Pituitary apoplexy: two very different presentations with one unifying diagnosis

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DECLARATIONS

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The following case reports illustrate two differing presentations of pituitary apoplexy, and then discuss appropriate investigation and treatment options.

Case 1

A previously healthy 64-year-old woman presented to the emergency room with a three-day history of feeling generally unwell, drowsiness and acute onset, severe headache. She had a decreased level of consciousness and a temperature of 39°C. No ophthalmoplegia, visual field defect or other focal neurological signs were present. She had a leucocytosis and raised C-reactive protein (CRP) with normal serum sodium. The chest radiograph was unremarkable and computed tomography (CT) of the brain was reported as showing involutional changes. Analysis of cerebrospinal fluid demonstrated 220 red cells per μL, 408 white cells per μL (83% polymorphs, 17% lymphocytes), proteinorrachia 1.7 g/L (NR 0.1–0.4) glucose 1.8 mmol/L and xanthochromia. The patient was presumed to have pneumococcal meningitis – the commonest cause of bacterial meningitis in this age group, and intravenous ceftriaxone was administered.

Five days into admission the patient's level of consciousness was improving but not at baseline. Severe headache and pyrexia continued. The cerebrospinal fluid was sterile. Further cranial imaging was arranged and MRI scan demonstrated a pituitary macroadenoma with evidence of recent haemorrhage (Figure 1). Goldmann perimetry confirmed intact visual fields. Hormone tests revealed panhypopituitarism (cortisol <30 nmol/L, thyroid-stimulating hormone [TSH] <0.1 mU/L [0.27–4.2 mU/L], free thyroxine 15.2 pmol/L [9–20], free tri-iodothyronine 3.7 pmol/L [3.4–5.6], follicle-stimulating hormone [FSH] and luteinizing hormone [LH] <0.5 pmol/L, prolactin <47 mlU/L, growth hormone [GH] <0.1 ug/L, insulin-like growth factor-1 [IGF-1] 9.5 nmol/L [3.7–32.9]).

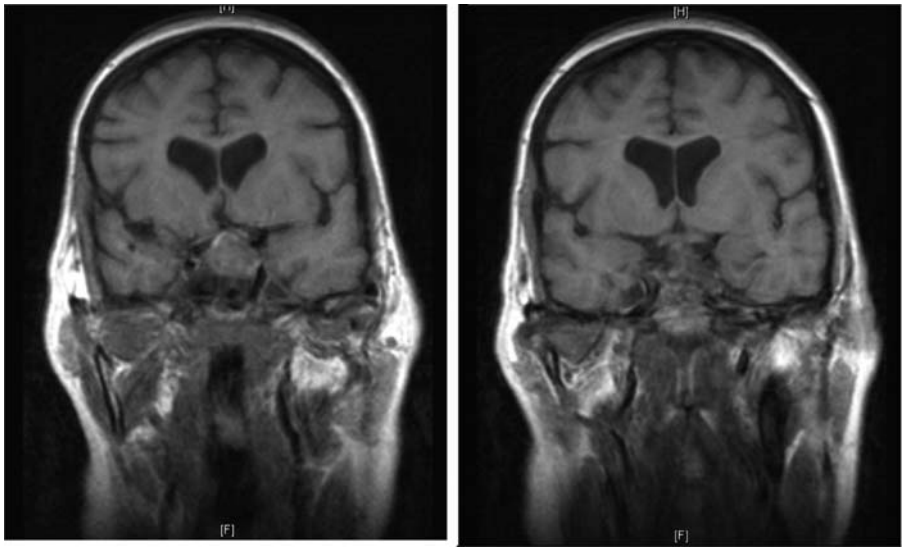
A diagnosis of pituitary apoplexy related to haemorrhage with resultant hypopituitarism was made. Hydrocortisone and thyroxine were commenced. After discussion with neurosurgical colleagues, it was agreed that operative intervention was not required. The patient was discharged home five days later. Although the patient continued to require pituitary replacement at follow-up three years later, imaging showed a reduction in the size of the pituitary mass.

Case 2

An 80-year-old man with history of hypertension (requiring three antihypertensive agents) and type 2 diabetes mellitus (managed with two oral hypoglycaemic drugs) was admitted with a fractured neck of femur following a low-trauma fall. He was admitted to the orthopaedic ward to await fixation. However, he became hypotensive and required ionotropic support and fluid resuscitation. His haemoglobin decreased (12.5 to 9.3 g/dl) and acute renal dysfunction developed. The blood glucose was well controlled. A TSH in the normal range (0.5 mU/L) was considered to have ruled out myxoedema. Imaging excluded thromboembolism and sepsis was clinically unlikely. An echocardiogram demonstrated good systolic function.

Four days after admission the patient was considered fit for hemiarthroplasty. Immediately postoperatively he became hypoglycaemic (BM

Figure 1
MRI brain showing a haemorrhagic lesion of the pituitary gland extending to the optic chiasm causing displacement of the optic nerve, consistent with pituitary macroadenoma



1.1 mmol/L) and progressively drowsy, with no focal neurology, including visual fields. Hyponatraemia and hypotension occurred. Full thyroid function testing showed hypothyroidism (free tri-iodothyronine 1.9 [3.4–5.6 pmol/L] and free thyroxine 6.4 [9–20 pmol/L]) with an inadequate pituitary response (TSH 1.0 mU/L [0.3–5.5]) prompting a diagnosis of pituitary apoplexy leading to insufficiency. A brain CT scan (Figure 2) showed macroadenoma with probable haemorrhage. An MRI was recommended, but due to his recent arthroplasty this could not be performed safely.

A diagnosis of macroprolactinoma was confirmed with prolactin level 17543 mU/L (50–480). Serum cortisol level was 47 nmol/L (120–500) with ACTH undetectable. Endocrinology team review concluded the patient had a chronic pituitary adenoma, as evidenced from his long-standing lack of testosterone (loss of secondary sexual characteristics and osteoporosis), improving diabetic control (on review of clinic notes HbA1c 7.6 in 2003 to 6.0 in 2005) and hyponatraemia, with acute presentation secondary to inability to mount a stress response.

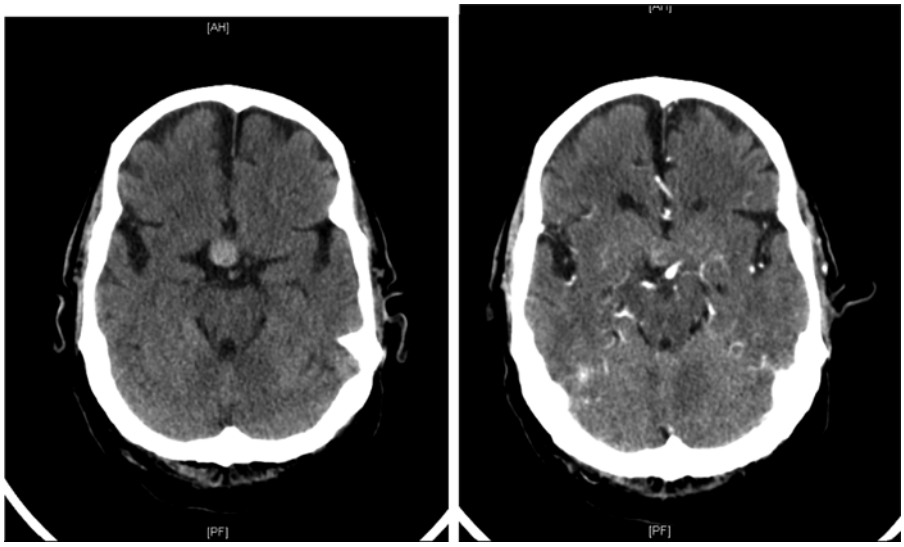
Cabergoline, hydrocortisone and thyroxine were introduced immediately (and testosterone subsequently), and at review four years later MRI confirmed haemorrhage into macroadenoma, now of reduced size, with controlled prolactin level 190 nmol/L (on dopamine agonist treatment).

Discussion

Pituitary apoplexy is a rare, under-diagnosed and potentially fatal condition usually resulting from haemorrhage or infarction of a pituitary tumour.[1,2] In the majority of cases there is no prior diagnosis of a pituitary tumour, increasing the difficulty of diagnosing apoplexy.[3] Other predisposing factors for apoplexy include anticoagulant therapy, bleeding disorders, diabetes, head injury, sudden changes in arterial or intracranial pressure and postpartum haemorrhage.[1]

Variability of clinical presentation poses a challenge. Leakage of infarcted tissue into the subarachnoid space may cause headache, altered level of consciousness, visual disturbance, fever or signs of meningism.[4,5] If the enlarged pituitary or haemorrhage extends laterally into the cavernous sinus ophthalmoplegia may occur. Superior expansion may cause visual impairment,

Figure 2
CT brain scan showing a hyperdense mass arising from the pituitary fossa, representing pituitary macroadenoma with haemorrhage



classically a bitemporal hemianopia. If the acute event is asymptomatic or subacute, patients present later with symptoms of hormonal deficiency.[6]

Patients with pituitary apoplexy, meningitis and subarachnoid haemorrhage can all present with headache, impaired consciousness and fever. To aid differentiation: pituitary apoplexy is favoured by bilateral ocular nerve palsy or ophthalmological signs and/or extended interval from headache to altered consciousness.[7] Biochemical markers of pituitary insufficiency such as cortisol deficiency should be sought and, as illustrated, judicious biochemical assessment of pituitary function is required. Although TSH is often measurable, a diagnosis of secondary hypothyroidism requires simultaneous measurement of the free thyroid hormones. Whole-brain imaging, especially CT, may obtain limited views of the pituitary fossa restricting diagnostic sensitivity. Thus, the gold standard modality is 'pituitary' MRI, which also better delineates haemorrhage.[5] Lumbar puncture is an important investigation in all patients presenting with fever, headache and impaired consciousness, but this may not diagnose pituitary apoplexy, which can show xanthochromia with raised red cell count and/or raised white cell and protein level.[8]

The management of pituitary apoplexy includes monitoring of fluid and electrolytes as secondary diabetes insipidus may occur.[5] Immediate high dose corticosteroid replacement should be considered, and emergency surgical decompression may be required in response to diminished level of consciousness, visual impairment or hypothalamic disturbance. Ocular paresis is reported to resolve in all patients, with acuity returning in 88% of cases.[5] Improved management of apoplexy has reduced mortality to 5%, with 50% of patients requiring long-term pituitary replacement therapy.[3,5]

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