J R Coll Physicians Edinb 2012; 42:119–23
http://dx.doi.org/10.4997/JRCPE.2012.206

An unusual case of sudden onset headache due to pituitary apoplexy: a case report and review of the new UK guidelines

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ABSTRACT Spontaneous pituitary apoplexy in the absence of a known pre-existing pituitary adenoma is a very rare cause of sudden onset headache, but can be potentially sight- and life-threatening. We describe a case of a 37-year-old man who presented to the Emergency Department with a severe headache, associated nausea, vomiting and features of meningism. A suspected clinical diagnosis of subarachnoid haemorrhage led to an urgent computed tomography scan of the head demonstrating a large pituitary macroadenoma. A diagnosis of pituitary apoplexy was suspected and he was transferred as an emergency case to the regional tertiary hospital for management. A further urgent magnetic resonance imaging scan showed haemorrhage into the pituitary adenoma, confirming pituitary apoplexy. We discuss this clinical condition and the new UK national guidelines which have recently been published to improve clinical assessment, investigation and management of patients with suspected pituitary apoplexy.

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KEYWORDS Pituitary apoplexy, sudden headache

DECLARATION OF INTERESTS No conflicts of interest declared.

INTRODUCTION

Pituitary apoplexy is a medical emergency caused by haemorrhage or infarction into a pituitary tumour. Patients present with a headache associated with nausea, vomiting, features of meningism or visual disturbance. The clinical presentation can mimic other more common neurological emergencies, such as subarachnoid haemorrhage or bacterial meningitis and should be considered as part of the differential diagnosis for patients presenting with the above features. There has previously been little consensus on the management of such patients. However the recently published UK guidelines aim to provide clear guidance on the investigation and management of these patients with proven or suspected pituitary apoplexy. Owing to the rarity of the condition and the fact that adequate expertise is likely to be lacking in local hospitals, it is recommended that patients be managed at a tertiary centre with neurosurgery, endocrinology and ophthalmology expertise on-site. Conservative management versus neurosurgical intervention should be considered. We discuss a case of a 37-year-old man who presented with symptoms of an acute intracranial pathology and whose initial imaging suggested pituitary apoplexy. We review the literature relevant to the condition and the new UK guidelines.

CASE REPORT

A 37-year-old male patient presented to the Emergency Department with a history of severe headache, which he described as pain over the frontal region with an abrupt onset, which had started the previous day. The headache was associated with nausea, vomiting, photophobia and neck stiffness. He was otherwise healthy, with no previous medical problems and was not on any regular medications. He had not suffered severe headache or migraine in the past, and had not noticed any previous visual disturbance. On initial assessment he looked unwell with a clammy and grey appearance, but was haemodynamically stable, with a blood pressure of 140/90 mmHg and a pulse rate of 50 beats per minute. His Glasgow Coma Score was 15/15. Neurological examination was normal, including preserved visual fields and normal range of eye movements. Fundoscopy was normal with no evidence of papilloedema. He had discomfort of neck flexion but Kernig's sign for meningism was negative. There was no skin rash. Blood tests revealed normal electrolytes and mildly elevated inflammatory markers with a white cell count of 14 x 10^9/cubic millimetre (normal <11) and a C-reactive protein level of 66 milligrams per litre (mg/L) (normal <10).

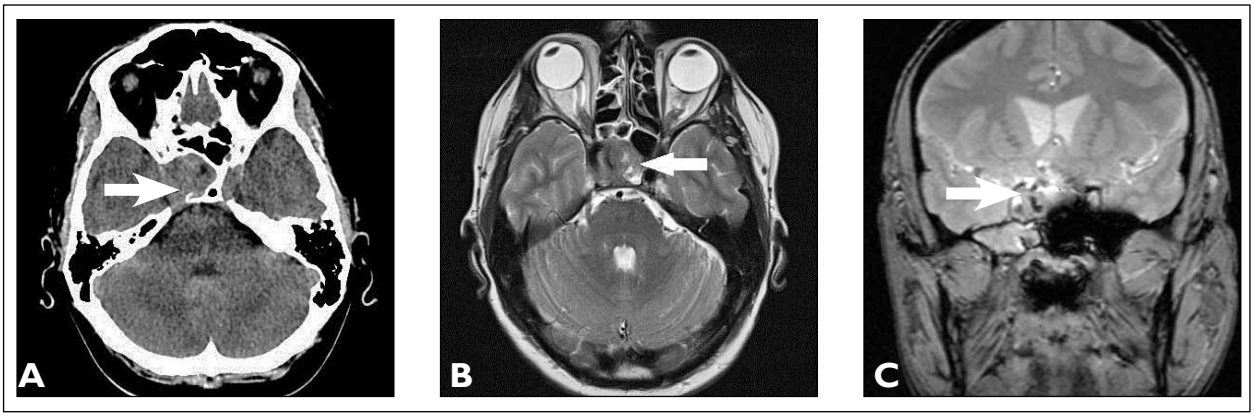

FIGURE 1A Computed tomography scan image showing the enlarged sella and the pituitary tumour. **FIGURE 1B** Magnetic resonance imaging (MRI) scan showing the same tumour. **FIGURE 1C** MRI scan showing haemorrhage within the tumour.

A differential diagnosis of either bacterial meningitis or subarachnoid haemorrhage was considered. The patient was treated empirically with intravenous ceftriaxone (2 grams stat) and an urgent computed tomography (CT) scan of the brain was arranged. This demonstrated a large pituitary macroadenoma, but no signs of acute subarachnoid haemorrhage (Figure 1a).

Over the next four hours, the patient's clinical condition worsened, with increasing headache, nausea and confusion. This raised the possibility of pituitary apoplexy as a potential diagnosis and the patient was commenced on intravenous steroid replacement therapy. The patient was discussed with specialists at a tertiary hospital and he was transferred for further imaging and management planning with a neurosurgical consultation. An urgent magnetic resonance imaging (MRI) scan demonstrated a large 25 mm enhancing pituitary macroadenoma which projected into the right cavernous sinus and anteriorly into the sphenoid sinus (Figure 1b). There was no significant suprasellar extension and the optic chiasma was not compressed. There was a small focus posteriorly in the lesion which was felt to show an increased T1 and T2 signal and low gradient echo signal which represented a small haemorrhage (Figure 1c).

The pituitary hormone profile was measured and demonstrated an elevated prolactin level with suppression of sex hormones, growth hormone and insulin-like growth factor; the thyroid profile was normal (Table 1). After a multidisciplinary discussion between the endocrine and neurosurgical teams, the patient was managed conservatively with steroid therapy. Emergency neurosurgical decompression was not deemed to be required.

DISCUSSION

Pituitary apoplexy is a rare medical emergency generally seen in patients with pituitary tumours. Patients typically present with sudden onset severe headache, associated with vomiting, visual impairment and reduced consciousness. First described in 1898 by Pearce Bailey,[1] it is caused by either haemorrhage into, as in the case of our patient, or infarction of a pre-existing pituitary tumour. In over 80% of cases, the pituitary tumour is unknown prior to the first presentation as apoplexy.[2] The earliest and most common symptom is one of severe headache and pituitary apoplexy should therefore be considered in the differential diagnoses for patients presenting with severe or sudden onset headache and the above additional symptoms.[3] Nausea is common in around 80% of cases.[3] Visual impairment, seen in 71%, is caused by lateral compression of the cavernous sinus, as a result of the sudden increase in sellar contents, which leads to ocular palsies, with the oculomotor nerve being the most common nerve involved. Extravasation of blood or necrotic tissue into the subarachnoid space can lead to features of meningism, including fever, photophobia and a reduced conscious level.[4] Acute secondary adrenal insufficiency is seen in around two-thirds of patients

TABLE 1 Pituitary hormone profile

Pituitary axis hormone	Measured level (reference range)
Prolactin	11040 mU/L (normal 0 to 450)
Luteinising hormone	1.7 U/L (normal 3.0 to 13)
Follicle stimulating hormone	1.1 U/L (normal 1.3 to 9.2)
Testosterone	2.5 nmol/L (normal 9 to 25)
Growth hormone	<0.07 µg/L (normal <0.4)
Insulin like growth factor	13 nmol/L (normal 15 to 37)
Thyroid stimulating hormone	0.86 mU/L (normal 0.3 to 4.7)
Free thyroxine	11.3 nmol/L (normal 9.5 to 21.5)

mU/L= milliunits per litre; **U/L**= units per litre; **nmol/L**= nanomoles per litre; µg/**L**= micrograms per litre

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with pituitary apoplexy and is the major cause of mortality associated with the condition.[2,3] It is an important diagnosis to consider in patients presenting with sudden onset headaches or features of meningism as it can be potentially sight- or life-threatening. Pituitary ischaemia can also be seen in other specific cases, for example in Sheehan's syndrome, where a large postpartum haemorrhage can lead to ischaemic pituitary necrosis within a normal pituitary gland, with resultant hypopituitarism.[4]

Recent UK national guidelines on the investigation and management of patients with suspected pituitary apoplexy contain recommendations related to the endocrinological and radiological investigations and management, including the issue of where these patients should be managed.[5] These guidelines have been drawn up following a consensus meeting about a condition that was previously poorly defined.[6] They reinforce the importance of considering pituitary apoplexy in the differential diagnosis of patients presenting with acute severe headache with or without neuro-ophthamological signs. The difficulty in making a positive diagnosis is recognised, as the clinical presentation often mimics other neurological emergencies such as subarachnoid haemorrhage and bacterial meningitis. This is similar to our patient, where intravenous ceftriaxone was administered to treat possible bacterial meningitis, prior to imaging or further investigation.

If pituitary apoplexy is suspected on clinical grounds then endocrine and radiology assessment is required. Endocrinological assessment includes measurement of insulin growth factor-1 (IGF-1), growth hormone, prolactin, thyroid stimulating hormone (TSH), free thyroxine (FT4), luteinising hormone (LH), follicular stimulating hormone (FSH), cortisol and testosterone or oestradiol, with over 80% of patients being deficient in at least one anterior pituitary hormone (as was the case in our patient).[2,3] Magnetic resonance imaging is the radiological imaging of choice, confirming the diagnosis in around 90% of patients.[3] The guidelines acknowledge that a CT scan is the most common initial investigation in the acute setting, which may only be diagnostic in identifying haemorrhage in 21% of cases[3] but is likely to identify a sellar mass. This again was the case in our patient.

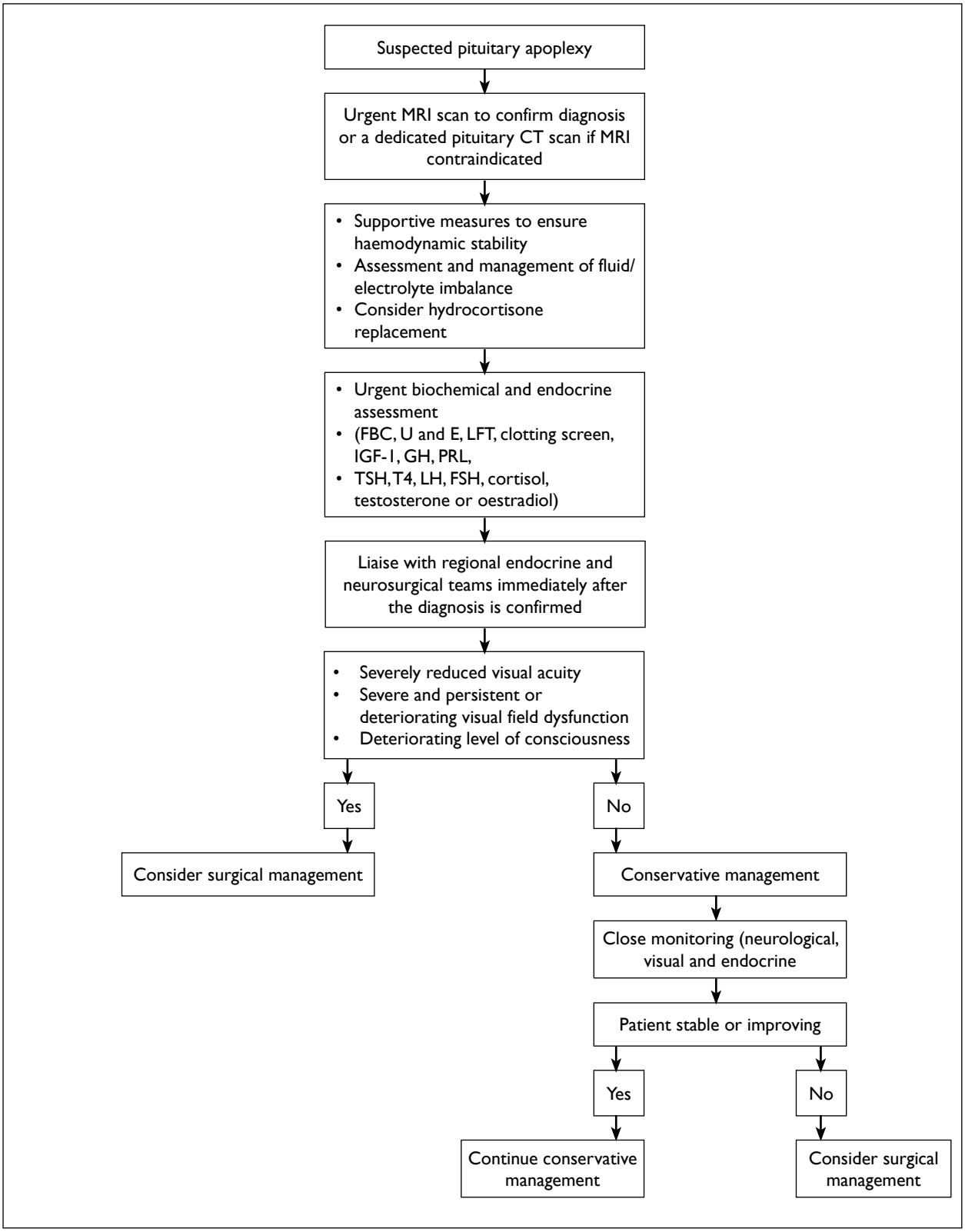
Initial management includes preservation of electrolyte and fluid balance alongside prompt corticosteroid replacement. The new guidelines recommend the use of hydrocortisone 100–200 mg as an initial bolus as the first-line treatment. If patients are haemodynamically unstable, this initial bolus can be followed by continuous infusion or six-hourly boluses and if unstable, then empirical treatment is recommended while confirmatory tests are carried out. The new guidelines reinforce the importance of management of such patients at a tertiary specialist centre with expertise in pituitary apoplexy, including a multidisciplinary approach involving endocrine, neurosurgical and ophthalmology input. It is recommended that cases are reviewed with the neurosurgical or endocrinology team at the earliest opportunity and transfer arranged to an appropriate centre once they are medically stable. Our experience with this patient was in keeping with the national guidance. The endocrinology team at the tertiary hospital provided advice and subsequently arranged transfer to them and liaised with the other specialist teams to ensure a smooth transition of care from a district hospital to the tertiary centre.

Further management after initial steroid replacement and transfer of care to an appropriate centre remains controversial as no randomised controlled trials have been performed to compare conservative medical management to neurosurgical management.[5] Published literature based on individual case series suggests that patients with mild neuro-ophthalmic signs improve with conservative management and careful monitoring, while patients with more severe signs, or who deteriorate, should be considered for early transsphenoidal resection of the tumour.[2,3,5] This strategy is reflected in the new national guidelines. Figure 2 (overleaf) provides a treatment algorithm for patients with suspected pituitary apoplexy, as recommended by the new UK guidelines.

CONCLUSION

Pituitary apoplexy can be caused by haemorrhage or infarction of the pituitary gland and should be suspected in patients presenting with sudden, severe headache, nausea or visual disturbance and meningism. It is a medical emergency and although rare, requires prompt recognition and treatment. The recently published UK guidelines underline the standards of investigation and management for these patients. Initial investigations include standard endocrine tests to define pituitary function and appropriate urgent neuroimaging, ideally by magnetic resonance, to confirm the diagnosis. Initial management is with fluid and electrolyte replacement and intravenous steroid replacements, followed by prompt discussion with and transfer to a tertiary centre where the patient can be managed with combined neurosurgical, endocrine and ophthalmology input. Further treatment includes both conservative management and consideration for neurosurgical intervention with transsphenoidal resection of the tumour to decompress the pituitary fossa.

FIGURE 2 Algorithm for the management of suspected pituitary apoplexy (Rajasekaran et al 2011).[5]



FBC= full blood count; **U and E**= urea and electrolytes; **LFT**= liver function tests; **IGF-1**= insulin growth factor-1; **GH**= growth hormone; **PRL**= prolactin; **TSH**= thyroid stimulating hormone; **T4**= free T4; **LH**= luteinising hormone; **FSH**= follicular stimulating hormone

KEY POINTS

- Pituitary apoplexy is a potentially sight-threatening and life-threatening condition.
- It is caused by haemorrhage or infarction into a pituitary macroadenoma.
- It is an important differential to consider in patients presenting with headache, nausea or visual disturbance, where a computed tomography (CT) scan of the brain demonstrates a pituitary macroadenoma.
- Patients with pituitary apoplexy should be managed in a tertiary centre by a multidisciplinary team comprising endocrinologists, neurosurgeons and ophthalmologists.
- Initial management is by intravenous steroid therapy, alongside fluid and electrolyte replacement.
- Patients with severe ophthalmological involvement, or who continue to deteriorate despite initial treatment may be considered for neurosurgical intervention.

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