Visual recovery following surgical intervention for pituitary apoplexy correlated with pre-operative optical coherence tomography

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ABSTRACT

Pituitary apoplexy is a rare but potentially fatal endocrinological emergency which can be difficult to diagnose as presenting symptoms vary significantly. Optimal management requires early diagnosis and collaboration between ophthalmology, endocrinology and neurosurgical services.

We present a case of pituitary apoplexy in a 52-year-old Caucasian female who was referred by her optometrist to Palmerston North Hospital Eye Clinic with a three-week history of sudden onset moderate bifrontal headaches, two weeks of non-specific peripheral visual changes and dense bitemporal inferior quadrantanopia on formal visual field testing. Ocular motility and slit lamp examination were unremarkable and retinal nerve fibre layer (RNFL) was relatively preserved on optical coherence tomography (OCT). MRI demonstrated a haemorrhagic pituitary macroadenoma elevating and compressing the optic chiasm without cavernous extension. Blood tests revealed mild hypothyroidism, hypocortisolism, hypogonadotropism and hyperprolactinaemia.

The patient was commenced on hydrocortisone and levothyroxine replacement and proceeded for urgent transsphenoidal tumour resection at Wellington Regional Hospital. Histology revealed a non-functioning macroadenoma. The patient was asymptomatic and visual field tests had normalised three weeks post-operatively. Six weeks post-operatively, thyroid function and cortisol levels were normal and replacement therapies were ceased.

Pituitary apoplexy results from infarction or haemorrhage of the pituitary gland, most commonly in the presence of an underlying pituitary adenoma.[1–3] As many pituitary adenomas are asymptomatic, pituitary apoplexy is often the first clinical manifestation.[1,4] Pituitary apoplexy occurs more commonly among macroadenomas (>10mm size) than microadenomas, though there remains debate over relative frequency among functioning and non-functioning macroadenomas.[1,3,5,6]

Predisposing factors for pituitary apoplexy include systemic hypertension, major surgery, pituitary surgery or pituitary-involving radiation therapy, head trauma, coagulopathies, dynamic pituitary function testing, high serum oestrogen, pregnancy/delivery and certain medications (including dopamine receptor agonists, ISMN, chlorpromazine, GnRH agonists and clomiphene). However, pituitary apoplexy may occur in the absence of any risk factors.[1,3,7,8]

Estimates of the incidence of pituitary apoplexy among patients with pituitary adenomas vary between 2% and 21%.[1,6,9,10] Incidence of pituitary apoplexy is highest in the fifth and sixth decade of life, with a slight male preponderance estimated between 1.1:1 to 3:1.[1,3,11] Some studies suggest subclinical pituitary apoplexy may be more common among females.[11]

Presenting symptoms vary significantly depending on severity, though often include headaches, nausea/vomiting and bitemporal visual field defects. Decreased visual acuities, ocular motility dysfunction, reduced level of consciousness, fevers and meningism may also occur. Diagnosis is confirmed by CT or MRI head. As endocrine abnormalities are common and potentially life-threatening, a pituitary function blood panel is recommended as part of initial work-up.[1,3,11]

Our case highlights the importance of collaboration between Ophthalmology, Endocrinology and Neurosurgical specialties in the effective diagnosis and management of pituitary apoplexy. The importance of visual field assessment as part of work-up for patients presenting with headache and visual disturbance is demonstrated. Treatment options for pituitary apoplexy and predictive factors for visual recovery including preoperative optical coherence tomography (OCT) are discussed.

Case presentation

A 52-year-old Caucasian woman was referred by her Optometrist to Palmerston North Hospital Eye Clinic with a three-week history of sudden onset moderate bifrontal headaches, two weeks of visual disturbance, which was described as peripheral "mottling" or "tunnelling", and dense bitemporal inferior quadrantanopia on formal visual field testing (Figure 1).

The patient's medical history was remarkable for pre-diabetes (HbA1c 44mmol/mol), hypertension, mild asthma and a previous left lower limb varicose vein treated by surgical stripping. The patient's menopause occurred three years prior. Medications included cilazapril 5msg PO OD, amlodipine 5mg PO BD and metformin 850mg PO BD. The patient had no known adverse medication reactions.

Upon examination, the patient was alert, oriented and appeared well. The patient was afebrile with a blood pressure of 142/78mmHg, and otherwise normal vitals. Visual acuities with glasses were 6/12 on the right and 6/30 on the left with no improvement with pinhole. Intraocular pressures were 14mmHg in both eyes with iCare tonometry. Ocular alignment and extraocular movements were normal—no ptosis, lid retraction or nystagmus was present. Pupils were equal and reactive with no relative afferent pupillary defect (RAPD), and colour vision was full on testing with Ishihara plates. Cranial nerve and limb power examinations were normal.

Slit lamp and dilated fundus examinations were normal. In particular, no ocular media opacities were present, and the optic nerves and maculae appeared healthy and well-perfused. Repeat formal visual field testing was not performed, given that this had been performed by the Optometrist the day prior. OCT demonstrated relatively preserved retinal nerve fibre layer (RNFL) while Ganglion Cell Layer (GCL) thicknesses were modestly reduced bi-nasally, particularly in the left eye (Figure 2).

Optic chiasmal pathology was suspected, with pituitary macroadenoma being the most likely differential. An MRI of the brain and orbits was requested to investigate further (Figure 3). This demonstrated widening of the sella and erosion of the dorsum sellae, with a heterogenous mass arising from the pituitary fossa, measuring 37x24x25mm with a fluid–fluid level. No normal pituitary tissue was visible, and the pituitary stalk was not identifiable. The lesion was consistent with a haemorrhagic pituitary macroadenoma (pituitary apoplexy) causing elevation and compression of the optic chiasm, without cavernous extension.

Initial blood tests demonstrated mild central hypothyroidism, hypocortisolism and hyperprolactinaemia. FSH of 3.0U/L and LH of 0.6U/L were below normal for post-menopausal state, suggestive of hypogonadotropism. Complete blood count, creatinine and electrolytes, liver function tests, INR, APTT, plasma ACTH, IGF-1 and GH were within normal range (Table 1).

The patient was commenced on Hydrocortisone 20mg PO mane, 10mg midi, 10mg nocte and levothyroxine 50mcg PO OD with endocrinology input. A CT head scan and dedicated pituitary MRI were performed for pre-operative planning, and the patient was referred to the Wellington Regional Hospital Neurosurgery Department. Tumour excision was performed by transsphenoidal approach four days following initial diagnosis. The procedure was uncomplicated, and the patient's recovery was uneventful other than intermittent headaches initially, which were severe at times but gradually settled over the course of two months. Histology showed a benign non-functioning pituitary macroadenoma and post-operative MRI demonstrated a small residual non-enhancing tumour mass present within the sella turcica measuring 16x5 x12mm with unchanged widening of the sella and erosion of the dorsum sellae (Figure 4).

The patient was reviewed in Ophthalmology clinic three weeks post-operatively with visual acuities of 6/4.5 in the right with glasses and 6/9+2 in the left with glasses, pin holing to 6/6+2. Slit lamp examination and dilated fundus examination were once again unremarkable. Formal visual field testing was performed, and demonstrated complete resolution of the inferior-temporal hemianopia in the right eye with a small central visual defect that was deemed artefactual, as it was not reproducible on subsequent testing. A small area of persistent temporal visual field loss was noted in the left eye (Figure 5), which corresponded to nasal GCL thinning on preoperative OCT (Figure 2). The patient's visual acuity and fields remained stable at subsequent follow-ups.

The patient attended follow-up with the endocrinology service six weeks post-operatively. 0900 serum cortisol was 358nmol/L after withholding hydrocortisone for 24 hours and therefore this medication was stopped. Thyroid function tests had normalised, with a T4 of 14.4 pmol/L and TSH of 1.28mU/L, and HbA1c improved to 40 mmol/mol. Therefore, levothyroxine and metformin

Figure 1: Results of Medmont Central Fast Threshold visual field testing by referring optometrist demonstrating dense bi-temporal inferior quadrantanopia, as well as early bitemporal superior field loss. Results were highly suggestive of optic chiasmal pathology.

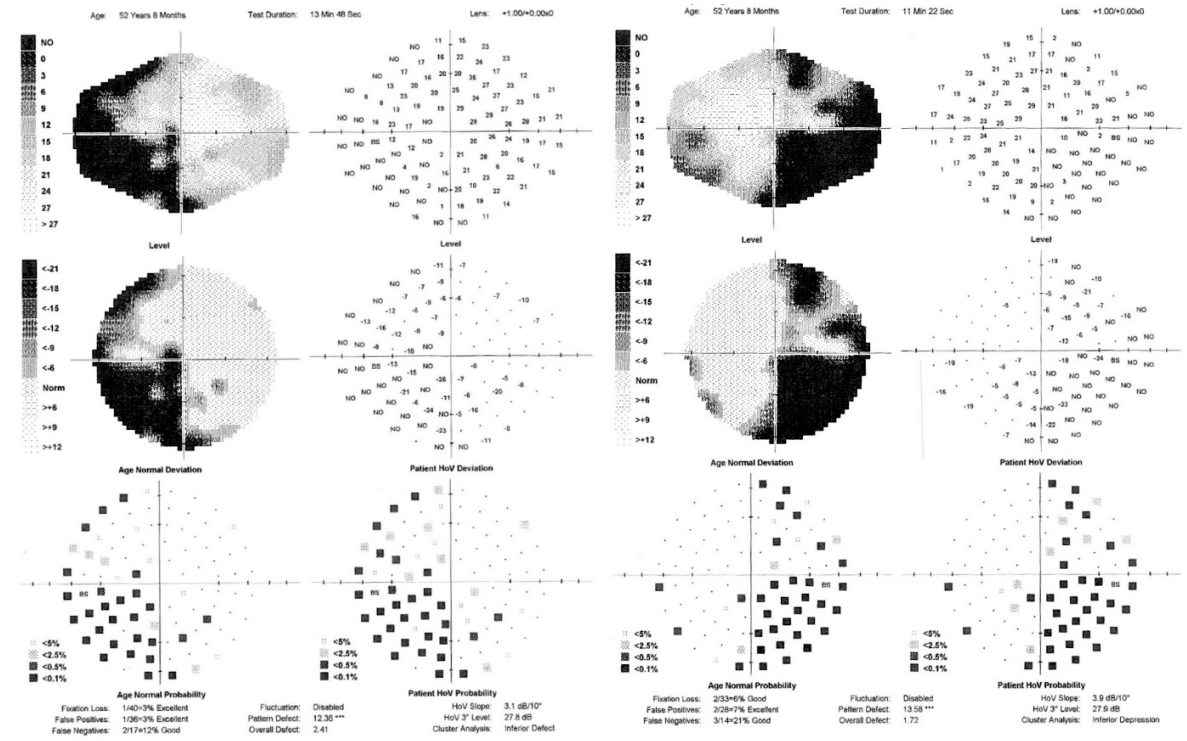


Figure 2: Pre-operative optical coherence tomography (OCT) scans of the retinal nerve fibre layer (RNFL) and ganglion cell layer (GCL), showing subtle generalised bilateral RNFL thinning as well as moderate bi-nasal GCL thinning particularly in the left eye.

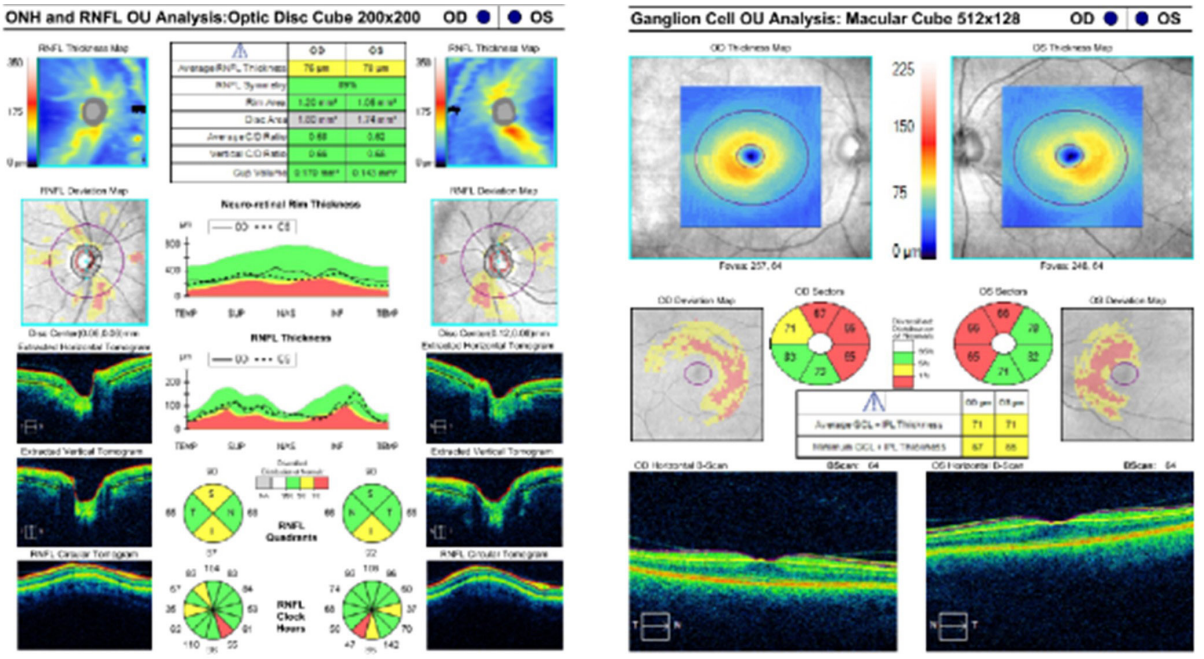


Figure 3: Pre-operative T1 TSE FLAIR Sagittal MRI (left) and T2 TSE Transverse MRI (right) demonstrating a heterogeneous pituitary mass with non-dependent fluid in the anterior mid-portion, consistent with a haemorrhagic pituitary macroadenoma (pituitary apoplexy). Optic chiasmal elevation was present with no cavernous sinus extension.

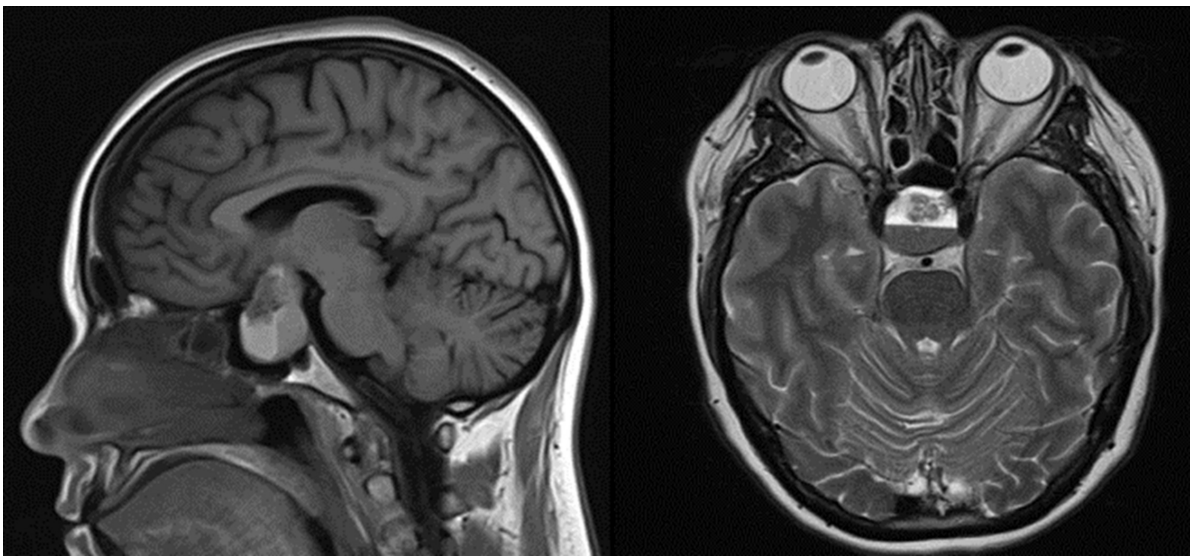


Figure 4: Post-operative T1 TSE Sagittal MRI (left) and T2 TSE Transverse MRI (right), demonstrating small residual pituitary tumour tissue with unchanged widening of the sella and erosion of the dorsum sellae. No elevation of the optic chiasm is seen.

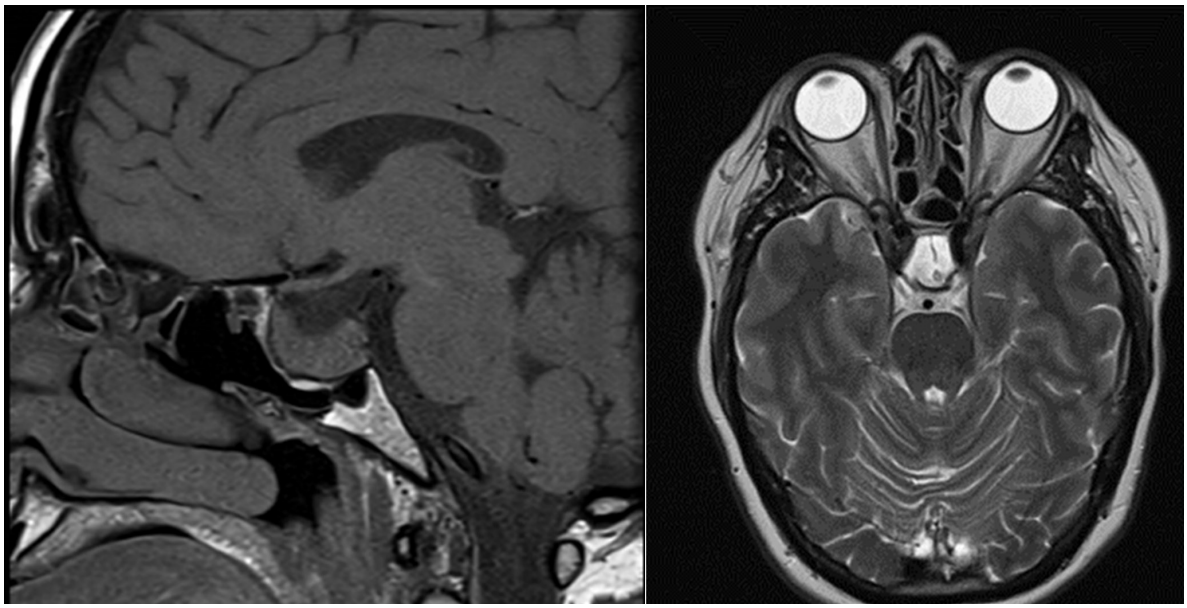
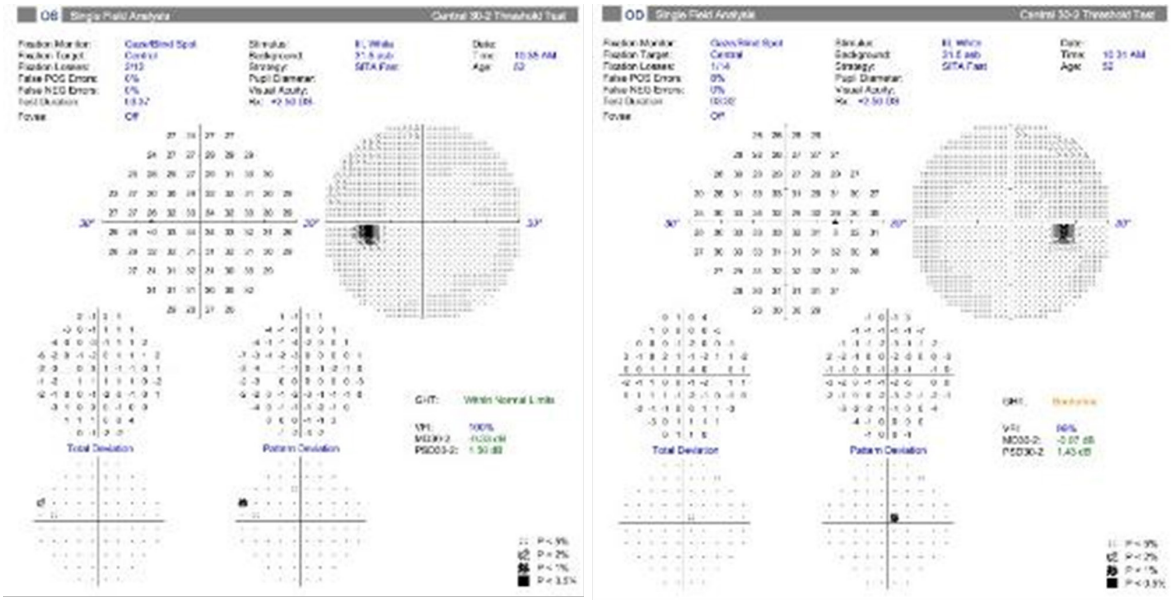


Table 1: Summary of hormone, electrolyte and renal blood results for our case. Hyperprolactinaemia, hypothyroidism and hypocortisolism resolved post-operatively, while mild hypogonadotropism persisted.

	Immediate pre-operative	1 month post-operative	6 weeks post-operative	4 months post-operative	Reference range
Cortisol (0900)	133 (L)	355*	358**		150–550nmol/L
ACTH (Plasma)	5.0	3.4			1.0–12.0pmol/L
TSH	1.36	1.28		2.06	0.27–4.2mU/L
Free T4	6.0 (L)	14.4		12.5	12.0–22.0pmol/L
Free T3	3.6 (L)	4.7			4.0–6.8pmol/L
hGH	0.12	0.12			<6ug/L
IGF-1	58	80			51–190ug/L
Prolactin	566 (H)	211			100–500mU/L
FSH	3.0 (L)	4.1 (L)			26–134U/L
LH	0.6 (L)	1.9 (L)			>20U/L
Oestradiol		<18 (L)			<180pmol/L
HbA1c		40			<41mmol/mol
Creatinine	77	67			45–90umol/L
Sodium	138	141		136	135–145mmol/L
Potassium	4.3	4.4		4.3	3.5–5.2mmol/L
Calcium (adjusted)	2.46	2.45			2.10–2.55mmol/L
Phosphate	1.08	1.16			0.8–1.5mmol/L

ACTH – adrenocorticotropic hormone; TSH – thyroid stimulating hormone; hGH – human growth hormone; IGF-1 – insulin-like growth factor-1; FSH – follicle stimulating hormone; LH – luteinising hormone.
*Cortisol level during replacement hydrocortisone therapy
**Cortisol level 24 hours after hydrocortisone withheld

Figure 5: Results of Zeiss HFA 30-2 SITA-Fast visual field testing one month post-operatively, demonstrating near-complete resolution of bitemporal visual defects. A small area of left temporal field loss was present and persisted on visual field testing at subsequent follow-ups.



were also stopped. Repeat thyroid function tests remained in the normal range six weeks after stopping levothyroxine.

Discussion

Clinical manifestations of pituitary apoplexy depend on the extent of haemorrhage, damage to the normal pituitary tissue and compression of surrounding structures such as the optic chiasm, hypothalamus, cavernous sinus and its contents.[2,3] Severe cases typically present with sudden onset severe headache followed by some combination of nausea/vomiting, ophthalmoplegia, visual loss, fevers, meningism or decreased level of consciousness occurring over hours to two days and can be life-threatening. However, symptoms in mild cases may be less pronounced and may have an insidious onset, as in the current case.[2,10] The differential diagnoses for patients presenting with headache and non-specific peripheral visual disturbance is wide and includes migraine, acute angle closure glaucoma, intracranial hypertension (idiopathic or otherwise), temporal arteritis, and optic neuritis among others. Visual field testing is fast, inexpensive and often useful in localising the area affected. In our case, characteristic bi-temporal visual field loss, particularly inferiorly, was highly suggestive of a pituitary lesion causing chiasmal compression. This resulted in prompt pituitary blood panel, MRI and early treatment.

There remains debate over the role and optimal timing of surgical decompression in pituitary apoplexy. No prospective trials exist due to the rarity of pituitary apoplexy. Case series and reports comparing conservative management and early decompression have varying conclusions, though significantly better visual outcomes have been demonstrated with surgical decompression compared to conservative management in patients with severely reduced visual acuity or visual field defects.[1,3] The UK guidelines for management of pituitary apoplexy advise that surgical decompression should be performed by an experienced pituitary surgeon within seven days of symptom onset in patients "with severe neuro-ophthalmic signs such as severely reduced visual acuity, severe and persistent or deteriorating visual field defects or deteriorating level of consciousness."[1] Reduced visual acuity and severe visual field loss were indications for early surgical decompression in the current case.

Pre-operative visual field defect, visual symptom duration and extensive retinal nerve fibre layer (RNFL) and ganglion cell layer (GCL) thinning on optical coherence tomography (OCT) are predictive factors for poor visual field recovery after surgical excision of pituitary adenoma.[12–15] Although these factors were identified in cases of adenoma without apoplexy, it is reasonable to

expect that such factors are relevant in pituitary apoplexy, given that visual field impairment is caused by direct compression of the optic chiasm in both conditions. In the current case, short visual symptom duration (two weeks) and preserved RNFL thickness on preoperative OCT suggested the potential for significant post-operative visual recovery despite a dense preoperative visual field defect. Nasal GCL thinning on pre-operative OCT, particularly in the left eye suggested the possibility of some persistent field loss, as was noted in the left temporal periphery post-operatively.

Pituitary apoplexy results in ischaemia, irreversible loss of healthy pituitary tissue and may lead to pituitary insufficiency. Some form of endocrine dysfunction is present in 80% of cases—most commonly deficiencies of growth hormone, gonadotropins and ACTH, hypothyroidism and hyperprolactinaemia.[1,3,11] Hypocortisolaemia results from impaired pituitary ACTH secretion and may cause electrolyte disturbance and haemodynamic instability, which may be life-threatening. Commencement of empiric hydrocortisone replacement therapy with Endocrinology input is recommended in cases of haemodynamic instability, altered level of consciousness or significant visual impairment. Patients with 09:00 serum cortisol less than 550nmol/L should be considered for hydrocortisone replacement therapy.[1] Hypocortisolism, hypogonadotropism and hypothyroidism were present in the current case pre-operatively without haemodynamic instability or hyponatraemia. Appropriate hydrocortisone and levothyroxine replacement were commenced with input from endocrinology. Hydrocortisone and levothyroxine replacement therapies were ceased six weeks following early surgical decompression, as the patient regained adequate pituitary function. This is consistent with findings from Liu et al, which demonstrated at least partial recovery of hormone deficiency after early surgical decompression.[11]

The diagnosis and management of pituitary apoplexy can be challenging. Patients may present acutely unwell or with very few symptoms. Visual field testing is a cheap, non-invasive investigation that can be very useful in identifying pituitary pathology, which may otherwise be missed. Pituitary blood testing is an important part of the initial work-up in cases of suspected pituitary apoplexy, as hormonal deficiencies are common. Serum cortisol testing is of particular importance as untreated hypocortisolism is potentially life-threatening. Significant visual and hormonal recovery may occur following early surgical decompression. The extent of postoperative visual field recovery in pituitary apoplexy may be predicted by similar factors as in pituitary adenoma without apoplexy, though further research in this area is warranted.

COMPETING INTERESTS

Nil.

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