Society for Endocrinology

Imperial College London

Imperial Pituitary Masterclass Meeting

Monday 25th September 2017

IMPERIAL PITUITARY MASTERCLASS MEETING 2017

APPROVED FOR 6 EXTERNAL CPD POINTS (RCP, LONDON)

ENDORSED BY THE SOCIETY FOR ENDOCRINOLOGY

Venue: Charing Cross Hospital, Imperial College Healthcare NHS Trust, London

08.30 - 09.00 Registration.

09.00 - 09.15 **Welcome.**
Dr Niamh Martin.

SESSION 1.

Chairs: Dr Rajee Baburaj and Dr Ben Whitelaw.

09.15 – 09:45 *Pituitary apoplexy – an update.*
Prof John Wass (Oxford University).

09.45 - 10.15 *Outcomes for craniopharyngiomas – a multi centre study.*
Dr Nigel Glynn (Bart's Health NHS Trust London).

10.15 - 10.30 Case presentation. *Adipsic diabetes insipidus complicated by hypothalamic obesity following recurrence of a craniopharyngioma.* S. Samarasinghe, L. Thurston, M. Martineau. West Middlesex University Hospital, London.

10.30 – 10.45 Case presentation. *Hyponatraemia and a vanishing pituitary mass.* E. Goodchild, N. Glynn. Bart's Health NHS Trust London.

10.45 – 11.15 BREAK.

SESSION 2.

Chairs: Mr Ramesh Nair and Dr Ben Field.

11.15 - 11.45 *Sodium balance and the pituitary.*
Prof Stephen Ball (University of Manchester).

11.45 - 12.00 Case presentation. *Acute pseudobulbar palsy and quadriparesis in a 23 year old man treated for hypopituitarism and severe hyponatraemia.* A. Dawson, T. Hampton, E. Maratos, J. Gilbert, B. Whitelaw. King's College Hospital NHS Foundation Trust, London.

12.00 - 12.15 Case presentation. *A rare case of a hypothalamic lymphoma who presents with confusion and dizziness.* S. Acharya, E. Maratos, S. Barazi. Kings Hospital NHS Foundation Trust, London.

12.15 – 12.30 Case presentation. *From Compensated Hypogonadism to Gonadotrophinoma*. M. Siddiqui, A. Sharma, A. Qureshi. Northwick Park Hospital, London North West Healthcare NHS Trust.

12.30 - 13.30 LUNCH.

13.30 - 13.40 LAPPS Update. Joy Ginn.

SESSION 3.

Chairs: Dr Paul Carroll and Mr Nigel Mendoza.

13.40 - 14.30 *Debate.* Patients with incidentally discovered pituitary adenomas less than 6mm and without evidence of hormonal hypersecretion should be discharged from endocrine clinic without further investigations.

For the motion: Dr Ben Whitelaw (King's College Hospital NHS Foundation Trust, London).
Against the motion: Dr Florian Wernig (Imperial College Healthcare NHS Trust, London).

14.30 - 14.45 Case presentation. *The Management of Aggressive Cushing's Disease.* R. Agha-Jaffar, N. Mendoza, A. Falconer, N.M. Martin, F. Wernig. Imperial College Healthcare NHS Trust, London.

14.45 - 15.00 Case presentation. *Cushing's disease: a difficult case, difficult imaging and difficult management*. E. Mills, R. Nair, F. Wernig, N.M. Martin, K. Meeran, J.F. Todd. Imperial College Healthcare NHS Trust, London.

15:00 - 15:30 BREAK.

SESSION 4.

Chairs: Dr Marcus Martineau and Dr Emma Hatfield.

15.30 – 16:00 *Late effects of cancer treatment and the pituitary.*
Dr Helen Simpson (University College Hospital, London).

16.00 - 16:15 Case presentation. *Cabergoline resistance in a giant prolactinoma – a surgical emergency.* E.C. Maratos, B. Whitelaw, J.Gilbert, T. Hampton, N.W.M. Thomas, S. Barazi. King's Hospital NHS Foundation Trust, London.

16.15 - 16:30 Case presentation. *A Difficult Case of Dopamine Receptor Agonist Resistance*. R.C. Troke, R. Ramli, G. Dawe, A. Gontsarova, A. Pambakian, N. Mendoza, E.C.I Hatfield, K.M. Meeran, N.M. Martin. Imperial College Healthcare NHS Trust, London.

16.30 - 16:45 Case presentation. *An Aggressive "Atypical" Pituitary Macroprolactinoma: What Else Can We Do?* L. Rich, K. Bradley. University Hospitals Bristol NHS Foundation Trust.

16.45 **CLOSING REMARKS AND FEEDBACK.**

Wireless Instructions

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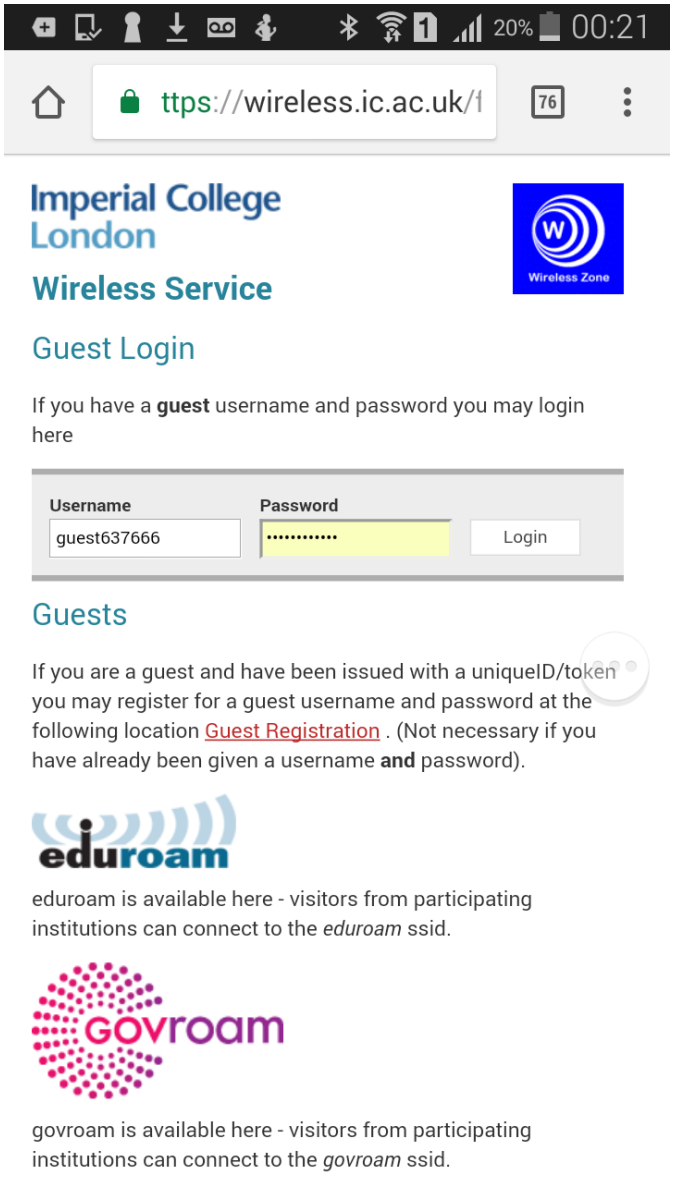

Adipsic diabetes insipidus complicated by hypothalamic obesity following recurrence of a craniopharyngioma. S. Samarasinghe, L. Thurston, M. Martineau. West Middlesex University Hospital, London.

Craniopharyngiomas arise from the remnants of the Rathke's pouch in the hypothalamic-pituitary region. Patients usually present with visual field defects, endocrinopathies and headaches. Proximity of the tumour to vital organs such as the hypothalamus and pituitary make surgical resection difficult. The hypothalamus plays a central role in the maintenance of osmotic balance through regulation of both antidiuretic hormones (ADH) and the thirst centre. The appetite/satiety centre is also located in the hypothalamus and both of these can be affected by damage from the tumour itself or during resection. It is the commonest cause of structural hypothalamic obesity.

We describe the case of an obese 56 year old female presenting to the emergency department with worsening confusion, visual impairment, electrolyte imbalance and severe hyperosmolality. She had a past medical history of three previous craniopharyngioma debulking surgeries, radiotherapy and a VP shunt in 1989 with subsequent use of human growth hormone (GH). The patient was diagnosed with secondary hypothyroidism and hypoadrenalism and started on levothyroxine and hydrocortisone. This potentiated manifestations of cranial diabetes insipidus (CDI). She was commenced on desmopressin and encouraged to drink. It was noted she had a completely absent thirst in response to a hypertonic stimulus despite regular prompting. The ADI significantly increased her morbidity (e.g. severe hypernatraemia, sleep apnoea, obesity, venous thromboembolism) and mortality risk.

Adipsic diabetes insipidus (ADI) is a rare condition consisting of central diabetes insipidus and a deficient or absent thirst response to hyperosmolality. Patients with ADI experience marked morbidity and mortality. Diagnosis and management of these patients is challenging and involves daily assessment of prescribed water intake with fixed antidiuretic therapy (desmopressin), close monitoring of electrolytes and fluid balance and morbidity screening.

Hyponatraemia and a vanishing pituitary mass. E. Goodchild, N. Glynn. St Bartholomew's Hospital, London.

Case History: A 36-year-old, previously healthy, gentleman complained of gradually worsening headache for several weeks. He came to hospital when he was awoken by worsening of the headache associated with vomiting and pre-syncopal symptoms. Investigations revealed severe hyponatraemia and with concentrated urine and elevated urine sodium concentration. He was also severely hypocortisolaemic. Cranial imaging revealed a suprasellar, complex cystic pituitary lesion. He was treated with intravenous saline and glucocorticoids; however, he continued to feel unwell and serum Na did not normalise. He was then treated with fluid restriction, while continuing glucocorticoids, and serum Na gradually returned to normal. He had panhypopituitarism, without polyuria, and was commenced on appropriate replacement. Neurosurgical team planned for transsphenoidal debulking; however, repeat pituitary imaging, six weeks later, revealed marked regression of the sellar mass.

Investigations: Biochemistry - Sodium 117 mmol/L, urine osmolality 726 mmol/kg, serum osmolality 68 mmol/L and urine sodium 62 mmol/L, fT4 6.1 pmol/L (10.5-24.5), TSH 0.68 munit/L, cortisol (random): 16 nmol/L, ACTH 19 ng/L, prolactin 101 munit/L , testosterone 0.8 nmol/l (8-29). Serum sodium improved to 125mmol/L after three days of fluid restriction, and to 138mmol/L upon discharge.

Imaging: CT and MRI head showed a cystic, suprasellar mass impinging upon the optic chiasm. Repeat imaging six weeks later demonstrated substantial shrinkage of the lesion which was now confined to the sella.

Current management: He remains on appropriate pituitary hormone replacement despite regression of the sellar mass. Following discussion at the pituitary multidisciplinary meeting we plan surveillance MRI and reassessment of pituitary hormone reserve.

Points for discussion: This case illustrates the complexity in the diagnosis and management of severe symptomatic hyponatraemia in patients with a newly discovered sellar mass. The differential diagnosis, management strategies and need for multidisciplinary input are worthy of discussion.

Acute pseudobulbar palsy and quadriparesis in a 23 year old man treated for hypopituitarism and severe hyponatraemia. A. Dawson, T. Hampton, E. Maratos, J. Gilbert, B. Whitelaw.
King's College Hospital NHS Foundation Trust, London.

A 23 year old previously well man presented to his local hospital with a two day history of vomiting, confusion and hallucinations after returning from a diving holiday. He was hypotensive (BP 70/30mmHg) with hypoglycaemia (capillary blood glucose 2.7mmol/L). Investigations demonstrated severe hyponatremia (Na 100mmol/L).
He was initially treated with intravenous normal saline and hypoglycaemia was corrected. Further urgent investigations showed a low random serum cortisol (138nMol/L) and stress doses of intravenous hydrocortisone were given. In total 4 litres of normal saline were administered over the first 24 hours. Neuroimaging demonstrated a T1 hyperintense pituitary lesion consistent with haemorrhage into a pituitary adenoma. Further investigations showed free T4 6.8 pmol/L (9-25), TSH 0.19 mIU/L (0.3-5.5), prolactin 708 mIU/L (100-410), LH 1.7 IU/L (1.5-9.3), testosterone 0.7 nmol/L (10-30). A working diagnosis of pituitary apoplexy and hypopituitarism was made.
After 9 hours of treatment sodium had risen to 108mmol/L, at 13 hours sodium was 117 mmol/L and 22 hours post admission sodium was 127 mol/L. The patient became haemodynamically stable and the confusion resolved. However, on the same day, he developed slurred speech and was found to have spastic quadriparesis with pseudobulbar dysfunction. MRI scan revealed changes consistent with osmotic demyelination.
The patient was transferred to the regional pituitary centre. There was no history of headache and no visual disturbance. The hypopituitarism was treated but the presumed haemorrhagic pituitary adenoma was managed conservatively.
Fortunately, with input from the speech and language and neurology occupational therapy teams, he made a complete neurological recovery within six months. He has remained well on full pituitary replacement.

Discussion:

Osmotic demyelination syndrome (ODS) is a well-recognised consequence of rapid hyponatremia correction. Serum sodium ≤105 mmol/L is the most clearly defined risk factor. An increase of less than 8 mmol in the first 24 hours is recommended. It was essential for this patient to be treated with saline and hydrocortisone initially, but current guidelines emphasise the importance of both monitoring the increase in sodium and intervening (with desmopressin and/or 5% dextrose) to break the rise. This case demonstrates the danger of allowing rapid correction of sodium without intervention.

A rare case of a hypothalamic lymphoma who presents with confusion and dizziness.

S. Acharya, E. Maratos, S. Barazi. Kings Hospital NHS Foundation Trust, London.

A 31 year old right handed stay at home mother presented to her local hospital with acute confusion. She had a one month history of progressive frontal headaches with features of raised intracranial pressure, memory problems, blurred vision and nausea. On further questioning, she had lost weight and stopped menstruating. The patient was otherwise fit and well with no significant past medical, drug, social or family history. On examination she was dehydrated but stable from a cardiorespiratory point of view. Neurological examination demonstrated no focal limb deficit and Ophthalmology input confirmed that she had normal visual acuity, visual fields and no papilloedema. Clinically, there were nor stigmata of systemic malignancy. Biochemistry showed that she had a sodium of 120mmol and a raised cortisol of 1197. Following paired urine and serum osmolalities, a diagnosis of syndrome of inappropriate ADH secretion was made.

A CT scan showed a 3x3 well circumscribed circular homogenously hyperdense lesion which enhanced with contrast in the hypothalamic region with some surrounding oedema and she was commenced on 8mg BD of dexamethasone. Within two weeks her lesion regressed in size, however the diagnosis of the mass was still a radiological mystery. A transphenoidal biopsy of the lesion was carried out and proved to be technically challenging due to its supra chiasmatic location and was complicated by post operative Diabetes insipidus treated with DDVAP and a CSF leak. The histology was consistent with high grade T-cell rich B-cell lymphoma (Bcl). She was treated with steroids and post-operative PET CT showed no intracranial metastasis.

Bcl is a rare tumour of the brain and spinal cord making up ≤1% of all lymphomas and ~1–3% of primary CNS tumours. It is most common in immune-compromised individual. Due to the absence of a typical clinical presentation, multiple neuroimaging appearances in keeping with a wide differential diagnosis, heterogeneity of the pathological morphology and no specific laboratory examination, the immunohistochemistry was key to gain accurate diagnosis. Most treatment of Bcl is a combination of surgery, chemotherapy and radiotherapy, however, the prognosis of Bcl remains poor, with a median survival time of 17–45 months following treatment. Making an early diagnosis of Bcl is challenging due to the variable and complicated clinical manifestations of the disease. This case highlights the need of a multidisciplinary team involving Neurosurgeons, endocrinologists, radiologists, pathologists and oncologists to coordinate care for such patients.

From Compensated Hypogonadism to Gonadotrophinoma. M. Siddiqui, A. Sharma, A. Qureshi. Northwick Park Hospital, London North West Healthcare NHS Trust.

A 79 year old frail gentleman was discovered to have an incidental 3 mm pituitary adenoma on MRI brain. He also had ischemic heart disease, a dilated thoracic ascending aorta and chronic kidney disease. Pituitary function testing revealed elevated gonadotrophin levels (FSH 23.4 IU/L and LH 9.1 IU/L) with adequate midmorning testosterone at 24.2 nmol/L, SHBG 106nmol/L, IGF-1 24.0nmol/L, prolactin 248 mIU/L, 9am cortisol 622 nmol/L, TSH 1.20 mIU/L with FT4 20.9 pmol/L and FT3 3.5 pmol/L. 24 hour urinary free cortisol levels were normal.

His calculated bioavailable testosterone was normal (5.17 nmol/L) and he was suspected to have a non-functioning adenoma and compensated hypogonadism. Pituitary imaging the following year showed a mild increase in the size of adenoma to 6mm which remained unchanged on subsequent scans. However during this time, the gonadotrophin levels have nearly quadrupled with most recent FSH 113.9 IU/L and LH 44.3 IU/L, and normal testosterone levels (ranging between 23.7 nmol/L to 26.3 nmol/L). Assay interference was excluded and alpha subunits were noted to be mildly elevated. The rest of the pituitary functions have been consistently unremarkable.

We suspect our patient has a non-functioning microadenoma and compensated hypogonadism. 4 years after diagnosis however, his 9 a.m. testosterone remains normal. A gonadotroph adenoma is an alternative explanation because hypersecretion of uncombined LH beta- and alpha-subunits has been described in patients with gonadotroph adenomas resulting in normal and even subnormal testosterone levels. Gonadotrophinomas are usually clinically silent and indistinguishable from other clinically non-functioning adenomas until immunohistochemistry is performed after pituitary surgery. Although a pituitary biopsy would be helpful, our patient is elderly, frail and has multiple co-morbidities and surgery/biopsy have not therefore been pursued.

Questions for the expert panel:

1. What do you believe is the most likely diagnosis?
2. Would you carry out additional tests?
3. What would you advise further in the management of our patient?

The Management of Aggressive Cushing's Disease. R. Agha-Jaffar, N. Mendoza, A. Falconer, N.M. Martin, F. Wernig. Imperial College Healthcare NHS Trust, London.

Background: Cushing's disease is a rare clinical condition of which 5-10% are secondary to ACTH producing macroadenomas.

Case Illustration: We report the case of a 35 year-old female who was found to have a pituitary mass in 2017. Past medical history included hypertension (diagnosed 2013) a left humeral neck fracture and sub-fertility for which she underwent in vitro fertilisation to achieve successful conception in 2015.

In January 2017, she developed headaches that were initially investigated with a CT head, which identified a pituitary mass and following this, a dedicated pituitary MRI. This demonstrated a pituitary macroadenoma extending into the suprasellar cistern and right cavernous sinus with no evidence of optic chiasm distortion.

A detailed examination noted signs consistent with hypercortisolaemia: bruising affecting her forearms and abdominal violaecous striae were documented. Body mass index measured 30.9 kg/m2 and blood pressure 148/95mmHg. A formal visual field assessment did not demonstrate a defect.

Subsequent biochemical investigations indicated cortisol excess: midnight salivary cortisol and urinary free cortisols were elevated (8.2 [<2.6] nmol/L and 473 [50-270] nmol/L respectively). A failure to suppress on both an overnight and a low dose dexamethasone suppression test further supported the diagnosis of Cushing's syndrome and inferior petrosal sampling confirmed the pituitary as the source of the excess ACTH production.

Treatment with metyrapone was commenced (at an initial dose of 250mg twice daily) and low molecular weight heparin introduced. Debulking of her tumour is scheduled.

Conclusions

Achieving long-term remission in this aggressive ACTH producing macroadenoma will be challenging. The authors would be grateful if the panel would advise on the preferred option for postoperative treatment. The following are currently under consideration: radiotherapy alone, radiotherapy followed by bilateral adrenalectomy or radiotherapy followed by medical therapy.

Cushing's disease: a difficult case, difficult imaging and difficult management. E. Mills, R. Nair, F. Wernig, N.M. Martin, K. Meeran, J.F. Todd. Imperial College Healthcare NHS Trust, London.

We report a 23-year old woman, who was referred with 18-months of secondary amenorrhoea, easy bruising, skin thinning, abdominal striae and hirsutism. Examination demonstrated typical Cushingoid features. Endocrine testing revealed a raised midnight cortisol of 512nmol/L; non-suppressed basal ACTH of 43.1ng/L and 48-hour cortisol of 345nmol/L following a low-dose dexamethasone suppression test; and a lack of diurnal cortisol variation during a cortisol day curve with an average of 537nmol/L. Inferior petrosal sinus sampling confirmed a central source for ACTH secretion with lateralisation to the left side of the pituitary. Pituitary MRI suggested possible heterogeneity within the left part of the gland, but no clear-cut specific lesion within it. The consensus of the Pituitary MDT was therefore to proceed with exploratory surgery of the left side of the pituitary to identify a surgical target or a left hemi-hypophysectomy in the event of a surgical target not being identified intraoperatively. Pending surgery, she was started on Metyrapone 250mg daily, which she did not tolerate due to lethargy and low mood; this was therefore discontinued.

However, following endoscopic transsphenoidal resection of the presumed pituitary lesion, her cortisol levels remained raised averaging 500-600nmol/L, confirming recurrent Cushing's disease. Post-operative histology revealed normal pituitary tissue rather than a corticoptroph adenoma. A Methionine PET/CT scan was therefore arranged to localise the tumour more effectively. Due to previous intolerance to Metyrapone, she was commenced on Fluconazole rather than Ketoconazole due to lesser liver toxicity. Titrated to Fluconazole 600mg twice daily, cortisol levels were controlled at 200-250nmol/L, along with restoration of normal menses. Unfortunately, the Methionine PET/CT did not reliably confirm a surgical target. Our patient was unkeen to undergo further pituitary surgery without a reasonable guarantee of cure. Along with the Pituitary MDT, she elected for a bilateral adrenalectomy to preserve pituitary function, future fertility and act as a definitive cure for Cushing's disease.

Questions to the panel:

- What experience do you have with the use of Fluconazole in the treatment of Cushing's syndrome?
- Do we have enough experience in interpreting Methionine PET/CT for difficult cases of Cushing's disease?
- Would you have encouraged repeat pituitary surgery or bilateral adrenalectomy in this patient's case?

Cabergoline resistance in a giant prolactinoma – a surgical emergency.

E.C. Maratos, B. Whitelaw, J. Gilbert, T. Hampton, N.W.M. Thomas, S. Barazi. Kings Hospital NHS Foundation Trust, London.

An 18 year old man presented with a 9 year history of headache, lethargy and failure to progress through puberty. On examination he had normal stature but delayed puberty with no axillary or facial hair and his voice had not broken. His bloods showed undetectably low gonadotrophin and testosterone, 9am cortisol of 26nmol/L and TSH 3mU/L, fT4 10.7mU/L. Prolactin was 278,000mIU/L. Visual fields tests demonstrated a dense bitemporal hemianopia and MRI revealed a 37 x 37 x 45mm mass expanding the sella and extending into the sphenoid sinus and parasellar regions with a significant suprasellar extension and chiasmal compression. The mass had areas of haemorrhage within it. The diagnosis of giant prolactinoma was made and he was commenced on 1mg cabergoline twice weekly as well as hydrocortisone and levothyroxine.

Initially there was a clear radiological and biochemical response. After 4 months of treatment the tumour had reduced in size from 45mm to 25mm maximal height and dilutional prolactin had fallen to within the normal range 174mIU/L (100-410mIU/L). There was a corresponding improvement in his visual field deficit. He was commenced on testosterone injections at this stage.

He then began to report new severe headaches and a repeat MRI showed a rapid increase in the mass to 34x34x34mm with marked displacement of the optic chiasm once more. The prolactin had risen to 404mIU/L and the visual fields again showed a dense bitemporal hemianopia.

The patient underwent an emergency endoscopic transphenoidal resection of the tumour with no immediate complications. His visual fields improved and postoperative prolactin was 232 (normal range). Histology confirmed a pituitary adenoma with focal prolactin positivity and Ki67 proliferation index of 1%.

A giant prolactinoma is defined as a purely prolactin-secreting tumour of greater than 4cm in maximum diameter. Giant prolactinomas are rare, comprising only 4.3% of prolactin secreting adenomas and 0.5% of all pituitary adenomas. Specific challenges to treatment include a lower rate of responsiveness to dopamine agonist treatment (60-70% compared to 80-90% response rate of normal prolactinomas) and a higher rate of visual failure. We present a case of cabergoline resistance in a giant prolactinoma and discuss the diagnostic and therapeutic challenges involved.

A Difficult Case of Dopamine Receptor Agonist Resistance. R.C. Troke, R. Ramli, G. Dawe, A. Gontsarova, A. Pambakian, N. Mendoza, E.C.I Hatfield, K.M. Meeran, N.M. Martin. Imperial College Healthcare NHS Trust, London.

In 2015 this 43 year old woman presented with a bitemporal hemianopia, galactorrhoea and amenorrhoea. A 4 cm pituitary lesion was confirmed on MRI, indenting the chiasm and invading the left cavernous sinus. Biochemistry revealed a prolactin of 188,000 mU/L accompanied by secondary hypoadrenalism and hypothyroidism. She was commenced on cabergoline 0.5mg twice a week, hydrocortisone and thyroxine.

Visual fields improved and prolactin fell to 49,000 mU/L by 6 months. However, a repeat MRI at one year suggested an increase in size of the pituitary macroadenoma, stretching the optic chiasm. In addition, the large central component of the adenoma demonstrated T1 shortening, consistent with recent haemorrhage. These MRI findings coincided with a deterioration in visual fields and a rise in serum prolactin 65,000 mU/L. Cabergoline was increased to 0.5mg four times per week, and the patient was discussed at the pituitary MDT with a decision made to surgically manage the lesion to alleviate the optic chiasm compromise. A haemorrhagic mass was evacuated and the pituitary adenoma was partially debulked. Histology confirmed cells which stained for prolactin, with a Ki67 index of 5%. The tissue was MGMT promoter methylation negative.

Following a smooth post-operative recovery, visual fields significantly improved. Immediately post-operatively, prolactin was 58,000 mU/L but by follow up at 8 weeks had risen to 107,000 mU/L despite increasing doses of cabergoline with good compliance. An observed cabergoline suppression test (4mg) showed a nadir prolactin of 84 000 mU/L supportive of dopamine receptor agonist resistance.

Six months after her surgery, she complained of partial left ptosis and developed 3rd, 5th and 6th nerve palsies with troublesome left trigeminal neuralgia consistent with further tumour growth, including within the left cavernous sinus. Repeat trans-sphenoidal surgery removed necrotic pituitary tissue (prolactin staining, Ki67 index 20%). However, serum prolactin continued to increase despite high dose cabergoline (1mg/day) to a peak of 128 538 mU/L. After further discussion at the Imperial Pituitary MDT, she received external beam radiotherapy (54Gy in 30 fractions) in April 2017 resulting in a significant fall in serum prolactin and reduction in tumour size.

Question for discussion:

We had many discussions about this patient regarding whether we should administer radiotherapy or trial temozolamide following her second surgery. Who would have favoured temozolamide?

An Aggressive "Atypical" Pituitary Macroprolactinoma: What Else Can We Do? L. Rich, K. Bradley. University Hospitals Bristol NHS Foundation Trust.

Prolactinomas are the commonest type of functioning pituitary tumour and the majority of these are responsive to treatment with dopamine agonists. However, resistance to standard medical therapy is well described and these cases may prove the most challenging to treat and we present one such individual; a 73 year old man who originally presented in 1994 with apoplexy and a prolactin of 161,000 on a background of 4 months of visual disturbance. Our patient underwent baseline trans-sphenoidal decompressive surgery with a good post-operative result. However, within 2 years his prolactin had started to rise and Bromocriptine failed to control tumour growth.

Eight years later, in 2002, he underwent his second trans-sphenoidal resection for progressive radiological and biochemical progression. Post-operatively, he also received 45Gy conventional radiotherapy. A prolactin nadir of ~1,000 was achieved by 2006 but Cabergoline had to be withdrawn around this time due to the development of psychosis that was chronologically related to dopamine agonist dose escalation. By 2009, with a prolactin of 18,900, a third trans-sphenoidal procedure was undertaken for visual protection and tumour control. Accelerated tumour growth and hyperprolactinaemia led to a debulking craniotomy in 2010 and a shunt insertion for the management of hydrocephalus. Between 2010 and 2011, 12 cycles of Temozolamide were administered and a post-operative prolactin of 3,100 fell to 526. From 2011 to 2014, tumour progression was slowly progressive and stereotactic radiosurgery (26Gy single fraction, chiasm dosage 4Gy) was offered. By June 2015, the situation necessitated the reintroduction of Temozolamide, to which the tumour was now unresponsive with both radiological and biochemical progression. In November 2015, after careful discussion and with psychiatry support, low dose Cabergoline was reintroduced. From then until early 2017 the prolactin showed a slow but gradual increase from 1,000 to around 3,000.

Tumour progression resulting in visual loss (prolactin ~10,000) led to a fifth debulking procedure in April 2017 with minimal anatomical or biochemical control being achieved. The histology showed an atypical tumour with elevated MIB-1 of 10% and p53 staining in 5%. FDG-PET and octreotide scans have confirmed highly avid disease but localised to the pituitary region. Options are now limited: Cabergoline has been increased to maximum tolerance, rapidly escalating Lanreotide has been added to the therapeutic regimen and Pasireotide (pending somatostatin receptor subtyping) is under active consideration. PRRT has not been pursued due to rate of tumour enlargement likely making it ineffective as well

as the therapy not being accessible currently. A further dose of conventional radiotherapy has also been offered despite the very high risk of significant visual impairment. Alternative medical therapies lack an evidence base and this gentleman’s prognosis for both visual preservation and life expectancy is now poor.