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## CASE REPORT

## Ischaemic pituitary tumour apoplexy and concurrent meningitis: a diagnostic dilemma

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**SUMMARY**

Pituitary tumour apoplexy is a rare but potentially life threatening clinical syndrome that mostly results from haemorrhage in the pre-existent tumour. Pure ischaemic subtype of apoplexy is even rarer. The presentation can be hard to differentiate clinically from bacterial meningitis. Moreover, the presence of one does not necessarily exclude the other and early diagnosis of both conditions is imperative for timely management. We report a case of ischaemic pituitary tumour apoplexy that may have precipitated in the setting of bacterial meningitis.

**BACKGROUND**

Pituitary tumour apoplexy is a potentially fatal clinical syndrome resulting from sudden expansion of the pituitary gland and subsequent mass effect on the surrounding structures with possibility of severe neurological, ophthalmological and endocrinological sequelae, especially acute adrenal crisis. It most often results from haemorrhage in the pituitary tumour, but apoplexy due to ischaemic infarction has been rarely reported. The clinical attacks are heralded by headache, nuchal rigidity, visual field defects, double vision and at times loss of consciousness.<sup>1</sup> With none of these symptoms specific to pituitary tumour apoplexy, it is not surprising that it is a great masquerader and can be easily overlooked. Cases have been reported where pituitary apoplexy mimicked the more common entity of meningoencephalitis.<sup>2,3</sup> Early identification of each of these entities is imperative for timely management, however, neither the presence of one excludes the possibility of the other nor does it establish the actual temporal relationship.<sup>4</sup> We are reporting a case of pituitary tumour apoplexy possibly triggered in the setting of concurrent central nervous system (CNS) infection and highlighting the typical MRI features of 'ischaemic' apoplexy in the absence of haemorrhage, emphasising the possibility of coexistence of the two entities.

**CASE PRESENTATION**

A 30-years-old woman presented to us with sudden onset of headache, fever and vomiting for 2–3 days along with right eye swelling for 1 day. The headache was right sided, moderate to severe in intensity and continuous. She complained of double vision. There was no history of loss of consciousness, altered mentation, seizures, night sweats or weight loss. On inquiry, she also reported an infrequent

dull generalised headache for the last 6 months for which she had been taking over the counter analgesics on pro re nata basis.

The examination revealed a young woman with an average height and built who had right orbital swelling which was non-pulsatile. There was no proptosis. Pupils were bilaterally 3 mm equal and reactive although sluggish on the right side. Right third and sixth nerve palsy was noted along with hypoesthesia to pinprick in V1 distribution and absent corneal reflex on the right side. Any visual field restriction was not identified by the confrontation method. Indirect ophthalmoscopy revealed Frisen Scale grade 1 papilloedema bilaterally. Neck stiffness and Kernig's sign were positive. Rest of the neurological examination was unremarkable. Formal ophthalmological assessment was not carried out.

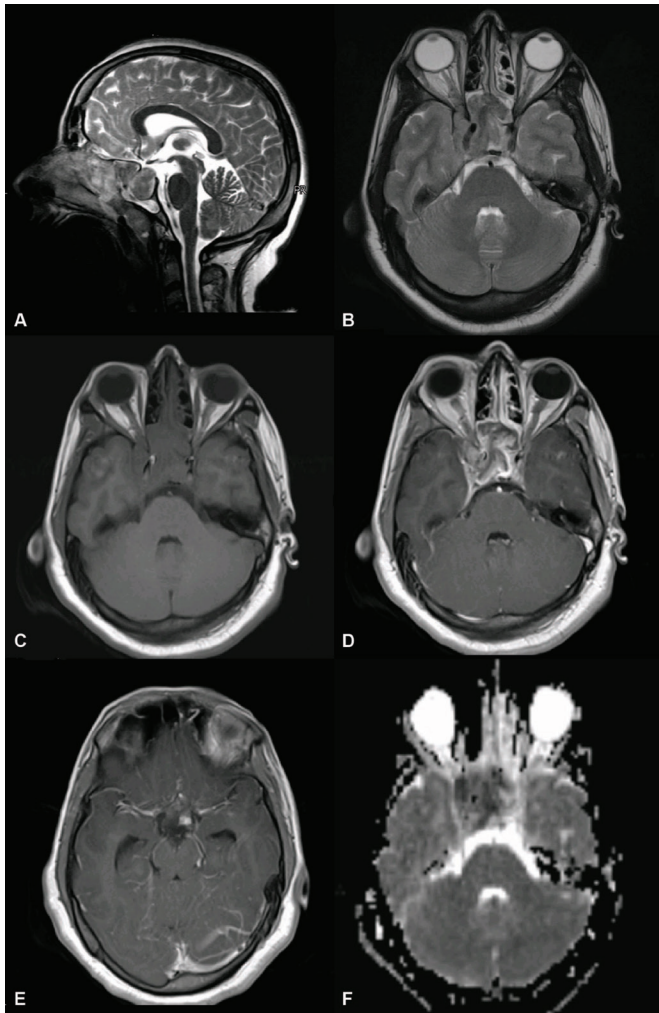
**INVESTIGATIONS**

The woman underwent contrast-enhanced MRI of the brain (figure 1) revealing predominantly hypointense signal intensity mass in the expanded sella with infrasellar and right parasellar extension on T2-weighted image. It was encasing the right internal carotid artery and right orbital apex. No suprasellar extension was identified. Mucosal thickening was appreciated in sphenoid sinus. An apparent diffusion coefficient sequence, showed diffusion restriction within the lesion. It was isointense to hypointense on T1-weighted sequence. Postcontrast T1-weighted axial sequence showed patchy peripheral enhancement with central non-enhancing area. There was significant basal meningeal enhancement as well. Based on overall MRI characteristics, diagnosis of fungal infection with meningitis was made with other possibility of ruptured epidermoid cyst with chemical meningitis. Magnetic resonance venography (MRV) did not show any evidence of cerebral venous sinus thrombosis (CVST). Cerebrospinal fluid (CSF) examination was done which showed total leucocyte count (TLC) of  $2.775 \times 10^9/L$  (range  $0-0.005 \times 10^9/L$ ) with 80% polymorphs. CSF glucose was 64 mg/dL with serum glucose level of 146 mg/dL and CSF protein level of 78 mg/dL (range 15–40 mg/dL). CSF Gram stain, acid-fast bacilli and fungal smears along with cultures were negative. First blood culture, drawn prior to starting antibiotics, grew pansensitive beta-haemolytic group A streptococcus. CSF cytology was negative for malignant cells. Blood TLC count was  $23.5 \times 10^9/L$  (range  $4-10 \times 10^9/L$ ) with 90.5%



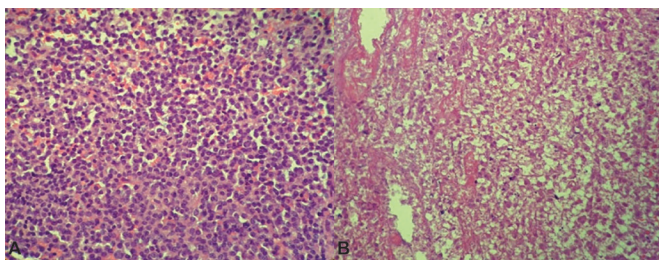
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**Figure 1** MRI brain showing a predominantly hypointense sellar mass lesion with mucosal thickening in sphenoid sinus on a T2-weighted sagittal image (A), encasing the right orbital apex (B). The lesion is predominantly isointense on a T1-weighted axial image (C). Postcontrast images showing peripheral contrast enhancement (D), 'pituitary ring sign', along with basal meningeal enhancement (E). Apparent diffusion coefficient map showing diffusion restriction within the lesion (F).

polymorphs. Serum galactomannan and beta-D-glucan assays were normal. As the nature of the sellar lesion was not clear, trans-sphenoidal biopsy was planned. Due to strong suspicion of concomitant CNS infection, the procedure was deferred till after 10 days of antibiotic and antifungal therapy. Contrary to our clinical impression, the histopathological features were found



**Figure 2** Histopathological analysis of the mass lesion obtained after a trans-sphenoidal biopsy reveals normal looking pituitary gland (A) as well as a segment of one of the large necrotic areas (B).

to be consistent with pituitary adenoma with extensive areas of infarction (figure 2). Periodic acid–Schiff–diastase staining was negative for any fungal organism. The adenoma was not stained for anterior pituitary hormonal profile. Serum hormonal profile was done after the biopsy and revealed monomeric prolactin level of 55.6 ng/mL (range 4.0–18.5 ng/mL), cortisol levels of 14.1 µg/dL (morning range 4.3–22.4 µg/dL), adrenocorticotropic hormone level of 80 pg/mL (normal <46 pg/mL), thyroid-stimulating hormone levels of 3.37 µIU/mL (range 0.5–8.9 µIU/mL) and follicle-stimulating hormone levels were 1.07 mIU/mL (midcycle range 0.2–17.2 mIU/mL). Short synacthen testing was not done.

#### TREATMENT

Intravenous antibiotics (ceftriaxone and vancomycin) and anti-fungal (amphotericin) medication were started empirically. Amphotericin was stopped after the biopsy result.

#### OUTCOME AND FOLLOW-UP

Amphotericin was stopped after biopsy results were obtained. The orbital swelling improved with time. Antibiotics were continued for a total of 14 days for underlying bacterial meningitis. Correlating the clinical, laboratory and radiological data, we made the diagnosis of ischaemic pituitary tumour apoplexy possibly precipitated by bacterial meningitis. Residual clinical deficit at follow-up after 1 month was partial right sixth nerve palsy.

#### DISCUSSION

Pituitary tumour apoplexy is a potentially life threatening but rare entity with reported incidence of less than 5%. The purely ischaemic subtype is even rarer.<sup>1</sup> Various theories have been proposed that may explain the pathogenesis of the ischaemic variety. An enlarging tumour within the confines of bony sella may compress its own blood supply leading to infarction. Pituitary tumours have particularly high metabolic demands along with reduced expression of vasogenic factors and relatively precarious blood supply which may result in a tumour simply outgrowing its feeding vessels and undergoing infarction.<sup>1</sup> Therefore, the presence of fever may have proved to be a tipping point in causing pituitary infarction in our patient who had a large pre-existent pituitary macroadenoma.

Leakage of necrotic cellular debris into the subarachnoid space following pituitary apoplexy may lead to chemical meningitis with resultant triad of fever, meningism and photophobia.<sup>5</sup> Such a situation would be difficult to label as definite bacterial meningitis unless the CSF Gram staining is positive, CSF antigen detection tests are positive or CSF cultures grow the pathological organism. Many times this criterion is not fully met in the clinical setting. However, the presence of particularly high CSF leucocyte count ( $2.775 \times 10^9/L$ ) with 80% neutrophils, low CSF to serum glucose ratio (0.4) and the fact that the first blood culture grew a potential bacterial pathogen, all strongly point towards the simultaneous occurrence of bacterial meningitis in our patient and can be labelled as probable bacterial meningitis.<sup>6</sup> The decision to continue with antibiotics for bacterial meningitis would be judicious in similar settings.

A vast majority (60%–80%) of pituitary tumour apoplexy occurs in otherwise asymptomatic patients with secretory adenomas being the most common underlying tumours.<sup>1,5</sup> Factors such as closed head trauma, hypotension and hypertension, pituitary irradiation, cardiac surgery, anticoagulation, oestrogen and dopamine agonist therapy, pregnancy and pituitary stimulation testing have been associated with increased risk.<sup>1</sup> CNS

infection and fever have not been reported as usual precipitants but meningitis is a recognised cause of vasculopathy and factors that may increase metabolic demand of the gland may precipitate infarction.<sup>4</sup>

MRI with dedicated sellar protocol is a sensitive study for imaging the pituitary gland and may visualise haemorrhage not seen on the CT scan. The absence of signal drop out on susceptibility weighted images excludes haemorrhage. Usually, the pituitary adenomas are isointense to hyperintense on T2-weighted image. The profound hypointense signal from the lesion on T2-weighted images in our case led us to initially suspect a fungal aetiology in our patient as the fungal hyphae containing paramagnetic elements like manganese, iron and magnesium return low signals on T2-weighted images.<sup>7</sup> Diffusion weighted imaging further aids in supporting early diagnosis of pituitary tumour infarction showing diffusion restriction in the infarcted tissue. Rim enhancement with central portion of isointense/slightly hypointense gland relative to grey matter (pituitary ring sign), on contrast enhanced T1-weighted MRI, is a typical manifestation in bland tumour infarction.<sup>8</sup> Sphenoid sinus mucosal thickening, as seen in our case, has been reported to be temporally linked with pituitary tumour apoplexy. Although its definite significance is unknown, in the setting of pituitary apoplexy it has been suggested to be an ominous sign requiring early surgical intervention.<sup>9</sup>

Most critical aspect of medical management after pituitary tumour apoplexy revolves around early identification and appropriate treatment of the potentially fatal acute adrenal crisis requiring prompt glucocorticoid administration. Hypothyroidism, hypogonadism and growth hormone deficiency may manifest progressively in the subacute to chronic phase. While there is continued emphasis on early recognition and

treatment of any hormonal insufficiency, the usage and timing of surgical decompression is debatable. As the pituitary tissue shrinks automatically following apoplexy, the definite surgical decompression is warranted only in cases with deterioration in conscious level and severe visual loss secondary to optic chiasmal compression.<sup>8</sup>

This case reinforces that pituitary apoplexy may coexist with CNS infection and mere absence of haemorrhage should not preclude one to consider pituitary tumour apoplexy as a diagnostic possibility.

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**Contributors** Case was seen by HH and SJS. The idea to report this case was put forward by HH and SSMA to which SJS agreed. After the review of literature, initial draft was prepared by HH and SSMA which was then reviewed by SJS who suggested and made some changes. All the authors participated in case writing.

**Competing interests** None declared.

**Patient consent** Gaurdian consent obtained.

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## Learning points

- ▶ Pituitary apoplexy is a clinical masquerade of infective meningitis and possibility of coexistence of both conditions should be kept in mind.
- ▶ Not all cases of pituitary tumour apoplexy are haemorrhagic, be wary of the pure ischaemic variety.
- ▶ The 'pituitary ring sign' is characteristic of ischaemic pituitary tumour apoplexy.

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