

LONDON  
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LCA

**Imperial College**  
London

**Pituitary  
Masterclass  
Meeting**

**Monday 28<sup>th</sup> September 2015**

## LCA PITUITARY MASTERCLASS MEETING 2015

08.30 - 09.00 Registration.

09.00 - 9.20 **Welcome.** Dr Niamh Martin (Consultant Endocrinologist, Imperial College Healthcare NHS Trust) and Dr Kate Haire (London Cancer Alliance).

### SESSION 1 ACROMEGALY.

Chairs Mr Ramesh Nair (Consultant Neurosurgeon, Imperial College Healthcare NHS Trust, London) and Professor Karim Meeran (Professor of Endocrinology, Imperial College, London).

09.20 - 09.40 *Update on treatments for Acromegaly*  
Dr Claire Higham (Consultant Endocrinologist, The Christie Hospital, Manchester).

09.40 Case presentation: *A challenging case of acromegaly complicated by heart failure.* P Valsalakumari, S Mehta, R Ramli, B Jones, A Mehta, N Mendoza, M Williams, K Meeran NM Martin, E Hatfield Imperial College Healthcare NHS Trust, London and Ealing Hospital NHS Trust, London.

09.55 Case presentation: *Old wine with a new label: Ipilimumab related hypophysitis.* M Joshi, G Maltese, D Kariyawasam, A Velusamy, U-King-Im Jean Marie, PV Carroll. Guys and St Thomas's Hospital NHS Trust, London.

10.10 Case presentation: *Factors predisposing to pituitary apoplexy: A tertiary centre's clinical experience.* J Milburn, A Abbara, D Joshi, S Clarke, R Ramli, A Comninou, A Mehta, B Jones, R Nair, N Mendoza, NM Martin, E Hatfield, A Sam, W Dhillon, K Meeran. Imperial College Healthcare NHS Trust, London.

10.25 - 10.40 **BREAK.**

### SESSION 2 CHALLENGES IN PITUITARY DISEASE.

Chairs: Mr Nigel Mendoza (Consultant Neurosurgeon, Imperial College Healthcare NHS Trust, London) and Dr Emma Hatfield (Consultant Endocrinologist, Imperial College Healthcare NHS Trust, London.).

10.40 *Radiotherapy options for managing cystic pituitary disease.*  
Dr Matt Williams, Consultant Clinical Oncologist, Imperial College Healthcare NHS Trust, London.

11.00 Case presentation: *A novel surgical approach for the management of giant invasive prolactinoma compressing the brainstem* N Margari, M: Vidyarthi, Z Khatami, S Chawda, J Pollock, E Marouf, N Stojanovic. The Royal London Hospital, Queens Hospital Romford and Woodlands Multispecialty Hospital Kolkata, India.

11.15 Case presentation: *Is antiplatelet therapy absolutely contraindicated in patients with a previous history of apoplexy?* D Joshi, J Milburn, A Abbara, R Ramli, A Comninou, A Mehta, B Jones, N Mendoza, N Hill, NM Martin, E Hatfield, A Sam, W Dhillon, K Meeran. Imperial College Healthcare NHS Trust, London.

11.30 *Cushing's disease – how to assess post-operative remission*  
Prof John Newell Price, Professor of Endocrinology, University of Sheffield.

12:00 Case presentation: *From non-functioning pituitary adenoma in adolescence to Cushing's disease in adulthood.* A Balasanthiran, E Hatfield, D Papadopoulou, A Mehta, B Jones, N Mendoza, N Martin, K Meeran. Imperial College Healthcare NHS Trust, London.

12:15 Case presentation: *A difficult case of Cushing's disease*. R Ramli, A Wren, D Papadopoulou, K Meeran, N Mendoza, E Hatfield, B Jones, A Mehta, NM Martin. Imperial College Healthcare NHS Trust, London and Chelsea and Westminster Hospital NHS Foundation Trust, London.

12.30 - 13.30 **LUNCH.**

### **SESSION 3 ADVANCES IN PITUITARY IMAGING.**

Chairs Dr Brynmor Jones (Consultant Neuroradiologist, Imperial College Healthcare NHS Trust, London) and Dr Gul Bano (Consultant Endocrinologist, St George's NHS Foundation Trust, London).

13.30 *Use of 11C-methionine PET in pituitary disease.*  
Dr Mark Gurnell, (Consultant Endocrinologist, University of Cambridge)

13.50 *Pituitary radiology for the non-radiologist*  
Dr Brynmor Jones (Consultant Neuroradiologist, Imperial College Healthcare NHS Trust, London).

14.10 Case presentation: *Detection of micro-thyrotropinoma with 11-C-Methionine PET-CT: switching the 'signal' on and off.* O Koulouri, A Steuwe, D Gillett, P English, D Halsall, N Antoun, A Hoole, H Cheow, N Burnet, M Gurnell. Addenbrooke's Hospital, Cambridge.

14.25 Case presentation: *The use of C-Methionine PET to identify a target for salvage surgery in acromegaly.* R Tan, B Whitelaw, T Hampton, G Vivan, S Aylwin. Kings College Hospital, London.

14.40 Case presentation. *An unusual case of a woman with prolactinoma and diabetes insipidus.* S Rafique, P Sathiskumar. Conquest Hospital, East Sussex Health Care Trust.

15.00 - 15.20 **BREAK.**

15:20 **LAPPS Joy Ginn.**

### **SESSION 4 THE PITUITARY AND NEURO-OPHTHALMOLOGY.**

Chairs: Dr Niamh Martin (Consultant Endocrinologist, Imperial College Healthcare NHS Trust, London) and Dr Paul Carroll (Consultant Endocrinologist, Guys and St Thomas', NHS Foundation Trust, London).

15.30 *Neuro-ophthalmology and the pituitary – what does one need to know?*  
Dr Alidz Pambakian, (Consultant Neurologist, Imperial College Healthcare NHS Trust, London).

15.50 Case presentation: *An interesting case of optic neuropathy.* I Ilesanmi, K Muralidhara. London North West Healthcare NHS Trust.

16.05 Case presentation: *Pituitary apoplexy complicated by a third nerve palsy – a mechanistic quandary?* D Joshi, A Abarra, R Ramli, A Comninos, J Milburn. S Clarke, A Mehta, B Jones, N Martin, E Hatfield, A Sam, W Dhillo, K Meeran. Imperial College Healthcare NHS Trust, London.

16.20 Case presentation: *Double trouble: dual endocrine pathology.* R Ramli, K. Steer, E. Hatfield, A Mehta, B Jones, N Mendoza, K Meeran, NM Martin. Imperial College Healthcare NHS Trust, London and London North West Healthcare NHS Trust.

16.40 **CLOSING REMARKS AND FEEDBACK**

*A challenging case of acromegaly complicated by heart failure.*

P Valsalakumari, S Mehta, R Ramli, B Jones, A Mehta, N Mendoza, M Williams, K Meeran NM Martin, E Hatfield  
Imperial College Healthcare NHS Trust, London and Ealing Hospital NHS Trust, London.

A 43 year old lady presented to her local hospital with a 2 month history of dyspnoea, weight gain and abdominal swelling. On admission she was noted to have features of acromegaly along with signs of congestive cardiac failure. She also gave a history of amenorrhoea for several months prior to the presentation and reported gradual deterioration of her vision. She had a past medical history of insulin-treated type 2 diabetes, hypertension and thyroidectomy for multinodular goitre. Investigations confirmed markedly elevated growth hormone (mean 94.2ug/l) and hypogonadotropic hypogonadism with a prolactin of 105mIU/l. Echocardiogram showed a severely dilated LV with significantly impaired global function (LVEF 25%). CT coronary angiogram and cardiac catheterisation studies demonstrated moderate stenosis in the mid LAD. MRI pituitary revealed a large pituitary macroadenoma compressing the optic chiasm and invading the right cavernous sinus. Formal visual field test results were unreliable. A diagnosis of acromegalic cardiomyopathy was made and she was started on monthly lanreotide autogel 120mg. She was referred to our centre for urgent neurosurgical review and to consider trans-sphenoidal surgery. Her case was discussed at our ICHNT Pituitary MDT meeting and a cardiology opinion obtained. It was felt that she was not suitable for general anaesthesia due to the high mortality risk associated with cardiac dysfunction. The plan was made to optimise heart failure medications, add cabergoline and up-titrate Lanreotide dose to 120mg every 3 weeks.

Further investigations showed mean growth hormone level of 26.4ug/l and IGF-1 68.5nmol/l. Despite increasing lanreotide dose and optimising heart failure treatment, she remained high risk for neurosurgery (LVEF 20%). At pituitary MDT review it was decided to proceed to pituitary radiotherapy and up-titrate the dose of lanreotide to 120mg weekly. Most recent results (6 weeks post completion of radiotherapy) show IGF-1 - 53.9nmol/l and growth hormone - 23.7ug/l. She remains on weekly lanreotide and cabergoline 500mcg.

Questions to the panel:

- 1) What other options shall we pursue to treat her acromegaly or should we simply wait for the radiotherapy to take effect?

*Old wine with a new label: Ipilimumab related hypophysitis.*

M Joshi, G Maltese, D Kariyawasam, A Velusamy, U-King-Im Jean Marie, PV Carroll.  
Guys and St Thomas's Hospital NHS Trust, London.

**Introduction:** The promising field of immunomodulatory cancer therapy has also seen the emergence of drug related hypophysitis, which was previously considered rare. We highlight two cases of ipilimumab related hypophysitis, during treatment for metastatic malignant melanoma.

**Case 1:** 82 year male, presented with 3 week history of severe fatigue & dizziness after receiving third cycle of ipilimumab for metastatic malignant melanoma. Investigations revealed cortisol 44 nmol/L, TSH 0.04 U/L, free T4 6.5 pmol/L, free T3 2.7 pmol/L, FSH 1.6, LH 0.3 U/L, testosterone 0.8 nmol/L, Na 120 mmol/L. MRI revealed right- sided soft tissue mass in the pituitary fossa, with hypo enhancing areas, likely to be adenoma and/or hypophysitis. Ipilimumab was stopped and he was started on started on hydrocortisone and levothyroxine replacement. Interestingly he also developed autoimmune thyrotoxicosis in March 2015. A repeat imaging in May 2015 showed an additional poorly enhancing cleft like tissue on left side of the gland, which could have been possible superimposed resolving hypophysitis.

**Case 2:** 58 year female, presented with headaches, fatigue of two weeks duration while being treated for metastatic melanoma. She had completed a 12 m duration of vemurafenib and was started on ipilimumab two months prior to presentation. Biochemistry revealed cortisol 18 nmol/L. TSH was 0.04 mU/L, T3 11.5, T4 28.2, LH 0.6 U/L, FSH 2.6 U/L, Oestradiol <44. She was started on hydrocortisone replacement. MRI Pituitary imaging in November 2014 demonstrated a pituitary based mass measuring 1.2x1.3x1.2cm, which was no longer evident on a follow up imaging on 20 March 2015 (following discontinuation of ipilimumab). Biochemistry showed some recovery of the gonadotrophin and thyroid axis, with persistent adrenal insufficiency.

**Learning points:** Endocrine dysfunction seen with the use of novel immune checkpoint inhibitors (including ipilimumab) used in cancer therapy is increasingly reported. Endocrinologists must be aware of the presentations and treatment of drug induced hypophysitis. The pattern of pituitary insufficiency & recovery seen with these agents may differ from non-drug induced hypophysitis.

**References:** 1. Faje et al , Ipilimumab related hypophysitis: a detailed longitudinal analysis in a large cohort of patients with metastatic melanoma. JCEM 2014;99(11):4078-85

*Factors predisposing to pituitary apoplexy: A tertiary centre's clinical experience.*

J Milburn, A Abbara, D Joshi, S Clarke, R Ramli, A Comminos, A Mehta, B Jones, R Nair, N Mendoza, NM Martin, E Hatfield, A Sam, W Dhillo, K Meeran  
Imperial College Healthcare NHS Trust, London.

**Abstract:**

Pituitary apoplexy is a rare clinical syndrome characterised by sudden onset headache as a result of haemorrhage and/or infarction into the pituitary gland, which may be accompanied by neuro-ophthalmic and hormonal deficits. Pituitary apoplexy may occur in 2-7% of patients with pituitary adenomas, often as a first presentation. A number of factors are thought to predispose to pituitary apoplexy including hypertension, coronary bypass surgery, anticoagulant use, oestrogen therapy, dopamine agonists, pregnancy, dynamic pituitary testing and head trauma. We reviewed our experience of pituitary apoplexy at Imperial College NHS Trust to identify how frequently predisposing factors to pituitary apoplexy were evident.

**Methods:**

Medical records of patients diagnosed with pituitary apoplexy at Imperial College NHS trust within the last 20 years were reviewed and putative predisposing factors recorded.

**Results:**

Sixty four patients with pituitary apoplexy were identified. The mean age of patients at diagnosis was 46 years, with a slight female preponderance 52% (33/64). Pituitary apoplexy was the first presentation in 73% (47/64) of patients. The majority of cases occurred in patients with non-functioning adenomas 75% (46/61) and in macroadenomas 88% (52/59). In half of patients (31/62) no cranial nerve abnormality was recorded; 31% (19/62) had cranial nerve 2 (CN2), 21% (13/62) CN3, and 13% (8/62) CN6 involvement.

A potential predisposing factor was identified in 44% (28/63) of patients. Nine percent (6/64) of patients were on antiplatelet agents such as aspirin or clopidogrel and 6% (4/64) of patients were on anticoagulants such as warfarin or heparin. More than a quarter of patients (17/61) had a diagnosis of hypertension. Almost a quarter of women (8/33) were diagnosed with apoplexy either during late pregnancy or puerperal period.

**Conclusion:**

This relatively large series of patients with pituitary apoplexy confirms that the majority of patients with pituitary apoplexy are diagnosed as a first presentation of a non-functioning pituitary macroadenoma and that hypertension, pregnancy and anticoagulant use are frequently observed predisposing factors.

*A novel surgical approach for the management of giant invasive prolactinoma compressing the brainstem*

N Margari, M: Vidyarthi, Z Khatami, S Chawda, J Pollock, E Marouf, N Stojanovic.

The Royal London Hospital, Queens Hospital Romford and Woodlands Multispecialty Hospital Kolkata, India.

**Abstract:**

**Introduction:** Prolactinomas constitute the largest subsection of all secretory pituitary adenomas. Most are microprolactinomas and are satisfactorily treated by medical management alone. Giant prolactinomas, measuring greater than 4 cm in diameter, are rare and usually occur more commonly in men. Dopamine agonists (DA) are the treatment of choice for all prolactinomas. Surgery is usually reserved for DA resistance or if vision is threatened by the mass effect of the tumour.

**Case report:** We describe the case of a 52 year-old woman with a giant invasive prolactinoma who required multiple surgical procedures. She was referred to the ophthalmology clinic with suspected thyroid eye disease. She gave a six-month history of feeling generally unwell and proptosis of the left eye with reduced vision. On examination she had left sided proptosis and ophthalmoplegia. Thyroid function tests revealed a TSH of 4.2 mU/L (range 0.5-5.5) and FT4 of 6.7 pmol/L (range 10-19.8). Pituitary function tests were requested urgently as TSH was disproportionately low relative to free T4. These were in keeping with hypopituitarism with prolactin grossly elevated at >500,000U/L (normal range 38-430). The patient did not report any galactorrhoea. She had become amenorrhoeic at the age of 42, which was attributed to menopause. Hypothyroidism was diagnosed three years before presentation, for which she was taking Levothyroxine 50 mcg once daily. Imaging demonstrated a large destructive mass of greater than 6 cm in maximum diameter centred on the sella and involving multiple compartments at the skull base. The tumour was compressing the brainstem and also extending into the left parasellar region to encase the left carotid. It also extended upwards to compress the optic chiasm and invade the left orbit along the superior oblique muscle and the optic nerve. She was commenced on Cabergoline and a replacement dose of hydrocortisone. A week later, she collapsed on the ward with a Glasgow Coma Scale of 7. An urgent computed tomography scan of the brain suggested minor haemorrhage within the tumour and acute hydrocephalus, which required emergency transsphenoidal debulking. The posterior portion of the tumour was not treated operatively at this stage in the expectation of future shrinkage with Cabergoline therapy. She required prolonged neurorehabilitation but made good progress and was discharged home. Three months later she presented again with sudden onset of tetraparesis, dyspnoea, slurred speech and pooling of saliva within the mouth. Imaging showed evidence of tumour apoplexy within the portion of tumour adjacent to the brainstem where there was now increased mass effect causing significant compression of the brainstem. Urgent debulking of the posterior portion of the tumour was indicated. This was done through a posterior approach via the suboccipital transtentorial route to safely access the large posterior fossa component of the tumour. Recovery was slow but uncomplicated. Treatment with Cabergoline was continued throughout. Imaging conducted six months later demonstrated a further decrease in the size of the tumour. The patient remained on Cabergoline 1 mg twice per week for a year after the initial presentation. At that time deterioration in visual acuity was noticed in the left eye, which was a result of further tumour expansion in the orbit. The dose of Cabergoline was increased to 1 mg daily with visual acuity returning to baseline as a result.

**Discussion:** This case highlights the importance of a multidisciplinary approach involving endocrinologists, biochemists, neuroradiologists and neurosurgeons to the management of such patients who present with florid neurological sequelae secondary to pressure effects. Although this presentation is uncommon, surgery via a suboccipital transtentorial approach may be considered the treatment of choice in suitable patients with giant invasive prolactinoma compressing the brainstem.

**Questions:**

- 1) What is the initial treatment for macroprolactinomas?
- 2) When would you consider surgery for macroprolactinomas?

*Is antiplatelet therapy absolutely contraindicated in patients with a previous history of apoplexy?*

D Joshi, J Milburn, A Abbara, R Ramli, A Comninou, A Mehta, B Jones, N Mendoza, N Hill, NM Martin, E Hatfield, A Sam, W Dhillon, K Meeran.  
Imperial College Healthcare NHS Trust, London.

**Case Presentation:**

An 88-year-old male was referred to the Stroke team at Charing Cross Hospital by his GP following a severe sudden onset headache, dizziness, blurred vision and confusion which started 4 days prior to seeking medical attention. His relevant medical background included a stable non-functioning pituitary macroadenoma, hypertension and hypercholesterolaemia. Two months prior to presentation he had been started on clopidogrel and aspirin for a transient ischaemic attack, with a subsequent carotid endarterectomy being performed for a 90 percent stenosis. On examination, the only significant finding was a complete left sided third nerve palsy with complete ptosis and a fixed, dilated left pupil. Blood tests revealed: sodium 120 mmol/L (133-145), thyroid stimulating hormone 0.76 mU/L (0.3-4.2), thyroxine 8.5 pmol/L (9-26), random cortisol 136 nmol/L, insulin-like growth factor-1 4.3 nmol/L (13-64), luteinising hormone <0.5 IU/L, testosterone 0.5 nmol/L and prolactin 809 mIU/L (125-625). Magnetic resonance imaging showed evidence of haemorrhage into the pituitary gland. In keeping with the history of sudden onset headache, neuro-ophthalmic signs on examination and findings on MR imaging, he was diagnosed with pituitary apoplexy. In view of this diagnosis, his antiplatelet therapies were suspended. His case was discussed in the pituitary multidisciplinary team meeting, and expectant management was recommended, unless further deterioration in his symptoms were to occur.

**Discussion:**

Anticoagulant use has been recognised as a predisposing factor for pituitary apoplexy. The incidence of pituitary apoplexy increases with advancing age, as does the incidence of medical conditions requiring antiplatelet therapies such as cerebro- and cardio-vascular disease. The occurrence of pituitary apoplexy soon after starting antiplatelet therapy following many years of stable pituitary disease indicates that this may have been a predisposing factor in this gentleman.

**Question for the expert panel:**

Would the expert panel recommend recommencement of his antiplatelet therapy following initial resolution of his symptoms, or would this now be contraindicated?



*From non-functioning pituitary adenoma in adolescence to Cushing's disease in adulthood.*

A Balasanthiran, E Hatfield, D Papadopoulou, A Mehta, B Jones, N Mendoza, N Martin, K Meeran.  
Imperial College Healthcare NHS Trust, London.

A 16 year old male was referred to our department for evaluation of short stature (height 144.5cm). Genital examination revealed Tanner stage III pubic hair and a 3cm penile length. Pituitary MRI demonstrated a pituitary macroadenoma with optic chiasmal displacement. Dynamic testing was undertaken: GnRH testing confirmed secondary hypogonadism and a glucagon stimulation test demonstrated a suboptimal growth hormone response. An overnight dexamethasone suppression test showed adequate suppression of cortisol.

Following discussion at the pituitary MDT and with the patient and family, a conservative approach towards management was adopted. Six-monthly visual fields and yearly MRI pituitary scans were organised alongside joint paediatric follow-up.

Several years after presentation, a repeat pituitary MDT noted a reduction in the size of the pituitary lesion, possibly related to haemorrhage. Bone age at this stage (aged 19 years) was '16' and radial and ulnar epiphyses had not yet fused. A testosterone-primed glucagon stress test showed an inadequate growth hormone response (peak of 0.75mcg/L). Growth hormone, testosterone and gonadotrophin replacement were undertaken in close co-ordination with the paediatric endocrinologists.

Eight years after presentation, the patient was noted to be clinically Cushingoid and this was confirmed biochemically. Inferior pituitary sinus sampling excluded an ectopic source of ACTH. The (now) small pituitary adenoma was the presumed source of ACTH and the patient was therefore referred for surgery and commenced on metyrapone therapy. Postoperatively, histology revealed a corticotroph adenoma. A post-operative cortisol day curve demonstrated persistent hypercortisolism (mean day curve cortisol 332 nmol/L). Following extensive multidisciplinary team discussion, a second procedure was undertaken. Following this, there was symptomatic improvement with weight loss and resolving striae. Histology following this procedure showed reactive changes with no evidence of adenoma. Mean day curve cortisol was 280nmol/L following this second surgery. The patient remains under close surveillance.

Questions:

Do the audience feel that this original presentation was due to a silent corticotroph adenoma?

What would be an appropriate follow-up strategy?

*A difficult case of Cushing's disease.*

R Ramli, A Wren, D Papadopoulou, K Meeran, N Mendoza, E Hatfield, B Jones, A Mehta, NM Martin. Imperial College Healthcare NHS Trust, London and Chelsea and Westminster Hospital NHS Foundation Trust, London.

A 29-year-old lady presented with features of Cushing's syndrome in October 2014. 24-hour urinary cortisol collections were elevated and a Low-Dose Dexamethasone Suppression Test (LDDST) confirmed ACTH-dependent Cushing's syndrome. MRI Pituitary showed a 4.5 mm right-sided pituitary adenoma and IPSS excluded an ectopic source of ACTH. She was commenced on metyrapone and underwent trans-sphenoidal pituitary surgery in January 2015. Histology confirmed a corticotroph adenoma with a Ki-67 index of 1%. Day 4, 5 and 11 post-operative cortisol levels were 215, 226 and 620 nmol/L respectively. A cortisol day curve 3 weeks post-surgery showed a mean cortisol of 298 nmol/L (0900 323 nmol/L, 1200 281 nmol/L, 1500 220 nmol/L, 1800 368 nmol/L) and a post-operative MRI pituitary scan showed possible small residual tumour in the right anterior sella. As she continued to feel unwell with ongoing headaches and leg swelling, she underwent a second trans-sphenoidal pituitary surgery in April 2015. Histology from this surgery showed normal adenohypophysis. The second surgery was complicated with a post-operative CSF leak and meningitis, which was treated surgically and a 2-week course of intravenous antibiotics. Although the patient reported improvement in her clinical symptoms and there was resolution of her hypertension, a cortisol day curve 6 weeks after her second surgery showed a mean cortisol level of 474 nmol/L (0900 475 nmol/L, 1200 479 nmol/L, 1500 560 nmol/L, 1800 371 nmol/L). Further investigations showed a raised sleeping midnight cortisol of 402 nmol/L and failure to suppress cortisol on an LDDST (T = 0 cortisol 449 nmol/L, T = 48 442 nmol/L; T = 0 ACTH 52.5 ng/L). Her case was discussed in a tertiary pituitary multi-disciplinary meeting and treatment options including bilateral adrenalectomy or pituitary radiotherapy were considered. She has been recommenced on metyrapone pending further intervention.

Questions to the panel:

1. Is this lady in remission from her Cushing's syndrome?
2. Does she need further intervention now or can we watch and wait?
3. What would be the preferred treatment option for this 29-year-old lady who is currently not in a relationship but who would like to consider pregnancy in the future?

*Detection of micro-thyrotropinoma with 11-C-Methionine PET-CT: switching the 'signal' on and off.*

O Koulouri, A Steuwe, D Gillett, P English, D Halsall, N Antoun, A Hoole, H Cheow, N Burnet, M Gurnell. Addenbrooke's Hospital, Cambridge

A 75-year-old woman presented with tiredness, palpitations and increasing size of a known multinodular goitre. She was found to have hyperthyroxinaemia with non-suppressed TSH (TSH 6.3 mU/L, FT4 89.1 pmol/L, FT3 11.7 pmol/L). Assay interference was excluded and a TRH stimulation test showed a flat TSH response (TSH 0' 6.1 mU/L, TSH 20' 6.8 mU/L, TSH 60' 8.5 mU/L), raising the suspicion of TSHoma. Pituitary MRI was originally reported as normal, but when repeated was suspicious for a right sided 4 mm microadenoma. <sup>11</sup>C-Methionine PET-CT showed a right sided 'hot' spot.

Long-acting somatostatin analogue (SSA) therapy led to complete TSH suppression after three injections (TSH 0.03 mU/L, FT4 39.5 pmol/L, FT3 7.2 pmol/L), however FT4 dropped unusually slowly from an initial concentration of 71.2 pmol/l to a nadir of 13 pmol/l twelve months later. Repeat PET six months after presentation (TSH 0.03 mU/L, FT4 36.4 pmol/L, FT3 6.8 pmol/L), showed absence of the initially discovered right sided hot spot, indirectly confirming that this was the site of excess TSH production.

One year after starting medical therapy, she developed hypoglycaemic episodes, which resolved after discontinuation of SSA. Recurrence of thyrotoxicosis was observed and repeat PET identified once again a 'hot' spot in the right sella. The diagnosis of a right sided microTSHoma was firmly established and this allowed referral for pituitary surgery.

*The use of C-Methionine PET to identify a target for salvage surgery in acromegaly.*  
R Tan, B Whitelaw, T Hampton, G Vivan, S Aylwin.  
Kings College Hospital, London. .

A 51 year old male presented with sudden onset severe headache. CT brain scan identified a pituitary mass without radiological evidence of acute haemorrhage. Visual acuity and fields were normal and there was no evidence of ophthalmoplegia. He was treated for suspected pituitary apoplexy with IV fluids and hydrocortisone. Initial pituitary function testing revealed a raised prolactin of 5758 mIU/L (100-410) and IGF-1 of 86.3 nmol/L (11.5-27.3). The patient was commenced on cabergoline.

Subsequent endocrine review revealed a 2 year history of symptoms consistent with acromegaly, including increase in hand and shoe size; coarsening of features and excessive sweating. Acromegaly was confirmed with an oral glucose tolerance test (OGTT) showing a paradoxical rise in growth hormone (19.5 mcg/L). The patient showed poor suppression of GH with a test dose of 100mcg octreotide, GH fell from 16.4mcg/L to nadir of 9.7mcg/L. Cabergoline was increased to maximal tolerated dose of 0.5mcg daily. A repeat interval MRI pituitary scan performed at 6 months demonstrated significant reduction in tumour size, however there was inadequate biochemical control of the acromegaly with IGF-1 and GH remaining significantly elevated.

The patient proceeded to endoscopic trans-sphenoidal surgery (TSS) which was uncomplicated. Histology demonstrated a pituitary adenoma (Ki67 4%), with immunohistochemistry showing strong staining for both prolactin and GH.

The patient noticed initial clinical improvement post TSS but follow-up at 4 months post TSS identified a persistently elevated GH (3.57mcg/L) and IGF-1 (86.3 nmol/L) and the patient noted return of headaches, snoring and sweating. No obvious residual tumour target was identified on review of post-op MRI pituitary imaging. The patient was referred for C-methionine PET scan to further evaluate for a target amenable to surgery. In the interim, he was started on Pegvisomant therapy.

C-Methionine PET revealed metabolic uptake on the left of the sphenoid sinus which the neurosurgeons were able to target with redo TSS. Review of biochemistry at 3 months post redo-TSS revealed near normal IGF-1 (28.5 nmol/L), nadir GH 0.81 mcg/L. The patient remains in remission, clinically well, off pegvisomant.

The case demonstrates C-Methionine PET can help detect a suitable surgical target for salvage surgery in patients with acromegaly in whom biochemical control has not been achieved with initial TSS.

*An unusual case of a woman with prolactinoma and diabetes insipidus.*

S Rafique, P Sathiskumar.

Conquest Hospital, East Sussex Health Care Trust

38 year old lady had a past history microprolactinoma (8mm) in 2010. She took bromocriptine and there was decrease in size of the tumour as per the MRI done in 2013. She stopped the medication when she became pregnant with her second child. Few days prior to delivery she developed transient right eye temporal visual impairment. 2<sup>nd</sup> day post delivery, she developed polyuria and polydipsia upto 11L. Her serum osmolality was 290 with a paired urine osmolality of 106, suggestive of diabetes insipidus. Her anterior pituitary hormone profile, except prolactin which was 5703, was otherwise normal including a short synacthen test. Visual fields were normal.

MRI pituitary showed 20x16mm low signal mass in sella just impinging optic chiasm suggestive of pituitary macroadenoma. She was started on 200 mcg desmopressin and cabergoline 500mcg weekly. Repeat MRI 2 months later showed significant decrease in size of the pituitary adenoma. A discussion with neuroradiologists, suggested thickening of pituitary stalk and a suggestion of hypophysitis. She is now 6 months post partum and asymptomatic, but still needs 200mcg desmopressin. Her prolactin is 476 on 750mcg weekly cabergoline. All other anterior pituitary hormones are normal and short synacthen test was negative repeated twice.

Our conclusion was that she had a microprolactinoma which enlarged in pregnancy to macroprolactinoma and which subsequently reduced in size with cessation of pregnancy and cabergoline. The diabetes insipidus which has persisted in spite of regression in size of pituitary tumor may be due to hypophysitis often seen post partum period.

The unusual learning point is that it presented with isolated diabetes insipidus, with normal ACTH and TSH. The other learning point is the importance of following up women with pituitary tumours in pregnancy.

Case presentation: *An interesting case of optic neuropathy.*  
I Ilesanmi, K Muralidhara.  
London North West Healthcare NHS Trust.

A 41 year old man originally from Afghanistan presented to the community ophthalmologist with reduced vision for a year. He worked as a cleaner in a bakery and managed to attend work prior to his clinic appointment. He gave a history of intermittent headaches but no vomiting, increased sweating, change in shoe size or shaving frequency.

On examination his visual acuity was counting fingers. He had brisk pupil response with no RAPD. There was bilateral pale optic discs hence this prompted a referral to the hospital. On further review, due to profound visual loss and pale optic discs, a provisional diagnosis of optic neuritis/neuropathy was made and an MRI orbit was booked along with optic neuropathy screen. His MRI showed a 5cm mass arising from the pituitary fossa with suprasellar extension and impingement on the optic chiasm. A referral to the Endocrine Team was made at this point.

He did not have any clinical features of pituitary hormone excess. His visual acuity was only finger counting with absent peripheral vision on confrontation. Not surprisingly, standard automated perimetry (Humphrey) showed severe constriction of the visual field.

His blood results showed a low prolactin at 28mIU/l, which did not change on dilution ruling out a 'hook effect'. His FT4 and T3 were 7.8 pmol/L and 2.8 pmol/L respectively with a TSH of 2.09 mIU/L. LH (2.1 IU/L) and FSH (4.2 IU/L) were within the normal range but testosterone was low 1.9. IGF-1 was low at 11.1 but cortisol was normal at 355. Urea and electrolyte, renal function and liver function were within the normal range.

He was discussed at the Pituitary MDT and an urgent referral to the surgeons was made. He underwent surgery on the 27/8/15 and remains well on Levothyroxine 50 micrograms daily. He will have regular neuro-ophthalmological evaluation for assessment of recovery of visual field.

In summary this is a young man who presents with a chiasmal syndrome with profound visual loss secondary to a large pituitary tumour. The late presentation may have resulted in an irrecoverable loss of visual field

*Pituitary apoplexy complicated by a third nerve palsy – a mechanistic quandary?*

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**Case History:**

A 29 year old lady was referred to Charing Cross hospital Accident and Emergency department from Moorfields' Eye hospital following a severe sudden onset occipital headache associated with acute onset ptosis and anisocoria. On examination she was haemodynamically stable and her visual fields, visual acuity and eye movements were uncompromised. However a left sided partial ptosis and left sided mydriasis consistent with an incomplete surgical third nerve palsy was evident.

She was reviewed by the neurosurgical team and a CT brain was arranged, which demonstrated high attenuation within the pituitary fossa in keeping with a diagnosis of pituitary apoplexy. An MR angiogram excluded a posterior communicating artery aneurysm and an MRI pituitary presented further confirmation of acute haemorrhage into the pituitary gland. She was treated supportively with parenteral corticosteroid cover for 24hours and close monitoring.

She was reviewed by the endocrinology team and no evidence of pituitary hormone insufficiency was detected. Blood results included: sodium 138 mmol/L (133-145), 9am cortisol 294 nmol/l, IGF-1 24.3 nmo/L (13.0-64.0), random growth hormone 1.15 mcg/L, oestradiol 178 pmol/L, FSH 1.15 iU/L, prolactin 488 mU/L (125-625), TSH 1.4 mU/L (0.3-4.2), fT4 11.5 pmol/L (9-26). Following partial improvement in her ptosis over the next 24 hours, she was discharged with outpatient follow up.

An MRI pituitary was performed six months later and a focal signal change within the posterior aspect of the pituitary gland was again noted in keeping with persisting intralesional haemorrhage within a pituitary microadenoma.

**Discussion:**

This lady presented with a clinical syndrome consistent with pituitary apoplexy resulting in a left surgical third nerve palsy. Review of her pituitary imaging demonstrated only small amount of bleeding within a microadenoma.

**Questions for discussion:**

What could the mechanism for the left sided surgical partial third nerve palsy given the relatively small amount of haemorrhage within the pituitary gland?

*Double trouble: dual endocrine pathology.*

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### **Case History**

A 39-year-old gentleman presented with features of thyrotoxicosis and was diagnosed with Graves' disease in 2014. He was initially commenced on Carbimazole, which he did not tolerate and was consequently given Propylthiouracil (PTU). Despite high doses of anti-thyroid medication for 18 months, he remained biochemically and clinically hyperthyroid. A thyroidectomy was planned as definitive treatment for his Graves' disease. Four days before his planned thyroidectomy, he developed double vision and was referred for urgent review by Neurosurgery at our centre. . On further questioning, he reported a 12-month history of lethargy and low libido. On examination, he had right 6<sup>th</sup> cranial nerve palsy and a partial right ptosis. A pituitary MRI showed a large suprasellar lesion with right cavernous sinus involvement. Biochemistry showed prolactin 37,384 mU/L (macroprolactin negative), testosterone 1.6 nmol/L, LH 1.5 IU/L, FSH 1.7 IU/L, T4 16.4 nmol/L, T3 7.2 nmol/L, TSH <0.01 mU/L, a morning cortisol 53 nmol/L and IGF-1 23.2 nmol/L (13-50 nmol/L). His case was discussed at the ICHNT Pituitary MDT meeting. His thyroidectomy was cancelled and he commenced cabergoline 0.5 mg/ week and hydrocortisone replacement. Serum prolactin fell quickly to 5456 mU/L after one dose of Cabergoline 0.5mg. Both the right-sided ptosis and 6<sup>th</sup> nerve palsy resolved. He demonstrated aggression and anger at out-patient review such that there were concerns regarding a further increase in cabergoline dose.

With regards to his thyroid dysfunction, TSH receptor antibody level was raised at 2.1 u/ml (reference range 0-0.3) with a persistently elevated fT3 and undetectable TSH. He elected for radioactive iodine treatment rather than thyroidectomy as a definitive cure for his Graves' disease. Nine weeks following radioactive iodine, he commenced thyroxine replacement consistent with our protocol (fT4 9.3 nmol/L). His TSH remains undetectable.

### **Question for discussion:**

1. Should he be offered pituitary surgery if his anger and aggression becomes such that he can no longer take dopamine agonists?