

High altitude-induced pituitary apoplexy

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ABSTRACT Sudden ascent to high altitudes beyond 2,438 m can cause life-threatening complications such as acute mountain sickness and high altitude cerebral and pulmonary oedema. We present a case of pituitary apoplexy in a young man who ascended to high altitude gradually, after proper acclimatisation. He developed headache, nausea, vomiting and persistent hypotension. Magnetic resonance imaging revealed an enlarged pituitary gland with haemorrhage. His hormonal estimation showed acute adrenal insufficiency due to corticotropin deficiency. The patient responded well to conservative medical management with hormonal replacement therapy. This is most likely the first reported case of high altitude-induced pituitary apoplexy in the literature.

Keywords: acute adrenal insufficiency, high-altitude illnesses, pituitary apoplexy
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INTRODUCTION

Altitude sickness in its commonly recognised forms consists of acute mountain sickness (AMS) as well as the two life-threatening forms – high altitude cerebral oedema (HACE) and pulmonary oedema (HAPE). Other well-documented but less common neurological conditions that occur in high altitude areas include transient ischaemic attacks, cerebral venous thrombosis, seizures, syncope, double vision and scotomas.⁽¹⁾ We present a rare case of high altitude-induced pituitary apoplexy. To our knowledge, this is the first reported case of pituitary apoplexy arising due to ascent to high altitude.

CASE REPORT

A 29-year-old male soldier, a resident of Lucknow (altitude 131 m from sea level), India, was posted to a high-altitude area. After a mandatory pre-induction medical examination and proper acclimatisation, he was inducted to an altitude of 4,572.0 m. After five days, he developed giddiness on getting up in the morning, which was associated with severe throbbing, global headache with nausea and non-projectile vomiting. There was no associated history of altered sensorium, diplopia or seizures. He was diagnosed with AMS and transferred to a lower altitude (914.4 m) by helicopter. Persistently low blood pressure (BP) levels were recorded (systolic 86–90 mmHg, diastolic 56–62 mmHg) by the treating attendant over the next two days in spite of adequate hydration and fluid resuscitation; hence, he was transferred to our centre.

On examination, the patient had a regular pulse of 68/min and BP of 94/60 mmHg with a postural drop of 18/10 mmHg. There were no crackles or wheeze on auscultation of the lungs. No cardiac murmur or focal neurological deficit was noted. There was no papilloedema on fundus examination. His investigations revealed a normal haemogram, coagulogram and routine biochemistry, including electrolytes. His electrocardiogram was

normal. Hormonal estimation showed inappropriately normal serum adrenocorticotropic hormone (ACTH) (5.2 pmol/L, normal range [NR] 1.3–16.7 pmol/L) with low basal serum cortisol (98.8 nmol/L, NR 138–690 nmol/L), normal thyroid function tests (free T4 16.9 pmol/L, NR 10.3–21.9 pmol/L; thyroid-stimulating hormone 2.8 mIU/mL, NR 0.34–4.25 mIU/L) and gonadal functions (serum testosterone 14.8 nmol/L, luteinising hormone 1.8 IU/L, follicle-stimulating hormone 2.6 IU/L).

Magnetic resonance (MR) imaging revealed an enlarged pituitary gland with haemorrhage (Fig. 1), suggesting pituitary apoplexy. The patient was managed with intravenous hydrocortisone 100 mg eight-hourly for the initial two days and then started on oral prednisolone (7.5 mg) in two divided doses. He symptomatically improved and his BP normalised to about 114/70 mmHg. On review after eight weeks, he remained asymptomatic. There was a reduction in pituitary size and the amount of subacute haemorrhage on repeat MR imaging (Fig. 2) compared to the previous MR images. He was reassessed for pituitary function after steroid replacement was discontinued for 48 hours. The patient still had evidence of adrenal insufficiency, which was confirmed by insulin tolerance test (basal 8 am serum cortisol 188.6 nmol/L and peak cortisol during insulin-induced hypoglycaemia 369.2 nmol/L [blood glucose 40 mg/dL]). Other pituitary hormonal profile was within normal limits. He was continued on tablet prednisolone 5 mg daily and is currently under follow-up.

DISCUSSION

Ascent to a height of more than 2,438.4 m without proper acclimatisation can result in serious medical illnesses, such as AMS, HAPE, HACE and high-altitude retinal haemorrhage. These high-altitude illnesses constitute as medical emergencies, as they can be fatal if treatment is delayed.⁽²⁾ The cardinal principle for the prevention of high-altitude illnesses is not to go too high too

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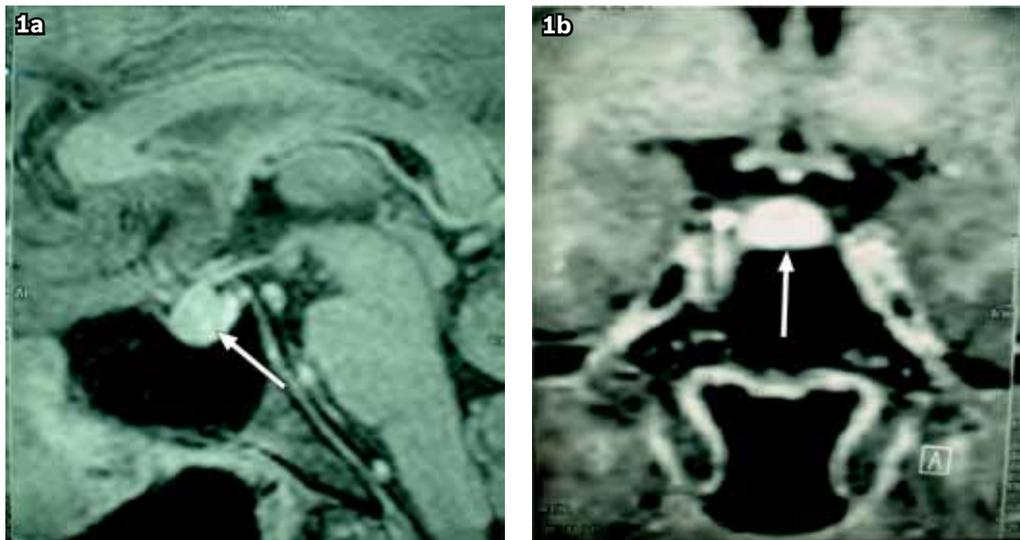


Fig. 1 (a) Sagittal and (b) coronal T1-W MR images of the pituitary gland show an enlarged pituitary gland with subacute haemorrhage.

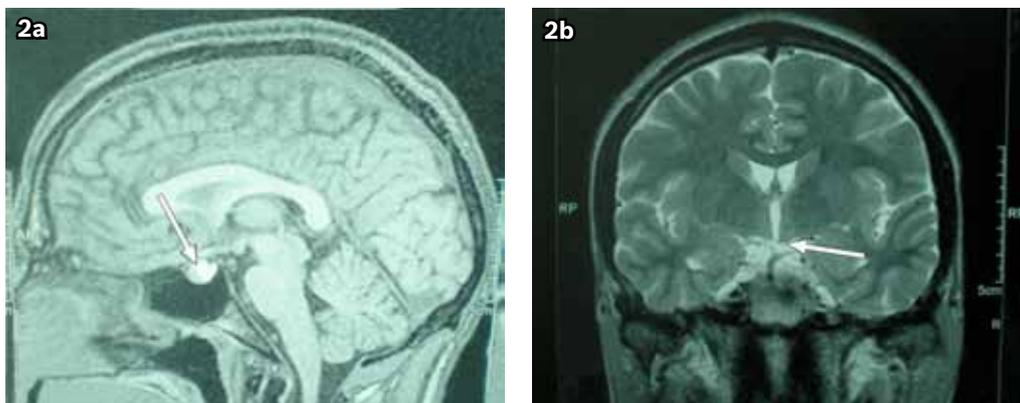


Fig. 2 Repeat (a) sagittal and (b) coronal T1-W MR images show an enlarged pituitary gland, which has decreased in size compared to the previous MR images with subacute haemorrhage.

fast. Thus, a proper acclimatisation protocol must be followed. The acclimatisation procedure followed by our organisation includes three stages: first stage (> 9,000 feet to 12,000 feet) consists of six days of graded routine activity; second stage (> 12,000 feet to 18,000 feet), four additional days of routine activity; and, third stage (> 18,000 feet), another four days of increasing activity level. Our patient had undergone proper acclimatisation according to the procedure laid out by the organisation.

AMS is the most common manifestation of high-altitude illness, which lies at one end of the spectrum. The other end of the spectrum includes life-threatening conditions such as HAPE and HACE. AMS usually develops after a lag period of 6–96 hours, but may occur immediately on induction to high altitude, with the onset occurring most often during the first day. Early signs of AMS include headache, which is usually bilateral, frontal, throbbing, aggravated by exertion and more frequently occurs in the morning on waking. Headache becomes more severe as the disease progresses and eventually stops responding to analgesics. Other symptoms include malaise, vomiting, shortness of breath on exertion and disturbed sleep. Untreated, this may resolve or may progress to HAPE or HACE. HAPE is characterised

by tachycardia, tachypnoea, cyanosis associated with bibasilar crackles in the lungs. Alteration in sensorium with stupor or coma may herald the onset of HACE. Our patient presented with the typical symptoms of AMS at the onset; however, AMS is more common after rapid ascent to a high altitude and within 3–4 days of arriving at high altitude. Our patient developed symptoms after five days of arrival to high altitude, where ascent was spread over ten days. Clinically, there was no evidence of HAPE or HACE, and he had no sign of pre-existing heart disease to explain his persistent symptoms and low normal-to-low BP. The presence of haemorrhage in the pituitary gland on MR imaging provided the clue to the possibility of adrenal insufficiency due to pituitary apoplexy. Further hormonal evaluation confirmed the presence of isolated adrenal insufficiency. Moreover, the patient improved with steroid supplement. However, there was no deficiency in other hormones, which is unusual. Our initial impression was that other deficiencies were not obvious likely due to delayed metabolism of the thyroid and gonadal hormones; hence, we re-evaluated the patient at eight weeks after steroid therapy was stopped. The re-evaluation showed persistent isolated adrenal insufficiency with a decrease in the size of the pituitary gland due

to absorption haemorrhage.

Autopsies of fatal cases of HACE have shown punctate as well as large haemorrhages in the white matter and the corpus callosum, as well as subarachnoid haemorrhages and thrombosis in the venous sinuses.⁽³⁾ This is the first case report of haemorrhage involving the pituitary gland at high altitude. Haemorrhage into the pituitary gland causes it to enlarge and expand into the suprasellar or cavernous sinus, impinging on neighbouring cranial nerves in the cavernous sinus, optic pathways or diencephalon. This results in presenting signs and symptoms such as ophthalmoplegia, visual loss, headache, altered consciousness and impaired pituitary function.^(4,5) Our patient had only isolated adrenal insufficiency without any neurological deficits. Acute adrenal insufficiency seen in 50%–80% of cases with significant pituitary apoplexy is due to loss of ACTH.⁽⁶⁾ Our patient did not have alteration of sensorium or neurological manifestations associated with HACE like hemiparesis, cranial nerve palsies (especially VI and VII), abnormal plantar reflex and papilloedema. Although urgent transsphenoidal surgical decompression is recommended for patients who remain clinically and neurologically unstable,⁽⁴⁾ we did not have to do that as our patient responded to conservative management.

Pituitary apoplexy has been reported in rapidly growing pituitary adenoma following postpartum haemorrhage and haemorrhagic shock (including from snake bite). However, it has been reported in normal subjects with normal pituitary function. The exact cause of pituitary apoplexy still remains elusive. Various predisposing factors have been described in the literature,⁽⁷⁾ but

none was present in our case. Although there was no evidence of pituitary tumour on MR imaging in our case, a pre-existing small tumour could not be ruled out. Hypoxia and low atmospheric pressure may cause cerebral vasodilatation and increased cerebral blood flow, which could predispose to haemorrhagic strokes.⁽³⁾ There is also increased metabolic demand to maintain internal milieu in the face of extreme cold climate, which may have put additional stress on the pituitary gland.

In cases of delayed onset of AMS-like symptoms in a subject ascending to high altitude with unexplained hypotension, pituitary apoplexy should be considered. Thus, we conclude that ascent to extreme altitudes is an independent predisposing factor for pituitary apoplexy.

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