



**Programme**

**&**

**Abstract Book**

## Programme

- 8:30           **Registration and Coffee**
- 9:25           **Welcome and Introduction**  
Mr M Powell & Dr G Conway
- 9:30           Two Cases
- Case 1: Case report of recurrent and malignant pituitary tumour  
                  S Sivappriyan, G Conway, S Baldeweg  
                  University College London Hospitals NHS Trust, London
- Case 2: Pituitary B-Cell Lymphoma Presenting as Horner's  
                  Syndrome  
                  P Grant, J Crane, N Thomas, R Marcus & S Aylwin
- 9:55           **Keynote lecture:**  
Aggressive Pituitary Tumours  
Professor Ashley Grossman  
Queen Mary, University of London, London
- 10:45          **Forum 1: Aggressive prolactinomas**  
**Chairs: Dr SE Baldeweg & Mr M Powell**
- Case 3: A complex case of recurrent Cushing's Disease  
                  HS Chahal, I Sabin, J Evanson, AB Grossman  
                  St. Bartholomew's Hospital, London
- Case 4: Temozolamide chemotherapy in an aggressive  
                  treatment-resistant prolactinoma  
                  L Srikugan, P Carroll & S Thomas  
                  Guy's & St Thomas' NHS Trust, London
- Case 5: Management Options for Aggressive Prolactinoma  
                  Resistant to Dopamine Agonists  
                  Lina Chong, Southampton General Hospital, Southampton
- Case 6: The clinical course of a patient with giant invasive  
                  prolactinoma : the need for multidisciplinary management  
                  M Vidyarthi, K Gungunah, E Marouf, Z Khatami, S Chawda, J  
                  Pollock and ND Stojanovic  
                  Queen's Hospital, Romford
- 11:35          **Coffee and Posters**
- 12:00          **Pituitary Foundation**  
Kit Ashley, Director
- 12:10          **Forum 2: A variety of pituitary cases**  
**Chairs: Dr G Conway & Miss J Grieve**

Case 7: Acromegaly Of Unexpected Origin  
P Sen Gupta, A A Roy, D M Berney, M Korbonits, A B Grossman  
St Bartholomew's Hospital, London

Case 8: Hypertrophic Pachymeningitis and Pituitary Pathology:  
Lymphocytic Hypophysitis or Cabergoline related Fibrosis?  
R Raghavan, E Mallam, N J Scolding, K J Bradley  
Bristol Royal Infirmary & Frenchay Hospital, Bristol

Case 9: Pituitary tumour causing thyrotoxicosis - or not?  
Whether to operate ...  
S Narayanaswamy & J Ahlquist  
Southend Hospital, Westcliff on Sea

Case 10: Difficulties in Management of Hypercortisolism  
FW Ahmed, D Sennik, J Wright, V Hordern, N Mendoza, F  
Roncaroli, A Mehta, K Meeran & D Russell-Jones  
Royal Surrey County Hospital & Hammersmith Hospital

13:00 **Lunch and Posters**

14:00 **A variety of pituitary cases**  
**Chairs: Dr M Vanderpump & Dr J Ahlquist**

Case 11: A complex case of recurrent Cushing's Disease  
HS Chahal, I Sabin, J Evanson, AB Grossman  
St. Bartholomew's Hospital, London

Case 12: Dilemmas in managing an aggressive non-functioning  
pituitary tumour  
H Courtney

Case 13: A difficult case of locally aggressive acromegaly  
K Vithian, J Kisalu, N Dorward, P M Bouloux  
Mid Essex Hospital NHS Trust & Royal Free Hospital

14:40 What's new in radiotherapy for pituitary tumours  
Dr Naomi Fersht, University College London Hospital, London

15:10 **Afternoon tea and Posters**

15:30 Three cases

Case 14: Hypophyseal Wegener's granulomatosis presenting  
with visual field constriction without pituitary dysfunction.  
P Plaha, E A C Pereira, M Hofer, O Ansorge, J Wass, S A Cudlip  
John Radcliffe Hospital & Churchill Hospital, Oxford

Case 15: The dilemmas of an endocrinologist  
L Srikugan, J Powrie  
Guy's & St Thomas' NHS Trust, London

Case 16: A change for the worse when thirst is not enough  
G Rayanagoudar, A Nicklin, B Hashim, J Thomas, SR Peacey, A  
Grossman

- 16:10      **Chairs: Mr M Powell & Miss Grieve**  
**Keynote Lecture**  
Endoscopic Pituitary Surgery: The Toronto and global  
experience  
Professor Fred Gentilli, Toronto, Canada
- 16:50      **Poster and presentation prizes**  
**Dr G Conway**
- 17:00      **Close**

## **Case 1: Case report of recurrent and malignant pituitary tumour**

**Author (s): Dr Siva Sivappriyan, Dr Gerard Conway, Dr Stephanie Baldeweg  
University College London Hospitals NHS Trust, London**

We would like to present one of our complicated Cushing's disease patients who had a rather malignant course of the disease with multiple recurrences and metastasis which posed a management challenge to our multidisciplinary team.

GB, 45 year old lady of Nigerian origin was initially diagnosed with pituitary dependant Cushing's disease in 1982 at the age of 18 years following investigations for amenorrhoea & weight gain. She also had bitemporal hemianopia and CT scan showed large pituitary macroadenoma with suprasellar extension and optic nerve involvement. She was treated with transfrontal hypophysectomy at the age of 18.

Over the next 20 years she further had several recurrences of her Cushing's disease clinically and bio- chemically including one pituitary apoplexy. This was treated with four further transphenoidal pituitary surgeries at different times. She also received pituitary radiotherapy, Photodynamic therapy and two gamma knife radiotherapy.

She further had bilateral adrenalectomy in 2003 following which she had recurrences of Nelson syndrome which was treated with pituitary surgeries and repeated chemotherapy. She also received gamma knife irradiation for her spinal metastases. She also developed hypopituitarism, corneal ulcer due to nerve damage as consequences of these.

Last year her tumour recurred again with extension into the prepontine space and severe invagination on pons. This was treated with another transphenoidal surgery. But unfortunately during the post op period she developed meningitis and pneumocephalus and despite the multi team intervention she eventually passed away.

Salient features of this case

1. Several recurrences of the disease
2. Resistant to the conventional therapy for the standard therapy

## **Case 2: Pituitary B-Cell Lymphoma Presenting as Horner's Syndrome**

**Author(s): Paul Grant, James Crane, Nick Thomas, Robert Marcus & Simon Aylwin**

### Case History:

A 73 year old previously well female presented with a 2 week history of fronto-occipital headaches, associated with visual disturbance, diplopia and a complete ptosis of the left eye.

Examination revealed a complete 3rd nerve palsy on the left hand side, other cranial nerves were intact and there was no visual field defect. We thought that her presentation may represent subacute apoplexy.

### Investigations:

Biochemistry was normal except for a moderately elevated ESR and gonadotrophin deficiency, with an otherwise normal baseline pituitary profile. An MRI of the brain did not reveal any haemorrhage but did show a sellar / suprasellar mass extending into the cavernous sinus and encircling the left carotid artery.

### Treatment:

The patient underwent transphenoidal hypophysectomy and she recovered well post operatively. The vision remained normal but there was no improvement in the 3rd nerve palsy. Post op Cortisol was normal and the patient was prescribed prn Hydrocortisone. The patient was discharged at day 5.

Her pituitary histology results were subsequently reviewed and this surprisingly showed diffuse, large B-cell lymphoma. Immunocytochemistry showed tumour cells positive for CD20, bcl2 and p53.

She re-presented with headaches and dizziness 12 days post operatively and was re-admitted. She was found to have hyponatraemia and her osmolalities and clinical picture were consistent with mild SIADH which responded to fluid restriction.

She was subsequently seen by the Haematologists who arranged a whole body CT scan and a bone marrow aspirate – this showed marrow involvement with non-Hodgkin's lymphoma. She was counselled and commenced on R-CHOP chemotherapy with intra-thecal methotrexate. Once her sodium levels were normalised she was discharged home and received the rest of her chemotherapy on an out-patient basis.

### Discussion:

The causes of a 3rd nerve palsy in this context would include pituitary adenoma, pituitary apoplexy, meningioma, craniopharyngioma and metastatic carcinoma. The key message is that a 3rd nerve palsy means something odd. Our patient had a deposit from a diffuse large B cell lymphoma. CNS lymphoma in the pituitary is rare. It accounts for less than 3% of all brain tumours. Most are diffuse large B cell lymphomas. Primary disease of the pituitary is extremely rare and constitutes only 3% of all CNS lymphomas. The hypothetical risk factors are; HIV/AIDS, Pituitary adenomas and lymphocytic hypophysitis.

### **Case 3: A complex case of recurrent Cushing's Disease**

**Author(s): HS Chahal<sup>1</sup>, I Sabin<sup>2</sup>, J Evanson<sup>3</sup>, AB Grossman<sup>1</sup>**

**<sup>1</sup>Department of Endocrinology, <sup>2</sup>Department of Neurosurgery, <sup>3</sup>Department of Neuroradiology, St. Bartholomew's Hospital, London**

We report a case of a female patient who presented aged 41 years with classical features of Cushing's syndrome due to a pituitary corticotroph microadenoma. She underwent transsphenoidal surgery with a significant improvement in the overall cortisol burden, but not an absolute cure (serum cortisol <50nmol/L at 09.00h). Two years later she underwent external beam radiotherapy. Over the next 10 years periodic cortisol day-curves (mean of 5 levels) demonstrated satisfactory control. However, 12 years after the original operation she complained of weight gain and hirsutism, and clinically had Cushingoid features with hypertension and type 2 diabetes. Her biochemistry showed a lack of diurnal cortisol variation and failure of cortisol suppression on the low-dose dexamethasone suppression test (2+48 serum cortisol 110nmol/L). A MRI demonstrated residual normal appearing pituitary, but no definitive adenoma. Medical therapy was commenced with ketoconazole, but she developed ketoconazole-induced hepatitis which required cessation of therapy. Due to the excess cortisol burden, intolerance to ketoconazole and the likelihood that long term metyrapone would increase the androgen burden, she underwent bilateral adrenalectomy at the age of 56 years; 5 years post-adrenalectomy she had marked skin hyperpigmentation and her plasma ACTH was elevated at 1024ng/L with an MRI showing a 4.9mm adenoma. Currently, aged 63 years (7 years post-adrenalectomy), her plasma ACTH level has increased to 1790 ng/L, with an MRI showing an increase in size of her residual tumour to 7.8mm; she remains on thyroxine, hydrocortisone and fludrocortisone replacement.

In summary, we present a 63 years old female patient with recurrent Cushing's disease who has had transsphenoidal surgery, external beam radiotherapy and bilateral adrenalectomy. We would like to ask the panel: 1) whether they would now consider further surgery or radiotherapy, radio-surgery, or simply follow-up with regular MRI; 2) should a bilateral adrenalectomy have been performed or would the panel have opted for long-term metyrapone treatment; and 3) is there a role for chemotherapy with temozolomide?

## **Case 4: Temozolamide chemotherapy in an aggressive treatment-resistant prolactinoma**

**Author(s): L Srikugan, P Carroll, S Thomas; Guy's & St Thomas' NHS Trust, London**

### **CASE HISTORY:**

A previously healthy 28 year old gentleman presented in 1996 with visual field defect secondary to optic chiasm compression from a large pituitary tumour. Prolactin was >150000mIU/l. He underwent trans-sphenoidal surgery (TSS) to prevent further visual loss. Histology confirmed an aggressive prolactinoma with increased mitoses. He exhibited panhypopituitarism post-surgery but hyperprolactinaemia persisted despite dopamine agonist therapy. He was treated with Leksell Gamma Knife irradiation in 2001. There was further re-growth with cavernous sinus invasion and cranial nerve palsy so he underwent two TSS and received further Gamma Knife irradiation during 2005–2007. Prolactin remained >12000mIU/l on cabergoline 1mg/day so he was treated with Capecitabine and Lomustine chemotherapy in 2008 – prolactin stabilised at 11,000mIU/l with stable tumour volume. However, six months later prolactin started to rise peaking at 44,811mIU/l.

Temozolamide chemotherapy was introduced in February 2010 with cabergoline 500mcg daily – tumour O<sub>6</sub>-methylguanine-DNA methyltransferase (MGMT) expression was not assessed pre-treatment. He underwent four temozolamide cycles, post-therapy prolactin being 20,831mIU/l with stable pituitary tumour volume. However within three months prolactin rose to 34,571mIU/l. Further temozolamide therapy is being considered.

### **DISCUSSION:**

Temozolamide, an alkylating drug, has varying degrees of success in aggressive prolactinomas. 12 – 24 cycles of temozolamide therapy have been reported for aggressive prolactinomas. Full responders appear to show biochemical improvement and tumour regression as early as six months into therapy. In our case prolactin had halved at six months but tumour volume had remained unchanged. He is currently asymptomatic but has a rising prolactin

What are the options of tackling the rising prolactin?

- Consider 8-12 further cycles of temozolamide with a view to simply preventing further tumour growth
- Combine Temozolamide with Capecitabine (as used for neuroendocrine tumours). Regression of an aggressive corticotroph tumour has been reported with just two cycles of CAPTEM; the tumour however recurred five months later.



## **Case 5: Management Options for Aggressive Prolactinoma Resistant to Dopamine Agonists**

**Author(s): Lina Chong**

A 64 year old gentleman presented with bitemporal hemianopia and headaches in 1999. Prolactin was 130000mu/L (55.4-276) and he had hypogonadotropic hypogonadism. Pituitary MRI showed a large pituitary mass extending into the clivus, invading the right cavernous sinus and sphenoid sinus, and compressing the optic chiasm. Cabergoline was commenced with rapid normalisation of prolactin, resolution of hemianopia and MRI evidence of significant tumour shrinkage. Testosterone replacement was initiated later that year.

In 2005, prolactin started to rise and in 2007, he developed a right CN IV palsy. Radiotherapy was administered in 2008. Cabergoline was titrated up to 2mg/day. There was concern over possible cardiac valvulopathy. Although cardiac MRI was reassuring, quinagolide was used instead as he was not responding to cabergoline. However, he developed suicidal ideation on high dose quinagolide so cabergoline was restarted.

In 2009, hydrocortisone and thyroxine replacement was commenced. Prolactin continued to climb, peaking around 30000mu/L. MRI in 2010 showed increased tumour size, wrapping around the carotid artery resulting in a complete right CN III palsy. He had debulking pituitary surgery to improve symptoms and obtain histological diagnosis.

Histology confirmed a prolactin secreting adenoma with rapid cell proliferation (evidence by Ki67 22%, presence of apoptosis and multiple small foci of tumour necrosis). Prolactin remained elevated post operatively. Following discussion in our pituitary MDT, he was referred for a trial of temozolamide.

### Questions

- 1) Is there a role for somatostatin analogue adjunctive therapy in resistant prolactinoma, particularly with pasireotide? Would scintigraphic imaging or tissue analysis for expression of SST receptor subtypes be of clinical use?
- 2) Although pituitary carcinoma is very rare, should we consider screening for evidence of metastatic disease and if so what investigation modality is best?
- 3) What is the likelihood of response to temozolamide, and if unsuccessful should alternative chemotherapy agent be considered?

## **Case 6: The clinical course of a patient with giant invasive prolactinoma : the need for multidisciplinary management**

**Author(s): M Vidyarthi<sup>1</sup>, K Gungunah<sup>1</sup>, E Marouf<sup>1</sup>, Z Khatami<sup>2</sup>, S Chawda<sup>3</sup>, J Pollock<sup>4</sup> and ND Stojanovic<sup>1</sup>**  
**Departments of Endocrinology<sup>1</sup>, Biochemsitry<sup>2</sup>, Radiology<sup>3</sup> and Neurosurgery<sup>4</sup>, Queen's Hospital, Romford, Essex.**

A 52 year-old lady was referred to the ophthalmology department with suspected thyroid eye disease. On examination the patient had reduced visual acuity (Snellen 1/60, LogMAR 1.3), proptosis and gaze palsy in all directions in the left eye. Thyroid function tests showed a TSH 4.2mU/l (range 0.5-5.5) and free thyroxine of 6.7pmol/l (range 10-19.8). Pituitary function tests were requested urgently as the TSH was disparately low compared with the thyroxine. These were in keeping with hypopituitarism, with prolactin elevated at >500,000U/l. An urgent endocrine opinion was therefore sought.

Pituitary imaging revealed a giant pituitary tumour eroding the skull base, invading the left orbit and compressing the brainstem. Treatment options were discussed with the patient. She initially rejected surgery, and so was started on a low dose of cabergoline. Her consciousness deteriorated a week after starting treatment and she had emergency tumour debulking, after which the patient improved significantly. Vision in the left eye as well as eye movements were partially restored. She was discharged on cabergoline, steroid and thyroxine replacement.

Six weeks later, she was admitted acutely with a collapse and limb weakness. A CT scan showed enlargement of the posterior fossa component of the tumour with further apoplexy in this region. She subsequently underwent further debulking of the tumour through the sub-occipital transtentorial approach. Recovery was uncomplicated, although she required inpatient rehabilitation. She remains on lifelong cabergoline, thyroxine and hydrocortisone.

Giant invasive prolactinoma in women are rare. This patient's case illustrates the need for close multidisciplinary team involvement in the management of these patients. The diagnosis in this case was made by a biochemist and the course of management was facilitated by close liaison between a neurosurgeon, endocrinologist and an ophthalmologist.

## **Case 7: Acromegaly Of Unexpected Origin**

**Author(s) P Sen Gupta<sup>1</sup>, A A Roy<sup>2</sup>, D M Berney<sup>3</sup>, M Korbonits<sup>1</sup>, A B Grossman<sup>1</sup>**  
**<sup>1</sup>Departments of Endocrinology, <sup>2</sup>Radiology & <sup>3</sup>Pathology, St Bartholomew's Hospital, London**

### Case History

A 53 year old lady was referred to endocrinology after a brain MRI, performed to investigate a retinal lesion picked up by her optician, revealed a pituitary mass lesion. Striking acromegalic features were noted seemingly of 2 years' duration, serum IGF-1 was 95µg/L (normal 23-70) and GH did not suppress following an oral glucose tolerance test. Visual fields were full to confrontation. She was also noted to be jaundiced and ultrasound revealed multiple liver lesions suggestive of metastases.

123I-MIBG with SPECT failed to demonstrate an MIBG-avid tumour. Liver biopsy showed a highly vascular neuroendocrine neoplasm favouring a lung primary. Revisiting the history and examination revealed a lobectomy 22 years previously for bronchial carcinoid, but with good interim health and new flushing episodes. CT staging confirmed liver metastases and pelvic bone sclerotic lesions but chemotherapy by the referring oncologist using lomustine and capecitabine did not result in tumour or plasma chromogranin A (904pmol/L [ $<60$ ]) regression. An octreotide scan showed somatostatin receptor positive bone and liver metastatic disease, and lanreotide autogel 90mg monthly was commenced.

Following lanreotide, there has been a notable symptomatic response, with falls in both IGF-1 (768 to 437ng/ml) and chromogranin A levels (904 to 262pmol/L), and stable tumour burden on CT over 12 months. Pituitary MRI has demonstrated shrinkage of the pituitary mass. Plasma GHRH was found to be grossly elevated at 8316ng/L ( $<30$ ).

### Discussion

This patient has a primary lung carcinoid recurring with ocular and liver metastases, and GHRH secretion causing presumed somatotroph hyperplasia and symptomatic acromegaly. Bronchial carcinoids can recur long after apparent remission, and ocular secondaries are a common manifestation. One should always consider the principle that the simplest all-encompassing explanation is likely to be the correct one, and thus that this patient's bronchial carcinoid, ocular lesion and acromegaly are all causally linked.

**Case 8: Hypertrophic Pachymeningitis and Pituitary Pathology: Lymphocytic Hypophysitis or Cabergoline related Fibrosis?**

**Author(s): Dr.Rajeev Raghavan<sup>1</sup>, Dr.Elizabeth Mallam<sup>2</sup>, Prof N.J.Scolding<sup>2</sup>, Dr.K.J.Bradley<sup>1</sup>**

<sup>1</sup>Department of Endocrinology, Bristol Royal Infirmary, Bristol, BS2 8HW

<sup>2</sup>Department of Neurology, Frenchay Hospital, Frenchay Park Road, Bristol

**Case History:**

A 51-year-old lady with a background of classical migraine and amenorrhoea conceived successfully via IVF, without prior endocrine assessment. Symptoms during the third trimester of pregnancy led to the diagnosis of a pituitary mass lesion (see table). Possible differential diagnoses, on subsequent endocrine review, included macroprolactinoma, microprolactinoma expanding intra-partum, or lymphocytic hypophysitis.

After six years of dopamine agonist therapy, the patient was admitted with progressive generalised headaches and vomiting (similar symptoms during initial presentation in pregnancy and different from usual migraine). Neurological assessment and follow up and repeat MRI demonstrated new diffuse meningeal thickening. Hypertrophic pachymeningitis (patchy widespread inflammatory thickening of meningeal dura-mater) was diagnosed.

Time-line	History	Prolactin (< 700 mIU/L)	Pituitary MR Imaging	Other Significant investigations
1998	Secondary Amenorrhoea	-----	-----	-----
2002	IVF therapy	-----	-----	-----
2002	Pregnancy 36 weeks-significant headaches, small left temporal field defect	-----	Macroadenoma	-----
2002	Rapid resolution of field defect post-partum without intervention	-----	-----	-----
2003	Persistent amenorrhoea 6 months post-partum, Cabergoline started	3188	Macroadenoma unchanged	-----
2004	Cabergoline 500mcg/week	36	Excellent involution of macroadenoma	-----
02/2008	Cabergoline reduced to 250mcg/week	33	Appearances unchanged	-----
08/2008	Disabling headaches	60	Appearances unchanged	CSF analysis-mild elevated protein,
01/2009	Pachymeningitis diagnosed. Cabergoline weaned & stopped 07/2009	41	Pachymeningitis, Pituitary unchanged	Extended Autoimmune profile normal, Gallium scan-normal
2009 to 2010	Headaches resolved within weeks of Cabergoline withdrawal	599 to 1990 (Latest-1230)	Complete resolution of meningeal thickening. Pituitary unchanged	

**Conclusion:**

Our case highlights the following

- Difficulties in retrospectively establishing aetiology of pituitary disorders presenting in pregnancy
- The rare association of treatment with an ergot-derived dopamine agonist (Cabergoline) and hypertrophic pachymeningitis.

Withdrawal of cabergoline (implicated in cardiac valvular fibrosis) coincided with rapid resolution of clinical and radiological features associated with pachymeningitis. Whilst this could be purely coincidental, a causal link cannot be definitively excluded.

## **Case 9: Pituitary tumour causing thyrotoxicosis - or not? Whether to operate ..**

**Author(s): Shakunthala Narayanaswamy and James Ahlquist  
Endocrine Unit, Southend Hospital, Westcliff on Sea, Essex.**

A 64 year old gentleman presented with atrial fibrillation but no specific thyrotoxic symptoms. He was otherwise euthyroid. TFT revealed TSH 4.3mU/L, FT4 35.3mU/L, FT3 11.9mU/L, raising the possibility of TSHoma. An MRI pituitary showed a 9x8mm lesion on the left of the gland, abutting the cavernous sinus, clear of the chiasm.

There was no other evidence of pituitary dysfunction. A thyroid isotope scan showed multinodular change. In view of the paucity of clinical features of thyrotoxicosis further consideration was given to alternative interpretations of TFTs, such as thyroid hormone resistance.

SHBG 103nmol/L (15-103nmol/L), TSH alpha subunit 0.5IU/L (<1.00). DNA analysis of T3 receptor was normal, arguing against thyroid hormone resistance. A T3 suppression test was performed, with additional TRH test before and after T3 suppression. There was a rise in T3 and SHBG as expected with T3 administration. Both the basal TRH test and the repeat after T3 suppression showed a greater than two fold rise in TSH after TRH (TSH 5.57mU/L rising to 11.29mU/L and 2.97 to 6.34mU/L respectively), supporting the diagnosis of thyroid hormone resistance. However, treatment with high dose T3 did not lead to significant suppression of TSH (basal TSH 5.57mU/L, day 12 TSH 2.97 mU/L), which would favour a diagnosis of TSHoma.

Correct diagnosis is relevant to management of his atrial fibrillation management; cardioversion would be arranged if hyperthyroidism is cured or excluded. A TSHoma remains likely as there was incomplete suppression of TSH during the T3 suppression test. However, against this is the absence of clinical features, the normal alpha subunit, and the normal rise of TSH after TRH.

Further investigations planned include TFT in his children to look for collateral evidence of thyroid hormone resistance, and a therapeutic trial of octreotide therapy. We invite the panel to discuss the diagnosis and further management.

## **Case 10: Difficulties in Management of Hypercortisolism**

**Author(s): Dr FW Ahmed<sup>1</sup>, Dr D Sennik<sup>1</sup>, Dr J Wright<sup>1</sup>, Dr V Hordern<sup>1</sup>, Mr Nigel Mendoza<sup>2</sup>, Dr Federico Roncaroli<sup>2</sup>, Dr Amrish Mehta<sup>2</sup>, Professor K Meeran<sup>2</sup> and Professor D Russell-Jones<sup>1</sup>**

**<sup>1</sup>Royal Surrey County Hospital**

**<sup>2</sup>Hammersmith Hospital**

A 50 year old lady first came to our clinic in 2006 for the assessment of a 3.4cms adrenal mass. She complained of abdominal distension, obesity, proximal muscle weakness, tiredness, bruising, thinning of the skins and hirsutism. These symptoms started few years earlier. She had osteopenia of her left hip, stress fractures in her feet and a rib fracture following a fall. Her past medical history includes tonsillectomy, hiatus hernia, ovarian cyst, spinal fusion, macular degeneration, glaucoma, diverticulosis and pacemaker for sick sinus syndrome.

On examination her BMI was 30.9kg/m<sup>2</sup> with weight centrally distributed. She had bruising, thinning of skin and buffalo hump.

Her cortisol level did not suppress after LDDST. Her ACTH level was 49ng/L. CRH test showed a 20% increase in cortisol (968nmol/L to 1427nmol/L) and 50% increase in ACTH (52ng/L to 117ng/L) respectively. However her pituitary CT scan was normal. It was decided in multidisciplinary meeting to proceed with left adrenalectomy. Histology showed left adrenal adenoma.

Following surgery in 2006 her symptoms improved. Investigations 6 months after surgery also normalised; cortisol level of <30 nmol/L following LDDST.

She represented in 2010 with symptoms of abdominal distension, proximal weakness and changes in facial appearance. Her investigations again were suggestive of ACTH dependent Cushing's. She was referred for petrosal sinus sampling.

Petrosal sinus sampling showed a basal IPS: P ratio  $\square$  2.0 indicating a pituitary source. A CRH stimulated ratio was also  $\square$  3.0. Interpretation for lateralization was difficult.

CT scan abdomen showed 10mm nodule within the body of the right adrenal gland.

Her case was discussed in our multidisciplinary meeting with Hammersmith Hospital. It was decided to perform CT head with pituitary reconstruction before any surgical option was considered. The patient was very distressed and keen to undergo right adrenalectomy.

CT pituitary was suggestive of pituitary adenoma, and pituitary surgery was offered to the patient.

Following pituitary surgery she improved symptomatically. This was confirmed by day 4, 9am cortisol of <20 nmol/L. Histology confirmed corticotroph adenoma.

## **Case 11: A complex case of recurrent Cushing's Disease**

**Author(s): HS Chahal<sup>1</sup>, I Sabin<sup>2</sup>, J Evanson<sup>3</sup>, AB Grossman<sup>1</sup>**

**<sup>1</sup>Department of Endocrinology, <sup>2</sup>Department of Neurosurgery, <sup>3</sup>Department of Neuroradiology, St. Bartholomew's Hospital, London**

We report a case of a female patient who presented aged 41 years with classical features of Cushing's syndrome due to a pituitary corticotroph microadenoma. She underwent transsphenoidal surgery with a significant improvement in the overall cortisol burden, but not an absolute cure (serum cortisol <50nmol/L at 09.00h). Two years later she underwent external beam radiotherapy. Over the next 10 years periodic cortisol day-curves (mean of 5 levels) demonstrated satisfactory control. However, 12 years after the original operation she complained of weight gain and hirsutism, and clinically had Cushingoid features with hypertension and type 2 diabetes. Her biochemistry showed a lack of diurnal cortisol variation and failure of cortisol suppression on the low-dose dexamethasone suppression test (2+48 serum cortisol 110nmol/L). A MRI demonstrated residual normal appearing pituitary, but no definitive adenoma. Medical therapy was commenced with ketoconazole, but she developed ketoconazole-induced hepatitis which required cessation of therapy.

Due to the excess cortisol burden, intolerance to ketoconazole and the likelihood that long term metyrapone would increase the androgen burden, she underwent bilateral adrenalectomy at the age of 56 years; 5 years post-adrenalectomy she had marked skin hyperpigmentation and her plasma ACTH was elevated at 1024ng/L with an MRI showing a 4.9mm adenoma. Currently, aged 63 years (7 years post-adrenalectomy), her plasma ACTH level has increased to 1790 ng/L, with an MRI showing an increase in size of her residual tumour to 7.8mm; she remains on thyroxine, hydrocortisone and fludrocortisone replacement.

In summary, we present a 63 years old female patient with recurrent Cushing's disease who has had transsphenoidal surgery, external beam radiotherapy and bilateral adrenalectomy. We would like to ask the panel: 1) whether they would now consider further surgery or radiotherapy, radio-surgery, or simply follow-up with regular MRI; 2) should a bilateral adrenalectomy have been performed or would the panel have opted for long-term metyrapone treatment; and 3) is there a role for chemotherapy with temozolomide?



## **Case 12: Dilemmas in managing an aggressive non-functioning pituitary tumour**

**Author(s): Hamish Courtney**

A 27 yr old male presented in 2005 with headaches, visual loss and hypopituitarism. There was no clinical or biochemical evidence of hormone hypersecretion. Imaging revealed a 2.8x2.5x1.9cm pituitary lesion which was removed with histology confirming a pituitary adenoma but with ACTH positivity and high Ki67 index. He was commenced on appropriate hormone replacement including GH.

In 2006, imaging showed a small amount of left cavernous sinus tissue only remaining.

In 2007 he had significant tumour recurrence and had repeat transphenoidal clearance with subsequent 30Gy external beam radiotherapy. A small stable tumour remnant remained on imaging.

In 2009 he presented with nasal discharge and was again found to have significant tumour recurrence. Lateral rhinotomy with tumour removal was performed but residual tumour was left in the cavernous sinus and clivus. He commenced temozolomide in 2010 with good radiological improvement.

The dilemmas to be discussed are firstly the future chemotherapeutic strategies for managing his tumour and secondly the management of his GH deficiency. His GH replacement was stopped after his second recurrence due to concerns regarding its possible effect on tumour growth, although the patient feels markedly symptomatic from possible GH deficiency.

### **Case 13: A difficult case of locally aggressive acromegaly**

**Author(s): Karunakaran Vithian : SpR in diabetes & endocrinology, Mid Essex Hospital NHS Trust**

**Judith Kisalu: Endocrine Specialist Nurse, Royal Free Hospital**

**Neil Dorward: Consultant Neurosurgeon, Royal Free Hospital**

**Pierre-Marc Bouloux: Consultant Endocrinologist, Royal Free Hospital**

A 42 year old gentleman was diagnosed with acromegaly in 2008 following a review in an ophthalmology clinic with headache and diplopia. The initial MRI showed a large macroadenoma compressing the chiasm and encasing the right internal carotid artery. A partial endoscopic transphenoidal resection followed by radical radiotherapy was administered. Lanreotide treatment was commenced in July 2008. In May 2010 he developed worsening headache with visual blurring and was diagnosed with apoplexy resulting in a re-do transphenoidal surgery in May 2010. Histology revealed an atypical pituitary tumour which did not stain for Growth Hormone or other pituitary hormones with proliferation index >50%. He therefore had one cycle of temozolomide chemotherapy. In July he presented to the Emergency Department in his local hospital with severe headache and loss of vision. On assessment he had complete ophthalmoplegia of the right eye and vision limited to the left lower temporal pole. He underwent emergency surgery that debulked his pituitary and cavernous sinus adenoma and gliadel wafers were inserted (one in the right cavernous sinus & three in the left). He represented to the endocrinology department at Royal Free Hospital 3 weeks after surgery with headache and visual blurring and the MRI showed increased size of residual tumour within the cavernous sinus.

Question to the panel / audience:

1. What would you do next to resolve his visual symptoms
2. What is the best long-term strategy to control this patient's locally aggressive tumour

**Case 14: Hypophyseal Wegener's granulomatosis presenting with visual field constriction without pituitary dysfunction.**

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The authors report a 48 year old woman with known systemic Wegener's granulomatosis and bitemporal superior quadrantanopia in whom magnetic resonance imaging, transphenoidal adenohypophysectomy and histopathology confirmed necrotising granulomatous hypophysitis causing optic chiasm compression.

Pituitary gland involvement in Wegener's granulomatosis is rare, first manifesting most commonly with central diabetes insipidus, sometimes with concomitant hypopituitarism affecting other hormonal axes and extremely rarely with visual symptoms.

The previously unreported presentation of hypophyseal Wegener's granulomatosis with bitemporal hemianopia but neither diabetes insipidus nor hypopituitarism is discussed.

Also, while granulomatous hypophysitis is most likely to present with DI amenable to medical management and visual symptoms are more likely to be due to concomitant cranial neuropathies than chiasmatic compression from pituitary enlargement in Wegener's granulomatosis, visual fields should be formally assessed and adenohypophysectomy considered after MRI in those with visual symptoms unimproved by corticosteroids in suspected hypophyseal WG.

## **Case 15: The dilemmas of an endocrinologist**

**Author(s): L Srikugan, J Powrie; Guy's & St Thomas' NHS Trust, London**

### **CASE HISTORY:**

A 60 year old gentleman presented with lethargy, cough and hypercalcaemia. Diagnostic CT and MRI revealed right renal tumour with pulmonary, left adrenal and splenic metastases as well as 2cm sella/suprasellar mass with stalk deviation and optic chiasm displacement.

He had normal Humphrey Visual Fields, no evidence of diabetes insipidus (DI); morning cortisol 353nmol, ACTH 29ng/l, fT<sub>4</sub> 11.3pmol/l (NR=12-22), fT<sub>3</sub> 3.6pmol/l (NR=3.1-6.8), total testosterone 2.2nmol/l, LH 1.8IU/l, FSH 2.6IU/l, IGF-1 1.6nmol/l, prolactin 95mIU/l. Pituitary adenoma rather than metastasis was considered because of the MRI appearance, absence of bone destruction, lack of metastases elsewhere in the brain and absence of DI.

Sunitinib 50mg daily was commenced to reduce tumour burden pre-nephrectomy. Nine weeks later CT showed significant reduction of renal tumour and metastases. He presented with headaches and diplopia a month later: brain MRI revealed bleeding around the rim of the pituitary adenoma. He was supplemented with hydrocortisone and thyroxine, and Sunitinib was continued. Imaging 4 months later revealed almost complete resolution of the initial sella mass and further renal tumour regression.

### **DISCUSSION:**

Distinguishing pituitary metastasis from an adenoma can be problematic. DI is seen less with pituitary metastases from renal carcinoma than other cancers. The parallel responses of the pituitary lesion as well as the primary tumour and other metastases to Sunitinib suggest metastatic pituitary lesion. However a response of an adenoma to Sunitinib remains a speculative possibility. Studies using pituitary adenoma cell cultures have demonstrated reduced [<sup>3</sup>H]thymidine uptake and DNA synthesis inhibition by protein tyrosine kinase inhibitors but no in vivo data exists.

Apoplexy has been reported amongst cases of renal carcinoma metastases. It is also likely that Sunitinib precipitated pituitary apoplexy either by its effects on tumour angiogenesis or the precipitation of haemorrhage. This may have been at least partially responsible for the tumour regression.

## **Case 16: A change for the worse when thirst is not enough**

**Author(s): G Rayanagoudar, A Nicklin, B Hashim, J Thomas, SR Peacey, A Grossman**

A 45-year old Afro-Caribbean patient presented 10 years ago with supra-orbital swelling and nasopharyngeal problems. Biopsy demonstrated features consistent with sarcoidosis. He had progressive loss of anterior pituitary function, followed by cranial diabetes insipidus, and a right homonymous hemianopia. MRI showed changes consistent with neurosarcoid in the hypothalamic sellar cistern region, with leptomeningeal thickening. He was commenced on prednisolone plus full pituitary hormone replacement, and underwent treatment with HCG and FSH to successfully achieve spermatogenesis resulting in conception and a successful pregnancy. He had repeated admissions with hyponatraemia thought to be secondary to the patient's liberal use of desmopressin.

Three months after weaning off the prednisolone and converting back to hydrocortisone he presented with a short history of confusion and fatigue. Visual acuity decreased dramatically in the left eye, correlating with disease progression on MRI. Films demonstrated widespread involvement of the optic chiasm and left optic radiation. A left afferent pupillary defect and optic atrophy were noted. Dexamethasone was started with good effect, and the confusion and visual acuity improved significantly. Desmopressin was stopped on admission due to hyponatraemia but three days later he developed polyuria with a lack of a proportionate increase in thirst; serum sodium 156 mmol/L; serum osmolality 330 mosmol/L; urine osmolality 204 mosmol/L. He was treated with intravenous fluids and desmopressin, and a strict fluid intake regimen, and his serum sodium and osmolality normalised. It was felt that neurosarcoid involvement of the hypothalamus had caused altered thirst sensation with consequential resetting of his osmostat, in addition to his diabetes insipidus. Treatment with external beam radiotherapy is now being considered.

Neurosarcoidosis is a complex problem where changes in pituitary and hypothalamic function, especially changes in thirst, render fluid balance particularly difficult to manage.