Commercial flight and patients with intracranial mass lesions: a caveat

Report of two cases


Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, London, United Kingdom; and Department of Anatomy, University of Malta, Msida, Malta

The authors report two cases of neurological deterioration following long commercial flights. Both individuals harbored intracranial space-occupying lesions. The authors assert that preexisting reduced intracranial compliance diminishes an individual’s reserve to accommodate the physiological changes resulting from a commercial flight. Airline passengers are exposed to a mild degree of hypercapnia as well as conditions that simulate those of high-altitude ascents. High-altitude cerebral edema following an ascent to great heights is one facet of acute mountain sickness and can be life threatening in conditions similar to those present on commercial flights. Comparable reports documenting neurological deterioration at high altitudes in patients with coexisting space-occupying lesions were also reviewed.

KEY WORDS • cerebral edema • intracranial pressure • air travel

COMMERCIAL airline passengers are exposed to rapid, although small, changes in cabin pressure. Similar barometric changes occur in nonacclimatized mountaineers during ascent to high altitudes and may result in AMS. Neurological symptoms associated with AMS develop once lower partial pressures of inspired O$_2$ result in cerebral hypoxemia. A more acute illness—HACE—develops when hypoxia-mediated cerebral edema is severe enough to lead to life-threatening neurological deterioration (Table 1).$^{10}$

Acute mountain sickness at altitudes greater than 3000 m is commonly reported. Nevertheless, death from HACE has occurred at altitudes as low as 2500 m.$^{12}$ Although passenger cabins on commercial aircraft are routinely pressurized to an altitude equivalent to 2440 m, hypoxia leading to neurological deterioration in response to air travel has not been previously reported. The lower levels of physical activity exhibited by airline passengers and the shorter duration of the imposed conditions during commercial flights may account for this discrepancy.

We present two cases of acute neurological deterioration following commercial air travel. An intracranial space-occupying lesion was known to exist in one of the patients, whereas a lesion was diagnosed only after the flight in the other.

Case Reports

Case 1

History. This 22-year-old man presented to a local emergency department with a 10-hour history of increasing headache, anorexia, polyuria, vomiting, hiccupps, and increasing drowsiness, which had begun during a transatlantic flight. Two years previously, he had sought medical advice because of headache. Cranial MR imaging had revealed an intraventricular mass lesion, and results of biopsy sampling had established a diagnosis of a xanthogranuloma of the choroid plexus. Symptomatic relief was obtained with the occasional administration of paracetamol; treatment was conservative. During the weeks before his flight he had been asymptomatic.

Examination. At presentation, results of a neurological examination showed a Glasgow Coma Scale score of 13 (eye opening 3, verbal response 4, and motor response 6), sluggish pupillary responses, chronic papilledema, lateral gaze nystagmus, generalized brisk reflexes, and truncal ataxia. Further deterioration in his level of consciousness necessitated intubation and artificial ventilation.

A CT scan revealed almost complete obliteration of the ventricular system by a nonenhancing tumor as well as effacement of the basal cisterns and sulci. An MR image confirmed the presence of a nonenhancing lesion distending the

Abbreviations used in this paper: AMS = acute mountain sickness; CT = computed tomography; HACE = high-altitude cerebral edema; ICP = intracranial pressure; MR = magnetic resonance; VEGF = vascular endothelial growth factor.
ventricles, which was associated with signs of significant chronically elevated ICP, that is, descent of the cerebellar tonsils below the foramen magnum and brain herniation through the biopsy bur hole (Fig. 1).

**Treatment and Posttreatment Course.** A 24-hour period of ventilation together with an elevated fraction of inspired \( \text{O}_2 \) and treatment with high-dose dexamethasone were followed by rapid and complete resolution of his symptoms. He was discharged to the care of a local neurosurgical unit.

**Case 2**

**History and Examination.** This 55-year-old woman presented with a reduced level of consciousness after a 14-hour flight. She had been completely asymptomatic before take-off but felt unwell during the flight, becoming progressively drowsy and then confused by the time the airplane landed. On admission to the local emergency department, she was confused and agitated. Her condition deteriorated rapidly and she suffered respiratory arrest. After intubation and ventilation, her pupils remained fixed and dilated. A CT scan revealed a large left-sided posterior fossa extraaxial hemorrhage, which was associated with signs of significant chronically elevated ICP, that is, descent of the cerebellar tonsils below the foramen magnum and brain herniation through the biopsy bur hole (Fig. 1).

**TABLE 1**

*Neurological signs and symptoms in AMS and HACE*

<table>
<thead>
<tr>
<th>AMS</th>
<th>HACE</th>
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<tbody>
<tr>
<td>headache; nausea &amp; vomiting; vertigo &amp; tinnitus; fatigue; irritability; mental slowness; insomnia; anorexia; &amp; retinal hemorrhage</td>
<td>severe headache &amp; vomiting; ataxia; cranial nerve palsies; impaired speech, sensory, &amp; motor functions; impaired memory; hallucinations; abnormal behavior; urinary incontinence; altered consciousness level; scotoma; blurred vision; papilledema; tremor; convulsions; &amp; death</td>
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* Modified from Hamilton, et al.

![Fig. 1](image1.png)  
**Fig. 1.** Case 1. **A:** Axial T₁-weighted MR image showing a ventricle distended by a nonenhancing tumor. **B:** Sagittal MR image demonstrating descent of the tonsils below the foramen magnum. **C:** Coronal T₁-weighted MR image revealing herniation of the cortex through the bur hole. **D:** Axial T₂-weighted MR image displaying streaks of increased signal in the splenium of the corpus callosum, representing early edema.
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lesion with surrounding edema, aqueduct obstruction, and acute hydrocephalus (Fig. 2).

**Treatment and Posttreatment Course.** Despite treatment with mannitol and the insertion of an external ventricular drain, the patient’s neurological condition did not improve, and death was confirmed by brainstem tests 24 hours later. In accordance with the family’s wishes, a postmortem examination was not performed.

**Discussion**

The potential risk of pressure changes during commercial air travel causing the expansion of trapped intracranial air in postoperative patients is known and well documented. However, we are not aware of any published report documenting progressive neurological deterioration precipitated by commercial flight in patients with intracranial mass lesions.

United States federal aviation regulations require occupied cabins to be pressurized to an altitude equivalent to no more than 2440 m. Furthermore, US regulations limit the pressure equivalent rate of ascent to not more than 5 m/second. This rate is comparable to rapid ascents to altitudes previously associated with AMS and HACE. Although the accompanying pressure changes are considerable, most persons tolerate these conditions with impunity. This circumstance may be a reflection of the relatively short duration of exposure as well as the lack of physical exertion in airline travel as compared with mountain climbing.

A model of the pathophysiology underlying AMS and HACE is emerging. At high altitudes, cerebral hypoxia triggers the upregulation of VEGF. In turn, the VEGF increases capillary permeability and contributes to cerebral edema. Note, however, that brain swelling attributable to ascent to high altitudes may occur without any associated symptoms. Preliminary study data indicate that the susceptibility for developing HACE is dictated by individual craniospinal anatomy: those with a smaller volume of cerebrospinal fluid are more likely to display symptoms.

Both of our patients presented with symptoms and signs of abnormally raised ICP that was precipitated by a long flight. These symptoms are also reminiscent of those associated with HACE. Although they were reversed with a return to sea altitude, artificial ventilation, O2 supplementation, and treatment with dexamethasone in one patient (Case 1), they proved fatal in the second patient (Case 2).

Data in the present cases support the hypothesis that a tight fit of the brain in the cranium reduces tolerance to mild brain edema. Both patients suffered from pathological entities that were likely to raise ICP and reduce intracranial compliance. We postulate that exposure to long commercial flights leads to mild cerebral hypoxia and edema not unlike those in AMS and HACE. Brain edema acts as a diffuse mass lesion and also decreases parenchymal compliance. Decompensation can further elevate preexisting raised ICP. Events that are normally well tolerated become significant when imposed on persons with preexisting pathological entities, given the lack of intracranial reserve.

Parallels can be made with data from three cases of previously unsuspected brain tumors that suddenly became symptomatic at high altitudes. Authors of another report describe the development of repeated, yet reversible, neurological signs in an individual with a subarachnoid cyst after ascent to an altitude of 4000 m.

A further mechanism may relate to increasing levels of inspired CO2 during commercial flights. Cabin air undergoes a degree of recycling as well as exchange with atmospheric air. This process leads to an increasing inspired fraction of CO2 levels in aircraft cabins during flight. The US federal aviation law specifies a CO2 level of less than 0.5% in the cabin air. Nevertheless, a mild degree of hypercapnia and hypercarbia would lead to the well-documented phenomenon of cerebral vasodilation. It is reasonable to suggest that this additive effect of mild hypercapnia would contribute to an elevated ICP in a decompensated individual.

Experience with MR imaging in acute HACE is limited. Intense T2 signal changes in white matter areas are described in severe cases, especially in the splenium of the corpus callosum, periventricular regions, and centrum semiovale. Patients with mild neurological dysfunction tend to exhibit only slight increases in T2 signal or normal imaging results. Abnormalities are thought to represent white matter vasogenic edema; available follow-up scans confirm complete resolution. These MR imaging changes are considered to be characteristic but not a prerequisite for the diagnosis of HACE. Magnetic resonance images were available in the patient in the first case. Although intense white matter changes were not present, a streak of mild increase in the T2 signal is visible within the splenium (Fig. 1).

Both AMS and HACE may be prevented by a more gradual rate of ascent and, early on, may be reversed by a return
to a low altitude. Treatments are aimed at reversing the underly- ing pathophysiological mechanisms. Cerebral hypoxia is treated with the administration of supplementary O2. A cetazolamide improves pulmonary gas exchange and thus cerebral oxygenation; reduced cerebrospinal fluid production also improves ICP.2,15 Dexamethasone downregulates VEGF expression and is used extensively to treat vasogenic brain edema.11,12 Predictably, data from randomized trials have shown that dexamethasone is useful in HACE prophylaxis and treatment.8,13,14,16,17

Although obviously rare, these two cases suggest that it is reasonable to caution patients with a known intracranial mass lesion about the possible risks of commercial flight. Prophylactic steroid agents, acetazolamide, and supplementary O2 may be considered for these patients during air travel. Air crews may wish to consider the use of supplemental O2 if passengers exhibit excessive drowsiness or abnormal behavior, including conduct resembling alcohol intoxication, a well-described presentation of AMS.

Conclusions

Patients with intracranial mass lesions may be at risk for neurological deterioration when exposed to cabin conditions commonly present on commercial flights. We propose that mild hypercapnia, possibly in concert with a mild form of HACE, may lead to clinically significant sequelae that could prove fatal when superimposed on preexisting conditions of raised ICP and decreased intracranial compliance. Patients known to harbor intracranial mass lesions should be counseled accordingly before they embark on commercial flights. Prophylactic steroid agents, acetazolamide, and supplementary O2 should also be considered.

References