Society for Endocrinology

Imperial College London

Pituitary Masterclass Meeting

Monday 26th September 2016

LCA PITUITARY MASTERCLASS MEETING 2016.

SPONSORED BY THE SOCIETY FOR ENDOCRINOLOGY.

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

REGISTERED FOR 6 EXTERNAL CPD CREDITS (ROYAL COLLEGE OF PHYSICIANS).

08.30 - 09.00 Registration.

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

SESSION 1.

Chairs: Dr Rajee Baburaj and Dr Emma Hatfield.

09.15 - 09.35 *Assessment of HPA axis function – time to challenge our cut-offs?*
Prof Tricia Tan (Imperial College London).

09.35 - 10.00 *Glucocorticoid replacement in pituitary disease – are we getting this right?*
Prof Karim Meeran (Imperial College, London).

10.00 - 10.15 Case presentation. *A challenging case of a woman with a suprasellar germ cell tumour and diabetes insipidus*. M Sutton-Smith, WM Kong. Northwick Park and Central Middlesex Hospitals, London.

10.15 – 10.30 Case presentation. *Presentation, natural history and management of pituitary LCH.* I Malik, PV Carroll. Guy's and St Thomas's Foundation Trust, London.

10.30 – 10.45 Case presentation. *Challenges and uncertainties in the management of IgG4-related disease.* S Hameed, K Meeran, C Pusey, A Mehta, B Jones, G Rose, D Bansi, F Wernig. Imperial College Healthcare NHS Trust and Moorfields Eye Hospital, London.

10.45 – 11.15 BREAK.

SESSION 2.

Chairs: Mr Ramesh Nair and Prof Karim Meeran.

11.15 - 11.35 *Interactive case presentation.*
Dr Amir Sam (Imperial College, London).

11.35 - 12.00 *Valvulopathy and dopamine agonists: an update.*
Prof Will Drake (Queen Mary University of London).

12.00 - 12.15 Case presentation. *A difficult case of macroprolactinoma.* P Plichta, J Randall. James Paget University Hospital NHS Foundation Hospital, Great Yarmouth, Norfolk.

12.15 – 12.30 Case presentation. *Cushing's disease due to atypical adenoma – pre-operative and post-operative challenges.* X Paraskevi, B Whitelaw, D Taylor, T, Hampton B Taylor, A King, NWM Thomas, J Gilbert. King's College Hospital NHS Foundation Trust, London.

12.30 - 13.30 LUNCH.

13.30 - 13.40 LAPPS Update. Joy Ginn

SESSION 3.

Chairs: Prof Will Drake and Dr Ben Whitelaw.

13.40 - 14.30 *Debate. This house believes that growth hormone replacement in growth hormone deficient adults is a waste of time and money.*
For the motion: Prof Maralyn Druce (Queen Mary University of London).
Against the motion: Dr Niamh Martin (Imperial College London).

14.30 - 14.45 Case presentation. *Nelson syndrome three years after bilateral adrenalectomy for Cushing's disease.* L Thurston, A Clifton, P le Roux, A Martin, DA Rodin. St Helier Hospital, Carshalton and St George's Hospital, London.

14.45 - 15.00 Case presentation. *Prolactinoma or Clival Chondroma: That is the question?* A Agha, N Karavitaki. University Hospital Birmingham.

15.00 - 15.25 *Mortality in patients with non-functioning pituitary adenomas.*
Dr Niki Karavitaki (University of Birmingham).

15.25 – 15.45 BREAK.

SESSION 4.

Chairs: Mr Nigel Mendoza and Dr Paul Carroll.

15.45 - 16.10 *Pituitary Surgery - It's Not Rocket Science!*
Mr Saurabh Sinha (Sheffield Teaching Hospitals NHS Foundation Trust).

16.10 - 16:25 Case presentation**.** *What is the best approach for recurrent Rathke's Cleft Cyst tumours?* R.Kehinde, NM Martin, N Mendoza, A Mehta, B Jones, P Lewis, K Meeran, E Hatfield, R Nair. Imperial College Healthcare NHS Trust, London.

16.25 - 16:45 Case presentation *Paediatric pituitary apoplexy.* E. Culpin, P. Dimitri, S. Sinha. Sheffield Children's Hospital, Neurosurgery, Sheffield.

16.45 **CLOSING REMARKS AND FEEDBACK.**

Wireless Instructions

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A challenging case of a woman with a suprasellar germ cell tumour and diabetes insipidus.

M Sutton-Smith, WM Kong.
Northwick Park and Central Middlesex Hospitals, London.

Abstract:
A 64-year-old woman was admitted to hospital with a community-acquired pneumonia and reduced GCS (10). She had a suprasellar germ cell tumour treated 50 years earlier (neurosurgical resection and radiotherapy) and had associated visual impairment, epilepsy and learning difficulties with panhypopituitarism requiring Hydrocortisone, Desmopressin and Levothyroxine therapy. She also had type 2 diabetes and a MRI-head scan one-year previously (worsening seizures) showed 3 inoperable meningiomas. She had previously been cared for by her mother and had been independently mobile being able to feed herself and communicate her needs until her hospital admissions. She was admitted to hospital one week after discharge to a nursing home following an 8-month hospital admission for a traumatic right-sided subarachnoid haemorrhage and subdural haematoma with overlying skull fracture and associated contrecoup subarachnoid haemorrhage, during which time her mother had died. On admission she was bedbound, doubly incontinent, unable to take food or fluids orally and reliably communicate her needs. During her admission her fluid balance was very challenging owing to her diabetes insipidus (DI) with recurrent severe hypo- and hypernatraemia. This was compounded by problems with her Desmopressin prescription and administration. Her management was further complicated by poor glycaemic control, seizures and difficulties with venous access. Her GCS fell (4) following an episode of severe hypernatraemia (Na 190 mmol/l) and her GCS remained persistently low thereafter. A MRI-head scan showed a large sellar mass measuring 50mm in sagittal dimension with suprasellar extension and right cavernous sinus and optic nerve/orbital involvement. Multiple extra-axial lesions, likely to represent leptomeningeal deposits were seen but there was no evidence of myelosis or hydrocephalus to explain her low GCS. She was switched from Hydrocortisone to Dexamethasone to reduce cerebral oedema and deemed unsuitable for neurosurgical intervention and later died from bronchopneumonia.

Discussion: This case highlights the critical role of the endocrinologist in the management of DI particularly in the light of recent national patient safety concerns and provides and opportunity to review the long term outcomes for childhood germ cell tumours.

Questions to the panel:
How would you manage a patient with the life-threating combination of adipisia, diabetes insipidus and insulin dependent diabetes mellitus outside the hospital setting?

Presentation, natural history and management of pituitary LCH.

I Malik, PV Carroll.

Guy's & St Thomas' NHS Foundation Trust, London.

Abstract:
A 26 year old previously healthy woman was seen in the endocrine clinic with elevated prolactin, headache, thirst and amenorrhoea. She also described pain in left thigh and was attending physiotherapy. Pituitary imaging demonstrated an avidly enhancing lesion in the infundibulum and the clinical history was consistent with diabetes insipidus which was confirmed with a water deprivation test. The differential for this presentation included inflammatory, granulomatous and neoplastic pituitary disease.

FDG-PET CT confirmed extensive avidity in the left femur and we considered LCH the likely unifying diagnosis. Bone biopsy at Stanmore confirmed this diagnosis.

The patient therefore had LCH presenting with pituitary disease and left femur involvement without other sites.

We considered management options and a number of management strategies have been employed in this condition. As the thigh pain was severe and limiting movement we delivered EBRT with instant resolution of symptoms and a complete metabolic response on PET CT.

We have observed the pituitary involvement radiologically using appropriate replacement. There has been no change in appearances over 12 months. Although there is more than one site of disease we are reluctant to use cytotoxic systemic therapy and plan to deliver low dose EBRT (~9 Gy) to the pituitary.

The clinical presentation, investigations and management of pituitary LCH will be discussed.

Challenges and uncertainties in the management of IgG4-related disease.

S Hameed[1], K Meeran[1], C Pusey[2], A Mehta[3], B Jones[3], G Rose[4], D Bansi[5] , F Wernig[1].
[1]Imperial Centre for Endocrinology; [2]Imperial College Renal and Transplant Centre;
[3]Department of Neuroradiology, Imperial College Healthcare NHS Trust; [4]Moorfields Eye Hospital, London, [5]Department of Gastroenterology, Imperial College Healthcare NHS Trust.

Abstract:
IgG4-related disease is an immune-mediated multi-systems condition. It presents with swelling and fibrosis of the involved tissues due to a lymphoplasmacytic infiltrate enriched in IgG4-positive plasma cells. The most common clinical presentations are IgG4-related pancreatitis and sclerosing sialoadenitis, but many other organs and tissues can be affected. Recently, IgG4-related pituitary involvement (infudibulo-hypophysitis) has been described in the literature. Biopsy is diagnostic. Albeit increasingly recognised, much uncertainty remains with regard to the natural course of the disease. As far as treatment is concerned, current consensus statements are based on case reports and case series only. The optimal treatment has yet to be established.

Here we report the case of a 61 year old man with a past history of chronic pancreatitis, asthma and transurethral prostate resection who initially presented to the neurologists with complex partial seizures. An MRI brain scan revealed a homogenously enhancing 8mm inflammatory mass of the pituitary stalk. Subsequent endocrine work up diagnosed secondary hypothyroidism and hypogonadism and replacement therapy was commenced. The pituitary lesion remained stable on serial imaging for four years when an increase in size was noted. This coincided with the appearance of painful bilateral exophthalmos as well as a flare up of pancreatitis. An orbital biopsy diagnosed orbital eosinophilic angiocentric fibrosis and a diagnosis of IgG4-related disease was made. High-dose prednisolone was commenced. Glucocorticoid treatment resulted in full resolution of the proptosis, marked improvement in his pancreatitis-related abdominal pain and steatorrhoea as well as significant reduction in the size of the pituitary lesion. He developed steroid-induced diabetes which had to be managed with insulin treatment. His eye disease was quiescent for six years when he presented with recurrence of the exophthalmos and high dose prednisolone was restarted for a year resulting in a marked clinical improvement. Unexpectedly, a pituitary MRI performed four months after stopping the second course of prednisolone showed a significant increase in the size of the infundibular lesion with mass effect on the optic chiasm. Extensive swelling of the eye muscles was also noted on the MRI which coincided with a recurrence of the exophthalmos. At this stage, he was offered treatment with rituximab, but elected for a further course of prednisolone treatment instead. After two months the eye signs had resolved completely. Repeat MRI of the pituitary is currently awaited.

Questions to the panel:
1) The periods of remission appear to become shorter and disease recurrences more severe. He already has developed steroid-induced diabetes. Should a steroid sparing-agent should be introduced now in order to prevent future relapses?
2) Rituximab has not been evaluated in a randomised-controlled trial in IgG4-related disease, but it would appear a more specific treatment than glucocorticoids for this condition. Would earlier treatment with rituximab have achieved better outcomes and more prolonged disease remission?

Clearly, only a well-coordinated and multidisciplinary approach can lead to successful management of this very complex and challenging condition. Evidence-based treatment guidelines are urgently needed.

A difficult case of macroprolactinoma.

P Plichta, J Randall.
James Paget University Hospital NHS Foundation Hospital, Great Yarmouth, Norfolk.

Abstract:
We describe a case of a 31 year old man with a history of schizophrenia (currently living in supported accommodation) who presented with a macroprolactinoma in 2009 with prolactin 12346mIU/L. Visual acuity and fields were within normal limits. He was initially treated with cabergoline titrating to a dose of 1 mg twice weekly with negligible effect on prolactin (presumed due to treatment with large doses of neuroleptic agents) and an increase in tumour size on MRI. He underwent transsphenoidal surgery in 2011 at Addenbrooke's Hospital. Histology confirmed a lactotroph adenoma with a MIB-1 index 5%, p53 3%. Post operatively, prolactin fell to 4860mIU/L. He has hypogonadotrophic hypogonadism which is treated with testosterone replacement.
Unfortunately, prolactin levels rose over the following 2 years to 8919mIU/L and it was felt that a tumour remnant on MRI was enlarging. He underwent a transnasal endoscopic procedure in February 2014, however only a fluid filled cavity was seen with no tumour visible. Post operatively there was an initial drop in prolactin concentration to similar levels to those seen after the initial surgical procedure. However, over time a gradual, significant raise in levels has been observed and the most recent prolactin is 8522mIU/L. Interpreting prolactin results has often been made difficult by increases to his antipsychotic treatment.
His case was discussed at the regional pituitary MDT in July 2015 where it was felt that there appeared to be little change in the size of what appears radiologically to be residual tumour although no tumour was visualised at the second operation. Methionine PET-CT scan was suggested as a functional imaging modality but unfortunately the patient did not have the PET scan as the appointment was sent to an old address and we have been informed that it cannot be rearranged at the present time.
We presented a difficult case of a patient with a macroprolactinoma resistant to dopamine agonist therapy with two previous surgical procedures and rising prolactin levels with an ongoing need for antipsychotic treatment.

Questions to the panel:
Should he have another trial of dopamine agonist treatment? Should he be considered for a further surgical procedure? Should he be considered for pituitary radiotherapy (the remainder of his pituitary function is within normal limits)? Or should we try again to obtain the PET scan?

Cushing's disease due to atypical adenoma – pre-operative and post-operative challenges.

X Paraskevi, B Whitelaw, D Taylor, T Hampton, B Taylor, A King, NWM Thomas, J Gilbert.
King's College Hospital NHS Foundation Trust, London

Abstract:
21 year old woman, presented with 2 year history of weight gain, hirsuitism, bruising, acne, muscle weakness and poor sleep. On examination she appeared Cushingoid with a rounded face, central obesity, purple striae and some proximal muscle weakness.

Investigations confirmed Cushing's: serum cortisol was 778 nmol/L and remained elevated following 1mg dexamethasone suppression test (623nmol/L). Post 8mg dexamethasone cortisol fell to 94nmol/L. Baseline ACTH was 49 ng/L. Midnight salivary cortisol measurements were elevated 65nmol/L (normal <10) and 24 hour urine free cortisol was 2014 nmol/24hr (normal <200).

MRI scan showed a 7mm left sided pituitary adenoma. The patient was planned to have trans-sphenoidal surgery but was given metyrapone pre-operative blockade for 4 months. Subsequent endoscopic transphenoidal surgery identified a sella tumour which was resected.

Post operatively the nadir cortisol remained detectable (99nmol/L). In view of this, re-exploration of the sella was performed 7 days after the first operation. Further tissue was removed from the sella and the subsequent post-operative cortisol level was undetectable (<30 nmol/L).

The histology from the first surgery showed an atypical pituitary adenoma, with strong immunostaining for ACTH. There was an elevated Ki67 of 15% and an increased mitotic rate (6 mitoses per 10HPF). The second surgery histology showed necrotic tissue.

Post-operatively she is hypopituitary (confirmed on IST) and takes hydrocortisone, levothyroxine, growth hormone and desmopressin.

Questions to the panel:
What are the indications, in Cushing's disease, for giving medical treatment prior to surgery?

What, if any treatment should this patient now be offered in view of the atypical histology?

Nelson syndrome three years after bilateral adrenalectomy for Cushing's disease.

L Thurston, A Clifton, P le Roux, A Martin, D A Rodin**.**
Departments of Endocrinology, Radiology and Surgery, St Helier Hospital, Carshalton and Departments of Radiology and Neurosurgery, St George's Hospital, London.

Abstract:
A 33 year old lady presented in 2011 with a classical history of Cushing's syndrome with 15kg weight gain, predominantly central obesity, hirsutism, acne and irregular menstruation. Her blood pressure was elevated but she was not diabetic. Investigations indicated that she had pituitary Cushing's disease. Serum cortisol failed to suppress during a 48 hour low dose dexamethasone suppression test (baseline cortisol 398 nmol/L; 48h cortisol 261 nmol/L) but suppressed in response to a 48 hour high dose dexamethasone suppression test (cortisol 57 nmol/L). ACTH was 37 ng/L. MRI pituitary gland was normal. She went on to have bilateral inferior petrosal sinus sampling (BIPSS) with CRH testing but this failed to confirm a pituitary cause for her Cushing's syndrome.

She was treated with metyrapone with a view to repeating her investigations after an interval. She declined further BIPSS and subsequent MRI did not show a pituitary tumour. By 2013 medical management had failed to control her symptoms and blood pressure adequately. Since she and her husband were keen to have a second child, she opted to have a laparoscopic bilateral adrenalectomy. Following this, there was rapid resolution of her Cushingoid features. She became pregnant in 2014 and had an uneventful pregnancy and delivery. She had regular endocrine monitoring and follow-up pituitary MRI scans after her bilateral adrenalectomy did not show a pituitary tumour. She continued treatment with hydrocortisone 5 mg tds and fludrocortisone 50 mcg od.

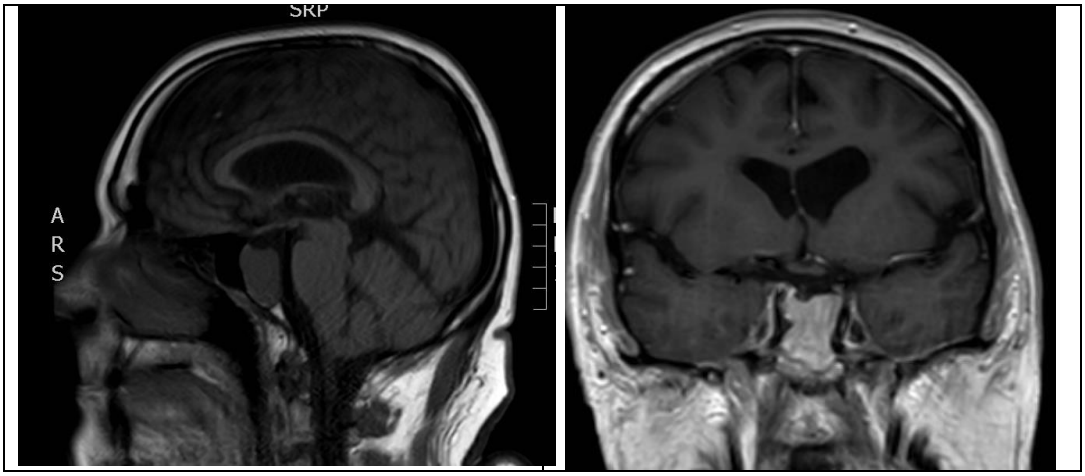
In 2016 she presented with widespread hyperpigmentation over the dorsum of both hands, over her face and oral mucosa. She had gained 4kg in weight, was feeling more tired and was hirsute again. Plasma ACTH was >1250 ng/L. Other anterior pituitary blood tests were normal: prolactin 681 mU/L, free T4 10.6 pmol/L, TSH 3.52 mU/L, FSH 4.0 IU/L, LH 4.9 IU/L, estradiol 384 pmol/L, and IGF-1 34.6 nmol/L. A further pituitary MRI scan showed a 12 x 7mm enhancing lesion on the right side of her pituitary gland. There was no invasion of the cavernous sinus or involvement of the optic chiasm. A diagnosis of Nelson syndrome was made three years after bilateral adrenalectomy and the patient has been referred to Neurosurgery.

This case demonstrates the risk of Nelson syndrome developing after treatment of Cushing's disease with bilateral adrenalectomy.

Prolactinoma or Clival Chondroma: That is the question?

A Agha, N Karavitaki.
University Hospital Birmingham.

Abstract:
Pituitary adenomas are soft tissue tumours with prolactinomas being the commonest among the functioning ones. Prolactin secreting macroadenomas are readily identifiable with their classical snowman appearance and its relation to the surrounding structures. We attempt to identify an unusual case where it mimicked clival chondroma. A 69-year-old retired self-employed engineer with past medical history of diabetes, pleural asbestos plaques, asthma and ischemic heart disease was referred with tingling in the left side of his face and some numbness in his left arm and problems with vision. He had also complained of decreased libido but no galactorrhea. His examination was grossly unremarkable with no visual field defect or any motor/sensory deficit. On investigating further with CT Head a soft tissue tumour was found extending towards the pituitary and involving central skull base with destruction of clivus. MRI confirmed clival lytic lesion with scalloped bony edges (see images) and he was referred to pituitary multidisciplinary team. His biochemical profile showed Prolactin of >9999mU/L, testosterone of 3.4nmol/L, LH 3.3 IU/L , FT4 13.5pmol/L. Despite the unusual radiological appearance he was diagnosed to have macroprolactinoma and started on cabergoline. The case signifies the importance of multidisciplinary approach in such cases where radiological findings alone may be misleading.



What is the best approach for recurrent Rathke's Cleft cyst tumours?

R Kehinde[1], NM Martin[1], N Mendoza[2], A Mehta[3], B Jones[3], P Lewis[4], K Meeran[1], E Hatfield[1], R Nair[2].
[1]Imperial Centre for Endocrinology; [2]Department of Neurosurgery, [3]Department of Neuroradiology; [4]Department of Histopathology, Imperial College Healthcare NHS Trust.

Abstract:
Rathke's Cleft cysts have been traditionally thought of as benign cysts that recur only rarely once drained. However when recurrence occurs, it can be difficult to decide how to prevent this. We are presenting two such cases.

Case 1
A 76 year old man presented in February 2016 with reduced vision in his left eye for one week. He has been blind in his right eye since childhood. A left visual field defect was confirmed and MRI revealed a cystic, suprasellar mass elevating and compressing the optic chiasm, suggestive of a Rathke's cleft cyst. Five days later, trans-sphenoidal resection of the pituitary mass was performed. Histology confirmed a Rathke's cleft cyst. Post-operatively, there was subjective improvement of his vision, although persistence of a partial left hemianopia on perimetry. Three months later he noticed rapid deterioration of vision in his left eye. Repeat MRI showed recurrence, with reduction in visual acuity to 6/12 (from 6/6). Serial perimetry also demonstrated progressive left visual field defect. Trans-sphenoidal drainage of the cystic mass was performed two weeks later. Since there was no improvement in post-operative MRI appearances, further drainage was performed a week later, with improvement of vision and on MRI. Post-operative visual fields also improved.

Case 2
A 58 year old man originally developed visual symptoms and bitemporal hemianopia due to a cystic pituitary mass. He underwent trans-sphenoidal surgery in 2001 and histology confirmed a Rathke's cleft cyst. Post operatively he had a persistent visual field defect and panhypopituitarism requiring hydrocortisone, thyroxine and testosterone replacement. He was monitored with perimetry and imaging. In 2010, whilst in Australia, there was a sudden expansion of cyst, presenting as acute visual deterioration, which required urgent decompression. Post-operatively his vision improved. Subsequently he returned to the UK and in 2012, he re-presented with sudden deterioration in vision and headaches, associated with significant increase in cyst size. The cyst was decompressed with visual field improvement, but was complicated by post-operative CSF leak. Recently (August 2016), he presented for the fourth time with sudden visual disturbance and a bitemporal hemianopia on perimetry. Pituitary MRI confirmed that the cyst had increased in size, displacing the optic chiasm. Extended trans-nasal endoscopic drainage of the Rathke's cyst was performed with improvement in vision.

Questions to the panel:
What options do we have to prevent further recurrence of these cystic lesions?
What is the best method of surveillance for recurrence of these tumours?

Paediatric pituitary apoplexy.

E Culpin, P Dimitri, S Sinha
Sheffield Children's Hospital, Neurosurgery, Sheffield.

Abstract:
Pituitary apoplexy is a rare endocrine emergency, resulting from ischaemia and necrosis of a pituitary tumour. There are few case reports in the literature describing this condition in children.
We describe a series of children presenting to our unit since 2010 with pituitary apoplexy.
Case Series: 5 children (3M, 2F; ages 13-16y - see Demographics Table) presented with headache and deteriorating vision. Only 1 of the children (child 5) was already known to have a pituitary tumour - a prolactinoma and was already on cabergoline.

Child	Age	Sex	Presentation	Initial Management	Timing of Surgery
1	16		Headaches Visual Loss Amenorrhoea Galactorrhoea	ETSS	During acute admission
2	15	M	Headaches Visual loss Cavernous sinus syndrome	Conservative	6 weeks later
3	14	M	Headaches Visual loss	ETSS	During acute admission
4	13	F	Headaches Visual loss Amenorrhoea	Conservative	16 months later
5	15	M	Headaches Visual loss	ETSS	During acute admission

[Demographics]

The apoplectic event was the first indication of a pituitary tumour in the other 4 children, all of whom also had biochemical evidence of a prolactinoma (PRL 10,626 - 47,100).
3 of the children required urgent endoscopic trans-sphenoidal surgery (ETSS) due to persistent visual loss. The other 2 were managed conservatively and able to be discharged home with improved vision and no headaches. However both subsequently presented with worsening vision and recurrent headaches requiring ETSS.
All 5 children had symptomatic improvement following surgery. Post-operative endocrinology showed normal prolactin levels.
Conclusions: Pituitary apoplexy is a rare condition that seems to have a higher relative incidence in children than adults. Our series suggests that the children are more likely to be adolescents and have a prolactinoma. All such patients required surgery, either as an acute or delayed procedure, for visual compromise. Further research into this rare condition is required to better understand the mechanisms.