapidly normalised on stopping domperidone. Attempts to wean glucocorticoid treatment, to improve Cushing’s and promote adrenal recovery, were hampered by flares of arthritis. Follow-up short synacthen test demonstrated persistent hypoadrenalism. She developed an episode of florid Cushing’s syndrome with proximal myopathy following administration of intra-articular steroid for joint pain by her rheumatologist. With glucocorticoid weaning (total hydrocortisone 20 mg daily) she developed postural hypotension. Electrolytes remained normal but aldosterone was undetectable (<60 pmol/l). This could represent primary adrenal insufficiency (on a background of autoimmune) or adrenal atrophy with loss of mineralocorticoid, becoming symptomatic on switch from prednisolone to hydrocortisone and dose weaning.

Plasma renin was not interpretable as she was taking Propranolol. Adrenal antibodies were negative. Fluorocortisone was introduced, but very small doses required as higher doses caused hypertension.

Conclusions and points for discussion
This case illustrates endocrine presentations of drug interactions. Itrazconazole inhibits microsomal enzymes including CYP3A4, resulting in delayed metabolism of drugs including domperidone and steroids. In our patient this caused galactorrhea, hyperprolactinaemia and symptomatic Cushing’s syndrome. We are developing patient alert cards to warn of such interactions. Itrazconazole may also inhibit enzymes of steroidogenesis. Polypathy and co-morbidity can cause difficulties in diagnosis and management. MRI pituitary was contra-indicated due to pacemaker and renin was uninterpretable due to propranolol.

DOI: 10.1530/endoabs.55.P31

P32
Clinical and biochemical acromegaly associated with a functioning pituitary FSHoma

Isabel Huang-Doran1,2, Olympia Koulouri1,2, Sue Oddy3, David Halsall2, Kieron Allison2, Dominic O’Donovan2, Richard Mannion2 & Mark Gurnell1,2
1Academic Endocrine Unit, Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Oxford, UK; 2Wellcome Centre for Human Genetics, Oxford, UK, 3Department of Clinical Endocrinology, Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, UK; 4Department of Endocrinology, The Royal Bournemouth Hospital, Bournemouth, UK.

Case history
A previously healthy 39 year-old male presented to his optometrist with visual disturbance. Visual field perimetry confirmed bitemporal hemianopia, prompting a referral to endocrinology. On questioning, he reported an increase in hand and shoe size, but no headache or diaphoresis. Examination revealed classic acromegalic features including prognathism, spatulate hands and prominent orbital margins, as well as marked bilateral macroadenoma.

Investigations
Clinical investigations included conventional biochemical evaluation of anterior pituitary function, MRI pituitary and testicular ultrasound.

Results and treatment
Biochemical findings were in keeping with acromegaly, with IGF1 64.4 nmol/l (9.5–45.0), basal GH 1.5 mcg/l and GH nadir of 1.2 mcg/l after a 75 g oral glucose challenge. FSH was elevated (107 UL (1.0–10.1)) with normal LH (1.2 (0.5–5.6)) and testosterone (3.9 nmol/l (8.0–29.0)). Anterior pituitary function was otherwise intact. MRI demonstrated a large pituitary macroadenoma with suprasellar expansion, displacing the chiasm and extending into the left cavernous sinus. Ultrasound revealed testicular volumes of 46 and 50 ml on the left and right respectively, without features of neoplasia. Transsphenoidal resection of the pituitary lesion resulted in normalisation of visual fields and partial reduction in testicular volumes. Postoperatively, IGF1 remained elevated (55 nmol/l), however the GH nadir improved to 0.48 mcg/l after oral glucose challenge. FSH reduced to 26.3 Ul. Testosterone, FT4 and cortisol were all below the normal range, so hormone replacement was commenced. MRI showed an intrasellar remnant with minimal suprasellar extension, no longer impacting on the optic chiasm. Histological analysis of the excised lesion confirmed a pituitary adenoma with predominant FSH staining, sparse LH staining, but no staining for GH. The possibility of coexistent ectopic GH or GHRH secretion was considered, however CT chest, abdomen and pelvis did not reveal an ectopic source, and no circulating GHRH was detectable by immunoassay. Serial follow up confirmed persistent mild elevation in IGF1 (1.1–1.4x ULN), GH nadir >0.6 mcg/l, and FSH between 30–40 Ul. MRI showed a slowly enlarging remnant in the pituitary fossa. Treatment with a somatostatin analogue was commenced, however there was no improvement in IGF1 or GH levels after 6 months. Repeat surgery is therefore planned.

Conclusions and points for discussion
This case (a) represents a functioning gonadotrophinoma in a male; (b) demonstrates clinical and biochemical evidence of GH excess without a somatotroph adenoma or hyperplasia, and without evidence for ectopic secretion; and (c) was refractory to somatostatin analogue therapy. Two further, similar cases have since been identified.

DOI: 10.1530/endoabs.55.P32

P33
A case of vitamin D-dependent rickets type 2A (VDDR2A), caused by compound-heterozygous mutations in the vitamin D receptor (VDR)

Victoria Stokes1, Alistair Pagnamenta2,3, Mark Stevenson1, Kate E Lines1, Brion Shine1, Jenny Taylor1,2, Tristan Richardson2 & Rajesh V Thakker1
1Academic Endocrine Unit, Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Oxford, UK; 2Wellcome Centre for Human Genetics, Oxford, UK, 3Oxford NIHR Biomedical Research Centre, Oxford, UK; 4Department of Clinical Endocrinology, Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, UK; 5Department of Endocrinology, The Royal Bournemouth Hospital, Bournemouth, UK.

Case history
Vitamin D-dependent rickets type 2A (VDDR2A) is an autosomal recessive condition caused by resistance to 1,25(OH)2D3, either through vitamin D receptor (VDR) mutations (type A) or abnormal expression of interfering proteins (type B). The possibility of coexistent ectopic GH or GHRH secretion was considered, however there was no improvement in IGF1 or GH levels after 6 months. Repeat surgery is therefore planned.

Conclusions and points for discussion
This case illustrates endocrine presentations of drug interactions. Itrazconazole inhibits microsomal enzymes including CYP3A4, resulting in delayed metabolism of drugs including domperidone and steroids. In our patient this caused galactorrhea, hyperprolactinaemia and symptomatic Cushing’s syndrome. We are developing patient alert cards to warn of such interactions. Itrazconazole may also inhibit enzymes of steroidogenesis. Polypathy and co-morbidity can cause difficulties in diagnosis and management. MRI pituitary was contra-indicated due to pacemaker and renin was uninterpretable due to propranolol.

DOI: 10.1530/endoabs.55.P31

Biochemistry at diagnosis showed a low adjusted calcium of 2.03 mmol/l (NR 2.25–2.55), low phosphate of 0.78 mmol/l (NR 1.29–1.79), elevated alkaline phosphatase of 1101 UL (NR <300), elevated parathyroid hormone of 1283 ng/l (NR <660), normal 25(OH)D3 of 20 mmol/l and high 1,25(OH)2D3 of 466–650 nl/l (NR 48–156).

Next generation sequencing was undertaken to expedite simultaneous analysis of the VDR and other possible genes involved in the aetiology of VDDR2B. This revealed compound heterozygous variants c.800C>T and c.1171C>T in VDR. These predict p.Ala267Asp and p.Arg391Cys alterations at evolutionarily conserved residues and were inherited from the father and mother, respectively.

Although neither variant was observed in Genome Aggregation Database, the p.Arg391Cys variant has been previously reported in a patient with VDDR2A.
Conclusions and points for discussion
We report a Caucasian female, who was born to non-consanguineous parents, with VDDR2A caused by compound heterozygous mutations of VDR. Of the reported kindreds with VDDR2A (n = 53), the majority with a known pedigree are the offspring of related, or likely to be related, parents (95%) and have homozygous mutations (92%). The prevalence is highest in Middle Eastern and South American populations (32 and 16% respectively), and only 11 and 14% occur in the North African and Caucasian populations, respectively. However, VDDR2A is less likely to be due to homozygous mutations in the Caucasian population (67% vs 92%), possibly reflecting the lower reported rate of consanguinity (17% vs 95%). In summary, this case illustrates the clinical utility of scientific advances in sequencing techniques and the increased likelihood of the occurrence of compound heterozygous mutations giving rise to VDDR2A in the Caucasian population.

DOI: 10.1530/endoabs.55.P33

P34
Hyperkalaemia in Conn’s syndrome masking hyporeninemic hypoadrenalism
Rebecca Rogers, Neil Burgess, Calum Ross & Kwin Swye Myint
Norfolk and Norwich University Hospital, Norwich, UK.

Background
Primary hyperaldosteronism (PHA) typically manifests as resistant hypertension, hyperkalaemia and metabolic alkalosis. We present a case of PHA who subsequently exposed type 4 renal tubular acidosis (RTA) after surgical intervention.

Case history
A 62 year old man underwent investigation for chronic resistant hypertension, which had failed to respond to titration of three antihypertensive agents including Perindopril, Amlodipine and Doxazosin. His medical history consisted of type 2 diabetes, microalbuminuria, dyslipidaemia and stage 3a chronic kidney disease (CKD). Average blood pressure recordings were typically 190/100 mm Hg on both arms, and fundoscopy revealed hypertensive retinopathy.

Investigations
Laboratory findings showed hyperkalaemia (potassium 3.4 mEq/l), alkalosis (bicarbonate 33 mmol/l) and mild hypernatraemia (sodium 147 mmol/l). CT imaging of the adrenal glands demonstrated a 17 mm left adrenal adenoma. Adrenal vein sampling lateralized aldosterone secretion, with an aldosterone: cortisol (ACR) being 53 times higher from the left adrenal gland.

Adrenal vein sampling lateralized aldosterone secretion, with an aldosterone: cortisol (ACR) being 53 times higher from the left adrenal gland.

Reference

DOI: 10.1530/endoabs.573492

P35
A case of cyclical Cushing’s syndrome
Vaithehi Kulendran, Rozana Ramli, Karen Chan, Anand Tana, Lucy Francis, Jeannie Todd, Karim Meenan & Emma Hatfield
Imperial College Healthcare NHS Trust, London, UK.

Case history
We present a 76-year-old woman with cyclical ACTH-dependent Cushing’s syndrome since 2002. She has two-yearly relapses with proximal myopathy, candidiasis, facial swelling and hypokalaemia that have been biochemically confirmed with Overnight and Low Dose Dexamethasone Suppression tests. Although her initial cycles were brief and uncomplicated, her most recent episodes led to prolonged hospital admissions. During her last admission, she became septic complicated by a bleeding pseudo-aneurysm in the liver, a right peroneal artery occlusion and bilateral deep venous thrombosis.

Investigations
Prior to admission, an MRI Pituitary in 2014 showed no clear adenoma. A subsequent MRI in 2017 showed no change. Inferior petrosal sinus sampling was inconclusive. A Ga68 DOTATATE whole body PET-CT was unable to locate any lesions as a source for ACTH. A CT chest, abdomen and pelvis demonstrated normal adrenal glands and stable calcified lung nodules. During her second admission, she had a fall in haemoglobin with deterioration in liver function tests. CT abdomen confirmed a 10 cm bleeding lesion in the left lobe of the liver. Following this, she developed necrosis of her right toes. A vascular duplex scan confirmed the presence of occlusions of bilateral superficial femoral vein and the right peroneal artery.

Results and Treatment
Her clinical deterioration coincides with rising cortisol levels (up to 2273 nmol/l). She became intolerant of Metyrapone and was switched to Fluconazole, which was uptitrated to 600 mg BD. There were concerns that her liver lesion could be a mycotic pseudo-aneurysm secondary to sepsis. She had an emergency embolisation, the pseudo-aneurysm was micro-coiled and required no further intervention. Given her bleeding risk, she was commenced on a heparin infusion for her thrombosis and thereafter, long-term treatment dose tinzaparin. Her necrotic toes were conservatively managed. Due to her frailty, a biopsy was not possible to ascertain whether the lung lesions could be a source of ectopic ACTH.

Conclusions and Discussion
This case illustrates the complexity of managing cyclical Cushing’s; the challenges in identifying the source of ACTH, and its management. Fluconazole was effective in the medical management of Cushing’s syndrome, acting on the same pathway as ketoconazole. Definitive treatment with bilateral adrenalectomy may be considered in the longer term. An established link between Cushing’s and pseudo aneurysms has been demonstrated in previously published clinical cases. This unusual case highlights the potential for serious adverse vascular sequelae of Cushing’s syndrome and the need for awareness of such complications.

DOI: 10.1530/endoabs.55.P35

P36
Severe necrotising pancreatitis secondary to hypertriglyceridaemia in pregnancy
Julia Graham1, Kirun Gunganah1, David Williams2, Catherine Lunken2 & Umashan Srirangalingam2
1Newham University Hospital, London, UK; 2University College London Hospital, London, UK.

Case history
A 35-year-old woman with known hypertriglyceridaemia presented with a one day history of abdominal pain, vomiting and fever. She was 14 weeks pregnant having conceived spontaneously following a period of infertility. She had discontinued her lip-lowering medication and was managed with diet alone. On examination, she was pyrexial, tachycardic (HR = 100 bpm), normotensive (BP = 111/71 mmHg), oxygen saturation was 96% on air and she had a tender distended abdomen. A fetal US confirmed a viable pregnancy. She was diagnosed with acute pancreatitis. Initial management was conservative but she developed acute respiratory distress syndrome (ARDS), requiring respiratory support and transfer to the intensive care unit.

Investigations
Venous blood gas showed a mild acidosis (pH 7.338), raised lactate (3.2 mmol/l) and glucose of 7.6 mmol/l. Blood investigations were limited by high levels of triglycerides precluding automated measurement. After multiple dilutions, triglyceride level was confirmed at 115 mmol/l and lipase level at 293 U/l. A CT abdomen demonstrated extensive peri-pancreatic fluid collections and peri-pancreatic fat stranding in keeping with acute necrotising pancreatitis presumed secondary to hypertriglyceridaemia.
Results and treatment

Initial management was focused on lowering the triglyceride levels. She was started on an intravenous insulin and heparin infusion and transferred to a tertiary centre for consideration of plasmapheresis. Her triglyceride level fell to 5.1 mmol/l with insulin and heparin alone. Plasmapheresis was not required. She was started on Fenofibrate, high-dose Omega3 and a low-fat diet which has maintained her triglyceride level below 5 mmol/l (currently 2.8 mmol/l). She subsequently developed a distended gallbladder and septicaemia requiring intravenous Tazocin, a gallbladder drain and a period of parenteral nutrition. Medical termination of pregnancy was discussed as a potential option to ensure maternal survival. She is currently 23 weeks gestation, approaching viability, with a growth scan showing normal growth but reduced uterine-artery-dopplers suggesting an increased risk of fetal-growth-restriction and placental insufficiency. Her care is being co-ordinated by a multidisciplinary team including hepatobiliary, obstetrics and metabolic medicine teams.

Conclusions and points for discussion

Acute pancreatitis in pregnancy has a high morbidity and mortality rate for both mother and fetus. Due to medical and ethical challenges, such cases must be managed via the multidisciplinary team. This case highlights the efficacy of insulin and heparin in lowering triglyceride levels. Plasmapheresis remains an option where triglycerides do not fall. It also highlights the importance of pre-conception care and effective use of diet, Omega3 and Fenofibrate in lowering triglyceride levels during pregnancy.

DOI: 10.1530/endobs.55.P36

P37
A rare case of congestive heart failure caused by idiopathic hypoparathyroidism

Niruthika Sithamparanathan, Kavitha Lakshmipathy, James Clark, Benjamin Field, Vidhu Nayyar & Sunil Zachariah
East Surrey Hospital, Redhill, UK.

Clinical Case

A 48-year old male presented with gradual onset of shortness of breath and atrial tachycardia requiring admission to intensive care unit. He was normally fit and well and did not have any history of thyroid/nearct surgery. He was an ex-smoker who drank more than 40 units of alcohol per week.

Investigations

Laboratory tests revealed low serum calcium of 1.03 mmol/l (2.15–2.6 mmol/l), high serum phosphate of 2.77 mmol/l (0.9–1.50 mmol/l) and low serum magnesium of 0.53 mmol/l (0.65–1.05 mmol/l). His potassium, alkaline phosphatase and renal function were normal. Electrocardiogram at admission showed atrial tachycardia with ventricular rate of 180 bpm, left ventricular hypertrophy, T wave depressions in leads V4-6 and prolonged QT interval. Chest x-ray showed cardiomegaly and features of pulmonary oedema. Urgent echocardiogram showed dilated and hypokinetic left ventricle with left ventricular ejection fraction of 27%. His parathyroid hormone was undetectable and he had normal thyroid function tests and vitamin D. He also underwent a coronary angiogram which was normal.

Treatment

Hypocalcaemia, hyperphosphataemia and undetectable parathyroid hormone is consistent with the diagnosis of primary hypoparathyroidism. He was initially treated with intravenous calcium gluconate and magnesium for several days until normalisation of serum calcium and serum magnesium. Following this, he was commenced on long term alfacalcidol and calcium supplementation. An echocardiogram done after three months of treatment showed improved left ventricular ejection fraction and normal left ventricular size. This patient is under long term follow-up with the cardiologist and the endocrinologists.

Conclusions

Dilated cardiomyopathy is a dangerous condition that can be associated with reversible conditions such as alcoholism, peripartum cardiomyopathy and various metabolic conditions. Hypoparathyroidism results in hypocalcaemia and hypomagnesaemia. Hypocalcaemia can cause prolongation of QT interval, ventricular arrhythmias and dilated cardiomyopathy. Calcium ion is important for the excitation of the myocardium and consequently its contractility. Cardiomyopathy associated with hypoparathyroidism can be reversed when it is adequately treated with calcium and vitamin D supplementation. In these cases, recombinant parathyroid hormone is rarely required. It is important to identify hypocalcaemia as a treatable cause of cardiomyopathy as this can prevent the development of life threatening sequela.

DOI: 10.1530/endobs.55.P37

P38
A case of pheochromocytoma with SDHA mutation

Lucy Millar1, Angela George2 & Daniel Morganstein1 2
1Chelsea and Westminster Hospital, London, UK; 2The Royal Marsden Hospital, London, UK.

A 58-year-old gentleman who was otherwise well presented with urinary symptoms. As part of his investigation for this he underwent a CT scan which showed an incidental 6 cm right adrenal mass compressing the inferior vena cava and superior pole of the right kidney with a 6-mm pulmonary nodule. He was subsequently found to have a raised urinary metanephrine of 48.8 (normal range 0–3.3) suggestive that the mass was a pheochromocytoma. Retrospectively he reported episodes of flushing, sweating, headaches and diarrhoea. Examination was unremarkable with a blood pressure of 136/84 and he did not take any medications including anti-hypertensives. An MIBG scan showed uptake within the adrenal mass. Having been established on phenoxybenzamine he underwent a radical adrenalectomy with right nephrectomy as there was invasion into the perinephric fat. On histological review the excision appeared complete and the tumour cells strongly expressed CD56, chromogranin, synaptophysin and NSE and S100 highlighted sustentacular cells, all of which supported a diagnosis of pheochromocytoma. The Ki-67 proliferation index was <2% suggesting low mitotic activity within the tumour. However, the tumour showed focal extension through the capsule and into the perinephric fat with lympho-vascular invasion within the large vessels of the perinephric fat and within the surrounding fibrous capsule. This histology gave an overall PASS of 6/20 with a score of <4 indicating a tumour will behave in a benign fashion. A gene panel test was performed which revealed a variant of unknown significance in the SDHA gene. Immunostaining showed loss of SDH expression suggesting this was pathogenic. Post-operatively he has had follow-up CT scans with 24 hour urinary metanephrine and gut hormone measurements at 2 months and 1 year. These have shown no evidence of residual or recurrent disease and stable appearance of the 6mm pulmonary nodule. He reports complete resolution of his symptoms.

Conclusions

Genetic predisposition to pheochromocytomas and paragangliomas is well recognised. The SDHA gene codes for one of the four subunits of the succinate dehydrogenase enzyme which converts succinate to fumarate. It is a tumour suppressor gene and alterations in this gene have been associated with pheochromocytomas and paragangliomas. The particular variant in this case has not previously been reported so it is therefore uncertain whether this alteration is associated with an increased risk of tumour development, however loss of immunostaining suggests it is pathogenic. This case also suggests that SDHA mutation associated pheochromocytoma can exhibit malignant behaviour.

DOI: 10.1530/endobs.55.P38

P39
Management of acromegaly in pregnancy and post-partum

Tamar Saeed, Bahram Jafar-Mohammadi, Christine May & Aparna Pal
Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, UK.

Case history

A 39 year old female presented reporting a 5-year history of swollen face, hands and feet, with associated joint pain. She was initially investigated for rheumatoid arthritis. She had no significant past medical history except for a previous miscarriage in 2014 and treatment for hypertension in a subsequent successful pregnancy. Post-partum she breastfed with no difficulty for 18-months but remained amenorrheic during this time. During 2016 she noticed increase in shoe and ring size, snoring and sweating. She felt increasingly tired, with a reduction in libido and experienced recurrent headaches with deterioration in her peripheral vision.

Investigations

Investigations demonstrated elevated IGF-1 level of 71 mmol/l (8.5–30.7 mmol/l) with growth hormone of 15.3 mcg/l. Her prolactin was 1717 MU/l. An MRI scan in August 2016 confirmed a large pituitary macroadenoma compressing the optic chiasm and eroding the fossa with right cavernous sinus invasion. She was advised to stop breast feeding, commenced on Lanreotide and Carbergoline, and referred to our centre for Transphenoidal surgery.

Results and treatment

She underwent transphenoidal adenectomy in December 2016. Post operatively there were no significant complications. Histology showed a somatotroph pituitary adenoma with a mixed densely and sparsely granulated pattern, no evidence of atypia, and a MIBI index < 1%. Lanreotide was continued post-operatively in view of the known residual tumour within the

DOI: 10.1530/endobs.55.P37
cavernous sinus. This was then confirmed on the post-operative MRI at 3 months. Biochemistry (on Lanreotide) showed IGFI of 24.3 nmol/l (6.4–31.0 nmol/l), growth hormone 1.2 mcg/l, LH 2.3 IU/l, FSH 5.9 IU/l and prolactin of 129 MU/l. In April 2017 her IGFI level was 20 nmol/l and random growth hormone was 2.3 IU/l. Prior to a complete biochemical post op assessment, she was keen to extend her family. Following discussion around the evidence of Lanreotide in pregnancy she and her husband chose to stop treatment. She conceived in May 2017 and the pregnancy is progressing without complication. She has expressed the wish to complete the pregnancy and breast feed off somatostatin analogue therapy.

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

DOI: 10.1530/endoabs.55.P39

P40
Diagnostic challenges in a patient with hitherto unexplained hyperinsulinaemic hypoglycaemia
Meenakshi Parsad
Royal Hampshire County Hospital, Winchester, UK.

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

DOI: 10.1530/endoabs.55.P40

P41
A not so sweet glucagonoma
Si Han Tan, Zhuo Min Chong & Isabel Howat
University Hospital Monklands, Lanarkshire, UK.

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

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

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

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

DOI: 10.1530/endoabs.55.P41

P42
Abstract withdrawn.

P43
SDH mutation and prolactinomas: case series
Richard Timms, Christine May, Aparna Pal & Bahram Jafar-Mohammadi
OCDEM, Churchill Hospital, Oxford, UK.

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

Case 1
61 year old gentleman, presented with a large right-sided carotid body tumour. Three years previously he had been diagnosed with a macroprolactinoma and continues to be managed on Cabergoline. Upon further review, the patient reported that his nephew had been diagnosed with two Phaeochromocytomas. There was no other family history. Genetic testing confirmed an SDHB mutation.

Case 2
40 year old gentleman was found to have a macroprolactinoma. On extensive history taking he reported a strong family history of phaeochromocytoma. Consequently, he underwent genetic testing, resulting in a diagnosis of SDHB mutation. He was also found to have a large right lung mass, which was confirmed to be a carcinoid tumour following resection. His investigations pre-surgery
identified mildly elevated metanephrines. He underwent surgery after appropriate alpha and beta blockade and subsequently metanephrines normalised.

Case 3
A gentleman diagnosed with a macroprolactinoma in his early 20’s. His mother was noted to have a confirmed paraganglioma syndrome secondary to a mutation in SDHC gene. His genetic testing has confirmed the same genetic mutation. His investigations including metanephrines and radiological scans have proved normal, apart from a small (6 mm) lung nodule that is under surveillance.

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

DOI: 10.1530/endoabs.55.P43
Clinical Update
Workshop A: Disorders of the hypothalamus and pituitary (I)
Diabetes Insipidus

**WA1**
Nephrogenic diabetes insipidus one year following discontinuation of lithium
Meenakshi Parsad
Royal Hampshire County Hospital, Winchester, UK.

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

DOI: 10.1530/endoabs.55.WA1

**WA2**
A complex case of diabetes insipidus in a patient with septo-optic dysplasia
Xilin Wu1,2 & William Drake2
1Queen Mary University of London, London, UK; 2St Bartholomew’s Hospital, London, UK.

An 18 year old gentleman was first reviewed in our endocrine adolescent transition clinic. He had been under the care of the paediatricians since birth, where he initially presented with developmental delay. This triggered investigations which led to the diagnosis of septo-optic dysplasia. At aged 12 he developed cranial diabetes insipidus (DI) and secondary hypothyroidism. This was managed with intranasal DDAVP (20ug BD) and thyroxine 125 µg. Due to an abnormal thirst threshold he was required to take up to 2.5 l/day of fluid to maintain sodium levels within the normal range. This was only achievable through the heroic efforts of his caring family. At that point his family were worried about his lack of ‘vitality’ and energy. Several O909 lhour serum cortisol levels of <100 nmol/l were measured therefore he was commenced on hydrocortisone replacement (5 mg BD). This however caused him to become hypernaetramia (Na 151 mmol/l). His fluid ‘prescription’ and DDAVP dose had to be adjusted accordingly, until a new equilibrium was established. A previous glucagon stimulation test documented evidence of growth hormone deficiency (GHD). However treatment was not initiated until the family raised concerns of his increasing lethargy, somnolence and increasing central obesity, 6 months after starting hydrocortisone replacement. He was commenced on GH replacement (0.3 mg OD). Although this greatly improved his level of alertness and short term memory, it led to decompensation of his DI, resulting in severe hypernaetramia: peak Na169 mmol/l. Disturbance of sodium balance with GH had been predicted, but the extent was unexpected and required inpatient correction. Septo-optic dysplasia is a congenital condition characterised by optic nerve hypoplasia, hypopituitarism and other midline brain defects. The evolving nature of the various endocrinopathies over time makes management of sodium and water balance especially challenging. ACTH deficiency is known to cause hyponatraemia. This may have been partially masked DI, which was revealed when he was commenced on hydrocortisone. The sodium-water equilibrium was again disrupted when he was started on GH replacement. Patients with GHD have sodium and water depletion. When GH replacement is initiated, there is usually stimulation of thirst, triggering an increase in fluid intake to match the sodium retention to keep serum sodium concentrations constant. However, due to hypothalamic dysfunction in our patient, this compensatory mechanism was lost, resulting in severe hypernaetramia. This case highlights the complex nature of sodium homeostasis and the profound effects the anterior pituitary hormones can have on that delicate balance.

DOI: 10.1530/endoabs.55.WA2

**WA3**
Lymphocytic hypophysitis in a pregnant patient with type 1 diabetes Shazia Hussain1, Mohammed Shahriar Huda1,2 & William Drake1
1St Bartholomew’s Hospital, London, UK; 2Royal London Hospital, London, UK.

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

DOI: 10.1530/endoabs.55.WA3

**WA4**
Extreme polydipsia as an emergency presentation of chronic undiagnosed central diabetes insipidus
Samantha Anandappa, Suhuyin Youin, Sheela Anpalakhan, Charmaine Llangarane, Cynthia Mohandas, Itoha Abedo & Arthur Ogunko Darent Valley Hospital, Dartford, UK.

Isolated Central Diabetes Insipidus is a rare condition characterised by deficiency of arginine vasopressin (AVP) which presents with polyuria and polydipsia. The reported prevalence of diabetes insipidus is 1 in 25,000. The pathogenesis of central diabetes insipidus is often uncertain however the known causes can be divided into acquired, through trauma or vascular injury as well as ineffective including malignancy, and congenital abnormalities which accounts for less than 10% of cases. Patients with this condition can often compensate through water consumption and therefore any disruption in their usual routine may lead to potentially fatal electrolyte disturbances. We present a 16 year old female patient who presented to the emergency department with increased water intake and lethargy. There was no previous medical history however it was reported that from the age of 3 years she had been obsessed with drinking water and the amount had steadily increased over the years where she was now consuming up to 15 litres per day. Her initial biochemistry was within the normal reference range (Sodium 144 mmol/l (133–146), potassium 4.1 mmol/l (3.5–5.3) and creatinine 51 umol/l (45–84)) and a provisional diagnosis of psychogenic polydipsia was made with paired osmolalities requested. She was limited to 4 l of fluid per day and following this her sodium level steadily increased over the subsequent 4 days to 156 mmol/l. The urine and serum osmolalities along with a water deprivation test revealed the diagnosis of central diabetes insipidus, the aetiology of which remains uncertain. MRI pituitary was performed measuring 5.7 × 5.5 × 13 mm, with normal stalk. She was commenced on desmopressin 100 mg three times three per day and since has had no further polyuria, polydipsia or nocturia. A detailed history and physical examination can often unmask clues within the underlying aetiology and provide a working diagnosis as to when the patient may have developed diabetes insipidus. Biochemical analysis and water deprivation test remain the gold standard for diagnosis. This case highlights the potential complications of
misdiagnosis and treatment of patients with central diabetes insipidus. It is also important to identify the changes in fluid intake that can occur through concurrent illness which requires monitoring in these individuals and can often be challenging manage with adjustments in fluid balance and DDAVP dose required to prevent extreme electrolyte changes.

**WA5**

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

Charmaine Ilarianarit, Samantha Anandappa, Arthur Ogunko, Cynthia Mohandas & Iopa Abedo

Darent Valley Hospital, Dartford, UK.

We present a case of a 79 year old gentleman who attended the emergency department with a one day history of acute confusion and hallucinations. His background included trans-sphenoidal surgery for a gonadotrophin pituitary macro-adenoma in 2012 with subsequent panhypopituitarism and post-operative diabetes insipidus. He also had a history of restless-leg syndrome for which he took Amitriptyline chronically, COPD and tablet-controlled diabetes mellitus. Of significant note, the patient had been discharged the previous week following an admission with painful legs and diagnosed with peripheral vascular disease thus confounding his picture as part of a conservative management plan. Blood tests showed an acute hypoponataemia with sodium 109 mmol/l and a normal full blood count, potassium, creatinine and urea. His baseline sodium was between 129 and 135 mmol/l over the previous year. There was no evidence of infection.

On initial assessment the patient was confused without any lateralising neurology. He was clinically euvo laemic and normotensive. A palpable bladder was noted. CT head and chest X-ray did not reveal acute pathology. The initial management plan was to hold Desmopressin, (DDAVP), commence intra-venous Hydrocortisone and catheretere. Paired osmolalities revealed a serum osmolality of 234 mosm/kg/H2O (normal value: 275–295), urinary osmolality of 583 mosm/kg/H2O, and urinary sodium of 103 mmol/l. He was managed with 2.7% hypertonic saline requiring two 100 ml infusions to raise the sodium above 5 mmol/l. The rate of correction exceeded 10 mmols within total 24 hours and therefore Desmopressin was re-commenced, initially at a lower dose. Acute hypoponataemia secondary to syndrome of Inappropriate anti-diuretic hormone, (SIADH), was diagnosed and deemed a consequence of recent commencement of Duloxetine, a dual re-uptake inhibitor of serotonin and noradrenergine. This patient was on long-term Amitriptyline, also a selective-serotonin re-uptake inhibitor, as well as Omeprazole and Desmopressin. Both SSR1 agents were permanently discontinued; Omeprazole another agent frequently associated with SIADH was switched to Pantoprazole. Sodium was slowly corrected to 135 mmol/l over a period of 72 hours, (low end of normal reference range). His cognitive impairment improved to baseline and he was discharged on his regular dose of oral Desmopressin and steroids. This case highlights how SSR1s potentiated the action of synthetic anti-diuretic hormone in a patient with central Diabetes-Insipidus. It is important to have awareness of SIADH as a side effect of common prescription medications and the cautions necessary for patients with possible diabetes insipids? How would you coordinate future treatment with Desmopressin and chemotherapy?

**WA7**

When opposites are one and the same

Desiree Seguna & Mark Gruppetta

Mater Dei Hospital, Msida, Malta.

Water balance disorders following neurosurgery are well recognised and may give rise to both hypo- and hypernatraemia. We present the case of a 42-year-old male who developed a triphasic response after extended transsphenoidal surgery for a pituitary stalk lesion. The patient presented with a 4 month history of unexplained frontal headaches and dizziness. MRI confirmed a 15x15 mm stalk lesion. Clinical examination including formal visual perimetry was unremarkable. Blood tests revealed primary hypothyroidism but were otherwise normal. His past medical history included hypertension and alcoholism. He was referred to the UK where he underwent extended transsphenoidal surgery. In the immediate postoperative period, he developed polyuria (670 ml/h) and polydipsia (500 ml/h) which led to a negative fluid balance (of 2 L over 12 hours), serum sodium of 142 mmol/l, high serum osmolality of 299 mOsmol/kg and low urine osmolality of 131. The patient was normoglycaemic and did not receive any diuretics. Desmopressin (initially subcutaneous then desmotabs) reduced the polyuria and, together with intravenous fluids (2 L of 5% dextrose/day between days 1 and 2) and ad libitum drinking, restored normonatraemia. Hydrocortisone 10-5-5 mg was started on the 6th postoperative day in view of a morning cortisol of 25 nmol/l. On the 7th day post-op he developed severe SIADH with a serum sodium of 120 mmol/l, which was managed conservatively with fluid restriction (1.5 l/day). He was clinically euvo laemic, with normal kidney function (creatinine 53 Umol/l). Despite fluid restriction, fluid intake exceeded urine output (19 ml/h) producing a positive fluid balance of + 1.5 l and a further fall in serum sodium to 119 mmol/l. Here the patient complained of headaches, unsteadiness and lethargy but no confusion or seizures. On day 12 the patient redeveloped polyuria (250 ml/hour) for which desmotabs 100mcgs daily were started. In anticipation of a triphasic response he was continued on ad libitum fluid intake and desmopressin was further increased to 100-200 mcgs as the patient was still waking up hourly to micturate. He was advised to omit one dose a week to allow excess water to be offloaded. On the 13th postoperative day he developed a serum sodium of 138 mmol/l, serum osmolality 299 mOsm/kg and urine osmolality of 79 mOsm/kg. Histology confirmed a pituicytoma (WHO grade 1); Ki-67 <1%. 

DOI: 10.1530/endoabs.55.WA7

A severe acute kidney injury requiring dialysis after which her renal function returned to baseline. Protocols to avoid Methotrexate toxicity require intravenous fluid at up to 250 ml/h so that a significant diuresis is achieved. Methotrexate toxicity was in part exacerbated by Desmopressin treatment which reduced the anticipated diuresis. Following chemotherapy and prior to discharge the patient’s Desmopressin was adjusted to achieve a normal fluid balance with stable sodium levels. Further cycles of chemotherapy are planned with down titration of Desmopressin under strict fluid input/output and serum sodium monitoring. How does this route to diagnosis differ from outpatient assessment of patients with possible diabetes insipids? How would you coordinate future treatment with Desmopressin and chemotherapy?

**WA8**

Challenges in management of cranial diabetes insipidus in critically ill patient

Manjima Uchambally

Sheffield Teaching Hospitals, Sheffield, UK.

Cranial diabetes insipidus in critically ill patients increase the complexity of fluid management. Well patients with cranial diabetes insipidus can drink enough fluid to replace their urine losses driven by their thirst mechanisms. In critically ill patients the thirst response cannot be relied upon. When fluid input is not adequate it results in hypernatremia. Here dextrose, water or hypo-tonic intravenous fluid is used. Complications related to this are high glucose levels, fluid overload and quick correction of hypernatremia. Treatment with desmopressin cause low urine output and anti-diuresis. Frequent monitoring serum sodium, urine osmolality and volume is very important. 39-year-old lady admitted to critical care with major haemorrhage following liver biopsy. Background Gestminna age 15, had a combination of chemotherapy and radiotherapy (craniospinal irradiation) which has left her with pan hypopituitarism with Diabetes insipidus. She takes Desmopressin 100micrograms in afternoon and 200 μg in the evening On
A previously well 49 year old woman was referred to our endocrine service with a 3-month history of polyuria and polydipsia. She described an eighteen month history of dermatomycetoma with no galactorrhoea and reported no change in her vision. Her past medical history included alopecia areata one year previously from which she made a full recovery. Clinical examination was normal including full visual fields to red-pin confrontation. Biochemistry identified serum sodium of 141 mEq/l, serum osmolality 292 mOsm/kg and urine osmolality 84 mOsm/kg. On the basis of the history and these investigations she was diagnosed with diabetes insipidus, felt likely to be central due to the acuteness of onset. She was started on DDAVP with good effect on her symptoms and this was titrated to a dose of 200 µg bd orally to achieve full control. Anterior pituitary function was normal (TSH 4.1 mU/l, 0900 h cortisol 238 nmol/l, LH 3.6 IU/l, FSH 4.1 IU/l, oestradiol 289 pmol/l, prolactin 383 mIU/l and testosterone 0.8 nmol/l). MRI scan of the pituitary showed a normal size pituitary but without a posterior bright spot consistent with a primary lung tumour. An inpatient MRI brain showed multiple metastases including one in the pituitary fossa. Her symptoms responded well to the introduction of both dexamethasone and desmopressin. Prior to discharge she underwent bronchoscopy which confirmed a diagnosis of adenocarcinoma of the right lung. She was ultimately treated with whole brain radiotherapy and palliative chemotherapy. During follow-up she became progressively more Cushingoid due to the high-dose dexamethasone required for symptom control and was diagnosed with steroid-induced diabetes mellitus. This case demonstrates the rarely encountered scenario of central diabetes insipidus due to pituitary metastasis. The possibility of this diagnosis was considered in the first clinic appointment hence the necessity of arranging more urgent investigation than for most suspected/possible DI cases.

DOI: 10.1530/endoabs.55.WA10
WA13
Cushing’s disease relapse associated with central diabetes insipidus
Ana Ferreira, Tiago Silva, Filipa Bastos, Isabel Manita,
Maria Carlos Cordeiro & Jorge Portugal
Garcia de Orta Hospital, Almada, Portugal.

Introduction
Central diabetes insipidus (DI) is a frequent complication of transphenoidal surgery for Cushing’s disease (CD). It can be transient or, more infrequently, permanent. The most common mechanism results from surgical neurohypophyseal damage rather than local mass effect from the pituitary adenoma.

Case report
A 40 years old woman was referred to our Endocrinology outpatient clinic at the beginning of 2015 for new onset hypertension, significant weight gain, mood disturbance, proximal muscular weakness and amenorrhea. After a year of follow-up, she was formally diagnosed with cyclic CD, hypogonadotrophic hypogonadism, central hypothyroidism, as well as a pituitary macroadenoma (12×16×15 mm) with pituitary stalk enlargement. She had surgery in March 2016, with no post-operative complications. Histology confirmed an ACTH positive adenoma. Her initial symptoms resolved, except for central hypothyroidism. She required hydrocortisone treatment for 5 months, with no adrenal insufficiency afterwards. About two years after surgery, the patient started complaining of increased thirst and water intake (3 to 4.5 l of water/day) and 24-hour urinary output. She also noted weight gain again. Further evaluation confirmed hypercortisolism relapse and revealed a new onset partial DI. MRI showed an increased thickness of the pituitary stalk (7×7×10 mm), more significant than before, associated with a residual lesion at this location. Other infiltrative disorders of the pituitary stalk were excluded. The patient was started on desmopressin and a new surgical procedure is under consideration.

Conclusion
This case illustrates a rare form of CD relapse, with associated DI, possibly related with the location of the residual lesion at the pituitary stalk. It should alert the clinicians to be aware for DI symptoms during follow-up, even a long time after surgery.

DOI: 10.1530/endoabs.55.WA13
Workshop B: Disorders of the hypothalamus and pituitary (II)
Management of Acromegaly

WB1
Gigantism presenting with visual failure
Craig E Stiles1,2 & William M Drake1
1St Bartholomew’s Hospital, London, UK; 2Queen Mary University of London, London, UK.

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

DOI: 10.1530/endoabs.55.WB1

WB2
A case of successful conception in a patient with acromegaly, post TSS after pre-treatment with a somatostatin analogue
Craig E Stiles1,2 & William Drake1
1St Barts, London, UK; 2Queen Mary University of London, London, UK.

A 35 year old lady presented to endocrine services with a background of attempted conception and oligomenorrhoea. Presenting features were typical of acromegaly including sweating, acne and median nerve entrapment. Growth hormone day curve showed unrelenting high levels of growth hormone. Serum IGF-1 was elevated at 154 nmol/l (normal 14.2–36.9). Other pituitary blood tests were within normal limits. A pituitary macroadenoma measuring 1.5×1.5×1.3 cm was found on MRI. There were no neuro-ophthalmic signs to suggest compression of the optic chiasm and the blood pressure was normal. The patient strongly desired future fertility and so a decision was taken to try and shrink down the pituitary tumour using somatostatin analogue therapy. It was hoped that this would better delineate the tumour from normal pituitary tissue, so that surgical resection might be less traumatic and would hopefully avoid damaging gonadotroph function. She underwent uncomplicated Transspheonidal surgery in 2012. The operation note mentions that a tumour was visualised on the left hand side of the pituitary gland as seen on the pre-op MRI. Histology showed a pituitary adenoma with cells staining strongly for growth hormone. Ki 67 = 1%. Appearances were consistent with a densely granulated somatotroph adenoma. Soft tissue changes associated with acromegaly disappeared after the surgery and the patient was left with normal pituitary function –the growth hormone level fell by 90% (compared to pre-op values). Normal menses returned and the patient subsequently had two successful pregnancies. Post-op MRI had shown a 6 mm area of tissue with reduced enhancement in the surgical bed which was thought to represent post-surgical change. Her serum IGF-1 remained mildly elevated (355 nmol/l, normal 109–284) and latterly she was put onto cabergoline (which proved ineffective) and more recently back onto a small dose of somatostatin (endonasally). Aside from elevated blood glucose levels in the aftermath of the surgery, his recovery was unremarkable. Histology reported a pituitary adenoma with production of growth hormone and prolactin. Recent IGF-1 at 3 months was 63.8 nmol/l and the patient is due to be seen in clinic very soon.

DOI: 10.1530/endoabs.55.WB2

WB3
Big hands result in a good catch
Ben Houlford
University Hospital Southampton, Southampton, UK.

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

DOI: 10.1530/endoabs.55.WB3
Workshop C: Disorders of the thyroid gland (I)
**Goitre and Thyroid Nodules**

**WC1**

Management of solitary toxic thyroid nodule

Rabia Arfan
Royal Berkshire Hospital, Reading, UK.

**Background**

Toxic thyroid nodules are difficult to manage medically. Surgical versus radioactive therapy can be chosen in light of risk and benefit for individual cases.

**Clinical case**

72 years old woman presented with 3 months history of hands tremor. There was no associated palpitations, weight loss, sweating, diarrhoea or mood change. She reported mild tiredness. She had never noticed any lump or pain in her neck. There was history of cold intolerance which had been a long standing problem and did not change recently. Her thyroid function was tested and showed T4 of 25.4 (12–22 μmol/l) with suppressed TSH <0.01 (0.27–4.2 mIU/l). She was started on carbimazole 5 mg daily by her GP and was referred to the Endocrine clinic. On treatment her tremors improved but did not settle completely. Clinically she was euthyroid. Her heart rate was 80/min and regular. There was no tremor or sweaty palms. There was no evidence of thyroid eye disease. Thyroid gland was not enlarged. The rest of systemic examination was unremarkable. Her repeated thyroid function on carbimazole showed TSH of 0.02 (0.27–4.2 mIU/l) and FT4 12 (12–22 μmol/l). Her TSH receptor antibodies and thyroid peroxidase antibodies were negative. Thyroid uptake scan was performed to evaluate the cause of hyperthyroidism which showed loculised increased uptake consistent with a solitary toxic nodule. Definitive treatment of her toxic nodule in form of surgery or radioiodine treatment was discussed with patient and she opted for surgery.

**Conclusion**

For solitary thyrotoxic nodules, surgical approach can be considered a better management option as it would preserve thyroid function but decision is dependant on patient’s preference.

DOI: 10.1530/endoabs.55.WC1

---

**WC2**

Toxic nodule: wait or treat?

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

68 years old female initially referred to endocrine clinic in November 2016 for assessment of fluctuating thyroid function. She had a history of long standing primary hypothyroidism, stable on treatment with 100 mcg Levothyroxine. In last one year, Levothyroxine was tapered and stopped due to persistent suppression of TSH and high normal Free T4. Last tests showed TSH of <0.01mIU/l and Free T4 of 27.1 pmol/l. She had ongoing complaints of feeling increasingly tired and generally unwell. She was clinically euthyroid with no evidence of thyroid eye disease. There was asymmetrical thyromegaly on right side with no compressive symptoms. Her thyroid function tests (TFTs) were normal with negative thyroid autoantibodies. Her TSH was 0.31 (0.27–4.20 mIU/l), T4 11.1 (10–23 pmol/l) and T3 5.9 (3.1–6.8 pmol/l). However, thyroid ultrasound showed a 2.7×3.5 cm right lobe nodule, characterised as U2. Repeat blood test revealed suppressed TSH (0.06 mIU/l), normal T3 (3.8 pmol/l) and T4 (12 pmol/l). Pituitary profile was normal for age. Suppressed TSH with increased T3/T4 ratio raised suspicion of a toxic nodule. She had a thyroid neontium uptake scan which confirmed dominant nodule in the right lobe of the thyroid. She was planned for Radio Active Iodine treatment but her thyroid function normalised and a decision was made to keep her under active surveillance. Over last 6 months, she had normal TFTs twice with improvement in symptoms. This is good learning case showing fluctuating toxic features in a thyroid nodule.

DOI: 10.1530/endoabs.55.WC2

---

**WC3**

Indeterminate thyroid nodule in a patient with Graves’ disease

S Samarasinghe1, P Avati2 & K Muraleedharan2
1Central Middlesex Hospital, London North West Healthcare Trust, London, UK; 2Department of Endocrinology, Imperial College London, London, UK.

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

DOI: 10.1530/endoabs.55.WC3

---

**WC4**

A common case of goitre, thyroid nodules and thyroid carcinoma

Dr David J Tansey & Dr James Gibney
Tallaght University Hospital, Tallaght, Dublin 24, Ireland.

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

DOI: 10.1530/endoabs.55.WC4
Workshop D: Disorders of the thyroid gland (II)
Thyroid Cancer

WD1

Abstract withdrawn.

WD2

An unusual route to the diagnosis of medullary thyroid cancer

Michael Gilroy1, Christopher Redford2, Julie Dunn1, Amita Patel1, Efstadia Kyroidimou1, Emma Baple1, Daniel Flanagan2 & Bijay Vaidya1
1Royal Devon and Exeter Hospital, Exeter, UK; 2Derriford Hospital, Plymouth, UK.

We describe a 68 year lady who was found to have bilateral adrenal masses (7 cm on the right side and 1.3 cm on the left) during investigations for gastrointestinal symptoms, in early 2016. Biochemistry revealed high urinary normetanephrines of 41.7pmol/24h (ref 0–3) and metanephrines of 40pmol/24h (ref 0–1.8). A PET and MIBG scan revealed uptake in both adrenal glands and therefore a diagnosis of bilateralphaeochromocytoma was made. The patient had complained of occasional palpitations and headaches, but no paroxysmal sweating or flushing. She had long-standing borderline hypertension not requiring treatment, and diet-controlled type 2 diabetes. In 1988 she had had a sub-total thyroidectomy for a large goitre at another hospital. The patient had a family history of thyroid disease. Her paternal aunt had a goitre removed and one of her sisters has autoimmune hypothyroidism. Her identical twin also has type 2 diabetes. Her mother had a stroke and osteoarthritis and her father died of a myocardial infarction. She has two daughters aged 38 and 41 years old. The patient underwent bilateral adrenoleucotomy in August 2016. Subsequent histology confirmed a right sidedphaeochromocytoma, with a PASS 9, and a left sidedphaeochromocytoma, with a PASS 4. Genetic screening revealed a previously reported ATA level C RET variant (p.Cys634Tyrc) confirmating a diagnosis of MEN 2A. This variant is associated with more aggressive form of medullary thyroid carcinoma. In light of these findings an ultrasound scan of her thyroid was performed in September 2016. This revealed two nodules measuring 13mm and 4mm in the right lobe, and a 10mm nodule in the right-sided isthmus. These nodules had entirely benign ultrasound appearances. Calciitonin and carcinomembrionyctic antigen (CEA) levels were normal. We were able to obtain the histology slides taken from the patients’ previous sub-total thyroidectomy. These had initially been reported, in 1988, as benign multi-nodular changes, but in retrospect a clear focus of medullary thyroid carcinoma was found. The question therefore was raised about whether the patient should now proceed to completion thyroidectomy, despite there being no definitive evidence of malignancy on ultrasound and 30 years having passed since her original thyroid surgery.

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

DOI: 10.1530/endoabs.55.WD2

WD3

A case of medullary thyroid cancer

Dhruvi Bhatt1, Muhammad Shaker2, Kim Ah-see2, Prakash Abraham1 & Alex Graveling1
1Department of Endocrinology, Aberdeen Royal Infirmary, Aberdeen, UK; 2Department of ENT, Aberdeen Royal Infirmary, Aberdeen, UK.

Case
A 61 year old female, presented to ENT in July ’17 with 6 month history of left sided neck swelling, gradually increasing in size over the last 1 month prior to presentation. She complained of tenderness over the swelling and pain and discomfort around her left shoulder. She denied any problems with her voice, breathing or swallowing. Her past medical history consisted of recurrent UTI’s, renal stones and mediastinal sponge kidney. She smokes 15 cigarettes per day and no family history of thyroid cancer. Examination-Left sided level V lymph nodes were hard and tender. An ultrasound guided fine needle aspiration was suggestive of medullary thyroid cancer (MTC). Despite a recent chest radiograph showing clear lung fields a CT neck and chest showed multiple lung nodules and adrenal deposits suggestive of metastatic disease. She was referred to Endocrinology in August ’17 for further investigations; Two urinary metaenamines, U&Es, TFFTs and calcium were all within normal range. CEA - 41.7 (0-3 mg/l) and calcitonin - 9,000 (0-15 ng/l) were both grossly elevated. Her case was discussed at the regional thyroid cancer MDT and she underwent bilateral neck dissection and total thyroidectomy in October ’17. Histology confirmed metastatic medullary thyroid cancer and an incidental 1.2 mm papillary microcarcinoma. She has made an excellent post operative recovery and her calcitonin 2 months post operatively has improved to 4,970 (0-15 ng/l). She is on Levotyroxine, alfalcacidol and calcichew post operatively. In view of her normal PTH we would aim to wean her off calcichew and alfalcacidol. Her MEN2 genetic testing was negative. She is awaiting a follow-up CT neck and thorax.

Discussion points
i) What is the most common presentation of MTC?
ii) What is the most important pre-operative investigation in patients with MTC?
iii) What percentage of MTC is thought to be genetic?
iv) What is the role of TSH suppression or high dose radioactive iodine in MTC?

DOI: 10.1530/endoabs.55.WD3

WD4

A thyroid lump presenting in pregnancy

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

A 34 weeks pregnant woman was reviewed in the joint antenatal clinic with over a month history of neck swelling. Her thyroid function tests showed TSH of 1.39 mIU/L and a free T4 of 11 pmol/L. An initial ultrasound of the neck revealed a solitary heterogeneous nodule in the right lobe of the thyroid consistent with U3 morphology (indeterminate). She was referred by ENT consultant and had a fine needle aspiration (FNAC). Cytology was consistent with features of papillary thyroid cancer (THY5). It has been discussed during Thyroid MDT with the recommendation to allow for completion of pregnancy first before offering any definitive thyroid treatment and to reconsider treatment 3 months postpartum. It was felt that she was a borderline candidate for hemithyroidectomy versus thyreoidectomy as the tumour was less than 4 cm. She had a delivery in December 2016. When assessed 4 weeks postpartum in the beginning of January 2017 she described globus type symptoms and felt the swelling of the neck has increased. On examination there was a 4-3 cm right thyroid nodule with no palpable lymph nodes. A repeated ultrasound of the neck showed an increase in size since the previous study. She underwent a total thyroidectomy in March 2017. A postoperative calcium and PTH were 2.32 mmol/L and 0.9 pmol/L respectively. Thyroid histology described a 40 mm encapsulated follicular variant papillary thyroid cancer with extensive vascular invasion pT2, R0. On follow up she has made an excellent recovery. The neck wound has healed well and her vocal cords were mobile on nasendoscopy. In April her thyroglobulin was less than 0.2 ng/ml, anti-thyroglobulin 28 IU/ml and TSH above 100 mU/L. There was no evidence of distant metastases on radioiodine scan. Her case was discussed at Thyroid MDT again and it was felt that she could either opt for therapeutic radioiodine or wait and see approach with ongoing oncology follow up.

DOI: 10.1530/endoabs.55.WD4

WD5

Hashimoto’s Thyroiditis and Thyroid cancer

Kazi Alam, Ragini Bhave & Miles Levy
University Hospitals Leicester NHS Trust, Leicester, UK.

A 40 year old lady presented to GP with few months history of palpitation, anxiety, frequent stools in April ’15. Clinical examination revealed moderate sized goitre, more prominent on right side, mobile, non-tender and no lymphadenopathy. Blood tests consistent with T3 toxicosis with FT3 10 (3.5–6.5), FT4 21 (9–25), TSH <0.05 (0.3–5.0) and thyroid peroxidase antibody positive at 562 IU/ml (0–60). Initiated on Carbimazole 20 mg once daily. US Thyroid (May ’15) showed features consistent with multinodular goitre. Right largest nodule solid cystic 3.8×2.2 cm. Left sided largest nodule 1.5×1.9 cm. FNA not performed due to hyperthyroidism. NM Thyroid Scan with uptake Technetium (July ’15) – cold nodule corresponding with the right largest nodule. Repeat US thyroid (September ’15) in view of above findings showed U2 nodule and FNA was benign (thy2). Carbimazole stopped in view of FT4 8.3, TSH 8.6.
She presented with worsening left neck pain in 2016. Repeat US thyroid reported no significant interval change in the right lobe nodule. There were two iso to hyperechoic nodules in the left lobe and ENT assessment was suggested. Reviewed in the ENT clinic August’16 and patient reported dysphagia for few months. US thyroid – no interval change. BTA U2 (benign) nodule. No FNA performed. ENT review again in May’17 with left otalgia and neck pain. MRI neck showed only multinodular goitre. Repeat US thyroid revealed right solid cystic nodule slightly increased in size, coarse calcification and FNA was thy4 (suspicious for malignancy). Underwent right hemithyroidectomy (pT2 follicular variant PTC). The background thyroid tissue shows features consistent with Hashimoto’s thyroiditis (diffuse lymphocytic inflammation with occasional secondary lymphoid follicles). As per MDT decision went for completion left hemithyroidectomy (pT2(m)NXMX) and referred for radioiodine treatment.

Discussion points

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

DOI: 10.1530/endoabs.55.WD5

WD6

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

Mariana Costache Outas 1 & Cosmin Giumele2,3
1Coltea Clinical Hospital, Bucharest, Romania; 2 Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; 3 Elias University Emergency Hospital, Bucharest, Romania.

We report a 21-year-old man who referred to endocrinologist following biopsy of a left-sided cervical mass. The pathological examination was diagnostic for medullary thyroid carcinoma (MTC). Physical examination was remarkable for a firm 3-cm nodule in right thyroid lobe and another 3 cm. firm nontender mass in left thyroid lobe. The calcitonin was 15,324 pg/ml, and carcinoembryonic antigen was 415 ng/ml. The calcium level was 10.3 mg/dl (<10 mg/dl) with unsuppressed parathormone of 37.1 pg/ml (15–65) and negative screening for pheochromocytoma. The ultrasound of the cervical region shows both thyroid lobes occupied by hypoechoic irregular masses with macrocalcifications and blood flow and metastatic bilateral adenopathies. The tomography of the chest revealed multiple bilateral nodular lesions (maximum 10 mm.) suggestive of pulmonary metastasis. The tomography of abdomen described hepatic lesions (>20) of sizes up to 22/17 mm. The patient was negative for germline RET mutations. The total thyroidectomy with central and cervical compartment dissection was carried out by a thyroid surgeon, as well as the exclusion of three out of four parathyroid glands. The patient received thyroid substitution therapy and active vitamin D supplement. A nadir for calcitonin of 16,646 pg/ml was registered three months following surgery. The follow up with repetitive tumor markers, and evaluation of tumors showed a slow progressive increase of calcitonin in 21.55% in 0.83 years (52% increase in 24 months) with the stable size of the pulmonary and hepatic metastasis and no tumor tissue in the cervical region.

Discussion

The study by Wells establishes the efficacy of Vandetanib in patients with locally advanced or metastatic MTC. This study included 15% patients that the progression of the disease was not documented before entry. The response rate to Vandetanib with sporadic MTC seems to correlate with RET mutations with better responsive rate (54.5%) when the mutation is present compared with the 32% in the patients who were negative for mutations (or have unknown mutation status). The relatively indolent tempo of disease in some patients with MTC makes the risk: benefit ratio of treatment unfavorable in patients with a low disease burden who experience slow progression and surviving rates of 100% at ten years when the doubling time of calcitonin is more than 24 months. In contrast, patients who are symptomatic, have a high disease burden or have rapidly progressing disease stand to benefit the most from treatment with Vandetanib.

DOI: 10.1530/endoabs.55.WD6

WD7

A challenging case of progressive follicular thyroid cancer

Shazia Hussain1, Carmel Brennan1, Nick Plowman1, Kate Newbold2 & William Drake1
1St Bartholomew’s Hospital, London, UK; 2Royal Marsden Hospital, London, UK.

A 60 year old gentleman with a history of renal stones presented 5 years ago with left sided flank pain. A CT of his renal tract showed an unexpected metastatic deposit in the left iliac crest. Cross-sectional whole body imaging, performed to locate the primary, also identified an expansile soft tissue mass in the T8 vertebral body and a predominantly cystic looking left sided thyroid nodule. He proceeded to have an iliac crest biopsy which was consistent with metastatic follicular thyroid cancer. A dedicated thyroid ultrasound scan showed a malignant looking thyroid nodule with no suspicious lymphadenopathy. He was referred for an urgent thyroidectomy. Post-operative histology was reported as widely invasive follicular thyroid cancer with evidence of vascular invasion and tumour necrosis. He was commenced on suppressive doses of Levothyroxine and was referred to our centre for radioiodine. A repeat look at his preoperative spinal imaging was worrisome for impending spinal cord compression from the T8 metastatic deposit. He, therefore, received urgent radiotherapy to this lesion and to the left ilium. After completing the radiotherapy he received radioiodine ablation. Post-ablation 1-131 scan showed iodine avidity in the thyroid bed, T8 and the left ilium. Over the next two years he received four therapy doses of radioiodine with good concentration in the metastatic deposits. His stimulated thyroglobulin fell from 6,840 µg/l to 3,544 µg/l. However, in May 2016, four months after his last radioiodine therapy dose, he reported worsening bone pain. His unstimulated thyroglobulin rose to >5,000 µg/l and a repeat MRI scan showed new acutabular deposits and a left pubic ramus pathological fracture necessitating more radiotherapy to this site. A repeat look at his post-therapy scans confirmed these sites as being non-iodine avid. In view of this, a PET scan was arranged to look for other non-iodine avid sites. Unfortunately, this identified multiple spinal and lung metastases. He was given bisphosphonate therapy and his case was brought back to the thyroid multi-disciplinary team meeting where funding for Sorafenib was discussed. However, the patient had done some of his own research and was keen to enrol in a clinical trial that specifically looked at treatment options which may restore iodine avidity to his advancing disease first. Differentiated thyroid cancers are usually responsive to radioiodine therapy. Refractory follicular thyroid cancers are rare and treatment options are limited. This case highlights the role of the multi-disciplinary team in managing these complex patients.

DOI: 10.1530/endoabs.55.WD7
Workshop E: Disorders of the adrenal gland
Newer imaging modalities show potential but are not widely available. Should this case illustrate the workup of a patient with primary hyperaldosteronism and gynaecomastia, 3–4 cm bilaterally. If this persisted or progressed, other medical investigations were unsuccessfully cannulated.

VE1

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

Ben Houlford
University Hospital Southampton, Southampton, UK.

A 42 year old gentleman was referred to endocrinology clinic by a consultant urologist due to an incidental finding of a 14 mm adrenal nodule on the patient’s right adrenal gland. He was originally seen by gastroenterology having been referred due his 7 year history of twice yearly attacks lasting around 30 min, comprising of flushing of the face, palpitations, burning sensation in his stomach, sweating, vomiting and loose bowel motions. The gastroenterology consultant did not feel this was a gastro problem and arranged CT chest/abdo/pelvis for exclusion of carcinoid and phaeochromocytoma. The CT scan showed a 13 mm left lower lobe lesion (likely bronchocle – suggested respiratory follow up), a left lower pole renal lesion (possible early neoplasm – for ultrasound and MDT follow up) and a right adrenal soft tissue nodule measuring 14 mm (referred to endocrinology). The urology consultant saw the patient who had now had an MRI and the renal lesion had been identified as a Bosniak 3 cyst (50% chance of malignancy). The plan was to monitor the cyst and likely excise it but only once the adrenal lesion had been dealt with. The MRI had shown this to not have characteristics typical of an adenoma with phaeochromocytoma being possible. A 24 hour urine collection for metanephrines had been sent with results awaited at this stage. The urologist organised an MIBG scan to further image the adrenal lesion. The patient was then seen in clinic in the endocrinology department. He and his wife were understandably anxious about all that was going on. The urine collection had demonstrated normetanephrine output of 2.15 (reference range 0–3.00), metanephrine output of 1.82 (reference range 0–1.40) and 3-methoxyxymetanephrine output of 2.52 (reference range 0.57–2.30). Chromogranin A and B results were also available and were within the reference ranges. A set of plasma metanephrines had been taken and these too were well within the reference ranges. The various results were explained to the patient and he was referred to the endocrinology MDT meeting. A repeat set of 24 hour urinary metanephrines was requested. The MIBG result was available not long after the clinic appointment and this showed an MIBG avid right adrenal nodule consistent with phaeochromocytoma. The endocrinology MDT meeting concluded this was an early phaeochromocytoma. The patient was referred for excision and alpha and beta blocking arranged. The lesion was excised uneventfully and histology confirmed the phaeochromocytoma diagnosis.

DOI: 10.1530/endoabs.55.WE1

WE2

Challenges in managing primary hyperaldosteronism

A 59 year old man was referred to Endocrinology from Neurology with a 2 year history of hypertension, and a 1 year history of mild hypernatraemia (146–148 mmol/l). He had a 1 year history of orthostatic symptoms, including invasive coronary angiogram which did not report any abnormality. Her blood pressure at his first attendance to the Endocrine Unit was 150/87. Investigations Blood pressure at his first attendance to the Endocrine Unit was 150/87. Aldosterone level was raised at 834 pmol/l with a suppressed renin (0.1 pmol/l). 24 hour urine collection for metanephrines had been sent with results awaited at this stage. The urologist organised an MIBG scan to further image the adrenal lesion. The patient was then seen in clinic in the endocrinology department. He and his wife were understandably anxious about all that was going on. The urine collection had demonstrated normetanephrine output of 2.15 (reference range 0–3.00), metanephrine output of 1.82 (reference range 0–1.40) and 3-methoxyxymetanephrine output of 2.52 (reference range 0.57–2.30). Chromogranin A and B results were also available and were within the reference ranges. A set of plasma metanephrines had been taken and these too were well within the reference ranges. The various results were explained to the patient and he was referred to the endocrinology MDT meeting. A repeat set of 24 hour urinary metanephrines was requested. The MIBG result was available not long after the clinic appointment and this showed an MIBG avid right adrenal nodule consistent with phaeochromocytoma. The endocrinology MDT meeting concluded this was an early phaeochromocytoma. The patient was referred for excision and alpha and beta blocking arranged. The lesion was excised uneventfully and histology confirmed the phaeochromocytoma diagnosis.

DOI: 10.1530/endoabs.55.WE1

WE3

Phaeochromocytoma: A reversible cause for hypertension

Eltaashra Ahmed
Queen Elizabeth The Queen Mother Hospital Margate, Margate, UK.

The case

The case described is a 49 year old lady referred to emergency department with history of episodic palpitations, headache and sweating with possible weight loss for last 14 years but symptoms now worse in the past few days. Past medical history was significant for modest hypertension with renal changes treated with Lisinopril. Patient stopped going to the gym recently as it seemed to exacerbate the symptoms. Patient recently registered with a new GP who in view of the above symptoms correctly organised 24-hour urine catecholamines and referred the patient to A&E. Systemic examination was unremarkable at time of admission with BP of 140/90, pulse rate of 72/min and RR of 14/min. However, patient seemed anxious. There was AV nipping and silver wiring on fundoscopy but no papilloedema or retinal haemorrhages. Rest of the systemic examination was unremarkable.

Results and management

The initial blood results were normal including sodium 139 mmol/l and potassium 4.3 mmol/l. Patient was referred to ambulatory care from A&E as clinically well. In view of strong suspicion of pheochromocytoma, patient was commenced on Phenoxybenzamine 10 mg twice daily and referred to urgent endocrine clinic. 24-hour urine catecholamine results showed grossly elevated urine noradrenaline 5410 nmol/24 h and adrenaline 1663 nmol/24 h (normal range 50–300 nmol/24 h and 20–70 nmol/24 h). Adrenaline was thought to be produced by the tumour. A 42 year old gentleman was referred to endocrinology clinic by a consultant urologist due to an incidental finding of a 14 mm adrenal nodule on the patient’s right adrenal gland. He was originally seen by gastroenterology having been referred due his 7 year history of twice yearly attacks lasting around 30 min, comprising of flushing of the face, palpitations, burning sensation in his stomach, sweating, vomiting and loose bowel motions. The gastroenterology consultant did not feel this was a gastro problem and arranged CT chest/abdo/pelvis for exclusion of carcinoid and phaeochromocytoma. The CT scan showed a 13 mm left lower lobe lesion (likely bronchocle – suggested respiratory follow up), a left lower pole renal lesion (possible early neoplasm – for ultrasound and MDT follow up) and a right adrenal soft tissue nodule measuring 14 mm (referred to endocrinology). The urology consultant saw the patient who had now had an MRI and the renal lesion had been identified as a Bosniak 3 cyst (50% chance of malignancy). The plan was to monitor the cyst and likely excise it but only once the adrenal lesion had been dealt with. The MRI had shown this to not have characteristics typical of an adenoma with phaeochromocytoma being possible. A 24 hour urine collection for metanephrines had been sent with results awaited at this stage. The urologist organised an MIBG scan to further image the adrenal lesion. The patient was then seen in clinic in the endocrinology department. He and his wife were understandably anxious about all that was going on. The urine collection had demonstrated normetanephrine output of 2.15 (reference range 0–3.00), metanephrine output of 1.82 (reference range 0–1.40) and 3-methoxyxymetanephrine output of 2.52 (reference range 0.57–2.30). Chromogranin A and B results were also available and were within the reference ranges. A set of plasma metanephrines had been taken and these too were well within the reference ranges. The various results were explained to the patient and he was referred to the endocrinology MDT meeting. A repeat set of 24 hour urinary metanephrines was requested. The MIBG result was available not long after the clinic appointment and this showed an MIBG avid right adrenal nodule consistent with phaeochromocytoma. The endocrinology MDT meeting concluded this was an early phaeochromocytoma. The patient was referred for excision and alpha and beta blocking arranged. The lesion was excised uneventfully and histology confirmed the phaeochromocytoma diagnosis.

DOI: 10.1530/endoabs.55.WE1

WE4

Challenging diagnosis of pheochromocytoma

Samantha Anandappa, Charmaine Ilangoarati, Itopa Abebo, Arthur Ogunko & Cynthia Mohandas
Darent Valley Hospital, Dartford, UK.

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

DOI: 10.1530/endoabs.55.WE2
adrenalectomy with normal post-operative levels of catecholamines and remains asymptomatic with a blood pressure of 133/80 mmHg on annual reviews and has discontinued all of her anti-hypertensive medications. There are important considerations when evaluating resistant and unusual cases of hypertension. Electrocardiogram changes with pheochromocytoma are common and up to 12% of patients will present with coronary syndromes. Elevated cardiac enzymes can be a prognostic indicator for those at risk of developing myocardial damage. It is therefore an important consideration in managing patients with chest pain/pain mimicking those with ischaemic ECGs. The general prevalence of pheochromocytoma in people diagnosed with hypertension is around 0.5% and this increases to 1.7% in the paediatric population. Less than 5% of incidental adrenal lesions prove to be pheochromocytoma. Of the cases identified approximately 30% will have a genetic predisposition which may alter treatment and surveillance. This patient did not have any features suggestive of syndromic association including multiple endocrine neoplasia, Von Hippel Lindau syndrome or neurofibromatosis however the case raises the importance of considering when and who to screen for genetic testing with a confirmed pheochromocytoma.

WE6
Case report of malignant hypertension secondary to Renal Artery Stenosis due to Fibromuscular Dysplasia in a young female patient
Meenakshi Parsad
Royal Hampshire County Hospital, Winchester, UK.

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

WE7
A hypertensive emergency post massive pheochromocytoma resection: catecholamines not to blame
Sam O’Toole1, Ali Rathore2, Morris Brown1 & Scott Akker1
1St Bartholomew’s Hospital, London, UK; 2Southend University Hospital, Southend, UK.

Case history
A 26 year-old lady was admitted from clinic with severe hypertension and bilateral papilloedema. Six weeks prior to admission she had undergone resection of a massive right upper quadrant lesion that was felt to be of hepatic origin. Histological analysis of the lesion revealed it to be an adrenal pheochromocytoma and she was thus referred to the endocrine service. Pre-operative biochemical assessment had not been performed but there was no evidence of any blood pressure abnormality or variation pre- or peri-operatively. Two weeks post-operatively she began to experience episodes of palpitations, sweating and hypertension and had attended the emergency department of her local hospital on a number of occasions and been commenced on doxazosin.

Results and treatment
Review of the surgical pathology confirmed the diagnosis of a pheochromocytoma with tumour present at the resection margin. Immunohistochemistry for the SDHB protein was negative, suggestive of a germline SDHx mutation. She was admitted to the High Dependency Unit for invasive blood pressure monitoring and commenced on IV labetalol alongside oral phenoxbenzamine given the previous diagnosis and incomplete resection. Urine and plasma metanephrines were subsequently normal. She was hypokalaemic on admission (K 3.2 mmol/l) and given the large size of the original lesion (18 cm), renovascular mediated hypertension was considered. This was confirmed biochemically and hyperreninemic hyperaldosteronism demonstrated (renin 18.3 mmol/l/h, aldosterone 1.014 pmol/l). Imaging confirmed infarction of the right kidney due to ligation of the renal artery with a DMSA scan confirming only a 5% contribution from the right kidney. Serum creatinine was normal. Her oral anti-hypertensives were rationalised to doxazosin and losartan. This combination was chosen to provide mechanism direct treatment of the current driver of hypertension, whilst providing alpha blockade given the incomplete pheochromocytoma resection and risk of local recurrence. The results of genetic analysis for germline mutations in pheochromocytoma-predisposing genes (and particularly SDHx genes given the negative SDHB immunohistochemistry) are awaited. Conclusions and points for discussion
This is an unusual and interesting case of acute secondary hyperaldosteronism due to inadvertent surgical ligation of the renal artery. The fact that the original operation was for an undiagnosed pheochromocytoma, which was incompletely resected, further complicates matters and led to an initial assumption of catecholamine-mediated hypertension. It provides an excellent opportunity to discuss:

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

DOI: 10.1530/endoabs.55.WE7
WE8
A pressing diagnosis in an adolescent
Sam O’Toole1, Nicola Tufton1, Lorena Arnez2, Laila Parvanta1 & Scott Akker1
1St Bartholomew’s Hospital, London, UK; 2St Mary’s Hospital, Newport, Isle of Wight, UK.

Case history
A 17 year old previously healthy male presented to his local emergency department with a generalised tonic seizure associated with severe hypertension (systolic blood pressure 240 mmHg) and tachycardia. He was intubated and admitted to the Intensive Care Unit. Antimicrobials to cover meningococcalis were commenced and his hypertension was managed with intravenous labetalol. He was extubated the following day. He had experienced headaches on a monthly basis for two years. They had become more severe and frequent in the weeks prior to presentation and were associated with paroxysms of sweating and palpitations. There was no suggestive family history. A 24 h urine collection was sent for metanephrines, however, given the significant suspicion of a pheochromocytoma, he was commenced on phenoxybenzamine and abdominal imaging was undertaken prior to diagnostic biochemistry becoming available. He was subsequently transferred to our centre for ongoing investigation and management.

Results and treatment
Initial blood tests demonstrated haemoconcentration with an acute kidney injury and active urinary sediment. CT and MRI demonstrated cerebral oedema within the occipital lobes and brainstem consistent with a diagnosis of posterior reversible encephalopathy syndrome (PRES). Urine metanephrine was significantly elevated with a normal metanephrine and 3-methoxytyramine. The magnitude of metanephrine elevation was significantly higher at 10x (8.8 upper limit of normal) compared to on transfer (24x). Abdominal imaging demonstrated a 4.1 cm left pheochromocytoma that was invading the renal vein. This lesion was MBG-avid. Two small inderminate pulmonary nodules were identified on thoracic imaging. Low molecular weight heparin was commenced in light of tumour thrombus in the renal vein. Phenoxybenzamine dose was uptitrated and propranolol subsequently added. After a number of weeks of outpatient blockade he underwent an open adrenalectomy and nephrectomy. Of note, his post-operative course was complicated by pneumonia and wound discharge. Phenoxybenzamine was discontinued on day 6 post operatively. His post-operative course was complicated by pneumonia and wound discharge. He was extubated the following day. He had experienced headaches on a monthly basis for two years. They had become more severe and frequent in the weeks prior to presentation and were associated with paroxysms of sweating and palpitations. There was no suggestive family history. A 24 h urine collection was sent for metanephrines, however, given the significant suspicion of a pheochromocytoma, he was commenced on phenoxybenzamine and abdominal imaging was undertaken prior to diagnostic biochemistry becoming available. He was subsequently transferred to our centre for ongoing investigation and management.

Conclusions and points for discussion
This case of a locally invasive pheochromocytoma in an adolescent who presented with PRES provides an excellent opportunity to discuss:
- The acute management of a pheochromocytoma crisis (particularly given the recent data and low dose benzamine)
- How pre-operative suspicion of a germline predisposition to pheochromocytoma development might influence imaging and surgical strategy
- Optimal surveillance strategy for this patient in particular and those with confirmed SDHx mutations generally

WE9
The case of a young man who originally presented with severely derranged electrolytes aged four days
Peter Jacob & William Drake
Department of Endocrinology, St Bartholomew’s Hospital, Barts Health NHS Trust, London, UK.

We would like to present the case of a twenty-six year old gentleman whose first presentation to hospital was aged 4 days old. At that time he was thought to be generally unwell with poor feeding and excessively somnolent. During his resuscitation he was found to have extremely deranged serum electrolytes with sodium 122 mmol/l and potassium 4 mmol/l. His electrocardiogram (ECG) was initially noted to be bizarre, with no clear rhythm. After resuscitation with IV fluid, glucose and insulin his potassium improved to 10 mmol/l and the ECG reverted back to sinus rhythm. Further investigations following his stabilisation showed that he had hyperkalaemia and raised levels of aldosterone and renin. A biochemical profile more in keeping with pseudohyposaldosteronism was made. It took a number of weeks to ascertain the daily sodium requirement given his very high urinary and sweat sodium concentrations. Once stable he was converted to a regime of oral slow sodium and calcium resonium, both at high doses: slow sodium 16 tablets per day and resonium 16 g daily. He has 3 younger siblings the elder two of which are unaffected. His youngest brother was noted by his mother to have excessively salty sweat and has gone on to have the same clinical diagnosis, although less severe in phenotype. There is no evidence to consanguinity. He has maintained a near normal life on the basis of intermittent additional dosing of calcium resonium and sodium when his potassium levels rose. Additionally he once needed hospital treatment during excessively hot weather and he became hyponatraemic due to profuse sweating. He has never had recurrent lung infections or skin disorders as a results of high sweat sodium content. In adult life he underwent screening for genetic causes of his condition and was found to have a homozygous mutation in the amiloride sensitive sodium channel subunit alpha. The c.1339dup pathogenic variant is predicted to cause a frameshift mutation and premature truncation p.(Tyr447Tyr*15). This is a mutation known to cause pseudohyposaldosteronism type 1. The disorder is estimated to affect 1 in 80,000 children and can be inherited in an autosomal dominant or recessive fashion depending on the gene affected. We aim to undertake further genetic testing in members of his family and continue genetic counselling. He continues to need careful management of electrolytes during intercurrent illness.

WE10
A case of mineralocorticoid hypertension with low postoperative cortisol
Hafiz Muhammad Zia-ul-Hussain
Beaumont Hospital, Dublin, Ireland.

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

Learning points:
1) Investigation of mineralocorticoid hypertension
2) What to do when your radiologist fails to cannulate both adrenal veins
3) Did this patient have 'Connshings' syndrome given the recent data and low cortisol post operatively

WE11
You can lead a patient to hospital, but you can’t make him have an adrenalectomy
Craig Thurtell & Alasdair Mackie
Ninewells Hospital and Medical School, Dundee, UK.

A 42 year old man was referred to the acute medical unit with accelerated hypertension in March 2015. He presented with headache and blunted vision due to posterior subcapsular cataract. Pre-treatment BP was 180/131 mmHg. Initial treatment included amlopidine, bendrofluamide and lisarsan. Prior to discharge, a 24 hour urine collection showed a significantly elevated urinary
noradrenaline level (3091 nmol/l, reference 0–473). Referral was made to the cardiovascular risk clinic for further investigation. Unfortunately, due to several missed appointments he was not followed up until May 2015. It transpired that the patient had a long-standing history of depression and substance misuse. He had previously taken alcohol to excess but more recently had replaced this with amphetamine in the form of ‘base’, the potent base form from which amphetamine (‘speed’) is manufactured. At review, 24 hour ambulatory BP measurement revealed severe, uncontrolled hypertension (mean daytime BP 164/104) with loss of the nocturnal dip. An ECG also showed LVH. A second 24 hour urine collection again showed elevated urinary noradrenaline (6445 nmol/l) and plasma normetanephrine was >25 000 pmol/l. The patient attended for an abdominal MRI scan in July 2015 which showed a large left adrenal lesion measuring 7.3 × 7.4 × 7.0 cm. Despite having the consequences of severe hypertension due to untreated phaeochromocytoma explained, this did little to encourage regular engagement or adherence to medication. In addition to substance misuse and the chaotic lifestyle ensuing, the patient also had anxiety issues around attending hospital. He eventually began to attend the endocrine service where he was offered weekly appointments – most of which were not attended. He was often found to be symptomatic of postural hypotension when he did attend. Biochemistry showed the development of mild non-PTH dependent hypercalcaemia. He declined to attend hospital on two occasions for adrenalectomy. He was eventually persuaded to attend on the third occasion where he had a short admission under endocrinology for pre-operative management prior to transfer to the surgical unit where he underwent adrenalectomy in November 2016. Histopathology confirmed this to be a phaeochromocytoma with a PASS of 9. No genetic mutations were found. Since adrenalectomy the patient has been lost to follow-up. This case demonstrates the extraordinary challenges of managing a patient with a phaeochromocytoma who also abuses amphetamines and has other mental health problems. It remains to be seen if the patient will re-present with recurrent metastatic disease given his elevated PASS.

DO: 10.1530/endobas.55.WE11

WE12
The octogenarian with a phaeochromocytoma: a new management dilemma
Tessa Glyn & Julia Thomas
Musgrove Park Hospital, Taunton, UK.

Increased use of abdominal imaging has resulted in vast numbers of adrenal incidentalomas being identified (Bovio et al., 2006). Guidelines exist for identifying hormone excess and diagnosing malignancy but there is little evidence about how to manage phaeochromocytoma in patients who are poor surgical candidates. We present the case of a frail 88 year-old lady who was found to have a right adrenal incidentaloma during assessment for abdominal pain. Mrs R is able to mobilise short distances with a frame. She has a history of falls associated with a postural hypotension, hypertension, previous transient ischaemic attacks, diverticular disease, fractures and a mastectomy for breast cancer. She was found to have a 28 mm right adrenal mass on CT-abdomen. Biochemical work-up showed significantly raised plasma metanephrines. A repeat supine resting sample confirmed a raised plasma normetanephrine at 2678 pmol/l (reference <450 pmol/l). Other biochemistry was normal. In Endocrinology clinic she described several years of symptoms, including a peculiar feeling in her head, a recurrent sensation of doom and intermittent palpitations. She was also found to be significantly hypertensive. She was not felt to be a surgical candidate in light of frailty and co-morbidities, and was equally not keen on embarking on an operation. The decision was made to manage her phaeochromocytoma conservatively. Doxazosin was chosen, due to its lesser side-effect profile compared to phenoxybenzamine. It was started at a low dose and slowly titrated, with weekly assessment in the Day Unit. Her blood pressure slowly improved but controlling her symptoms remains problematic. With gradual titration and encouraging good salt and water intake, postural symptoms have been minimal and she has not experienced falls. This case raises several important points about how to manage phaeochromocytoma in patients who are poor surgical candidates and highlights the importance of multidisciplinary teamwork.

DO: 10.1530/endobas.55.WE12

WE13
Primary hyperaldosteronism presenting following a miscarriage
Layla Thurston, Sheharyar Qureshi & Marcus Martineau
West Middlesex University Hospital, London, UK.

Case history
A 35 year-old female was found to be significantly hypertensive (181/91 mmHg) following a first trimester miscarriage (at 8 weeks gestation) during her first pregnancy.

Investigations
Blood tests demonstrated moderate hypokalaemia (2.6 mmol/l) with a normal serum sodium (140 mmol/l) and eGFR (>90 ml/min). ECG showed hypokalaemic changes with prolongation of the PR interval and T wave flattening. To avoid potential misinterpretation, additional blood tests were performed prior to commencing antihypertensive therapy. Her potassium was replaced intrave-

ously and an aldosterone: renin ratio was performed. Results
Aldosterone 940 pmol/l, Renin <0.2 nmol/l per h with a ratio of >4700. Testing was repeated a week later, Aldosterone 1180 pmol/l, Renin <0.2 nmol/l per h with a ratio >5900. A saline infusion test (with 2 litres of 0.9% NaCl) was undertaken and further bloods drawn. Aldosterone 1380 pmol/l, Renin <0.2 nmol/l per h with a ratio of >6900 supporting a diagnosis of primary hyperaldosteronism. Adrenal MR imaging identified a 2 cm right adrenal lesion with loss of signal on the out of phase image in keeping with benign, lipid-rich adenoma.

Management
Given her suitability for a laparoscopic adrenalectomy, adrenal venous sampling (AVS) was undertaken in order to localise the source of aldosterone hypersecretion (results pending).

Conclusion
This patient was asymptomatic and her hypertension and hypokalaemia only identified following early pregnancy loss (with progesterone acting as a potential aldosterone antagonist). Whilst her MRI is suggestive of an adrenal adenoma, it is important that her initial blood results and imaging are interpreted in concert with AVS in order to guide targeted removal of the appropriate gland. 35% of cases of primary hyperaldosteronism are caused by a unilateral adenoma whilst 60% are the result of bilateral adrenal hyperplasia (bilateral idiopathic hyperaldosteron-ism). Whilst a laparoscopic adrenalectomy is the treatment of choice for unilateral aldosterone-secreting adenomas (with around 70% of patients being cured for hypertension following surgery); medical management (with Aldosterone antagonists such as Spironolactone/Eplerenone) should be considered in the management of bilateral disease.

DO: 10.1530/endobas.55.WE13

WE14
Hyponatraemic hyperaldosteronism in surgically cured Conn’s syndrome
James Pittaway, Simon Coppack, Rob Carpenter & William Drake
St Bartholomew’s Hospital, London, UK.

A 53 year old gentleman from Ghana was referred to our clinic for further management of his Conn’s syndrome. This had been diagnosed at another hospital 3 years previously when he presented with hypertension and hypokalaemia on the back of 14 years of poorly controlled hypertension. Serum aldosterone was raised at 3178 pmol/l and serum renin mass was 3.9 mU/l. MRI revealed a 5 mm nodule in the medial limb of the right adrenal gland. He was initially commenced on medical treatment with spironolactone and then eplerenone but although these medications controlled his blood pressure and hypokalaemia well, caused him troublesome gynaecomastia. Repeat biochemistry, imaging and adrenal venous catheter studies re-affirmed the diagnosis and strongly pointed to the right adrenal lesion as the source of his hyperaldosteronism without evidence of cortisol co-secretion. Referral was made to the endocrine surgical service for consideration of adrenalectomy. However given this gentleman’s morbid obesity with a BMI > 50 kg/m2 with uncontrolled OSA, the anaesthetic and surgical risk was considered too great in the context of a medically controllable condition (albeit with severe side-effects). He was seen in the obesity clinic and with little improvement on oral weight control agents went on to have a gastric banding procedure. This precipitated weight loss of 40 kg and enabled a successful laparoscopic right adrenalectomy following the year. Post-operatively he still required two antihypertensive agents for presumed non-aldosterone mediated hypertension. In the follow up to this, he was admitted to our hospital from clinic when follow up biochemistry revealed hyperkalaemia of 7.7 mmol/l. Venous blood gases revealed a normal anion gap metabolic acidosis (HCO3 17 mmol/l, pH 7.306). Reassessment of his renin-aldosterone axis showed hyponatraemic

DO: 10.1530/endobas.55.WE14

Society for Endocrinology: Endocrine Update 2018

A 41 year old man was referred to the endocrine service at St Barts hospital. He had previously had a GP check-up and was found to be hypertensive, this led to him having an ultrasound KBUI, an abnormality was detected which resulted in a CT abdomen being performed. The CT abdomen showed a 38×33 mm well-defined right adrenal lesion and the patient was referred to endocrinology. Upon review, the patient had been having palpitations for the past year - particularly when strain on the lavatory but also unprovoked when resting - and episodes of sweating. The palpitations had provoked multiple attendances to A+E and he had had a 24 hour Holter monitor, which was unremarkable. Examination was unremarkable aside from a blood pressure of 140/90, HR 100bpm on Verapamil. A 1 hour urinary metanephrine measurement was performed, which showed elevated 24 hr normetadrenaline of 11,544 nmol/day (normal <4400) and 24 hr metadrenaline of 2,203 nmol/day (normal <2000). 3-Methoxytyramine levels were normal. Plasma calcitonin was subsequently found to be raised to 21 ng/l (normal <10). Gut hormones were within normal limits, but HbA1c was elevated at 45 nmol/mol. The patient was admitted for alpha blockade with metadrenaline of 2,203 nmol/day (normal <4,400) and 24 hr metadrenaline of 2,203 nmol/day (normal <2000). 3-Methoxytyramine levels were normal. Plasma calcitonin was subsequently found to be raised to 21 ng/l (normal <9.52). Gut hormones were within normal limits, but HbA1c was elevated at 45 nmol/mol. The patient was admitted for alpha blockade with phenoxybenzamine and IV fluid filling, he was subsequently beta blocked with propranolol. He also underwent an ultrasound of the thyroid, which showed some small nodules, but none were felt to display any worrying features. The patient is currently awaiting a right sided adrenalectomy. It highlights the issues of managing both primary aldosteronism and non-aldosterone mediated hypertension in complex patients with comorbidities and also the management of hypertension in aldosterone deficiency.

DOI: 10.1530/endoabs.55.WE15

WE16
Challenging case of recurrent pheochromocytoma and metastatic paraganglioma
Jan Klepacki, Jane Dymott & Prakash Abraham
Endocrinology, Aberdeen Royal Infirmary, Aberdeen, UK.

Background
A 59 year old woman presented with recurrent symptoms of catecholamine excess (episodic headache and sweating). She was initially diagnosed in another centre to have a right adrenal pheochromocytoma in 2002. She had suggestive symptoms, elevated urine catecholamines and a right adrenal mass on CT Adrenals. MBIG was however negative and they had proceeded with a right adrenalectomy and histology confirmed a pheochromocytoma. She also had type 2 DM, anxiety and degenerative lumbar spine. In 2010 she presented to our centre with recurrent symptoms. Urine adrenaline was found to be elevated at 404 nmol/24h (Normal <100). CT abdomen revealed 16mm recurrent right adrenal mass but no uptake on MBIG. However PET scan showed mild metabolic activity in the nodule. Genetic screen didn’t find any known mutation for VHL1, SDHB, SDHD, RET, MEN 2, TMEM127 genes. The recurrent adrenal mass was resected and histology shown benign pheochromocytoma with lesion extending to excision margins.

Subsequent 24h urine metaadenalines were normal. The patient started complaining of episodic recurrence episodic of her symptoms two years later and intermittently thereafter. However urinary and plasma catecholamines were within normal limits. Neurological investigations (MRI brain, CSF, EEG) didn’t reveal significant abnormality. In 2015 urinary collection shown new elevation of urinary meta-adrenaline at 1.96 (Normal <1.4) Repeat samples were similar after stopping amitryptiline. In March 2016 CT abdomen revealed a new 13x16mm nodule in upper pole of right kidney. However yet again in July 2017 SPECT CT MBIG images show no abnormal foci of uptake. Urinary meta-adrenaline elevated at 2.7. Phenoxybenzamine titration was commenced and she had resection in September 2017. Histology has shown incomplete excision of metastatic paraganglioma and she has expressed unwillingness for a fourth operative procedure. Subsequent urinary catecholamines and meta-adrenalinens returned to normal level.

Discussion
This case illustrates the challenges in diagnostic process and identification of pheochromocytoma and paraganglioma due to inconclusive functional investigations (MBIG and PET CT). Given incomplete excision further reoccurrence is very likely and there will be challenges ahead in choosing further surgical therapy (given her reluctance) and limitations in medical management options including 131I-mIBG therapy.

DOI: 10.1530/endoabs.55.WE16

WE17
Back to the basics!
Faisal Hasan & Andrew Johnson
Southend Hospital, Bristol, UK.

A 42 year old lady initially presented in Poland with haematuria while she was on holiday over Christmas. She had some tests including an ultrasound of the kidney which showed a mass adjacent to the left kidney. The haematuria had settled and she was feeling well apart from non-specific back ache. She worked in a cake factory which she continued to do here in the UK. Her GP requested another ultrasound of her kidneys which showed a solid mass adjacent to the left kidney and a CT abdomen was advised (Feb 17) which found a mass anterior to the left kidney. The radiologists suspected this was arising from the tail of the pancreas. As it was part cystic and part solid, a diagnosis of probably pancreatic cyst adenoma was made. An MRI was requested which demonstrated a 5 cm complex solid and enhancing left retroperitoneal mass but the origin was uncertain, differentials included solid pseudo-papillary pancreatic tumour or retroperitoneal sarcoma. She was reviewed in the Sarcoma MDT and they recommended a laparoscopic biopsy or a surgical excision. She then went on to have a FNA under EUS which stained like an NET. She then was discussed at the hepatobiliary MDT and a NET MDT referral was made who suggested an MBIG scan and 24 hour urine metadrenaline. Meanwhile, she was referred to Endocrinology. In our clinic, on direct questioning she had no symptoms related to adrenaline excess. Her past medical history included an appendectomy, a resected meningioma and high cholesterol. There was no family history suggestive of MEN or a genetic paraganglioma syndrome. On examination, her blood pressure was 213/103 mm Hg. She appeared a fit lady with no stigmata of underlying illness. Her pulse rate was regular. She was commenced on Phenoxybenzamine and slow sodium at this point. An MIBG scan done a month later confirmed the diagnosis of left active secreting adrenal pheochromocytoma. She successfully underwent a left laparoscopic adrenalectomy.

Discussion
We did not find any mention of her high BP recordings in any of the correspondence from the GP and various MDTs. If they had noted a finding of significantly raised BP in a previously fit lady with a lesion around the kidney, a possibility of a pheochromocytoma would have been considered much earlier and intermittently thereafter. However urinary and plasma catecholamines were within normal limits. Neurological investigations (MRI brain, CSF, EEG) didn’t reveal significant abnormality. In 2015 urinary collection shown new elevation of urinary meta-adrenaline at 1.96 (Normal <1.4) Repeat samples were similar after stopping amitryptiline. In March 2016 CT abdomen revealed a new 13x16mm nodule in upper pole of right kidney. However yet again in July 2017 SPECT CT MBIG images show no abnormal foci of uptake. Urinary meta-adrenaline elevated at 2.7. Phenoxybenzamine titration was commenced and she had resection in September 2017. Histology has shown incomplete excision of metastatic paraganglioma and she has expressed unwillingness for a fourth operative procedure. Subsequent urinary catecholamines and meta-adrenalinens returned to normal level.
Workshop F: Disorders of the gonads
Gynaecomastia and Sex Steroid & Sex Steroid Replacement in Females

WF1
Sex steroid replacement in primary amenorrhoea due to Turner’s syndrome
Nithya Sukumar1,2, Aamir Naeem1 & Sailesh Sankar3
1University Hospitals Coventry and Warwickshire, Coventry, UK; 2Warwick Medical School, University of Warwick, Coventry, UK; 3Consultant Endocrinologist, Watford General Hospital, Watford, UK.

Case history
FK is an 18 year old female, who attended the Turner’s syndrome clinic in our tertiary centre with primary amenorrhoea. Her family are originally from Ghana but she was born in Italy and lived there until moving to the UK in 2016. She was born full-term by normal delivery and Turner’s syndrome was diagnosed at 3 months of age due to characteristic phenotypic features. She was managed by the paediatric endocrinologists in Italy and was on growth hormone injections for around 10 years until it was stopped at age 16. She was on the Eoverl 25 patch whilst in Italy for a few years and had 1 episode of spotting at age 14 years. There has been no further menstrual bleeds. Since coming to the UK, she did not receive any further hormonal treatment, until her first appointment in the Turner’s syndrome clinic when she was started on Ethinylestradiol. She has not had any menstrual bleed since this was commenced 4 months ago. She has no other developmental issues or past medical history. She was doing a Diploma in Childcare in college. Drug history: Ethinylestradiol 10 mcg OD, Cholecalciferol 800 IU OD. On examination: height 147.5 cm, weight 60 kg, BP 120/70. No webbed neck or swollen hands or feet.

Investigations
TSH: 1.11 mIU/L (NR 0.27–4.2); Free T4: 17.0 pmol/L (NR 9.0–26.0); TPO antibodies: 9; FSH: 55 IU/L (postmenopausal 26–153); LH: 11 (postmenopausal 8–58); Fasting blood glucose: 4.4 mmol/L; 25-hydroxy vitamin D: 29 nmol/L; USS pelvis: Both kidneys appear normal in sizes and echogenicity. Normal sized anteverted uterus, endometrial thickness 1 mm. Echo: Bicuspid AV with no stenosis or regurgitation detected. No-dilated aorta with no evidence of coarctation seen. Audiology: Seen by ENT, reports normal.

Treatment
Since she did not have a menstrual bleed with ethinylestradiol 10 mcg, we increased the dose to 20 mcg OD. During telephone review 4 weeks later, this had resulted in 2 occasions of breakthrough bleeding. Therefore a note was sent to her GP to prescribe Norethisterone 5 mg BD for 5 days for endometrial protection. Since she did not have a menstrual bleed with ethinylestradiol 10 mcg, we increased the dose to 20 mcg OD. During telephone review 4 weeks later, this had resulted in 2 occasions of breakthrough bleeding. Therefore a note was sent to her GP to prescribe Norethisterone 5 mg BD for 5 days for endometrial protection. During her next clinic appointment, we plan to discuss with her about starting the combined oestrogen-progesterone pill or patch.

Conclusions and points for discussion
This is a useful case to highlight the optimal sex steroid replacement in a girl with Turner’s syndrome, primary amenorrhoea and premature ovarian insufficiency, who has attained final height.

DOI: 10.1530/endoabs.55.WF1

WF2
Diagnosis and management of functional hypothalamic amenorrhoea – a case report
S Samarasinghe1, P Avari2 & K Muralidhara1
1University Hospitals Coventry and Warwickshire, Coventry, UK; 2Warwick Medical School, University of Warwick, Coventry, UK.

Functional hypothalamic amenorrhoea (FHA) is an endocrine disorder secondary to a deficiency of pulsatile gonadotrophin-releasing hormone (GnRH) secretion. It is not related to hypothalamic-pituitary organic lesions, endocrine or systemic disease. The clinical profile is dependant on the degree of GnRH suppression – it can range from an inadequate luteal phase to hypothalamic amenorrhoea. The incidence of FHA ranges from 15% to 48% of the secondary amenorrheas. We present the case of a 21-year-old female of Romanian origin referred to clinic with amenorrhoea. She attained menarche between the ages of 11–13 years and had regular periods for a year. After this time, her periods became more irregular and this was thought to be secondary to weight gain. The patient subsequently lost 8–58); Fasting blood glucose: 4.4 mmol/L; 25-hydroxy vitamin D: 29 nmol/L; USS pelvis: Both kidneys appear normal in sizes and echogenicity. Normal sized anteverted uterus, endometrial thickness 1 mm. Echo: Bicuspid AV with no stenosis or regurgitation detected. No-dilated aorta with no evidence of coarctation seen. Audiology: Seen by ENT, reports normal.

Treatment
Since she did not have a menstrual bleed with ethinylestradiol 10 mcg, we increased the dose to 20 mcg OD. During telephone review 4 weeks later, this had resulted in 2 occasions of breakthrough bleeding. Therefore a note was sent to her GP to prescribe Norethisterone 5 mg BD for 5 days for endometrial protection. During her next clinic appointment, we plan to discuss with her about starting the combined oestrogen-progesterone pill or patch.

Conclusions and points for discussion
This is a useful case to highlight the optimal sex steroid replacement in a girl with Turner’s syndrome, primary amenorrhoea and premature ovarian insufficiency, who has attained final height.

DOI: 10.1530/endoabs.55.WF1

WF3
Honesty is always best
Shazia Hussain, Helen Storr & William Drake
St Bartholomew’s Hospital, London, UK.

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

DOI: 10.1530/endoabs.55.WF3
A 27 year old was referred to endocrine clinic for investigation of longstanding gynaecomastia. He had noticed loss of early morning erections. He never fully grew a beard and had no children. This was associated with temporal hair recession and intermittent headaches. On examination he appeared to be of asthenic built and youthful. He was tall with his upper body being longer than lower. He had widely spaced breasts and long arms. His testicular volume on examination was 1–2 ml bilaterally. His visual fields were full on confrontation. His bloods showed an FSH of 44.0 mIU (1–12) and LH of 22.4 mIU Testosterone levels of 3.7 nmol/l (8.64–29), sex hormone binding globulin levels of 41 nmol/L (18.3–54.1) and a Free Androgen Index of 9.0 (42–200). He was investigated for hyper-gonadotrophic hypogonadism and consented for genetic testing for Karyotyping. His genetic testing confirmed a diagnosis of Klinefelters and he was commenced on testosterone replacement therapy. As he was unable to make testosterone, replacement was required to alleviate the symptoms that he had long suffered with including mood problems, lethargy and sexual dysfunction plus the long term benefit on bone and cardiovascular health, also reducing the risk of developing type 2 diabetes. Review a few months later showed a noticeable improvement in energy levels, mood elevation, and hair growth on arms and increased sex drive. His repeat blood tests showed Testosterone levels of 45.2 nmol/l (8.64–29). He generally felt much better and was terrified of any deviation from this relief and asked for the IM equivalent after being told that Testogel supplies were extremely scant. It was therefore agreed to start him on IM Nebido (Testosterone Undecanoate 250 mg/ml) 1gm every 12 weeks. Dosing will be varied on the basis of trough levels and regular full blood count monitoring during the course of treatment.

DOI: 10.1530/endoabs.55.WF4
Workshop G: Disorders of the parathyroid glands, calcium metabolism and bone
Hypocalcaemia Including Vitamin D Deficiency

WG1
Calcium homeostasis after parathyroidectomy
Ramesh Kumar & LNR Bondugulapati
Wrexham Maelor Hospital, Wrexham, North Wales, UK.

We describe a 82 year old patient with background history of thyrotoxicosis (had total thyroidectomy), primary hyperparathyroidism (had parathyroidectomy 12 years back at another hospital - two glands removed). She was on l-thyroxine, alfacalcidol 1 μg/day and CaCO3 500 mg BD. She remained stable for 7 years on this cocktail. In February 2017, she was admitted with acute confusion and was found to have adjusted ca level of 4.57 with AKI, normal magnesium. No recent changes in medications and there was no obvious precipitating event (apart from AKI although this may well be the other way round). Other workup for hypocalcaemia was negative (including CT CAP). She was discharged prior to Endo review (Ca 2.68) with no alfacalcidol/CaCO3 at all. Her renal function was back to baseline. Understandably, she was readmitted after 3 days with parathesias, pins and needles in both hands and her Adj Ca was 2.01. She was re-started on CaCO3 500 mg bd and alfacalcidol 500 μg once daily with improvement in calcium levels (Adj Ca 2.2). However, 10 days post-discharge, she was readmitted with hypocalcemia (1.82; Mg 0.56). She was treated appropriately and discharged on CaCO3 500 bd, alfacalcidol 1mg daily. In April 2017, she was re-admitted with Adj calcium of 3.33. Her alfacalcidol was reduced to 750 μg, CaCO3 to 500 mg OD and Ca levels have been stable since (2.1–2.25). Corrected calcium levels: 4.57-3.30-2.68-2.01-2.1-1.90-3.33-2.21-2.18

Conclusion

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

Questions

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

DOI: 10.1530/endoabs.55.WG1

WG2
Refractory hypocalcaemia due to pseudo hypoparathyroidism
Aaiha Saqib, Jennifer Tremble & Debbie-Ann Charles
Queen Elizabeth Hospital, Lewisham and Greenwich NHS Trust, London, UK.

A 27 year old, Caucasian female was admitted with vomiting and found to have severe hypocalcaemia. On clinical examination she had a normal stature, oval face; she was not brachydyactylic and did not have dental hypoplasia. Biochemically she had serum Ca of 1.49 mmol/l (2.15–2.50), a serum Phosphate of 1.50 mmol/l (0.9–1.45) and Vitamin D levels of 59 nmol/l (>35 sufficient for majority population). Her serum parathyroid hormone was elevated at 304.5 ng/l (15–65). She had a 24-h urine collection which showed a urine creatinine of 9.46 mmol/l (3–18), Urine Calcium 0.42 mmol/l, 24-h Urine Calcium of 0.33 mmol/l (0–7.5) and Calcium/creatinine ratio of 0.04 mmol/mmol. She was treated with IV calcium infusion and diagnosed as Pseudo hypoparathyroidism. On taking a further history we find out that she had symptoms of severe hypocalcaemia including perioral paraesthesia, numbness/tingling in the fingers, severe muscle cramps. Her mother had taken her to GP severally since the age of 9 with symptoms of severe hypocalcaemia, when her arms will go in a spasm, with tingling around her mouth and ophthalmoplegia. She was advised to be fed sugary drinks and was told this was due to low blood sugars and that she has a squint at times. She had no other medical problems, no family history and not found to have developmental delay. The first time she had her blood tested was age 21, two weeks after her son was born when she presented to ED as she was unable to cope at home due to severe muscle cramps and lasshery. On that occasion she was discharged home with oral calcium tablets. From age 21–27 she was seen in ED six times, admitted for IV calcium infusion twice. Three years since diagnosis she continues under endocrine follow up and is being treated with Calcichew D3 and Alfacalcidol. She is now age 30 and the management of her hypocalcaemia remains a challenge. With oral therapy we have been unable to achieve serum calcium above 1.80 mmol/l despite being Vitamin D replete. She is asymptomatic when her serum calcium levels are between 1.6 and 1.8 mmol/l. She is now also hypothyroid Free T4 11.1 pmol/l (12.0–22.0) and TSH 9.95 mIU/l (0.27–4.20) thyroid antibodies are awaited. She is waiting genetic testing.

DOI: 10.1530/endoabs.55.WG2

WG3
Parathyroid hypoplasia - an uncommon cause of hypocalcaemia
Annalisa Montebello & Sandro Vella
Mater Dei Hospital, Msida, Malta.

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

PTH: 10 pg/ml (15–65 pg/ml)
Vitamin D: 27 (30–100 ng/ml)
Flow Cytometry:
CD3 (T Lymphocytes): 609 cells/μl (723–7,737 cells/μl)
CD4 (Helper/Inducer T Lymphocytes): 418 cells/μl (404–1,612 cells/μl)
CD8 (Suppressor/Cytotoxic T Lymphocytes): 174 cells/μl (220–1,129 cells/μl)
CD3: 56% (56–86%)
CD4: 39% (33–58%)
CD8: 16% (13–39%)
CD4/CD8: 2.4 (1–3)

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

DOI: 10.1530/endoabs.55.WG3

WG4
Generalised convulsions as a presentation of severe hypocalcaemia secondary to Vitamin D deficiency: An uncommon presentation of a common condition
Samantha Anandappa, Lavarniya Rajakumar, Dora Affam, Siva Sivappriyan & Jesse Kumar
Maidstone Hospital, Maidstone, UK.

A 36 year old female patient presented to the emergency department with a generalised tonic-clonic seizure. She had a past medical history of epilepsy and tuberous sclerosis. Her medication prior to hospital admission was Tegetrol which had controlled her seizures well for many years. On admission, the adjusted calcium level was 1.4 mmol/l with a raised ALP 508 UI and a phosphate within the normal reference range at 1.1 mmol/l. Magnesium was also within the normal reference range at 0.8 mmol/l. On further investigation there was an elevated
Parathyroid hormone level 39.2 pmol/l (1.6–6.9) and her Vitamin D was undetectable at <30 nmol/l. Despite repeated IV calcium gluconate infusions and vitamin D supplementations calcium levels did not improve consistently. X-ray of her hands demonstrated periosteal new bone formation around the proximal phalanges which was in keeping with the features of Tuberous Sclerosis. After calcium levels supplemented with IV replacement she was discharged with Alfacalcidol 1.5 micrograms twice daily and sandocal 1,000 four times a day.

Ergocalciferol 300,000 IU was administered as an intramuscular injection. Epilepsy is a common disorder and the medications administered to prevent recurrent seizures often have multiple side effects. Tegretol, carbamazepine, is a cytochrome P450 inducer and as a consequence of this action can lead to changes within in bone mineral density, including deficiency of vitamin D and hypocalcaemia. It is reported that approximately half of the people treated with such medications develop bone metabolism abnormalities and therefore it is important to initiate surveillance in these patients to prevent fractures as well as seizures from electrolyte disturbance. This case highlighted the difficulties in managing hypocalcaemia and also stressed the importance of looking for a secondary cause. In addition, we raise an important issue of pharmacovigilance in antiepileptic therapy especially for induced Vitamin D deficiency and consequent electrolyte balance.

DOI: 10.1530/endoabs.55.WG4

WG5
Multifactorial hypocalcaemia in a patient presenting with sepsis
Santoshkumar Rajkumar & Andrew Smith
Princess Royal Hospital, Haywards Heath, UK.

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

DOI: 10.1530/endoabs.55.WG5
Workshop H: Miscellaneous endocrine and metabolic disorders
Hypoglycaemia & Neuroendocrine Tumours

WH1
A daughter’s diagnosis
Laxmi Manohar Rao Balmuri1, Lauren Morris2, Clare Mummy1, Jennifer Beynon2 & Basir Isa1
1Manchester Royal Infirmary, Manchester, UK; 2Salford Royal Foundation Trust, Manchester, UK; 3Wythenshawe Hospital, Manchester, UK.

Case
An 89 year old gentleman was admitted to hospital following a collapse at home. His capillary blood glucose was found to be 1.4 mmol/l by the paramedics. He had experienced multiple collapses at home in the preceding 2 weeks. Each time, he had been found to be hypoglycaemic but treated and discharged from A&E. He complained of reduced appetite, weight loss and change in bowel habit. The patient’s past medical history included a large fibroma of the left pleura which was being managed conservatively. He was also known to have atrial fibrillation, COPD, bronchiectasis and CCF with severe systolic impairment.

Investigations
Blood tests revealed an elevated CRP (45 mg/l) with normal WCC (7.9 x 109/l), mild anaemia (HB 11 g/l), elevated ALP (146 IU/l) and normal renal function. A CT scan showed the known large pleural fibroma and a new smaller lesion in the right upper lobe of uncertain aetiology. Following transfer to the endocrinology ward, the patient experienced a further episode of hypoglycaemia and the venous glucose was found to be 1.9 mmol/l. Insulin and C-peptide levels were also found to be low at 11 pmol/l and <94 pmol/l respectively. A SST was normal and IGF-1 and IGF-2 levels were analysed. Results showed IGF-2:IGF-1 ratio 16.7 (10). Despite regular feeding, supper and overnight snacks he remained significantly hypoglycaemic especially overnight with no awareness of symptoms. He was commenced on Prednisolone 30mg daily and his hypoglycaemia improved. Surgical resection of the lesion commenced.

Discussion
Dooge-Potter syndrome is a rare cause of hypoglycaemia. In this condition, hypoglycaemia is mediated by the secretion of IGF-2 from a fibrous tumour.

Conclusions and points for discussion
Endogenous hyperinsulinaemic hypoglycaemia is a rare but well recognised and significant complication of gastric bypass surgery. Exogenous insulin administration is an important cause of hypoglycaemia and requires a high threshold of suspicion to detect. The co-existence of both is highly unusual and this case provides an excellent opportunity to discuss:

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

DOI: 10.1530/endoabs.55.WH2

WH2
An unexpected cause of hypoglycaemia post-bariatric surgery
Sam O’Toole1, Simon Coppuck2 & Scott Akker1
1St Bartholomew’s Hospital, London, UK; 2The Royal London Hospital, London, UK.

Case history
A 54 year-old gentleman was transferred as an inpatient from another centre for investigation and management of refractory hypoglycaemia following a revision gastric bypass. He was requiring a continuous infusion of 20% dextrose on the ward, the patient experienced a further episode of hypoglycaemia and the venous glucose was found to be 1.9 mmol/l. Insulin and C-peptide levels were also found to be low at 11 pmol/l and <94 pmol/l respectively. A SST was normal and IGF-1 and IGF-2 levels were analysed. Results showed IGF-2:IGF-1 ratio 16.7 (10). Despite regular feeding, supper and overnight snacks he remained significantly hypoglycaemic especially overnight with no awareness of symptoms. He was commenced on Prednisolone 30mg daily and his hypoglycaemia improved. Surgical resection of the lesion commenced.

Discussion
Dooge-Potter syndrome is a rare cause of hypoglycaemia. In this condition, hypoglycaemia is mediated by the secretion of IGF-2 from a fibrous tumour.

Conclusions and points for discussion
Endogenous hyperinsulinaemic hypoglycaemia is a rare but well recognised and significant complication of gastric bypass surgery. Exogenous insulin administration is an important cause of hypoglycaemia and requires a high threshold of suspicion to detect. The co-existence of both is highly unusual and this case provides an excellent opportunity to discuss:

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

DOI: 10.1530/endoabs.55.WH2

WH3
Somatostatin analogue therapy in a patient with von Hippel-Lindau disease and multiple pancreatic neuroendocrine tumours
Sam O’Toole & William Drake
St Bartholomew’s Hospital, London, UK.

Case history
An 11 year old girl was diagnosed with von Hippel-Lindau disease (VHL) on cascade genetic screening due to a positive family history and was enrolled in a VHL surveillance programme. She developed bilateral pheochromocytomas and underwent staged bilateral adrenalectomies at the age of 12 and 14. At the age of 16, she was discovered to have a 2.5 cm tail of pancreas pancreatic neuroendocrine tumour (pNET) on routine surveillance imaging. This enlarged during follow up and additional smaller pNETs in the pancreatic body became visible. At the age of 19, she underwent a distal pancreatectomy and splenectomy. Her mother had a progressive metastatic pNET and there was considerable understandable family anxiety surrounding the diagnosis.

Results and treatment
Histology confirmed a 35 mm grade 2 pNET with a Ki67 index of 10%. Tumour was present at the resection margin with no evidence of lymph node metastases. A second 1 mm grade 1 pNET was also present and was completely excised. During post-operative imaging surveillance, three new pNETs developed within the tail, body and uncinate process which all grew on sequential examinations. She was asymptomatic and chromogranin A and fasting gut peptides were normal. All lesions were avid on Gallium DOTA-TATE imaging confirming somatostatin receptor expression. Given the rate of lesion growth, in combination with her family history of malignant disease, intervention was deemed necessary. However, given the lesion locations, there was a high risk of pancreatic insufficiency with further surgical resection and there were significant concerns about her ability to manage the resultant pancreatic insufficiency. She therefore underwent a trial of primary somatostatin analogue therapy which was well tolerated without adverse effects. After 6 months of treatment, reimaging demonstrated that all pNETs had significantly reduced in size and met RECIST criteria for partial response. This response has been maintained for over 18 months.

Conclusions and points for discussion
This case of a young woman with recurrent multifocal pNETs in the context of VHL provides an excellent opportunity to discuss:

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

DOI: 10.1530/endoabs.55.WH3

WH4
A tricky case of hypoglycaemia
Su Ann Tee1, Naveen Siddaramaiah2, Jeremy French1, Christopher Boot1, Taimur Gulfam1, Ahmed Al-Sharefi1, John Leeds1 & Robert Andrew James1
1St Richard’s Hospital NHS Foundation Trust, Newbury, UK; 2South Tees Hospitals NHS Foundation Trust, Northallerton, UK.

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

Conclusions and points for discussion
Endogenous hyperinsulinaemic hypoglycaemia is a rare but well recognised and significant complication of gastric bypass surgery. Exogenous insulin administration is an important cause of hypoglycaemia and requires a high threshold of suspicion to detect. The co-existence of both is highly unusual and this case provides an excellent opportunity to discuss:

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

DOI: 10.1530/endoabs.55.WH2
neuroendocrine tumours may have separate multiple malignancies, and there is a
difficulties in diagnosing tumours of neuroendocrine origin, and illustrates various
remains under close monitoring. This case highlights the potential diagnostic
progression of the lesions, further surgery or radioactive iodine was withheld. She
the lung nodules were probable metastases from thyroid cancer all along. The
neck but showed two areas of uptake in the left lung; USS neck showed no local
of thyroid cancer recurrence. Repeat radioiodine scan showed no uptake in the
thyroglobulin levels started to increase markedly, which raised the suspicion
thyroglobulin was 166 ug/l, with negative thyroglobulin antibodies. A year later,
vascular invasion and extrathyroidal extension, hence completion thyroidectomy
Histology showed a 20 mm papillary thyroid carcinoma with capsular and
neuroendocrine markers. Meanwhile, FNA of her thyroid nodule showed Thy1,
Histology from her breast resection was reviewed and negative for TTF1 and
lesion was too close to the pulmonary artery to safely excise. She then had an
neuroendocrine tumourlet; Ki-67 index
the left lower lobe lesion showed a typical carcinoid tumour with an adjacent
lung. She was referred for biopsy and/or resection of these lesions. Histology of
hypothyroidism following radioactive iodine for toxic multinodular goitre.
mammography. Past medical history included type 2 diabetes, asthma, and
A 68-year-old lady presented with a right-sided breast lump detected on routine
Su Ann Tee1, Robert Andrew James1, George Petrides1, Robert Allcock2 &
neuroendocrine tumours
DOI: 10.1530/endoabs.55.WH4

WH5
NET or Not? A case illustrating potential difficulties in detecting neuroendocrine tumours
Su Ann Tee1, Robert Andrew James1, George Petrides1, Robert Allcock2 & Petros Perros1,3
1Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK;
2Gateshead Health NHS Foundation Trust, Gateshead, UK; 3Institute of Genetic Medicine, Newcastle University, Newcastle, UK.

A 68-year-old lady presented with a right-sided breast lump detected on routine
mammography. Past medical history included type 2 diabetes, asthma, and
hypothyroidism following radioactive iodine for toxic multinodular goitre. Staging CT showed 2 presumed metastases in the left lung, and one in the right
lung, which was referred for biopsy and staging of these lesions. Histology of the
left lower lobe lesion showed a typical carcinoid tumour with an adjacent
neuroendocrine tumourlet; Ki-67 index <5%. Unfortunately, the left upper lobe
lesion was too close to the pulmonary artery to safely excise. She then had an
OctreoScan which was negative. Her breast carcinoma was removed and
tamoxifen was commenced. An incidental thyroid nodule was also noted and
further work-up organised. Her case was discussed in the Neuroendocrine MDT. Histology from her breast resection was reviewed and negative for TTF1 and
neuroendocrine markers. Meanwhile, FNA of her thyroid nodule showed Thy1,
repeat FNA showed Thy 3f so she proceeded to have a left diagnostic lobectomy. Histology showed a 20 mm papillary thyroid carcinoma with capsular and
vascular invasion and extrathyroidal extension, hence completion thyroidectomy
was performed. Post-operatively she received 3.7Gy of radioactive iodine. Initial
post-ablation scan did not show any extrathyroidal uptake, and stimulated
thyroglobulin was 166 μg/l, with negative thyroglobulin antibodies. A year later,
thyroglobulin levels started to increase markedly, which raised the suspicion
of thyroid cancer recurrence. Repeat radiodine scan showed no uptake in the
neck but showed two areas of uptake in the left lung; USS neck showed no local
recurrence; and repeat OctreoScan showed non-specific activity in the left lung.
Serial CTs showed a 4 mm increase in the left-sided lesion, with stable
appearances of the right-sided nodule. Rediscussion in the MDT concluded that the
lung nodules were probable metastases from thyroid cancer all along. The
diagnosis was explained to the patient, and due to her lack of symptoms and slow
progression of the lesions, further surgery or radioactive iodine was withheld.
She remained under close monitoring. This case highlights the potential diagnostic
difficulties in diagnosing tumours of neuroendocrine origin, and illustrates various
diagnostic modalities and multidisciplinary expertise available. Patients with
neuroendocrine tumours may have separate multiple malignancies, and there is a
possible association documented in the literature. It is of paramount importance
to involve patients in decision-making and consider their symptoms and
expectations, as it may be inappropriate to offer treatment when the benefits are
unclear.
DOI: 10.1530/endoabs.55.WH5

WH6
Insulinoma presenting with nocturnal seizures
Craig E Stiles1,2, Stephen Daly1 & Marlyn Druce1,2
1St Barts Hospital, London, UK; 2Queen Mary University of London, London, UK.

A 29 year old lady presented to an outside hospital with 1 year’s history of episodes of confusion in the mornings. The patient’s partner had noticed 2–3
times a week she awoke with episodes of confusion, minimal communication, stereotyped lip smacking and winking lasting up to 20 min. She had one nocturnal
tonic-clonic seizure abroad, requiring A+E attendance. She was then seen by a
neurologist, had a normal sleep deprived EEG and was diagnosed with focal
epilepsy and started on lamotrigine. She subsequently had two further episodes of
nocturnal/early morning tonic-clonic seizure whilst in the UK, on anti-epileptic
medications. A CBG of 1.2 mmol/l was recorded by the ambulance service after
one of these seizures. After this, she would wake herself in the night to consume a
banana and a can of Coca Cola, which prevented further seizures. She had
experienced some weight gain. Family history was remarkable for type 2 Diabetes Mellitus in a grandmother and thyrotoxicosis in her mother. Physical examination was unremarkable. A 72-hour fast was planned, however, the patient had an
episode of hypoglycaemia prior to the test starting, with a lab glucose of 1.6 mmol/l, insulin was inappropriately detectable at 9.8 μmol/l with a c-peptide of
765.6 pmol/l. A urinary sulphonylurea screen was negative. Results were
compatible with insulinoma. Other blood parameters were normal. MRI pancreas showed a 1 cm soft tissue lesion arising from the pancreatic tail, this lesion was
avid on 68Gallium-Dotate PET-CT. No evidence of metastatic disease was seen.
The patient was referred for surgery. Management of the hypoglycaemia was
challenging. The patient had a disappointing response to escalating doses of
diazoxide, still requiring a midnight snack to prevent hypoglycaemia. Octreotide
was unhelpful and resulted in nausea and reduced intake, leading to re-admission
with further hypoglycaemic episodes. Symptoms persisted despite the addition
of anti-emetic medication and the octreotide was stopped and preinsulone
commenced and the dose gradually increased to 10 mg morning, 5 mg evening until
the hypoglycaemic episodes were abolished. Diazoxide induced oedema was
managed with Bendroflumazine. The patient underwent a distal pancreatectomy
and splenectomy. Histology showed a completely excised 13mm NET, Ki67
<1% with no evidence of vascular invasion. Immunohistochemistry showed
expression of chromogranin and synaptophysin with weak staining for insulin.
Post-operatively, there have been no further hypoglycaemic episodes.
DOI: 10.1530/endoabs.55.WH6

WH7
A rare cause of funny turns and weight gain
Pui San Yap & Alex Graveling
NHS Grampian, Aberdeen, UK.

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

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

Discussion

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

DOI: 10.1530/endoabs.55.WH7

WH8

Multiple endocrine neoplasia type 1: Can we talk about day-to-day ‘routine’ patients?
Andreas Selberher1,2, Victoria Stokes1 & Rajesh Thakker1
1Academic Endocrine Unit, University of Oxford, Oxford, UK; 2Medical University of Vienna, Vienna, Austria.

A 35-year-old patient was referred to a tertiary referral unit for further investigation of severe watery diarrhea. Infectious agents had already been excluded. Biochemistry revealed a strikingly raised serum calcium concentration of 4.09 mmol/l (NR 2.1–2.65 mmol/l), chromogranin A was grossly elevated at 293 U/l (NR 2–18 U/l) and vasoactive intestinal peptide (VIP) was also raised at 130 pg/ml (NR 10–60 pg/ml). Computed tomography (CT) of the abdomen demonstrated an eight-centimeter mass in the body of the pancreas which led to the working hypothesis of a VIP producing neuroendocrine tumour as the cause of this patient’s condition. Molecular genetic testing showed a deletion of 4 base pairs in exon 2 resulting in a truncation of the Menin protein at codon 116, leading to a diagnosis of MEN1, with a suspected VIPoma and primary hyperparathyroidism. Screening for other manifestations of MEN1 did not reveal any pituitary abnormalities, however genetic testing of family members revealed that the patient’s 9 year old son carried the same mutation. As a bridging therapy to surgery somatostatin-analogues were administered which led to a cessation of diarrhea and allowed the patient to undergo a total pancreatectomy. Intraoperatively an incidental pancreatic lesion and PET scan showed metabolically active pancreatic lesion which led to the working hypothesis of a VIP producing neuroendocrine tumour as the cause of this patient’s condition. Molecular genetic testing showed a deletion of 4 base pairs in exon 2 resulting in a truncation of the Menin protein at codon 116, leading to a diagnosis of MEN1, with a suspected VIPoma and primary hyperparathyroidism. Screening for other manifestations of MEN1 did not reveal any pituitary abnormalities, however genetic testing of family members revealed that the patient’s 9 year old son carried the same mutation. As a bridging therapy to surgery somatostatin-analogues were administered which led to a cessation of diarrhea and allowed the patient to undergo a total pancreatectomy. Intraoperatively an incidental pancreatic lesion and PET scan showed metabolically active pancreatic lesion which led to the working hypothesis of a VIP producing neuroendocrine tumour as the cause of this patient’s condition. Molecular genetic testing showed a deletion of 4 base pairs in exon 2 resulting in a truncation of the Menin protein at codon 116, leading to a diagnosis of MEN1, with a suspected VIPoma and primary hyperparathyroidism. Screening for other manifestations of MEN1 did not reveal any pituitary abnormalities, however genetic testing of family members revealed that the patient’s 9 year old son carried the same mutation. As a bridging therapy to surgery somatostatin-analogues were administered which led to a cessation of diarrhea and allowed the patient to undergo a total pancreatectomy. Intraoperatively an incidental pancreatic lesion and PET scan showed metabolically active pancreatic lesion which led to the working hypothesis of a VIP producing neuroendocrine tumour as the cause of this patient’s condition. Molecular genetic testing showed a deletion of 4 base pairs in exon 2 resulting in a truncation of the Menin protein at codon 116, leading to a diagnosis of MEN1, with a suspected VIPoma and primary hyperparathyroidism. Screening for other manifestations of MEN1 did not reveal any pituitary abnormalities, however genetic testing of family members revealed that the patient’s 9 year old son carried the same mutation. As a bridging therapy to surgery somatostatin-analogues were administered which led to a cessation of diarrhea and allowed the patient to undergo a total pancreatectomy. Intraoperatively an incidental pancreatic

DOI: 10.1530/endoabs.55.WH8

WH9

Persistant hypoglycaemia post bariatric surgery
Tessa Glyn & Robert Andrews
Mugrosve Park Hospital, Taunton, UK.

Postprandial Hyperinsulinaemic Hypoglycaemia reportedly occurs in 0.1 to 0.3% of patients after Roux-en-Y Bypass procedures. In our Bariatric Surgery Service we seem to be seeing this complication more frequently. Most patients can be managed in a step-wise approach, but we have a few patients who appear refractory to conventional treatment. This case illustrates one such patient. Mrs P was referred to the Weight Management service in 2011, aged 45. She weighed 108 kg, with a BMI of 40 kg/m². She had type 2 diabetes, but no other past medical history and was working in a high profile job. A Roux-en-Y bypass was performed in November 2011, with no immediate complications. She successfully lost 25% of her body weight and by April 2012 weighed 79.2 kg. Towards the end of 2015 she was re-referred with symptoms of severe fatigue, poor concentration and mood changes. She had been signed of sick by occupational health. Investigations revealed no evidence of anaemia, or vitamin deficiency and a normal cortisol response to synacthen. Treatment with a course of thiamine and Pabrinex initially improved her symptoms but they then returned. Despite denying symptoms of dumping syndrome and hypoglycaemia, a decision was made to proceed with Continuous Glucose Monitoring (CGM). This revealed hypoglycaemia 2–3 hours after meals. A clinical diagnosis of hyperinsulinaemic hypoglycaemia was made and she was referred to the dietitian. Changing her diet initially improved her symptoms but they then returned. Acarbose and diltiazem were next tried without success. Liraglutide, followed by octreotide, were then trialled, which resulted in only temporary improvement. Due to the persistence of her hypoglycaemia a CT pancreate, 72 h fast & octreotide scan were performed ruling out an insulinaemia. In early 2017 she successfully returned to work on Prednisolone, quick-acting insulin with meals, Octreotide and with a CGM funded through exceptional funding. In the last 3 months however, her hypoglycaemia has not responded to this regimen and she has had to take early retirement. Her most recent CGM download shows she spends 19% of her time with a blood glucose <4 mmol/l and 5% <3 mmol/l. She is adamant that she does not want further surgery. Various options have now been discussed including trialing a dual insulin and glucagon pump. This case illustrates the devastating effects that Hyperinsulinaemic Hypoglycaemia can have on someone’s quality of life. More evidence is needed to support new treatments to reduce hypoglycaemia in this cohort of patients who appear refractory to conventional therapy.

DOI: 10.1530/endoabs.55.WH9

WH10

Insulin independent hypoglycaemia in malignancy: An unusual case
Thomas Crabtree
Derby Teaching Hospitals NHS Trust, Derby, UK.

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

DOI: 10.1530/endoabs.55.WH10
Pancreatic neuroendocrine tumors are rare neoplasms of this organ. The majority of them are tumors without hormonal activity. Approximately 35% of the pancreatic neuroendocrine tumors (pNETs) are functional, the most common of which is an insulinoma. We present a 57 year old lady with dyspepsia, nausea and Fe deficiency anaemia for more than a year. On examination had a epigastric mass, endoscopy was consistent with a well differentiated endocrine grade 2 tumor. Octeotide scan showed increased uptake. CT abdomen: large enhancing mass with calcification extending from pancreas to stomach, spleen and portal vein. Discussed with wessex carcinoid MDT. Underwent a left upper quadrant clearance: Total gastrectomy, distal oesophagectomy, pancreatectomy, spenectomy, Roux-en-Y reconstruction, portal vein resection and anastomosis. Histology confirmed a well differentiated pancreatic endocrine carcinoma with nodal, vascular and perineural invasion, staging PT3N1R1 excision. Post operatively developed diabetes, hypo unawareness, and malnutrition, treated with insulin pump and dexcom G4 CGM and high dose creon. Timely and right intervention saved patients life. We would like to emphasize that in this case Octeotide imaging & contrast CT can be effectively helpful especially in conjunction with other useful diagnostic methods which are handled in pancreatic tumor’s. We put emphasis on corrected and extended histopathological report which determines further management according to prognostic and prediction factors of patients with neuroendocrine pancreatic tumor.

DOI: 10.1530/endoabs.55.WH11
Additional Cases
CB1
Hyperthyroidism in an elderly patient with normal thyroid on USS, negative hypogonadism and dilemma following liver toxicity
Artemis Vogazianou & Helen Simpson
UCLH, London, UK.

An 82 year old lady was admitted with acute stroke on 3/1/18, confirmed on MRI. She was found to be in AF and had thyroid function tests checked on 4/1/2018, with TSH 0.01 (0.27–4.20) mIU/l and FT4 52.8 (12.0–22.0) nmol/l. She was commenced on Carbimazole 20 mg OD. TPO and TSH-receptor antibodies were both negative. An ultrasound scan confirmed a normal thyroid without any features of Grave’s disease or thyroid nodules. Clopidogrel 75 mg OD and Atorvastatin 40 mg OD were also started. She was discharged on 17/1/2018, to a rehabilitation unit for further physiotherapy input. She progressed satisfactorily, but on routine bloods done on 20/1/2018, she was found to have acutely deranged LFTs, with ALP 700 (35-104) IU/l (81 on 5/1/2018), ALT 147 (10–35) IU/l (12 on 5/1/2018), bilirubin 6 (0–20) mg/dl (7 on 5/1/18). The patient was clinically well. Her statin was discontinued, but she remained on Clopidogrel 75 mg OD and Carbimazole 20 mg OD. She was re-admitted on 29/1/2018 for further investigations. ALP had improved slightly to 522 IU/l, ALT 52 IU/l and Bilirubin 4 mg/dl. The γ-GT was 949 IU/l. The liver ultrasound showed a thin-walled gallbladder with a 1.5 cm gallstone and it was felt that this was most likely a cholestatic picture due to a passed gallstone in view of rapid resolution. By 29/1/2018, TSH was 0.06 (0.27–4.20) mIU/l and FT4 16.3 (12.0–22.0) nmol/l just over 3 weeks after commencing Carbimazole 20 mg OD. There is suspicion that this may have been Thyroiditis (not contrast-related as CT-angiogram on 3/1/2018 and deranged LFTs on 4/1/2018). Given the recent history of AF and stroke, she was continued on Carbimazole but at a much reduced dose of 5 mg OD. She has returned to the rehabilitation unit and remains clinically well. Given the patient had been recently commenced on a number of medications with potential effects on liver function, including statins (hepatitis; jaundice; hepatic failure) and clopidogrel (hepatitis and acute liver failure), as well as Carbimazole (cholestatic jaundice) there was a dilemma about how to proceed, especially given potential effects on liver function, including statins (hepatitis; jaundice; hepatic failure). Given her clinical picture there was no clear account of jaundice. Further investigations, including liver biopsy were not possible.

DOI: 10.1530/endoabs.55.CB1

CB2
Diagnosis and management of male hypogonadism
S Samarasinghe & R RA Khanal
1Northwick Park Hospital, Harrow, UK; 2West Middlesbrough University Hospital, Isleworth, UK.

Gonadotropin-releasing hormone agonists are a class of drugs used to treat male hypogonadism, also known as hypogonadism in men. These drugs can cause a temporary decrease in sex hormone levels, which can result in decreased sexual function and decreased muscle mass. They can also cause systemic side effects, such as hot flashes and sweating.

CB3
A case of asymptomatic hypercalcemia...
Muhammad Fahad Arshad1,2, Gerard Jayamanne1 & Surinder Kang1
1Sheffield Teaching Hospitals, Sheffield, UK; 2Doncaster Royal Infirmary, Donca, UK.

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

Reference

DOI: 10.1530/endoabs.55.CB3

CB4
Curious case of hypercalcaemia in pregnancy
Sanesh Pillais & Ruth Mcinerney
Chesterfield Royal Hospital, Chesterfield, UK.

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

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

Investigations
PTH was 12 (15–60) and 25-OH vitamin D was 115.8 reflecting supplementation. Serum ACE was normal A PTHrP was undetectable, however this was taken 3 months for interval assessment of the lesion. The patient was diagnosed with primary hyperparathyroidism with a plan to initiate testosterone replacement therapy (the primary treatment option). Current guidelines on the management of sexual problems in men advocate pre-treatment assessment to rule out prostate cancer in men over the age of 40 years. Men with erectile dysfunction and diminished libido and documented testosterone deficiency are candidates for testosterone therapy once a diagnosis of hypogonadism is confirmed. After the initiation of therapy, total testosterone, sex hormone binding globulin (SHBG) and albumin levels should be monitored. The aim of therapy should be a total testosterone level of at least 15 nmol/l.

DOI: 10.1530/endoabs.55.CB4
Post-operative hypocalcaemia in a patient with a metastatic pancreatic neuroendocrine tumour

Nithya Sukumar1,2, Gregory Kaltas1 & Martin Weickert1
1University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK, 2Warwick Medical School, University of Warwick, Coventry, UK.

Case history
Mrs SC, a 56 year old female was referred to the endocrine registrar with hypocalcaemia (corrected calcium 1.93 mmol/l). She was day 3 post-hemihysterectomy for liver metastases from a primary pancreatic tail neuroendocrine tumour (NET). She had paraesthesia and numbness of her fingers and toes but no spasms. Chvostek’s sign was negative and there were no ECG changes. Past medical history includes severe hypocalcaemia in September 2016 which was found when she presented acutely with abdominal pain. CT abdomen done as a part of the work-up showed a 4.5 cm lesion in the tail of the pancreas and 3× liver metastases, which was subsequently confirmed to be a primary pancreatic NET on SRS octreotide scan and biopsy. She had an open distal spleno-pancreatectomy in 2017 for resection of the primary tumour. Aside from this she had previous breast cancer (in remission) and oesophagitis. Drug history: Octreotide 200 micrograms daily, Pamidronate.

Investigations
At diagnosis (09/2016)
Corrected calcium: 4.01 mmol/l (NR 2.1–2.58)
Phosphate: 0.63 mmol/l (NR 0.8–1.4)
PTH: <0.6 pmol/l (NR 1.1–4.2)
25-hydroxy vitamin D: 24 nmol/l
eGFR: >60 ml/min per 1.73 m²

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

Day 3 post-operative (5/1/2018)
Corrected calcium: 1.94 mmol/l
Phosphate: 1.46 mmol/l
Magnesium: 0.80 mmol/l (NR 0.7–1.0)
eGFR: >60 ml/min per 1.73 m²

Treatment
The sudden post-operative hypocalcaemia was due to loss of PTHrP secretion after removal of the liver metastases. This confirmed the suspicion that her initial hypercalcaemia was due to PTHrP secretion from a NET, which has been described in case reports. This paraneoplastic syndrome tends to occur with metastatic pancreatic NETs and is often responsive to somatostatin analogue therapy or peptide receptor radiotherapy causing hypocalcaemia. In the acute setting, she was given IV calcium gluconate until her calcium increased to >2.1 mmol/l. The Cinacalcet and Alendronic acid was stopped and she was started on Adcal D3 2 tablets TDS. Her calcium on discharge was 2.19 mmol/l.

Conclusions and points for discussion
This is an unusual case of a PTHrP secreting metastatic pancreatic NET causing hypocalcaemia initially and then hypocalcaemia after surgical resection. It is important to monitor calcium levels closely in such patients in the post-operative period.

CB5

DOI: 10.1530/endoabs.55.CB5

A case of primary hypoparathyroidism with hypocalcaemia

Monzoor Quader
Walsall Manor Hospital, Walsall, UK.

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

Questions for the panel:
1. Are these collapses related to Hypocalcaemia?
2. How can we get the calcium to normal level as there was an episode of AKI with hypercalcaemia?
3. Was the AKI related to Hypercalcaemia?

CB6

DOI: 10.1530/endoabs.55.CB6

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

Ryzan Nizar & Tony Robinson
Royal United Hospital, Bath, UK.

79 year old male had been admitted due to multiple falls within a space of 24 hours. On admission, he had a full set of bloods which showed hypercalcaemia and no other significant abnormality. His past medical history included Prostate Cancer, Type 2 Diabetes and Urinary retention for which he had a long-term catheter in situ. His current medications were Linaclapitin, Apixaban, Bicalutamide and simple analgesia. Initially, he was fluid resuscitated, which seemed to improve his calcium slightly but his calcium levels remained well above 3 despite of 2 high dose D3 injections. He was then discharged with instructions to take 50,000 Units of Cholecalciferol and was discharged with instructions to take 50,000 units once a week for 5 weeks. However, he was back in the hospital within 3 weeks of discharge and his Vitamin D box was empty. Looking through this patient’s previous calcium levels it was noted he had never had high calcium levels and in fact, if anything at times it was low prior to admission. However, Vitamin D levels at 63 mmol/l they were certainly not very high. We went on to check a 1.25 OH vitamin D level. This level came back at 199 pmol/l (55-139) which was much higher than the normal range.
Discussion
A normal CT scan, as well as a negative serum protein electrophoresis and negative urine BJP, excluded malignancy as a possible cause of his hypercalcemia. A suppressed PTH at admission prior to treatment also excluded Hyperparathyroidism as a cause. In conclusion, this was a patient with hypercalcemia due to Vitamin D toxicity with normal serum 25-OH Vitamin D levels and raised 1-25 OH Vitamin D levels.

DOI: 10.1530/endoabs.55.CB7

CB8
Peripartum calcium conundrum in a lady with pseudohypo parathyroidism
Muhammad Waseem Ashlam & Miles Levy
Leicester Royal Infirmary, Leicester, UK.

Pseudohypo parathyroidism during pregnancy can lead to challenging calcium fluctuations and can lead to maternal and foetal morbidity. There are limited case reports and no established management guidelines. Maintaining calcium level in healthy range during pregnancy is required to minimise the risks of associated complications. We report a case of Pseudohypo parathyroidism type 1a in 30 year old lady, who was initially referred to us by her general physician with calcium, of 1.63 mmol/l, raised phosphate levels of 1.71 mmol/l and raised parathyroid hormone; she volunteered the symptoms of feeling non specifically tired for few years, and it was only over the last few months that she had experienced carpopedal spasm and symptoms that would relate specifically to hypocalcemia. On examination she had a short stature, rounded face and a short 5th metacarpal all indicating pseudohypo parathyroidism type 1a. She had no evidence of subcutaneous calcification and the rest of the examination was unremarkable. She was referred for genetic counselling and was started on Alfacalcidol and Sandocalc to improve her symptoms, MRI brain was arranged as she mentioned balance issues which revealed symmetrical pathological mineralisation of the globi pallidi, heads of caudate nuclei and cerebellar dentate nuclei. In due course she conceived spontaneously and maintaining calcium in optimum range became even more challenging then pre conception. Her Alfacalcidol was increased to 1.5 µg BD. She was seen in joint endocrine anti natal clinic and was found to have high blood pressure and her US revealed polyhydramnios and had to be given IV Calcium Gluconate to optimise the calcium levels, despite fluctuating calcium levels she delivered a healthy female baby at term but her calcium was ever so resilient it plummeted to 1.58 mmol/l two months after delivery, despite being non lactating mother. Her Alfacalcidol was increased to 1.5 µg TDS in order to raise the serum calcium. This case highlights the implications of mother’s conditions on developing foetus and re emphasises the importance of close monitoring and planning of pregnancy but also in post partum period and necessitates the genetic workup of new born.

DOI: 10.1530/endoabs.55.CB8

CB9
An unusual case of hypocalcaemia
Syed Bitat & Godwin Simon
Basilion and Thurrock University Hospitals NHS Foundation Trust, Basildon, UK.

Case history
A 34 year old Chinese male was referred by GP as routine blood test which was done as part of investigation for ongoing hair loss that revealed hypocalcaemia. Patient was asymptomatic with no tingling sensation, numbness or anaesthesia. There was no history of carpopedal spasm, muscle pain or cramps. He does not give any history of symptoms suggestive of malabsorption. His PMH include Mild asthma and Eczema for which he was not on any regular medication. Social history of note he lives with his parents and have no partner. He works in IT and stays mostly indoors. He does not smoke or drink alcohol. There is no family history of problem with calcium or any bony deformity. On examination Chvostek’s and Trousseau’s sign was negative. No bony deformity noted. Systemic examination was essentially normal.

Investigations
FBC- Normal, Renal function, Adjusted calcium- 1.57, PTH 75.7, Phosphate 1.0, Magnesium 0.81, Vitamin D 16.3 ALP 117 TSH 2. ECG-Normal sinus rhythm and QTc. Vitamin B12, folate and ferritin- Normal.

Results and treatment
The results supported a clinical diagnosis of secondary hyperparathyroidism due to vitamin D deficiency. Patient was started on Cholecalciferol 40 000 units once a week for 8 weeks then 20 000 units once a week for 8 weeks. He was also started on Calcium carbonate 1000 mg three times daily for 3 months. Patient was subsequently followed up in the endocrine clinic for 2 years where he missed couple of his appointments. His Vitamin D level normalised after initial replacement and remained between 71 to 87. His Adjusted calcium remained low between 1.9 and 2. The patients PTH remained high and was 24.2. After initial vitamin D replacement patient was on Cholecalciferol 10 000 units OD and Calcichew 2 tablet daily which was continued for 2 years with patient denying any compliance issue. His most recent blood test showed PTH 15.5, Adjusted calcium 2.1 and Vitamin D 135. All other biochemical test was normal.

Discussion
Differential diagnosis includes 1) Hypocalcaemia due to Vitamin D deficiency with secondary hyperparathyroidism or Pseudohyoparathyroidism Type 2 or 1b. Point for discussion-1) Is there any other test will be helpful to confirm the diagnosis like PTH infusion and measurement of urinary cAMP(where done in UK) or Xray hand or measure 1 25 OH Vit D and genetic test for Pseudohyoparathyroidism. 3) Is there any other treatment that can achieve normocalcaemia like alpha-calcidol.

DOI: 10.1530/endoabs.55.CB9

CB10
A 60 year history of recurrent hypoglycaemia
Evgenia Foteinopoulou1, Kevin Colclough2 & Mark Strachan3
1Western General Hospital, Edinburgh, UK; 2Royal Devon and Exeter Hospital, Exeter, UK; 3Western General Hospital, Edinburgh, UK.

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

DOI: 10.1530/endoabs.55.CB10

CB11
Spontaneous hypoglycaemia in an elderly man with suspected bladder cancer
Craig Thurtell & Chris Schofield
Ninewells Hospital and Medical School, Dundee, UK.

An 87 year old man was referred to our endocrine service from the medicine for the elderly team for investigation of suspected hypoglycaemia. He had several
co-morbidities but did not have diabetes mellitus. There was a 6 month history of ‘funny episodes’ characterised by lethargy, profuse sweating and confusion. The symptoms resolved a few minutes after eating. One such episode occurred while attending his GP who arranged for blood to be drawn. The plasma glucose was 1.9 mmol/l hence satisfying Whipple’s triad. A CT chest, abdomen and pelvis performed prior to referral to investigate unexplained weight loss revealed an endoluminal lesion in the bladder thought to represent a localised tumour as well as pleural thickening (secondary to asbestos exposure) and a possible small left sided empyema. Considering the patient’s relative frailty and already proven hypoglycaemia, it was decided to arrange an immediate inpatient stay on our ward to complete the necessary investigations. A short Synacthen test showed a peak cortisol of 1008 mmol/l thereby excluding adrenal insufficiency. A few hours into an overnight fast he became hypoglycaemic and blood drawn at the time demonstrated hyperinsulinaemic hypoglycaemia – plasma glucose 1.8 mmol/l, insulin 36 mU/l (ref. range 3–17) and c-peptide 3.19 mmol/l (0.36–1.12). The sample was delayed in reaching the laboratory for at least a few hours which may have had deleterious effect on insulin and c-peptide prior to analysis. The elevated results, however, still supported a diagnosis of endogenous insulin excess. The respiratory physicians reviewed his radiology and attempted an US-guided pleural aspiration but the tap was dry. The patient was followed up as an outpatient thereafter. A follow-up CT scan showed no change in the thorax but did reveal a 13 mm rounded lesion in the tail of the pancreas possibly representative of a small insulinoma. Investigation by our urology colleagues confirmed a high-grade transitional cell carcinoma of the bladder. This was successfully treated with intravesical BCG therapy. Due to the patient’s frailty and wish not to undergo surgery, the hypoglycaemia has been successfully managed with diazoxide alone. This case demonstrates a (probable) insulinoma in an elderly patient presenting with spontaneous hypoglycaemia. Insulinoma has been described at the extremes of age and cannot be thought of exclusively as a condition of middle age. The case also highlights the need to investigate and manage patients taking into account their own wishes and co-morbid state.

DOI: 10.1530/endoabs.55.CB12

**Recurrent hypoglycaemia, post sleeve gasterectomy, new approach**

Assaad Aldafter
Noor Specialist Hospital, Manama, Bahrain.

A 29 years old lady she has Diabetes mellitus type II, and obesity so she did sleeve gasterectomy and she was happy that her sugar was well controlled then later in complete remission. She has later recurrent symptoms of hypoglycaemia and intolerable, when Hba1c done was habc 6.8%. She was started on Glucobay tablet 50 mg before each meal. Next visit she come, she was happy that her sugar is well controlled with treatment but her medicines is finished. After requiring how many tablet she took per day she was using before every simple meal or snack and total of 6–10 tablet per day. Her Hba1c was 6.1. She was tolerating 10 tablet per day without troubles. Q1, how many times we prescribe Glucobay per day to be allowed? Q2, studies of symptomatic hypoglycaemia post sleeve should be employed. Q2 whether should give limit of tablet of Glucobay prescribed.

DOI: 10.1530/endoabs.55.CB13

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

Punith Kempegowda1,2, Samina Kauser1, Lisa Shepherd1 & Mohamed Salih Ahmed1
1Heart of England NHS Foundation Trust, Birmingham, UK; 2Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK.

**Background**

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

Case presentation

A 42-year-old Caucasian female presented with recurrent episodes of weakness and confusion, increasing in frequency for 5 years. She was previously diagnosed with type 1 vasovagal syncope, cephalic migraine and temporal lobe epilepsy for these symptoms; none entirely explaining the whole phenomenon. Patient’s capillary glucose incidentally measured during one such episode was 1.9 mmol/l and hence referred to the endocrine department for further evaluation. There was no history of chest pain, palpitations, syncope or syncope during these episodes. There were no specific triggers or relationship with meals. Apart from Parkinson’s disease in some family members, rest of the medical history was unremarkable. On examination, the patient was hemodynamically stable and clinically unremarkable with a BMI of 20.9 kg/m². 24-hour fasting test demonstrated low but detectable levels of insulin (14 pmol/l) and c-peptide (121 pmol/l) with suppressed ketones (0.2 mmol/l) while the patient was hypoglycemic (2.2 mmol/l); sulphonilurea screen was negative. However, the patient had abnormally high insulin (187 pmol/l), c-peptide (1797 pmol/l) with hyperinsulinaemia (2.2 mmol/l) during mixed meal test. Rest of the endocrine hormonal assessment including gut hormone profile was within normal limits. CT scan of her abdomen revealed a 4.0 x 3.1 cm mass within the head and uncinate process of the pancreas.

Management and outcome

Patient developed a severe rash with diacoxide and life-threatening hypoglycaemia with octreotide when used as medical treatment for insulinoma. Medical therapy was hence discontinued and the patient went on for surgical resection of the mass following discussion with the neuroendocrine multidisciplinary team. Histology confirmed benign insulinoma and patient reported no further hypoglycaemic episodes since the surgery. Genetic testing was not considered as this was a single lesion with normal serum calcium and no family history of neoplasms.

**Conclusion**

Detectable levels of endogenous insulin with severe hypoglycaemia should prompt further investigations to rule out insulinoma. One should consider a possibility of insulinoma with an exaggerated insulin response to a mixed meal test. A close watch is recommended when patients are initiated on medical treatment for insulinoma.

DOI: 10.1530/endoabs.55.CB14

**Insulinoma – a cause of recurrent hypoglycaemias**

Annalisa Montebello & Sandro Vella
Mater Dei Hospital, Msida, Malta.

A 72 year old lady presented to endocrine clinic in January 2016 with a history of frequent episodes of feeling increasingly lightheaded, tremulous, sweaty and hungry. All symptoms resolved after eating. Her family doctor had twice documented a capillary glucose lower than 4 mmol/l. Continuous blood glucose monitoring was performed but there were no episodes of hypoglycaemia picked up. She was admitted for a 72 h fast in September 2016. Her capillary blood glucose readings never dropped to below 2 mmol/l during the test. At the end of the fast, a plasma glucose, insulin, C peptide, pro insulin, beta hydroxybutyric acid levels and urine for sulphonylurea were taken revealing:

Fasting Glucose: 2 mmol/l (3.88–5.38 mmol/l)
Insulin: 7.8 μU/ml (2.6–25 μU/ml)
C peptide: 1.5 ng/ml (1.1–4.4 ng/ml)
Pro Insulin: 12.1 pmol/l (<11 pmol/l)
Beta hydroxybutyric acid: 1687 μmol/l (Up to 270 μmol/l)
Urine for sulphonylurea: negative.

These results were diagnostic of an insulinoma. Magnetic resonance (MR) imaging of the pancreas in December 2016 failed to show any pancreatic lesions. An endoscopic ultrasound (US) of the pancreas was performed showing a 13 x 6 mm hypoechoic homogeneous lesion at the body of the pancreas. Pancreatic core biopsies confirmed a Grade 1 (low grade) neuroendocrine tumour. A repeat MR pancreas in May 2017 showed a 9mm focus of restricted diffusion at the junction of the body and tail of the pancreas which probably corresponding to the neuroendocrine tumour seen on endoscopic US. Subcutaneous Octreotide was prescribed to prevent hypoglycaemia. The patient underwent successful distal pancreatectomy in July 2017. Localisation of tumour was guided by on table intra-operative US. She was noted to have high capillary blood glucose readings post operatively and an oral glucose tolerance test confirmed a diagnosis of diabetes mellitus (fasting blood glucose of 10.44 mmol/l, second hour 21.9 mmol/l). She is currently managed on oral glucose lowering agents and is doing well. Insulinomas are the commonest neuroendocrine tumours. They arise from pancreatic islet cells and may secrete insulin in short bursts thus causing...
rapid fluctuation in blood glucose levels. 90% are benign tumours, 5% are malignant. Diabetes mellitus is one of the main complications post operatively.

DOI: 10.1530/endoabs.55.CB14

CB15
A rare cause of elevated testosterone levels in an adult female
Shazia Hussain, Anju Sahdev & William Drake
St Bartholomew’s Hospital, London, UK.

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

DOI: 10.1530/endoabs.55.CB15

CB16
DHEA: is it fountain of youth or medical need?
Rakshit Kumar, Saba Hafeez & Anand Velusamy

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

DOI: 10.1530/endoabs.55.CB16
Author Index

Abedo, I WA4, WA5 & WE4
Abraham, P WD3, WE16 & WE2
Adaln, M P17
Adlan, M P12
Aflam, D WG4
Ab-see, K WD3 & WE4
Abraham, P WD3, WE16 & WE2
Adaln, M P17
Affam, D WG4
Ah-see, K WD3
Ahmad, E WE3
Ahmed, MS CB13
Akker, S OC4, P28, WE7, WE8 & WH2
Al-Sharefi, A WH4
Alam, K WD5
Aldafter, A CB12 & WE12
Allcock, R WH5
Allinson, K P32
Anandappa, S WA4, WA5, WE4 & WG4
Andrew James, R WH4
Andrews, R WH9
Anguelova, L OC9
Ann Tee, S WH4
Anpalakhan, S WA4
Anthony, J P16
Arfan, R WC1
Arnez, L P10 & WE8
Arshad, MF CB3
Arshad, S OC3
Aslam, MW CB8
Avari, P WC3 & WE1
Aylinwin, SJB OC3
Bakhit, M OC3
Bano, G OC1 & P11
Banu, Z OC5 & P07
Baple, E WD2
Bastos, F WA13
Beirne, P P19
Berney, D OC4
Best, J P18
Beynon, J WH1
Bhake, R WD5
Bhatt, D WD3
Bidmead, J OC3
Bisambar, C P03
Bittat, S CB9
Bondugulapati, L WG1
Boot, C WH4
Brackenridge, A P18
Bravis, P V24 & P30
Brennan, C WD7
Brown, M OC2, P14, WE6 & WE7
Burgess, N P34
Calvo-Latorre, J P10
Carpenter, R WE14
Carroll, P WC2
Carty, D OC6
Chan, K P35
Charles, D WG2
Cheow, H P14
Chicco, M P30
Chika-Ezerioha, Dl WF4
Chok, YL P07
Chung, TT P14 & P15
Church, D OC8
Clark, J P37
Colclough, K CB10
Collier, A P03
Coppack, S WE14 & WH2
Cordeiro, MC WA13
Cordiner, R OC6
Crabtree, T WH10
Cranton, T P13
Cross, S P28
Daly, S WH6
Dawson, A P29
Dede, A P13
Dhere, A OC9
Diaz-Cano, S OC3
Drake, W CB15, P14, P15, WA2, WA3, WA9, WB2, WD7, WE14, WE6, WE9, WF3 & WH3
Drake, WM WB1
Drume, M WH6
Du, Y OC7
Dunn, J WD2
Duthie, F P03
Dymott, J WE16
Ehrenstein, M OC8
Ferreira, A WA13
Field, B P37
Flanagan, D WD2
Foteinopoulou, E CB10
Fox, J P20
Francis, L P35
French, J WH4
Gannon, D P07
Garg, S OC2
George, A P38
Gibney, J WC4
Gibson, J OC6
Gilroy, M WA6 & WD2
Giulea, C WD6
Glyn, T WE12 & WH9
Goodchild, P E14 & WE6
Gorvin, CM P27
Graham, J P36
Grant, J P09
Graveling, A WD3, WE2 & WH7
Green, F WA11
Gruppetta, M WA7
Gulfam, T WH4
Gunganah, K P36
Gurnell, M P15 & P32
Hafeez, S CB16 & WC2
Halsall, D OC8, P09 & P32
Hameed, A OC1 & P11
Hannan, F P13
Haque, M OC3
Hasan, F WE17
Hassoun, S WA11
Hattfield, E P35
Hodgson, S OC1
Houlford, F WB3 & WE1
Howat, I P41
Huang-Doran, I P32
Hussain, S CB15, WA3, WD7 & WF3
Ilangaratne, C WA4, WA5 & WE4
Isenberg, D OC8
Issa, B WH1
Jacob, P WE9
Jafar-Mohamadi, B OC9
Jafar-Mohammadi, B P27, P39 & P43
James, RA WH5
Jayamanne, G CB3
Johnson, A WE17
Joshi, R OC7
Kaltsas, G CB5
Kang, S CB3
Kariyawasam, D P18
Kauser, S CB13
Kaushal, R CB2 & P04
Keat Cheah, S P09
Kempegowda, P CB13
Kim, D P11
Kirresh, O P15
Klepaci, J WE16
Kline, G P26
Koulouri, O P32
Krishnan, S P09
Kulendran, V P35
Kumar, J WG4
Kumar, R CB16, WC2 & WG1
Kummaraganti, S P19
Kurzawinski, T P14
Kyriakakis, N P19
Kyrodimou, E WE2
Lakshmipathy, K P37
Lam, F OC8
Lawrence, V OC4 & P10
Leeds, J WH4
Levy, M CB8 & WD5
Lewis, D OC3
Li, APZ P18
Lindsay, R OC6
Lines, KE P33
Lunken, C P36
Lynch, J P19
MacInerney, R P05
Mackenzie, F OC6
Mackie, A WA10 & WE11
Maltese, G P18
Manita, I WA13
Mannion, R P32
Manohar Rao Balmuri, L WH1
Manova, Y OC8
Margar, N OC10
Martineau, M P01 & WE13
Mathews, A P09
Matson, M P14
May, C P39 & P43
McInerney, R CB4
Meeran, K P35
Mehta, S OC10
Menon, R OC5
Millar, K P04
Millar, L P38
Millson, V P29
Mohamed, M WA11
Mohandas, C WA4, WA5 & WE4
Montebello, A CB14 & WG3
Morganstein, D OC7, P25, P31 & P38
Morris, L WH1
Mumbay, C WH1