

CASE REPORT

Uncontrolled diabetes as a rare presenting cause of pituitary apoplexy

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SUMMARY

Pituitary apoplexy is a rare endocrine emergency. The extent to which hyperglycaemia is a contributory risk factor in the precipitation of pituitary apoplexy is not known. A 38-year-old man with poorly controlled diabetes presented to the emergency department with sudden onset of nausea and headache with drooping of his right eyelid for about 4 days. On physical examination, he had orthostatic hypotension, ptosis of the right eye, lateral and downward positioning of the eye and absent pupillary reflex. Visual field testing of the left eye revealed superolateral quadrantanopia. MRI of the brain showed pituitary macroadenoma with necrosis. Investigations showed hyperglycaemia, decreased T3, T4 with normal Thyroid stimulating hormone (TSH), low serum Leutinizing hormone (LH), Follicle stimulating hormone (FSH), testosterone and low normal serum prolactin levels. About 21% of non-functioning pituitary adenomas present with apoplexy as was seen in our patient. It is likely that his uncontrolled diabetes precipitated this episode of apoplexy as hyperosmolarity and dehydration, caused by hyperglycaemia can lead to changed pituitary microvascular environment increasing the risk of pituitary infarction.

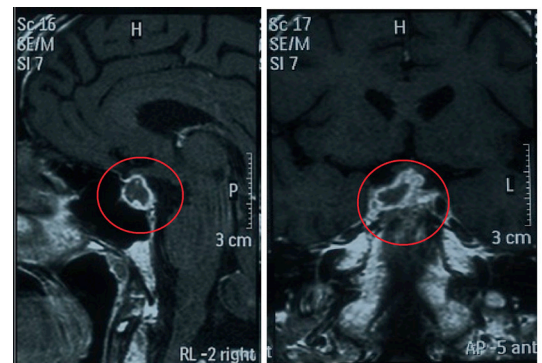


Figure 2 T1W image on the MRI of the brain showing a lesion arising from the right side of pituitary, which is hypointense suggestive of pituitary adenoma with peripheral enhancement and central necrosis suggestive of apoplexy.

BACKGROUND

Pituitary apoplexy is a rare endocrine emergency. Through this case, we postulate that uncontrolled diabetes is a risk factor for pituitary apoplexy.

CASE PRESENTATION

A 38-year-old, Indian Hindu, man presented to the emergency department with sudden onset of headache, nausea and vomiting with closure of the right eye over the course of 4 days. His headache was diffusing, non-pulsating in nature, with increased severity in the early morning and with coughing. The vomiting was projectile, non-bilious with no haematemesis. There was no history of fever, altered sensorium, seizures, neck stiffness or photophobia. The patient had been diagnosed with type 1 diabetes 15 years ago and was not taking his medications as prescribed. There was no significant family history. The patient had no history of using alcohol, cigarettes or recreational drugs.

On examination, he was afebrile with a pulse rate of 98/min, regular, and blood pressure was 112/84 mm Hg in both arms supine but had postural hypotension with blood pressure of 90/70 mm Hg standing. BMI was 22.3 kg/m². On neurological examination, he had ptosis of the right eye, which was shifted down and out (figure 1), with an absent pupillary reflex. Visual field testing of his left eye revealed superolateral quadrantanopia; however, the right eye could not be assessed due to ptosis. Fundus examination had changes of non-proliferative diabetic retinopathy. The rest of the neurological examination was normal. Cardiovascular,



Figure 1 Ptosis is seen in the right eye and the right eye is shifted down and out.



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respiratory and gastrointestinal systems examination was unremarkable.

INVESTIGATIONS

Routine investigations including full blood count, serum electrolyte, renal function test and liver function tests were within normal limits. His fasting and postprandial plasma glucose was 376 mg/dL and 450 mg/dL, respectively, with HbA1C of 9.3% (diabetic > 6.4%) and urinary microalbumin:creatinine ratio of 262 mg/g (30–300 mg/g-microalbuminuria). Urinary ketones were negative and arterial blood gas analysis was within normal limits. Serum C-peptide level (random) was reduced to < 0.30 ng/mL (normal 0.81–3.85 ng/mL) compatible with the known diagnosis of type 1 diabetes mellitus.

In view of the sudden onset of his signs and symptoms, an MRI of the brain was ordered that showed a lesion $1.9 \times 1.3 \times 1 \text{ cm}^3$ arising from the right side of the pituitary, which was hypointense on T1W image and shows peripheral enhancement with central necrosis (figure 2). It extended superiorly impinging on the optic chiasma and also involved cavernous sinus, abutting the right oculomotor nerve. The patient had a T3 of 0.40 ng/mL (0.60–1.81 ng/mL) and a T4 of 3.20 µg/dL (5.01–12.45 µg/dL), with an inappropriately low TSH of 2.73 µIU/mL (0.35–5.50 µIU/mL). Early morning serum cortisol level was also low at 3.53 µg/dL (4.30–22.40 µg/dL), serum LH was 1.35 mIU/mL (1.50–9.30 mIU/mL), FSH was 1.30 mIU/mL (1.40–18.10 mIU/mL), serum testosterone (random) was 10 ng/dL (14–76 ng/dL) and prolactin was 2.40 ng/mL (2.10–17.70 ng/mL). These clinical investigations were suggestive of central hypothyroidism with a probable lack of Adreno corticotrophic hormone (ACTH)-driving cortisol insufficiency and hypogonadotropic hypogonadism. Growth hormone axis was not tested at this stage. On the basis of the MRI findings of a pituitary macroadenoma with necrosis and relevant clinical findings, a diagnosis of pituitary apoplexy was made.

TREATMENT

The patient was initially started on intravenous fluids and insulin infusion for hyperglycaemia. After the diagnosis of pituitary apoplexy, steroid supplementation (injection hydrocortisone 50 mg six hourly) and tablet levothyroxine (1.6 µg/kg body weight) were started. His condition improved over the next 48 hours, and he was shifted to subcutaneous insulin therapy (basal-bolus regimen) and oral steroids (tablet hydrocortisone [20 mg/day] in divided doses). A neurosurgical opinion was sought, and subsequent trans-sphenoidal removal of the pituitary macroadenoma was performed.

OUTCOME AND FOLLOW-UP

The histopathological examination of the removed tumour was suggestive of a non-functioning pituitary adenoma.

DISCUSSION

Pituitary apoplexy is a rare endocrine emergency to be suspected when the presentation includes features of raised intracranial pressure along with acute ophthalmoplegia, visual field defects or altered sensorium. The peak age of presentation is in fifth to sixth decade with a male preponderance with a ratio of 1.1–2.25:1.^{1–4} About 21% of non-functioning pituitary adenomas present with pituitary apoplexy as was seen in our patient.⁵ It occurs more commonly in men as pituitary adenomas are more commonly detected at the stage when a macroadenoma has developed in comparison to women where menstrual

irregularities, or galactorrhoea, tends to lead to an earlier detection at the microadenoma stage. In about 80% of the cases, an apoplectic episode uncovers the presence of an adenoma.⁶

Although pituitary apoplexy may occur without any identifiable cause, various known precipitating factors for an apoplectic episode are hypertension, sudden changes in arterial blood pressure, anticoagulant therapy, head trauma, dynamic testing of pituitary functions especially with TRH and Gonadotropin releasing hormone (GnRH), oestrogens, dopamine agonist, somatostatin analogues and radiation therapy.^{2,6}

The presentation of pituitary apoplexy is variable. Symptoms, such as ophthalmoplegia, results from pressure on surrounding structures, such as the third, fourth, fifth and sixth nerves in the cavernous sinus, visual field defects are due to pressure on the optic chiasma, hormonal deficiencies due to pituitary necrosis and headache due to raised intracranial pressure. Symptoms in our patient initially resulted from an undiagnosed enlarged pituitary adenoma impinging on the optic chiasma and extending into the cavernous sinus with tumour necrosis precipitating acute cortisol deficiency. In the accident and emergency department, sudden onset of third nerve palsy in the presence of uncontrolled diabetes was initially thought to be due to diabetes. However, it is important to note that the pupillary reflex is preserved in various medical causes of third nerve palsy as the presumed pathology is infarction of the nerve trunk compared with surgical causes where extra ocular pressure over the nerve trunk causes loss of the pupillary reflex. In our patient, absence of pupillary reflex in the presence of sudden onset of ptosis made us to think about intracranial pathology as a cause of his third nerve palsy.

However, it is likely that his hyperglycaemia precipitated the apoplectic episode as the resultant hyperosmolarity and dehydration leads to a changed pituitary microvascular environment, which increases the risk of pituitary apoplexy.² It could be argued that the apoplectic episode itself was responsible for the uncontrolled hyperglycaemia due to a state of physiological stress on the body, but as the counter-regulatory hormones associated with a rise of plasma glucose in stressful situations were low in our patient, it is unlikely that physiological stress leads to hyperglycaemia. Also, the presence of a raised HbA1c level indicated pre-existing hyperglycaemia. However, the contribution of diabetes as a risk factor in the occurrence of pituitary apoplexy is still not known and has rarely been described in the literature,⁶ a review revealed one case report describing uncontrolled diabetes associated with pituitary apoplexy where degenerative changes in the gland's microvasculature had been described as a possible aetiology.⁷ The other possible mechanisms for precipitation of pituitary apoplexy in our patient could be blood pressure fluctuations due to autonomic neuropathy secondary to long-standing diabetes.

The immediate management of pituitary apoplexy includes careful monitoring of fluid and electrolyte balance, steroid supplementation and supportive measures. Once the patient recovers from the acute episode, they can be continued on a maintenance dose of steroids. The controversy in the management of pituitary apoplexy is regarding the conservative or the neurosurgical management of the patient. Few retrospective studies suggest better visual and endocrinological outcomes with early neurosurgical intervention.^{8–10} However, recent retrospective studies show that there is no difference in neurological or endocrinological outcome between conservatively and surgically managed patients.^{11,12} Although there is a general consensus that patients who are clinically and neurologically unstable with a reduced level of consciousness or progressive visual deficit should undergo urgent surgical decompression,¹³ but there are no defined criteria for such intervention. Our patient had a

progressing visual deficit so had trans-sphenoidal removal of his pituitary adenoma.

Lack of knowledge about an existing pituitary adenoma makes it difficult to think about pituitary apoplexy as a differential diagnosis, leading to delay and potential mismanagement of a patient such as this with increase in mortality and morbidity.

Learning points

- ▶ Uncontrolled diabetes should be considered a risk factor for pituitary apoplexy.
- ▶ Look for a surgical cause of ptosis when there is absent pupillary reflex.
- ▶ Patients with a pituitary macroadenoma and apoplexy, who are clinically or neurologically unstable with a reduced level of consciousness or a progressive visual deficit should undergo urgent surgical decompression.

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