The 9th Clinicopathological Conference on Pituitary Disease

Institute of Child Health, London, 28th March 2007

Programme

9:25 Welcome and Introduction — Mr Michael Powell (London)

9:30 Keynote Lecture

Prolactin, what's new - differentiating stalk compression and when to stop treatment of prolactinoma
Professor John Wass (Oxford)

10:20 Forum 1 - Cases – Focus on Prolactin
Chair: Dr Mark Vanderpump (London) and Mr Michael Powell (London)

(Cases will be presented at approximately ten to fifteen-minute intervals)

Panel:		
	Professor Ashley Grossman	Endocrinology, London
	Professor John Monson	Endocrinology, London
	Dr Peter Trainer	Endocrinology, Manchester
	Professor John Wass	Endocrinology, Oxford
	Dr Nick Plowman	Radiotherapy, London
	Dr Gordon Plant	Ophthalmology, London
	Dr Andy Platts	Neuroradiology, London
	Professor John Pickard	Neurosurgery, Cambridge
	Professor Nicolas de Tribolet	Neurosurgery, Switzerland
	Mr Kanna Gnanalingham	Neurosurgery, Manchester
	Dr John Jane Jr	Neurosurgery, Charlottesville
	Dr Federico Roncaroli	Histopathology, London

1. When is cabergoline-associated irritability an unacceptable side effect?
Barrington-Ward E, Martin NM, Hatfield ECI & Meeran K (London)

2. Emerging macroprolactinoma with intolerance to cabergoline therapy.
Raghavan R, Close CF & Andrews RC (Taunton)

3. Dilemmas in the management of macroprolactinoma with co-existent schizophrenia
Caputo C, Wren AM, Martin NM, Hatfield ECI & Meeran K (London)

4. Would the audience have attempted withdrawal of cabergoline?
Banerjee A, Williamson C, Hatfield ECI, Martin NM and Meeran K (London).

5. An Erosive Pituitary Tumour
Kelly P, Benjamin J, Chawda S, Parsons M & Stojanovic N (Romford)

11:30 Coffee

11:50 Forum 2 – Cases - Aggressive Pituitary Disease
Chair: Dr Stephanie Baldeweg (London) and Miss Joan Grieve (London)

6. Wegener's Granulomatosis
Swamy A, Clark J & Gurnell M (Cambridge)

7. Pituitary carcinoma causing acromegaly: treatment options
Shaikh H, Martin NM, Hatfield ECL & Meeran K (London)

8. A Case of Severe Cushing's Disease
Lawrence V & Grossman A (London)

9. A case of malignant Cushing's?
Joharatnam J, Chammas N, Mehta A, Mendoza N, Bassett D, Martin NM, Hatfield ECI & Meeran K (London)

12:45 Lunch

13:30 Keynote Lecture

Unbiased, whole genome analysis of pituitary adenomas
Professor William Farrell (Keele University School of Postgraduate Medicine)

14:00 Forum 3 – Miscellaneous Pituitary Cases
Chair: Dr James Ahlquist (Southend) and Dr Gerard Conway (London)

10. Reversible Hypopituitarism after Postpartum Lymphocytic Hypophysitis
Fernandez A, Karavitaki N & Wass JAH (Oxford)

11. Management options for an intra/suprasellar cystic lesion with difficult histology
Barrington-Ward E, Martin NM, Roncaroli F, Mendoza N and Meeran K (London)

12. A Diagnostic Conundrum
Khalifa S & Baldeweg S (London)

13. Cushing's Disease Diagnosed Following Stroke.
Nathan Y & Seal L, Sugihara C (London)

14. Management of Incidental Non-functioning Pituitary Macroadenoma
Fonia A, Muralidhara K, Goulden P, Barnes DJ & Kumar J (Maidstone and Tunbridge Wells)

15. Pituitary Apoplexy
Chakrabarti S & Johnston C (Hemel Hempstead)

16. A Deceiving Prolactinoma
Kassim SB & Courtney CH (Belfast)

17. A Case of Rapidly Developing Total Pituitary and Visual Failure.
Kelly PA, Sabin I, Alusi G, Evanson J, Plowman PN, Monson JP & Drake WM (London)

18. Pituitary metastasis
Jindahra P, Powell M & Plant GT (London)

15:20 Afternoon Tea

15:40 Focus on Ophthalmology and Pituitary Disease Cases

Dr Gordon Plant (London)

16:00 Focus on Pituitary Surgery - Transition to pituitary endoscopy

Dr John Jane Jr (Charlottesville)
Mr Kanna Gnanalingham (Manchester)

16.30 Close

Programme Organising Committee March 2007

Dr James Ahlquist **Dr Stephanie Baldeweg**
Dr Gerard Conway **Ms Joan Grieve**
Mr Michael Powell **Dr Mark Vanderpump**

Forum 1 - Cases – Focus on Prolactin
Chair: Dr Mark Vanderpump (London) and Mr Michael Powell (London)

1. When is cabergoline-associated irritability an unacceptable side effect?

Barrington-Ward E, Martin NM, Hatfield ECI & Meeran K.
Endocrine Unit, Imperial College Faculty of Medicine, Hammersmith Hospitals, London

In 2000, a 32-year-old anaesthetist presented with a 2-year history of reduced libido and erectile dysfunction. His prolactin was elevated at 260,901mU/L, associated with hypogonadotrophic hypogonadism and secondary hypothyroidism. Visual fields were normal on perimetry, however, MRI revealed an extensive pituitary tumour measuring 4 by 4 by 5 cm, with extension around the right internal carotid artery and right optic tract. He commenced cabergoline 250mcg twice a week and his prolactin levels fell to 281 mU/L within 8 months. This was associated with resolution of his secondary gonadal and thyroid dysfunction. Consistent with his biochemical improvement, successive MRIs showed substantial shrinkage of his tumour. His cabergoline was gradually increased to 500mcg three times a week which successfully suppressed his prolactin to 95 mU/L. Recently, in outpatient clinic, he has raised after concern about irritability. He feels this is becoming an issue both at home and at work. He would therefore, like to stop his cabergoline, since he believes this is responsible for his irritability. Our question to the expert panel is:
Now that this gentleman has had successful reduction is the size of his macroprolactinoma with suppression of his prolactin, is it safe to stop cabergoline or should we advise him despite the associated side effects, to continue his cabergoline?

2. Emerging macroprolactinoma with intolerance to cabergoline therapy.

Raghavan R, Close CF & Andrews RC.
Department of Diabetes & Endocrinology, Musgrove Park Hospital, Taunton and Somerset NHS Trust, Taunton, TA1 5DA [Rajeev.Raghavan@tst.nhs.uk]

A 44-year-old man with complex symptoms, modest hyperprolactinaemia (800), low-normal testosterone, and normal pituitary MR scan was offered DA treatment but declined. Tests one year later showed further increase in PRL (1440), low testosterone and low gonadotrophins. cabergoline was not tolerated so bromocriptine and testosterone replacement offered. Over the next 3 years prolactin ranged 2000-4000 but, despite repeated attempts, patient was unable to take treatments. Pituitary MR scan at 5 years reported normal but at 7 years pituitary enlargement clearly visible with PRL rising to 16000. Restarted cabergoline but was again only able to tolerate 500mcg/wk, without full PRL suppression. Declined testosterone replacement (priapism), stopped cabergoline and declined alternative DAs. Currently hypogonadal with enlarging pituitary adenoma, and PRL 11000.

Points for discussion:
1. Modest hyperprolactinaemia with normal scan at diagnosis subsequently developing a macroprolactinoma with significant hyperprolactinaemia and hypogonadism.
2. Complex symptoms and management issues secondary to uncommon adverse effects.
3. Most appropriate choice for further management, acknowledging complexity of issues, risks and benefits.

3. Dilemmas in the management of macroprolactinoma with co-existent schizophrenia

Caputo C, Wren AM, Martin NM, Hatfield ECI & Meeran K
Endocrine Unit, Imperial College Faculty of Medicine, Hammersmith Hospitals, London

A 35-year-old male was referred to our hospital in December 2003 after a seizure resulting in a fall. CT brain showed a parietal contusion and incidentally a large pituitary macroadenoma expanding the pituitary fossa. Definition of the pituitary lesion was poor, but the patient declined further imaging. His past history included epilepsy and schizophrenia, requiring psychiatric inpatient treatment. Medications included olanzapine and phenytoin. Prolactin was markedly elevated at 78,438 mU/L (NR 50-400). Other baseline pituitary function was normal. Perimetry showed bilateral temporal hemianopia, however cooperation was variable. He was carefully commenced on carbergoline, 500mcg weekly under psychiatric inpatient review. Olanzapine was changed to quetiapine which exhibits less D2 antagonism. After 2 weeks on cabergoline, the prolactin reduced to 16 000 mU/L. Eight months post-discharge, compliance deteriorated along with his psychiatric condition requiring psychiatric admission. Cabergoline was maintained at 500mcg weekly, and nadir prolactin was 1000-3000 mU/L. Transsphenoidal surgery was contemplated to allow definitive cure, withdrawal of dopamine antagonist and more aggressive treatment of his schizophrenia. However, this was balanced against the risks of possible panhypopituitarism, including diabetes insipidus, and the difficulties likely to be encountered in managing hormone replacement in the face of psychiatric co-morbidity. After multiple failed attempts, to re-image his pituitary due to claustrophobia, recent improvement in his psychiatric condition allowed an MRI under anaesthesia. This showed significant reduction of tumour mass. In the last month, he has been readmitted as a psychiatric inpatient due to a further worsening of his psychiatric condition. At present, he continues on his cabergoline. Our questions for the expert panel are:
1. Is there a role for debulking the macroprolactinoma to potentially allow a reduction in cabergoline dose and improve his psychiatric state?
2. Would radiotherapy be an option to shrink his tumour or is this outweighed by the risk of subsequent panhypopituitarism and variable compliance with pituitary hormone replacement?

4. Would the audience have attempted withdrawal of cabergoline?

Banerjee A, Williamson C, Hatfield ECI, Martin NM and Meeran K.
Endocrine Unit, Imperial College Faculty of Medicine, Hammersmith Hospitals, London

Women should be encouraged to breastfeed their babies if they wish, due to the nutritional, immunological and psychological benefits. A woman with a macroprolactinoma is usually not able to consider breast-feeding because she is on carbergoline throughout the pregnancy to prevent the macroprolactinoma enlarging.

A 31-year-old lady presented with secondary amenorrhoea and a prolactin of 15,704; MRI pituitary confirmed a macroadenoma abutting the optic chiasm, and with infiltration into the right cavernous sinus. Formal perimetry showed visual fields were intact. She was commenced on carbergoline. 250 mcg /twice weekly, increased at 3 months to 500 mcg twice weekly. One month later, her menses returned, and the patient immediately conceived. The patient was reluctant to take cabergoline but at 18/40 developed visual field impairment, and agreed to restart with subsequent increasing dose titrated against visual field loss. Unfortunately this pregnancy was complicated by severe pre-eclampsia and a placental abruption at 34/40, resulting in a stillbirth. Thereafter, she was diagnosed with factor V Leiden heterozygosity. Post partum the cabergoline was increased further to 500mcg once daily (3.5mg/wk) with the aim of shrinking the tumour as much as possible. Subsequently the patient had two successful pregnancies managed on cabergoline with increasing doses up to 6mg/wk titrated to visual fields and size of adenoma on MRI. On both occasions she did not breast feed. She was treated with aspirin and clexane for her thrombophilia.

She conceived unexpectedly now at the age of 36 years. As for her previous pregnancies she increased her cabergoline from 500mcg/twice a week to 500mcg/day from the first trimester. Visual fields were monitored with formal perimetry and remained normal. The patient considered the possibility of breast-feeding. At 29/40 she had a repeat MRI scan showing no change in size of the adenoma and subsequently, reduced her cabergoline to 500mcg/ 5 times a week. The aim was to gradually wean her off cabergoline prior to delivery in order to enable breast-feeding. Three weeks later a repeat pituitary MRI showed an increase size of the adenoma, now encasing the right common carotid artery within the cavernous sinus but not abutting the optic chiasm. Her visual fields remained normal. This lady is currently 34/40 gestation.
Which of these possible management options would the panel recommend for the remainder of this lady's pregnancy?:

1. Wait and change nothing since the tumour will regress after delivery.
2. Increase the cabergoline to 0.5mcg/day and do not give her the option of breast-feeding.
3. Reduce the carbergoline further with the aim of stopping prior to delivery to enable breast-feeding.

5. An Erosive Pituitary Tumour

Kelly P[1], Benjamin J[2], Chawda S[3], Parsons M[4] & Stojanovic N[1]
Queen's Hospital Romford, Departments of Endocrinology[1], Neurosurgery[2], Diagnostic Imaging[3] and Chemical Pathology[4]. (p.a.kelly@qmul.ac.uk)

A 41 year-old male Black Cab driver presented with a severe frontal headache for 12 hours; two months ago he was referred to ENT for a suspected CSF leak. He was flushed and pyrexial with neck stiffness; CSF rhinorrhoea was apparent. Meningitis was confirmed on lumbar puncture and ceftriaxone and aciclovir were started. MRI of the maxillary sinuses showed a 2.5 x 2.5 x 2.5 cm mass in the fossa involving the body of the sphenoid bone and invading the right cavernous sinus, suggestive of a skull base neoplasm, such as a chordoma. Endocrinology review revealed loss of libido, sparse body hair, gynaecomastia, galactorrhoea and 15 ml testes bilaterally. Acuity, the fundi and the fields were normal. There were no signs of systemic malignancy. Basal endocrinology revealed no diabetes insipidus, hypogonatrophic hypogonadism and growth hormone deficiency; thyroid function was normal, the 9am cortisol was 458 nmol/L. Prolactin was 92390 miu/L (53 – 360). A lactotroph macroadenoma was diagnosed and dedicated pituitary and skull base imaging was arranged showing destruction of the base of the skull, sphenoid and pituitary fossa; a pituitary mass extending into the right cavernous and sphenoid sinus, the parasellar region; the right optic nerve was abutted and tissue was apparent in the region of the right optic canal; the chiasm was not compressed. Cabergoline 250 mg once weekly was commenced with a consequent fall in the prolactin. Transsphenoidal repair of the leak was successfully undertaken three weeks later with no complications. Post operatively, on cabergoline 500 mg/week, the prolactin has fallen to 447 miu/L; hypogonadotrophic hypogonadism, growth hormone and partial ACTH deficiency are present.

Forum 2 – Cases - Aggressive Pituitary Disease
Chair: Dr Stephanie Baldeweg (London) and Miss Joan Grieve (London)

6. Wegener's Granulomatosis

Swamy A, Clark J & Gurnell M.

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A 60-year-old lady presented with 11 weeks history of polydipsia and polyuria. She drank 12 litres of fluids per day. She also suffered from dry cough, intermittent nosebleeds, shortness of breath on exertion and tiredness for 2 weeks. She had a melanoma excised from her back 20 years ago and had endometrial carcinoma 3 years ago, which was well-differentiated and treated with total abdominal hysterectomy and

bilateral salpingo-oophorectomy. On examination, she was overweight, euvolemic and had normal vital signs. Systemic examination was unremarkable. Endocrine investigations demonstrated partial hypopituitarism with FT4 6.7pmol/l (9.8-23.1), TSH 1.12mU/l (0.35-5.5), FSH 0.9U/L (21-140) and LH <0.3U/L (16-75). Her prolactin was normal at 430mU/L (60-550). Short synacthen test was unexpected with baseline cortisol of 1257nmol/L rising to 2069nmol/L after 30 minutes. A subsequent 24-hour urinary free cortisol and overnight low dose dexamethasone suppression test were normal. Cranial diabetes insipidus was confirmed by a water deprivation test. Her ESR was noted to be grossly elevated at 110 mm/hr. Chest x- ray showed cavitating lung lesions in the right middle and lower lobes. CT scan of the chest demonstrated further cavitating lesions in the left lung and CT scan of the abdomen revealed a 3cm mass in the right adrenal gland. MRI of the pituitary showed a 2.5cm mass with central hypodensity. Visual fields were intact. Immunological screen showed ANA 0.3units (0-0.9), ANCA MPO 1AU/ml (0-6), ANCA-PR3 8AU/ml (0-6) increasing to 50AU/ml subsequently, serum ACE 13U/l (15-70), IgG 14g/L (5.4-16.1), IgM 3g/L (0.8-4.0), IgA 1g/L (0.5-2.0). At this stage our working diagnoses were partial hypopituitarism (hypothyroidism and hypogonadism) with diabetes insipidus due to either Wegener's granulomatosis or metastatic disease (+/- an adrenal incidentaloma/carcinoma). VATS biopsy of lung lesions revealed a necrotic inflammatory mass with features consistent with vasculitis. There was no evidence of malignancy. She developed haematuria with no casts on urinalysis. Urine albumin-creatinine ratio was 29.0mg/mmol (0-2.5). Ultrasound of the kidneys revealed small sized kidneys. An ENT review revealed bilateral crusting lesions posterior to Little's area. Nasal biopsy showed non-specific inflammatory changes. Ophthalmic review showed mild retinal vasculitis with cotton wool spots. The adrenal mass was found to be non-functioning following various biochemical and imaging studies (biopsy was refused). She received endocrine replacement with thyroxine and desmospray. For her presumed Wegener's Granulomatosis, she was treated with immunosuppressive therapy, with IV IgG followed by high dose oral Prednisolone and then at a maintenance dose of 5mg daily and has made excellent progress.
This case illustrates an unusual cause of both anterior and posterior pituitary failure.

7. Pituitary carcinoma causing acromegaly: treatment options

Shaikh H, Martin NM, Hatfield ECL & Meeran K
Endocrine Unit, Imperial College Faculty of Medicine, Hammersmith Hospitals, London

We describe the case of a lady who presented in July 1996 at the age of 47 years with typical features of acromegaly, an elevated mean growth hormone (GH) level (58.4mU/l) and an extensive pituitary mass confirmed on MRI. She subsequently went on to have in the same year debulking transcranial pituitary surgery and a year later radiotherapy which led to a decrease in serum IGF-1 levels after 6 months (from 158nmol/l to 89.5 nmol/l). Histology confirmed a pituitary adenoma which stained for GH. Despite the above procedures in September 1998, the IGF-1 level had increased (to 111.5nmol/l) which led to the commencement of lanreotide intramuscularly 30mg every 14 days. Her acromegaly was difficult to control with somatostatin analogues but consecutive MRI scans revealed a stable pituitary lesion. The patient noticed a right sided neck lump which was removed for histological examination in February 1999 and was found to be cytomorphologically identical to the pituitary adenoma and immunostained also for GH. Following the neck lump dissection IGF-1 levels dropped (60nmol/l). Lanreotide was discontinued and six weeks later octreotide and MIBG scans were found to be negative hence lanreotide was stopped. In February 2000, the patient's IGF-1 levels increased (122nmol/l) and the patient began complaining of increased sweatiness leading to recommencement of lanreotide. Neck MRI scans revealed enlarged lymph nodes and in June 2000 a neck dissection was performed with histology confirming 10 nodes out of 20 contained metastatic pituitary metastases with positive immunostaining for GH and cell cultures confirmed production of GH. Six months post surgery the serum IGF-1 levels decreased (62.7nmol/l) with an improvement in symptoms. She then went on to have another relapse due to further neck metastases which led to a second neck dissection in 2003. At review 4 years later she still has an undetectable GH level.
We would like to pose the following questions to our expert panel:
1. Could any parameters have predicted malignant change in this lady's somatotroph adenoma at diagnosis?
2. Should she now have any further medical management?

8. A Case of Severe Cushing's Disease

Lawrence V & Grossman A,
Dept. of Endocrinology, St. Bartholomew's Hospital, London (v.j.Lawrence@qmul.ac.uk)

A 26-year-old man was referred from Trinidad with extremely severe Cushing's. He had cortisol levels in the 4000-5000nmol/l range with ACTH 300-500 ng/ml and a severe hypokalaemic alkalosis (K+ < 2mmol/l even on replacement and K sparing diuretics + ACE inhibitor). Initial clinical suspicion was that this was an ectopic ACTH secreting tumour but he had a 7mm pituitary adenoma on MRI (predominantly right sided), no cross sectional or bronchoscopic evidence of an ectopic source and BIPSS showing CRH stimulated gradients of 3 and 5 on the right and left respectively (ie apparent lateralisation contrary to MRI). He was managed with an etoposide infusion (+cortisol replacement) and his clinical course complicated by several life threatening fungal, bacterial and viral (CMV) infections culminating at one point in cardiac arrest. A diagnostic procedure was scheduled to be performed two weeks before this presentation.....

9. A case of malignant Cushing's?

Joharatnam J, Chammas N, Mehta A, Mendoza N, Bassett D, Martin NM, Hatfield ECI & Meeran K
Endocrine Unit, Imperial College Faculty of Medicine, Hammersmith Hospitals, London

A 47-year-old retired district nurse presented in 2000 with clinical features of Cushing's syndrome. Biochemical investigations confirmed Cushing's syndrome: low dose dexamethasone suppression test (LDDST) T =48h cortisol 368nmol/L, 9 AM ACTH 17.0ng/L. An MRI scan revealed a solitary non-enhancing 5mm focal lesion in the left side of the pituitary gland and inferior petrosal sinus sampling (IPSS) confirmed a central source of ACTH. A diagnosis of pituitary-dependent Cushing's disease was made and she underwent transsphenoidal surgery (TSS) in December 2000. A post-operative LDDST was indicative of remission (T= 48h cortisol <30nmol/L) and dynamic pituitary function testing post-operatively confirmed secondary hypoadrenalism and hypothyroidism. Therefore, she commenced hydrocortisone and thyroxine replacement. Three years later, in 2003, she showed evidence of clinical recurrence, which was confirmed biochemically (LDDST T=48h cortisol 199nmol/L). An MRI scan showed a small remnant of pituitary tissue and repeat TSS was performed in August 2003. A post-operative LDDST confirmed cure. Eighteen months later, she demonstrated a further recurrence of her Cushing's disease, which was once again confirmed biochemically. A repeat MRI scan showed an empty pituitary fossa. She underwent bilateral adrenalectomy in July 2005. A repeat MRI in Jan 2007, performed 18 months after her bilateral adrenalectomy, showed a new lesion: a small 5 mm area of abnormal soft tissue to the left of the pituitary fossa, between the lateral border of the sella and the cavernous sinus. This may represent a residual or recurrent pituitary adenoma. In view of its location, this newly-visualised tissue is not suitable for surgical resection. Currently ACTH measured 2h after her morning hydrocortisone dose is 178ng/L.
In view of this new finding on MRI and this patient's history of aggressive disease, should she undergo pituitary radiotherapy now?

Forum 3 – Miscellaneous Pituitary Cases
Chair: Dr James Ahlquist (Southend) and Dr Gerard Conway (London)

10. Reversible Hypopituitarism after Postpartum Lymphocytic Hypophysitis

Fernandez A, Karavitaki N & Wass JAH
Oxford Centre for Diabetes, Endocrinology and Metabolism (afernamed@hotmail.com)

A 34-year-old woman presented 9 months after normal delivery (previous uneventful pregnancy) with a 7-month history of fatigue, nausea, weight loss, amenorrhoea, inability to breastfeed. Investigations: 9.00am cortisol<2nmol/l, ACTH<5ng/l, FSH 0.6IU/l, LH<0.1IU/l, oestradiol <40pmol/l, prolactin 588mU/l(<400), IGF-I 8.86 nmol/l(14-47), fT4<2pmol/l, TSH 34.75mU/l, high anti-TPO antibodies, normal pituitary MRI. Lymphocytic adenohypophysitis was the presumed diagnosis co-existing with primary hypothyroidism. After >1 year of amenorrhoea, she had spontaneously two periods and became pregnant, while the other

deficiencies persisted. In lymphocytic adenohypophysitis, hypopituitarism can rarely be reversible and spontaneous pregnancies have exceptionally been reported. Awareness of this may prevent unwarranted lifelong replacement.

11. Management options for an intra/suprasellar cystic lesion with difficult histology

Barrington-Ward E, Martin NM, Roncaroli F, Mendoza N and Meeran K
Endocrine Unit, Imperial College Faculty of Medicine, Hammersmith Hospitals, London

A 43-year-old gentleman presented with increasingly blurred vision with evidence of a bitemporal hemianopia both on direct confrontation and perimetry. Pituitary MRI revealed an extensive cystic, haemorrhagic pituitary mass with suprasellar extension and optic chiasmal compression. Transphenoidal hypophysectomy was performed. Histological examination showed a cyst lined by squamous epithelium in keeping an epidermoid cyst, Rathke's cyst with squamous metaplasia or craniopharyngioma. Post-operatively, his visual fields initially improved, with small residual bilateral superior temporal defects. He required full pituitary replacement therapy. One year after surgery, MRI demonstrated significant tumour re-growth. Initially, the patient remained asymptomatic and conservative management was adopted. However, subsequent MRIs showed progressive enlargement of the tumour with the development of right temporal upper quadrantopia on perimetry. He was listed for surgery, but on admission for this, perimetry had spontaneously normalised and therefore, plans for surgery were postponed. Does this gentleman require radiotherapy in addition to further transphenoidal surgery if this may be a craniopharyngioma? If histology remains inconclusive, what should be our plan of action?

12. A Diagnostic Conundrum

Khalifa S & Baldeweg S
Department of Endocrinology, UCH, London

We would like to present this challenging case with diagnosis conundrum. Mrs ZA is a 40-year-old Somali lady who was found to have a pituitary macroadenoma during routine brain imaging for investigation of amenorrhoea and headache. She was also complaining of tiredness. On assessment she was found hypotensive with low random cortisol, low TSH and low fT4. An MRI pituitary scan showed 1.7 cm macro adenoma with suprasellar extension but no optic chiasm compression. She was started on Hydrocortisone 10mg + 5mg + 5mg and thyroxin 50ug. These are the blood results.

	Nov 05	Mar 06	Jul 06	Oct 06
TSH	0.21	3.0	0.13	1.95
fT4	8.8	3.8	8.1	11.3

	Mar 06	Oct 06
LH	4.9	2.9
FSH	5.9	7.2
Oestradiol	234	115
Prolactin	< 10	< 10

SST	0 min	30 min	60 min
Cortisol	290	746	838

GTT/GH	0 min	30 min	60 min	90 min	120 min
GH	0.8	0.5	0.5	0.4	0.3
Glucose	5.3	8.5	9.4	9.3	7.4

She remained on hydrocortisone for about 3 months before she was advised to stop on the awareness of the normal SST result. Five months after presentation the headache resolved spontaneously. A follow up pituitary MRI nine months later showed a dramatic decrease in the size of the pituitary gland. It is now entirely contained in the fossa and it is actually smaller than one would expect for the patient's age. There was no signs haemorrhage or infarction.

The questions to the panel would be:

1. what causes the pituitary adenoma / enlargement to shrink?
2. why was the prolactin level unrecordable despite suprasellar extension?
3. could it be lymphocytic hypophysitis?

13. Cushing's Disease Diagnosed Following Stroke

Nathan Y, Seal L & Sugihara C
Department of Endocrinology St Georges Hospital London (yashib@doctors.org.uk)

A 57-year-old retired roofer was initially referred in March 2006 to the endocrinology clinic by the stroke team, after suffering from a hemorrhagic stroke. He described a 5-year history of fatigue, central obesity and facial plethora. In 2003 he was suffering from reduced libido and reduced orgasmic function, at this time he was discovered to have a testosterone level of 6.6 and was commenced on testosterone replacement. There was no record of his gonadatrophins values at this point. Since then he commented on progressive increase in weight, easy bruising and proximal myopathy symptoms. He had been hypertensive since 1999 but was not diabetic. He reported no improvement of his fatigue symptoms on the testosterone replacement, and his ejaculatory failure and lack of libido continued. On examination he was found to have a blood pressure of 135/77 with no postural drop, he appeared to have florid cushingoid facies and centripetal obesity, intrascapular fat pad, and easy bruising, his testes were 15mls bilaterally and of good texture. Baseline investigations revealed IGF-1 15.4, Prolactin 334, FSH 0.2, LH < 0.1, testosterone 14.5, SHBG 23, Testosterone/ SHBG ratio 63 and ACTH 80(0-50). An overnight dexamethasone test did not suppress from 800 to 534.
A low dose/ high dose dexamethasone test showed cortisol levels of 614 on day 1, 326 on day 3 and 147 on day 5. Gut peptide screen was normal. A pituitary MRI revealed an infiltrating tumour eroding the floor of the pituitary fossa and body of the sphenoid and invading the clivus, there was noted to be suprasellar extension. His vision was recorded as R 6/9, L 6/6 and was noted to have a homonymous hemianopia following his cerebrovascular accident
He was commenced on metyrapone therapy 250mg tds. Inferior petrosal sinus sampling confirmed a right sided pituitary lesion, his baseline samples were suggestive of ectopic ACTH but CRH testing on the right the ACTH rose from 63 to 491 and on the left from 62 to 141, peripherally from 49 to a peak of 62, confirming pituitary dependant Cushings. He was referred to the neurosurgical team for an urgent opinion. After this consultation it was decided that he should undergo neurosurgical intervention by Caldwell luc approach and that he would also need postoperative radiotherapy. He underwent joint surgery from both the neurosurgical and maxillofacial teams and made a good post-operative recovery. He developed E coli urinary sepsis post operatively and was treated .A post operative overnight dexamethasone suppression test showed a cortisol of 202, and It was felt he should be commenced on ketoconazole 200mg bd as he had found it increasingly difficult to tolerate metyrapone pre operatively. He was admitted 10 days later to the medical ward with progressive weakness and general malaise and sore throat symptoms, he denied any urinary or CSF leak symptoms. His random cortisol at this time was 91 and it was felt that he had developed relative cortisol deficiency secondary to the ketoconazole. He was started on hydrocortisone orally 40mg, 20mg, 20mg and was treated with oral antibiotics. He was discharged home on a reducing course of hydrocortisone as he was clinically well. However he represented 24 hours later with visual hallucinations and increasing confusion, he underwent a lumbar puncture to rule out meningitis/ encephalitis. The results were normal and a neurological opinion was sought, at this time he was on 20mg, 10mg, and 10 mg of hydrocortisone. It was felt that the hallucinations were most likely due to metabolic disturbance post operatively. He was discharged on the above dose of hydrocortisone and follow up arranged together a hydrocortisone day profile and octeotide scan organized in view of the fact that there may be an ectopic ACTH source and an EEG organized in order to rule out atypical epilepsy. The EEG showed abnormal and episodic focal delta activity in keeping with a structural lesion. Octreotide scan was reported as normal. His latest day profile shows intrinsic cortisol production with an ACTH of 37 and his dose has been reduced to 10mg for 2 days and then 5mg once a day. He is currently undergoing postoperative radiotherapy.

Diagnostic and treatment issues were:
1. Initial misdiagnosis of secondary hypogonadism causing testosterone deficiency
2. Patient requires complex pituitary surgery as apposed to transsphenoidal surgery for large invasive tumour
3. Post-operative treatment of ketoconazole may have caused Addison's disease.
4. His underlying cerebrovascular pathology may have contributed to his current neurological status.

5. He still has endogenous high levels of cortisol suggesting that he still has functioning tumour; does he require further surgery?

14. Management of Incidental Non-functioning Pituitary Macroadenoma

Fonia A, Muralidhara K, Goulden P, Barnes DJ & Kumar J
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A 52-year-old Caucasian man was found to have a pituitary macroadenoma during routine brain imaging for changes in mood, memory and sexual function. He was evaluated for endocrine dysfunction and was found to have isolated growth hormone (GH) deficiency on combined pituitary function tests and an MRI showed 13 x 9 x 10mm cystic macroadenoma (Hardy's classification - grade A) that did not extend to the optic chiasm. He was treated with GH replacement at standard doses to improve his mood and this was later stopped due to dependent oedema and no improvement in AGHDA score (scoring complicated by history of depression). He was re-evaluated 4 years later with combined pituitary function tests, which were normal, although he did not achieve adequate hypoglycaemia for growth hormone response (table 1). IGF-1, however, was normal at 23.8nmol/L (normal range 11-44nmol/L). A repeat MRI scan revealed an increase in the size of the adenoma (13 x 16 x 17mm) with no encroachment onto the optic chiasm.

Incidental non-functioning pituitary macroadenomas need careful endocrine and imaging follow-up, and the treatment needs to be tailored to the patient's informed choice and the endocrine deficiency. The potential for growth non-functioning pituitary macro-incidentalomas has been reported, however, there is no consensus as to time for surgical intervention due to lack of adequate studies. We would like to discuss the management options of these tumours and their follow-up in regards to their size (Hardy's classification) and growth hormone deficiency.

Table 1: Combined Pituitary Function Test

Time (min)	Glucose (mmol/L)	Growth hormone (mcg/L)	Cortisol (mol/L)	TSH (mU/L)	FSH (IU/L)	LH (IU/L)	Prolactin (mIU/L)
0	-	< 0.10	280	0.87	4	2	238
30	2.7	0.73	360	5.64	7	11	
60	3.0	5.46	699	4.05	7	12	
90	3.9	5.41	726	-	-	-	-
120	4.4	3.48	542	-	-	-	-

15. Pituitary Apoplexy

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A 41-year-old man presented with sudden onset left sided headache. His past medical history included metallic aortic valve replacement and warfarin anticoagulation. He initially had no focal neurological symptoms but went on to develop a partial left third nerve palsy. CT was initially reported as normal but when reviewed pituitary apoplexy was noted. He was already panhypopituitary and due to the risks associated with warfarin and the need for anticoagulation with his metallic valve, he was managed conservatively. His ophthalmoplegia completely resolved within weeks although he remains panhypopituitary. This case would lead to the discussion of diagnosis of pituitary apoplexy and best management of pituitary apoplexy with ophthalmoplegia.

16. A Deceiving Prolactinoma

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A 49 year old man presented in 2000 with a history of sudden onset frontal headache nausea, vomiting and visual loss in his right eye. On examination he had a right third nerve palsy. His level of consciousness deteriorated rapidly to a GCS of 9/15. Imaging revealed a pituitary fossa tumour with suprasellar extension and high density areas within the tumour suggestive of haemorrhage. He proceeded to emergency decompression with good clinical improvement post-operatively.
A pre-operative prolactin returned at 2200 mU/l and following surgery was 889 mU/l. Histological examination revealed necrotic tissue with some fragments consistent with a pituitary adenoma. On follow up he has required thyroxine for secondary hypothyroidism and testosterone replacement for hypogonadotrophic hypogonadism. No further prolactin measurements were made until 2005, when his prolactin was 17900 mU/l, subsequently confirmed at 21400 mU/l. He was commenced on Cabergoline and his most recent prolactin was <40 mU/l. MRI imaging in 2001 and 2005 show an excess of soft tissue in the pituitary fossa.
1. While the initial management may not have been altered, are prolactin measurements during and immediately after apoplexy unreliable in distinguishing patients with macroprolactinomas, who may require different follow up?
2. What is the optimal follow up of patients who have had pituitary apoplexy?

17. A Case of Rapidly Developing Total Pituitary and Visual Failure.

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A 40-year-old woman had suffered with four months of nocturnal thirst and polyuria, sweats, amenorrhoea, cold intolerance, dry skin, severe myalgia, lassitude and intermittent headaches. Visual failure had developed insidisously with central field loss; carpal tunnel syndrome had been diagnosed three weeks prior to admission. An MRI brain revealed an enhancing hypothalamic/pituitary mass. She had a 12-year-old son whom she had breastfed; menses returned spontaneously, she had never suffered with spontaneous galactorrhoea. On examination she was euthyroid, pulse 80bpm, blood pressure 90/60 mmHg with no drop; the rest of the examination was normal. The pupils were equal and reactive to light and accommodation, gaze was conjugate, the discs were clear; the fields showed partial blindness bitemporally and red-desaturation bilaterally over the midline. Anterior and posterior pituitary failure was evident on investigation, the prolactin was 2065mU/L. Pituitary imaging showed an inhomogenously enhancing lesion involving the hypothalamus, pituitary and optic chiasm. CT chest/abdomen was normal. The presence of rapidly developing visual failure, anterior and posterior pituitary failure and the absence of extracranial malignancy made us consider the diagnosis of an intracranial germ cell tumour. CSF and serum were negative for α-fetoprotein and β-HCG and chemotherapy was withheld. Dedicated pituitary imaging showed an enhancing pituitary lesion with possible thickening of the stalk and chiasm. Dexamethasone, cabergoline and thyroxine were commenced pending trans-sphenoidal biopsy. At biopsy a normal looking gland was seen under a thinned fossa. However, on incision of the pituitary, under tension, copious dark, altered clot with golden flecks (suspicious of cholesterol) appeared; a soft, yellowish mass with old haemorrhage within it was seen and removed. Post-operatively growth hormone, gonadotrophin and TSH deficiency and diabetes insipidus were present; the hypothalamo-pituitary-adrenal axis was intact. Initial histology suggested haemorrhage and granulomatous inflammation; outside review of the histology suggested however that this was low grade mesenchymal tumour of the sella region. Serial imaging has not revealed a primary mesenchymal tumour. She has remained well on follow up on

replacement thyroxine, cyclo-progynova and desmopressin.

18. Pituitary metastasis

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A 48-year-old female presented with a 5-week history of painless progressive blurred vision over left visual field. There was no history of weight loss, loss of libido, loss of body hair, cold intolerance, polydipsia, nor polyuria. Past medical illness included breast cancer 20 years ago with lumpectomy and radiotherapy. She had cancer recurrence 12 years ago with mastectomy and ovarian metastasis 2 years ago. On examination, VA was 6/9 on the right and HM on the left. Left RAPD was detected. Fundus examination showed a mildly swollen disc at the left. Visual field revealed bitemporal hemianopia. MRI brain demonstrated a suprasellar mass. Resection of the tumour confirmed a metastasis. The imaging features of this tumour which pointed towards that diagnosis will be discussed together with a review of clinical features of pituitary metastases.