

Programme

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Abstract Book

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KARL STORZ - ENDOSCOPE

Programme

08:15	Registration
09:15	Welcome and introduction Mr M Powell & Dr S E Baldeweg
09:20	Case 1 – Pasireotide therapy in a patient with acromegaly, Cushing's and hyperprolactinaemia secondary to a pluripotential pituitary tumour <i>Author(s): Azraai Nasruddin, Rajesh Rajendran, Simon Barker, Derek Sandeman University Hospital Southampton</i>
9:40	Key note lecture: Pasireotide in acromegaly and Cushing's disease Dr Diego Ferone University of Genova
10:20	Forum 1 – Case presentations – Corticotroph adenomas Chairs: Dr S E Baldeweg & Mr M Powell Case 2 – Clinically significant Cushing's Disease with Discordant Biochemistry - ? Cyclic Cushing's <i>Author(s): S Zac-Varghese, P Behary, F S Wernig, R Fikr, K Meeran. Imperial College London</i> Case 3 – An unusual case of Complicated Cushing's <i>Author(s): N Rashid, M Thomas, J Grieve, P Hyatt, SE Baldeweg University College London Hospitals</i> Case 4 – An aggressive ACTH- secreting pituitary macroadenoma in a patient with congenital adrenal hyperplasia - a pituitary feedback tumour <i>Author(s): D Cavlan¹, F Afshar², R Carpenter^{1,2}, D Lowe^{1,2}, PN Plowman^{1,2}, M Himonas³, GM Besser^{1,2} ¹Department of Endocrinology, St Bartholomew's Hospital, London ²The London Clinic Centre for Endocrinology ³Nicosia General Hospital, Cyprus</i>
	Case 5 – Watch Out for the Silent Ones <i>C. Izzi-Engbeaya, R. Sharma, A. Al-Nahas, B. Jones, A. Mehta, N. Mendoza, N. Martin, K. Meeran. Charing Cross Hospital, London</i>
11:20	Coffee and posters
11:50	Echocardiography for patients treated with dopamine agonists- an update Professor Will Drake St Bartholomew's Hospital, London

12:20	Forum 2 – Case presentations – Infections Chairs: Dr M Vanderpump & Miss J Grieve Case 6 – Pituitary tuberculosis presenting with panhypopituitarism and bitemporal hemianopia <i>Author(s): E Panteliou, A Mian, V White, J Grieve, D Berney, J Evanson, W M Drake</i> <i>St Bartholomew's Hospital, London</i>
	Case 7 – Tuberculosis in the pituitary fossa – a common pathology in an uncommon site <i>Author(s): Dr Kalpita Majumdar, Dr Maria Barnard</i> <i>Whittington Hospital, London</i>
	Case 8 – Hypopituitarism in a patient with HIV and toxoplasmosis <i>Author(s): K Jeyaraman, D L Morganstein</i> <i>Chelsea and Westminster Hospital, London</i>
13:05	Lunch and posters
14:00	Pituitary Foundation
14:15	Genetics in pituitary disease – an update Professor Marta Korbonits St Bartholomew's Hospital, London
14:45	Forum 3 – Case presentations - Diabetes Insipidus Chairs: Dr Ahlquist & Miss J Grieve Case 9 – A Case of Severe Gestational Diabetes Insipidus <i>Author(s): J W Pomroy, M A Cohen</i> <i>Barnet General Hospital</i>
	Case 10 – One drink too many! <i>Author(s): Dr Ashwini Swamy, Dr Smitha Nalla, Dr John Clark</i> <i>West Suffolk Hospital</i>
	Cases 11 – When 15 pints isn't one too many! <i>Author(s): Mr A Kailaya-Vasan, Professor R Ross & Mr S Sinha</i> <i>Royal Hallamshire Hospital, Sheffield</i>
15:30	Afternoon tea and posters
15:45	Key note lecture: Extracapsular resection of prolactinomas Ian McCutcheon The University of Texas MD Anderson Cancer Center, Houston

16:30	Forum 4 – Case presentations – Prolactinomas Chairs: Dr M Vanderpump & Mr M Powell Case 12 – Temozolomide therapy in an aggressive macroprolactinoma with late-onset dopamine agonist resistance – does temozolomide therapy modify sensitivity to dopamine agonists? <i>Author(s): Azraai Nasruddin, Simon Barker, Derek Sandeman, Geoff Sharpe University Hospital Southampton</i>
	Case 13 – Incidental haemorrhage in prolactinomas. Is it of any clinical significance? <i>Author(s): K N Sarwar, M S B Huda, V Van de Velde, L Hopkins, S. Luck, R Preston, B M McGowan, P V Carroll, J K Powrie King's College London</i>
	Case 14 – Prolactinoma co-secreting growth hormone <i>Author(s): A Ihuoma, J A Ahlquist, Southend University Hospital</i>
17:15	Poster and presentation prizes Dr S E Baldeweg
17:30	Close

Abstracts for orally presented cases

Case 1 - Pasireotide therapy in a patient with acromegaly, Cushing's and hyperprolactinaemia secondary to a pluripotential pituitary tumour

***Author(s): Azraai Nasruddin, Rajesh Rajendran, Simon Barker, Derek Sandeman
University Hospital Southampton***

We report the preliminary response to pasireotide in a patient with a pluripotential pituitary adenoma.

A 65 year old man presented with impotence in 2008 with hyperprolactinaemia (prolactin 12550mU/L). He had acromegalic features, diabetes, hypertension and left ventricular hypertrophy. Basal GH was elevated (32 micrograms/L) with failure to suppress on glucose tolerance testing. Pituitary MRI revealed a 2cm macroadenoma. He was commenced on cabergoline and underwent transsphenoidal surgery in December 2008. GH levels improved but remained elevated and octreotide LAR was commenced.

Despite octreotide LAR 30mg/month he had inadequate control (IGF-1 771micrograms/L, mean GH 4.7micrograms/L). Imaging showed significant residual tumour extending to the left cavernous sinus. He declined radiotherapy and underwent further debulking transsphenoidal surgery (April 2011). Histology from this surprisingly stained for ACTH but not GH or prolactin. We reviewed his initial histology which showed an adenoma staining for GH, prolactin and ACTH.

He subsequently developed fatigue and weight gain. Results showed secondary hypothyroidism and elevated midnight salivary cortisol (15.8/19.1nmol/L). Further testing confirmed hypercortisolaemia (24hr UFC 451nmol/L, cortisol 177nmol/L following 1mg dexamethasone, cortisol 105nmol/L following the LDDST) with normal ACTH levels. IGF-1 remained elevated (314microgram/L) with mean GH of 2micrograms/L on octreotide. With the biochemical and histological findings we concluded he had concurrent acromegaly and pituitary Cushing's.

We recommended radiotherapy but opted for a trial of subcutaneous pasireotide (0.6mg twice daily) to begin with on the basis that it may treat both conditions. Within 2 months he reported significant improvement in well-being. GH levels improved (mean GH 0.2micrograms/L, IGF-1 64micrograms/L). However hypercortisolaemia persists (24hr UFC 436nmol/L, midnight salivary cortisol 8.6/11.4nmol/L). Repeat imaging at three months shows change in tumour appearance (loss of contrast enhancement). We conclude that there has been a partial response to pasireotide. We are considering radiotherapy with continued pasireotide as bridging therapy.

Case 2 – Clinically significant Cushing's Disease with Discordant Biochemistry - ? Cyclic Cushing's

Author(s): S Zac-Varghese, P Behary, F S Wernig, R Fikr, K Meeran.
Imperial College London

A 49 year old gentleman presented with clinical features of Cushing's syndrome. He had a two year history of 15 kg weight gain, had developed type 2 diabetes mellitus and had recently fractured his left fibula.

He had been previously investigated in Malaysia. He was found to have an elevated random cortisol of 1,922 nmol/L and he had failed an overnight dexamethasone suppression test with a cortisol following suppression of 330 nmol/L with an ACTH 70 ng/L. He also had reports of an MRI pituitary scan which did not suggest an obvious pituitary lesion and a CT abdomen which was reported as normal although the adrenal size was not commented on.

Physical examination revealed central obesity and abdominal striae. We repeated two dexamethasone suppression tests (results below). In addition, two 24 hour urine collections for urinary free cortisol were obtained. The first was elevated at 281 nmol/L (normal values <270) and the second normal 217 nmol/L. Anterior pituitary investigation did not reveal any other abnormality.

Time	Cortisol (nmol/L)	ACTH (ng/L)
9am Day 0	580	83.2
9am Day 1	41	23.5
9am Day 2	185	62.7

Time	Cortisol (nmol/L)	ACTH (ng/L)
9am Day 0	562	-
9am Day 1	889	138
9am Day 2	28	38

Our patient has clinical features of Cushing's although his biochemistry is discordant. This may fit with cyclic Cushing's. Cyclic Cushing's is demonstrated by episodic hypercortisolaemia and is most commonly caused by Cushing's disease although has although been reported to be associated with Ectopic ACTH secretion. The mechanism of periodicity is unknown but may include infarction, necrosis, tumour calcification or patient stress. Our patient is still under investigation and inferior petrosal sinus sampling has been arranged.

Case 3 – An unusual case of Complicated Cushing’s

Author(s): N Rashid, M Thomas, J Grieve , P Hyatt, S E Baldeweg
University College London Hospitals

Introduction:

Cushing’s syndrome is broadly categorized into ACTH dependent (Pituitary & ectopic source) and ACTH independent (adrenal source). Localizing source of Cushing’s can sometimes be a cumbersome diagnostic process.

Reversible dilated Cardiomyopathy is rare complication of Cushing’s which can significantly compromise patient’s clinical condition and quality of life.

Case History:

A 25- year- old male patient presented with rapid onset weight gain, muscle weakness and occasional headaches as well as severe dyspnoea, orthopnea and PND. There was no significant past medical or family history. He was not on any regular medication and denied exogenous steroids intake. He had clinical features consistent with florid Cushing’s syndrome and congestive cardiac failure. Cardiac MRI suggested severe dilated Cardiomyopathy with EF 23% which was treated medically. His screening investigations for Cushing’s showed discordance with clinical picture. He had high 24 hour urine free cortisol on 2 occasions but suppressed < 28 on LDDST. Two early mornings ACTH levels were undetectable and prompted investigations for adrenal source. CT and MRI adrenals failed to localize an adenoma. Alternative sources were then explored. Pituitary MRI and subsequent dynamic pituitary MRI were entirely normal apart from stalk deviation to left side. No ectopic source of disease was found on Gallium octreotide PET CT. Rest of the Pituitary function tests were satisfactory. He had IPSS which showed strong lateralization to left side of pituitary. He was started on Metyrapone in the interim while awaiting surgery.

Repeat cardiac MRI showed improvement in cardiac function (EF 41%). He had pituitary surgery twice within a week as post operative cortisol remained high (785nmol/L) after first surgery. Second surgery has rendered him pan-hypopituitarism but cured Cushing’s disease.

Conclusions:

Diagnosing Cushing’s syndrome and identifying the source can sometimes be challenging and require more invasive investigations.

Reversible dilated Cardiomyopathy as a complication of Cushing’s needs early recognition and optimal cardiac treatment.

Case 4 – An aggressive ACTH-secreting pituitary macroadenoma in a patient with congenital adrenal hyperplasia - a pituitary feedback tumour

Author(s): D Cavlan¹, F Afshar², R Carpenter^{1,2}, D Lowe^{1,2}, PN Plowman^{1,2}, M Himonas³, GM Besser^{1,2}

¹Department of Endocrinology, St Bartholomew's Hospital, London

²The London Clinic Centre for Endocrinology

³Nicosia General Hospital, Cyprus

A Cypriot woman with an unremarkable past history and two children developed secondary amenorrhoea aged 38, and a year later galactorrhoea. Serum prolactin was 3000mU/l (125-625mU/l). A pituitary MRI scan demonstrated a macroadenoma pressing on the optic chiasm, right optic nerve and both cavernous sinuses. She underwent transsphenoidal surgery and following this her headaches resolved and regular menses returned.

After 7 years her symptoms returned; repeat MRI showed regrowth of the tumour and she was referred to our department. Serum prolactin was 530mU/l, 9am cortisol 514nmol/l with no features of Cushing's syndrome. She had a second transsphenoidal operation and histology showed a tumour immunostaining for ACTH.

During the subsequent conventional pituitary radiotherapy she developed clinically marked Cushing's syndrome. Now the serum cortisol was 995nmol/l only falling to 793nmol/l during a 48 hour low dose dexamethasone suppression test (<50nmol/l). A 17-hydroxyprogesterone level was elevated at 336nmol/l (<10nmol/l). An adrenal CT showed bilateral adrenocortical hyperplasia, and genetic analysis confirmed the diagnosis of congenital adrenal hyperplasia with 21-hydroxylase deficiency (homozygous positive for the 1683G>T mutation). Genetic analysis of family members showed that her mother was affected by 21-hydroxylase deficiency, while her father and her own two daughters were carriers.

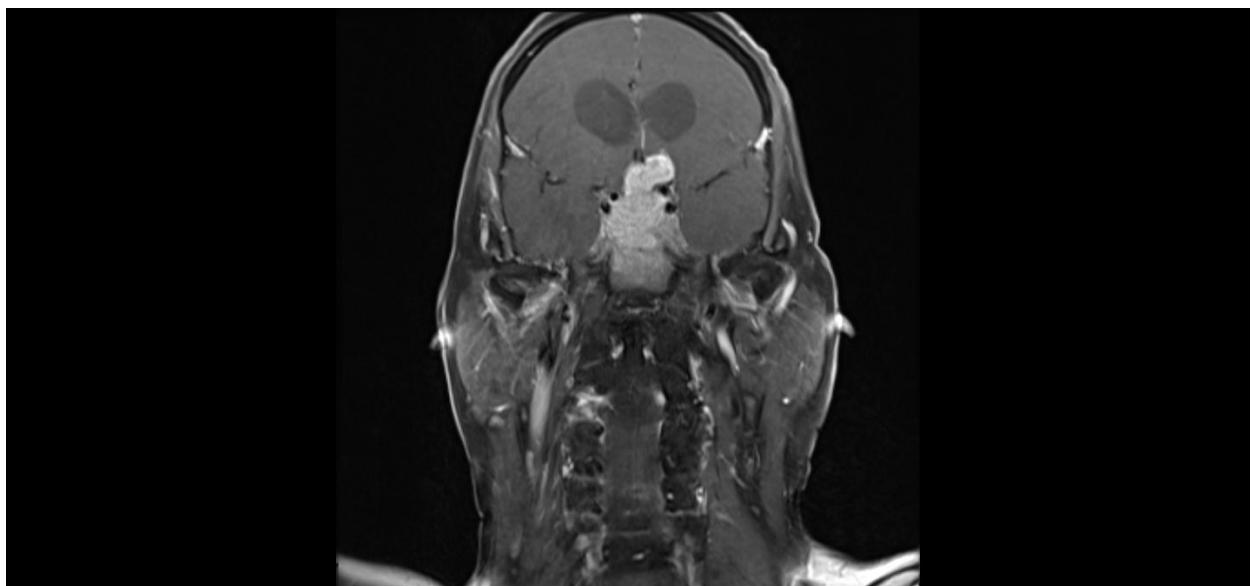
After 4 months further tumour regrowth necessitated stereotactic gamma-knife radiotherapy leading to tumour shrinkage remaining static over the ensuing decade.

Pituitary "feedback tumours" typically show hyperplasia developing in the longstanding absence of an inhibitory signal from a failing peripheral endocrine gland, most commonly hypothyroidism or hypogonadism. In this instance the lesion was an aggressive tumour without hyperplasia (the reticulin network was destroyed) and was associated with 21-hydroxylase deficiency. We discuss mechanisms for tumour development and for the delayed presentation of clinical Cushing's syndrome in this case.

Case 5 – Watch Out for the Silent Ones

C Izzi-Engbeaya, R Sharma, A Al-Nahas, B Jones, A Mehta, N Mendoza, N Martin, K Meeran.
Charing Cross Hospital, London

A 65-year-old man went to see his GP with a 6 month history of progressive unsteadiness. His past medical history included hypertension and hypercholesterolaemia, which were treated with amlodipine and simvastatin respectively. An MRI of his brain was requested and it revealed an extensive pituitary macroadenoma infiltrating the central skull base and causing hydrocephalus (see image). Clinical examination was unremarkable apart from a bitemporal hemianopia that was confirmed by formal visual field assessment. He was not incontinent and his AMT was 8/10. His pituitary profile was normal apart from secondary hypogonadism. Histology from a biopsy of the lesion showed that 20% of the neoplastic cells were ACTH positive, Ki67 index was 2% and there was no p53 over-expression. Furthermore 60-70% of the neoplastic cells expressed MGMT (O-6-methylguanine-DNA methyltransferase).



He did not have signs of Cushing's Disease and his cortisol suppressed to 19nmol/l after a 48-hour low dose dexamethasone suppression test. The risks of non-curative surgery were deemed to outweigh the benefits, therefore trans-sphenoidal surgery was not performed. He was referred to the Oncologists and started temozolomide in Dec 2012.

Question:

1. What is the experience of other centres with temozolomide treatment for silent corticotroph adenomas which are positive for MGMT?

Case 6 – Pituitary tuberculosis presenting with panhypopituitarism and bitemporal hemianopia

Author(s): E Panteliou, A Mian, V White, J Grieve, D Berney, J Evanson, W M Drake

St Bartholomew's Hospital, London

A 35 year old Bangladeshi man presented with a short history of headaches, fevers, night sweats, weight loss, reduced libido and erectile dysfunction, polydipsia, polyuria and nocturia. He last visited Bangladesh in 2009, denied TB contacts and his chest X-ray was normal.

His pituitary profile was as follows: cortisol: 122 nmol/L (200-600), TSH: 0.03 mIU/L (0.3-4), free T4: 7.0 mmol/L (10.5-24.5), IGF-1: 109 ng/mL (109-284), FSH: 1.8 IU/L (1-10), LH: 0.4 IU/L (1.8-8), testosterone 0.7 nmol/L (9-27), dehydroepiandrosterone 0.6 umol/L (2.3-10), SHBG 30 nmol/L (17-50). His biochemistry showed a sodium of 146 mmol/L (133-146), serum osmolality of 302 mOsm/kg (275-295), urine osmolality of 468 mOsm/kg (50-1200) and HCG<1 IU/L (0-3 IU/L).

On MRI, pituitary volume was satisfactory, the stalk and chiasm were normal and there was no evidence of granulomatous disease.

A diagnosis of panhypopituitarism was made and was discharged in good health on levothyroxine, hydrocortisone, testogel and desmopressin with an intention to repeat the MRI scan in 3 months.

2 months later he presented to Moorfields Eye Hospital with blurred vision, diplopia and headache. On examination his visual acuity was reduced to 6/24 in the right and 6/18 in the left eye and there was a bitemporal hemianopia.

A repeat MRI showed a markedly enlarged pituitary extending into the suprasellar region, stretching the optic chiasm. A presumptive diagnosis of tuberculous hypophysitis was made.

He underwent urgent transphenoidal surgery for deteriorating vision and, immediately post-operatively was started on rifampicin, isoniazide, pyrazinamide, moxifloxacin and pyridoxine. His vision recovered after surgery. A clinically concerning hepatitis (peak ALT 417 IU/ L) was managed by temporary discontinuation, followed by gradual, staged reintroduction of therapy and he was discharged taking rifampicin, isoniazid, ethambutol, moxifloxacin and pyridoxine.

Histology showed widespread necrotizing granulomatous inflammation, epithelioid macrophages, multinucleated giant cells compatible with TB. No neoplastic changes were noted.

Case 7 – Tuberculosis in the pituitary fossa – a common pathology in an uncommon site

**Author(s): Dr. Kalpita Majumdar, Dr. Maria Barnard
Whittington Hospital, London**

Intrasellar tuberculomas are extremely rare. We present the complex case of a woman who was treated for a pituitary tuberculoma.

A 25-year old woman was referred to Endocrinology with a history of bi-temporal headaches, amenorrhea, sub-fertility and weight gain. She had been reviewed in the Respiratory clinic the previous year with clinical and radiological findings of pulmonary tuberculosis, but no histological confirmation. A 7-month course of empirical anti-tubercular therapy led to significant improvement.

In the endocrine clinic, the patient was had secondary hypothyroidism, the remaining pituitary functions were normal. MR scan of the pituitary fossa revealed a large sellar mass, extending into the supra-sellar space. The patient underwent a trans-sphenoidal hypophysectomy at our regional neuro-endocrine centre. Histology of the resected mass revealed a necrotising granulomatous hypophysitis with no acid-fast bacilli (AFB). Tuberculosis of the pituitary was considered most likely. Anti-tuberculous therapy was recommenced for one year, with a slightly delayed but good radiological response to treatment.

Although the first reported case of a sellar tuberculomas was from Britain in 1924, there are very few reports from the Western hemisphere. Sharma et al, who have reported the largest series on intrasellar tuberculosis so far, have described a 100% incidence of headaches and 38% incidence of endocrine disturbances including the amenorrhea-galactorrhea syndrome. A concomitant history of systemic tuberculosis is not always present. The clinical and radiological features of these lesions mimic a typical pituitary adenoma. Our patient continued being amenorrheic and it was especially surprising to note low cortisol levels during pregnancy, which is a state characterised by raised cortisol levels (secondary to higher cortisol binding globulin). It is important to be aware of these hormonal variations as we are more likely to see and deal with unusual infections that are no longer restricted to the 'developing' world.

Case 8 – Hypopituitarism in a patient with HIV and toxoplasmosis

***Author(s): K Jeyaraman, DL Morganstein
Chelsea and Westminster Hospital, London***

We present a 44year old gentleman with HIV since 1996 who was treated for cerebral toxoplasmosis in 2010. He subsequently developed absent sex drive, erectile dysfunction and loss of body hair. He also reported dizziness on standing and intermittent dull headaches, but no loss of consciousness or collapses, or episodes of severe or sudden onset headaches. His medications include Truvada, Ritonavir and Darunavir. He denied use of anabolic steroids. Examination showed no postural drop, normal visual fields, normal secondary sexual characteristics and 15-20ml bilateral testes.

Initial investigations showed low testosterone, LH and FSH consistent with hypogonadotrophic hypogonadism. Given his constellation of symptoms, he went on to have investigations to rule out panhypopituitarism. Repeat testosterone levels were low (2.2 nmol/l) with low LH (1.0 IU/L) and FSH (1.3 IU/L). LH and FSH showed inadequate response to GnRH stimulation in keeping with hypopituitarism. There was normal cortisol response to synacthen stimulation. Prolactin (39 mu/L), IGF1 (3.4 nmol/l) and growth hormone (<0.05 mcg/l) were low. Thyroid function test was normal. He is due to have glucagon stress test to assess his growth hormone reserve following which hormone replacement will be discussed with him. Pituitary MRI with contrast showed features consistent with empty sella and loss of pituitary volume since previous studies, which had not shown any evidence of an adenoma, making apoplexy unlikely. We hypothesise that he developed hypopituitarism secondary to cerebral toxoplasmosis.

Only two previous cases have been reported of toxoplasmosis presenting as hypopituitarism in HIV patients. Endocrine disorders in HIV infection are often a result of opportunistic infections of endocrine organs. The clinical manifestations may be subtle and may be overlooked, particularly in the setting of chronically and severely ill patients. Recognition and prompt treatment is essential in these cases.

Questions for the panel include:

- Should we perform endocrine tests on all HIV positive patients with toxoplasmosis?
- Was the hypopituitarism likely to have developed at the time of infection or as a late phenomenon. Would earlier recognition have changed outcome?

Case 9 – A Case of Severe Gestational Diabetes Insipidus

Author(s): J W Pomroy, M A Cohen
Barnet General Hospital

A 39 year old lady of African origin who was 33 weeks pregnant with monochorionic diamniotic twins presented with a week's history of vomiting and confusion. She was severely dehydrated and tachycardic (pulse 140 bpm), BP 127/75. She described polyuria and polydipsia of 4L/day for several weeks. The obstetricians proceeded directly to emergency caesarean section for foetal distress.

Investigations revealed profound hypernatraemia (167mmol/L), acute kidney injury (creatinine 259umol/L) and grossly deranged LFTs (ALT 1300iu/L, ALP 590iu/L, Bili 29umol/L) consistent with acute fatty liver of pregnancy (AFLP).

On endocrine review she was polyuric (400 ml/hr) with urine osmolality 128 mosm/kg and serum osmolality 337 mosm/kg diagnostic of diabetes insipidus (DI). She was transferred to HDU where she was given 2mcg DDAVP IM with hourly measurement of urine osmolality (mosm/kg). Urine osmolarity increased by more than 50% following DDAVP excluding nephrogenic DI.

The differential diagnosis of acute DI in pregnancy includes pituitary apoplexy, lymphocytic hypophysitis and gestational DI. Anterior pituitary function and MRI pituitary were normal implicating gestational DI.

AFLP resolved 12 days after caesarean section. She was discharged with 100mcg DDAVP po which was withdrawn after 6 weeks indicating resolution of DI.

Gestational DI is thought to be due to inactivation of endogenous AVP by placental vasopressinase. It appears to be more severe in patients with AFLP where it has been proposed that associated hepatic dysfunction leads to reduced clearance of placental vasopressinase.

Fortunately exogenous DDAVP appears to be relatively resistant to placental vasopressinase.

The gestational DI in our patient was particularly severe and this is likely to have been contributed by twin pregnancy and gross hepatic dysfunction.

Loss of biological activity of arginine vasopressin during its degradation by vasopressinase from pregnancy serum.

Gordge MP, Williams DJ, Huggett NJ, Payne NN, Neild GH, Clin Endocrinol. 1995 Jan;42(1):51-8.

Case 10 – One drink too many!

Author(s): Dr Ashwini Swamy, Dr Smitha Nalla, Dr John Clark
West Suffolk Hospital

40 years old previously fit IT Consultant presented with three years history of polyuria and polydipsia which was preceded by a viral illness. He consumed 10-12 pints every day and passed urine every 2 hourly with nocturia. He had suffered from occasional headaches. His symptoms were so disruptive that he had organised to work from home to accommodate his health needs. Examination was unremarkable.

Baseline investigations revealed hypernatraemia (148 mmol/l), with normal full blood count, ESR, fasting glucose, and a negative autoimmune screen. Endocrinology demonstrated him to have hypogonadotropic hypogonadism (testosterone 1.0 nmol/l, FSH 1.7 IU/L, LH 1.5 IU/L). He was eucortisolemic, euthyroid and normoprolactenemic.

Water deprivation test was suggestive of cranial diabetes insipidus.

Water Deprivation Test

Time	Urine volume	Plasma osmolality (mosmol/kg)	Sodium Mmol/l	Urine osmolality Mosmol/kg	Weight (kg)
08:00	2130 mls	298	141	98	98.2
09:00	795 mls				97.5
10:00	958 mls	300	144	94	96.9
11:00	861 mls				96.2
12:00	628 mls	308	147		96.0
13:00	673 mls				95.6
14:00	590 mls	313	150	133	95.3
15:00	350 mls				95.0
DESMOPRESSIN 2mcg im. at 15.05					
16:00	177 mls			334	97.5
17:00	69 mls			498	98.6
18:00	51 mls			586	99.7
19:00	57 mls			476	100

A contrast MRI revealed appearances of an empty pituitary fossa with an enhancing 'bulky' pituitary stalk/ hypothalamus.

DDAVP therapy was associated with marked improvement in symptoms.

CT scan (chest, abdomen pelvis) did not reveal evidence of Langerhans cell histiocytosis.

He awaits treatment of hypogonadism and further characterization of the pituitary lesion.

Cases 11 – When 15 pints isn't one too many!

***Author(s): Mr A Kailaya-Vasan, Prof R Ross & Mr S Sinha
Royal Hallamshire Hospital, Sheffield***

We present this case of a 30yr old lady who has a hypothalamic lesion of unknown pathology. She presented with headaches, lethargy and confusion and subsequent imaging revealed an enhancing hypothalamic lesion.

A biopsy was initially attempted but was unsuccessful. Post-operatively the patient deteriorated acutely and blood tests demonstrated a serum sodium of 174mmol/L. It was also noticed that she was passing large amounts of dilute urine and a diagnosis of diabetes insipidus (DI) was made. Interestingly, following stabilisation the patient reported a detailed history stating that she was tall as a child, had early menarche aged 9, stopped growing at the age of 11 and had put on a significant amount of weight. Importantly, she described regular episodes of polyuria and polydipsia where she started drinking 15 pints of water per day. This started three years earlier when she was pregnant. As this was not recognised prior to surgery, placing the patient NBM resulted in her severe hypernatraemia.

Pharmacological therapies for both DI and hypopituitarism were commenced and a tissue diagnosis was attempted via trans-sphenoidal surgery, however this was non-diagnostic. Despite surgical debulking and pharmacological management, she remained symptomatic and surveillance imaging a year later revealed re-growth of the lesion. Trans-sphenoidal surgery was repeated and histological analysis demonstrated chronic inflammatory changes. Interestingly, her lesion demonstrated an impressive response to steroids and azathioprine. In addition, the patient reports a family history of sarcoidosis. Although a tissue diagnosis has not been obtained, given these findings a provisional diagnosis of neurosarcoidosis has been made. This is further supported by upper zone groundglass opacification seen on HRCT chest imaging, albeit these features are not entirely typical.

In conclusion, we present a case which highlights the dangers of not recognising diabetes insipidus pre-operatively and also describe an unusual lesion that may be neurosarcoidosis.

Case 12 – Temozolomide therapy in an aggressive macroadenoma with late-onset dopamine agonist resistance – does temozolomide therapy modify sensitivity to dopamine agonists?

***Author(s): Azraai Nasruddin, Simon Barker, Derek Sandeman, Geoff Sharpe
University Hospital Southampton***

We present a 66 year old man who presented in 1999 with a large macroadenoma with suprasellar extension and prolactin of > 120,000mU/L. He had good response to cabergoline with significant tumour shrinkage and normalisation of prolactin. However resistance to cabergoline gradually developed between 2003-2007 with rising prolactin despite cabergoline doses of up to 7mg/week and tumour enlargement with invasion of the right cavernous sinus resulting in headaches, ptosis and diplopia. Trial of tamoxifen and switching to quinagolide/bromocriptine did not help. External beam radiotherapy was delivered in 2008 with improvement in symptoms and significant fall in prolactin but between 2009-2010 rapid tumour growth occurred.

Transcranial debulking surgery was performed in 2010. Histology confirmed aggressive prolactinoma (Ki67 index > 20%). Post-operatively tumour growth persisted with a prolactin doubling time of 3 months. He was commenced on temozolomide (300mg daily for 5 days/cycle) for 8 cycles, completed in September 2011. He remained on cabergoline therapy at an average dose of 3-4mg/week.

Gradual fall in prolactin was observed from > 30,000 at the start to 3680 at the end of temozolomide therapy with resolution of headaches and ptosis but with persistent diplopia. Prolactin continued to fall reaching a nadir of 1060 in May 2012 with progressive tumour shrinkage on MRI imaging at 3 and 10 months post-therapy. We therefore decided to wean down the dose of cabergoline but this resulted in recurrence of headaches and nausea with rising prolactin levels. Cabergoline dose was promptly increased back to 4mg/week with abrupt fall in prolactin which is now maintained around 1000.

Our case demonstrates good response to temozolomide with ongoing fall in prolactin over a year following cessation of therapy with partial return of sensitivity to cabergoline. This suggests a possible role of cabergoline as adjunctive therapy in combination with temozolomide in resistant prolactinomas.

Case 13 – Incidental haemorrhage in prolactinomas. Is it of any clinical significance?

Author(s): KN Sarwar, MSB Huda, V Van de Velde, L Hopkins, S. Luck, R Preston, BM McGowan, PV Carroll, JK Powrie
King's College London

Background: Incidental pituitary haemorrhage in prolactinomas is a common radiological finding. The clinical significance, associations and outcome of this are largely unknown. Most reports describe surgically treated macroprolactinoma and non-functioning adenoma, and there are few data in a clinic prolactinoma population.

Aims: To characterise the prevalence, natural history and risk factors associated with pituitary haemorrhage in a large clinic prolactinoma population.

Method: A retrospective case-note analysis of 368 patients with prolactinoma attending Guy's and St. Thomas' Hospitals between 2000 and 2008. Presence of haemorrhage was noted on magnetic resonance imaging (MRI).

Results: Pituitary haemorrhage was found in 25 patients, giving an overall prevalence of 6.8%, and was significantly more prevalent in macroprolactinoma (20.3%) than in microprolactinoma (3.1%) ($p<0.0001$). Three patients had classical pituitary apoplexy. The majority of patients in the haemorrhage group had macroprolactinomas (16/25 (64%)) and the majority were female (22/25 (88%)). The proportion of females with macroprolactinoma was also higher in the haemorrhage group (14/16 macroprolactinomas (87.5%)) than in the non-haemorrhage group (36/63 macroprolactinomas (57.1%)) ($p=0.02$). The majority of patients were treated conservatively (92%) with 87% of patients having complete resolution of their haemorrhage within 26.6 ± 5.2 (mean \pm standard error of mean) months. Anticoagulant therapy, diabetes, hypertension and type of dopamine agonist therapy were not associated with pituitary haemorrhage. After adjustment for confounders, the presence of macroprolactinoma (odds ratio 9.00 95%CI 3.79- 23.88 $p<0.0001$) and being female (odds ratio 8.03 (95%CI 1.22-52.95, $p=0.03$) were independently associated with haemorrhage.

Conclusion: These data show that haemorrhage is relatively common in macroprolactinoma where 1 in 5 develop haemorrhage, but is also present in microprolactinoma. The vast majority were clinically silent and resolved spontaneously with only dopamine agonist therapy. We present novel data showing that women, particularly with macroprolactinoma, were more likely to develop haemorrhage in comparison to men.

Case 14 – Prolactinoma co-secreting growth hormone

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A 49 year old man was found to have a pituitary mass on CT head whilst being investigated for headache. MRI showed a pituitary mass measuring 2.2cm x 2.2cm x 1.6cm close to the optic chiasma but not compressing it. Visual fields were normal. Prolactin was elevated at 27971mu/L(NR 0-331mu/L) so Prolactinoma was diagnosed. He had hypogonadotrophic hypogonadism, LH 1.7u/L, FSH 3.1u/L, and Testosterone 6.7nmol/L. Thyroid and adrenal axes were normal.

Despite treatment with a fairly high dose of cabergoline 500mcg daily, the pituitary mass after two years has not shrunken much (1.8cm x 1.5cm x 1.6cm). Interestingly, though the prolactin level has fallen to 1370mu/L, the IGF1 levels have risen progressively from a mildly raised baseline level of 295 to 870 and later on 1229ng/ml(NR 94-252ng/ml). In addition there was no suppression of the Growth hormone(GH) on OGTT, basal 3.1ng/ml and nadir 2.3ng/ml. He does not look acromegalic and apart from snoring and bilateral carpal tunnel syndrome, he does not have other symptoms of GH excess.

The current plan is to recheck the GH/IGF1 after temporarily stopping the dopamine agonist and administer an octreotide challenge test to assess response to somatostatin analogue.

This case demonstrates that a co-secreting tumour may present as a large prolactinoma without clear evidence of acromegaly.