High-altitude corneal oedema associated with acetazolamide

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To the Editor: A healthy 37-year-old woman with no eye disorders or prior eye surgery climbed from 1 980 m to 5 681 m on Kilimanjaro. She took acetazolamide, a carbonic anhydrase inhibitor, as prophylaxis against acute mountain sickness. She had no mountain sickness, but developed progressive painless blurred vision during her summit attempt on day 5. Her husband noted that her eyes looked opaque.

She descended to a local hospital. On ophthalmological examination 22 hours after beginning the descent her vision was improving, to 6/18 in the right eye and 6/24 in the left eye. There were superficial punctate lesions in the lower third of one cornea, consistent with minor abrasions from flying volcanic dust. Folds in Descemet's membrane suggested corneal oedema. The findings on fundal examination appeared normal, although visualisation was poor. Intra-ocular pressures were 13 mmHg in both eyes.

Twelve hours later, vision had improved to 6/9 and 6/12 and folding of Descemet's membrane had lessened. Visual impairment resolved over 2 days.

Follow-up examination several weeks later in Johannesburg was unremarkable. The anterior chamber was normal. Central corneal thickness was normal, 0.535 mm in the right eye and 0.543 mm in the left eye. A subsequent endothelial analysis showed a typical endothelial cell density, 2 537/mm^2 in the right eye and 2 555/mm^2 in the left eye. Central corneal thickness was unchanged from the previous examination.

The corneal endothelium is a thin-cell monolayer at the posterior surface of the cornea, facing the anterior chamber of the eye. It regulates corneal hydration by various active transport mechanisms, causing water flow from out of the stroma into the anterior chamber.[1] Endothelial oxygen supply is predominantly by transcorneal diffusion from the atmosphere. Impairment of endothelial oxygenation impairs fluid transport and promotes corneal oedema.

The decrease in the partial pressure of atmospheric oxygen during rapid high-altitude ascent is associated with mild, asymptomatic corneal swelling.[2,3] This oedema decreases as the endothelium adapts to the hypoxic environment. In the normal eye, the endothelium's adaptive reserve is probably sufficient to ensure that the severity and rate of hypoxic exposure typically experienced by climbers do not produce clinically significant problems. To our knowledge, there are no reports of high-altitude corneal oedema producing symptoms in previously healthy climbers.

Visual impairment due to high-altitude corneal oedema in association with other factors has occasionally been reported, however.[4,5] Symptomatic hyperopic shift may occur in persons who have had prior radial keratotomy, which alters the cornea's refractive state.[4] Another suggested mechanism is reduced endothelial function, such as occurs in Fuchs' corneal dystrophy. In a 77-year-old man who developed corneal oedema after a rapid ascent to 3 800 m, the limited adaptive reserve of the diseased endothelium to hypoxia was suggested to have caused the decompensation.[5]

In the current patient, with a normal endothelium and no prior surgery, acetazolamide may have contributed to the marked corneal oedema by impairing the endothelial adaption to hypoxia. Carbonic anhydrase pumps are important endothelial pumps regulating fluid movement.[1] Acetazolamide, a carbonic anhydrase inhibitor, produces corneal swelling by inhibiting these pumps. We suggest that oral acetazolamide may have produced sufficient endothelial inhibition, while simultaneously facilitating ascent by reducing symptoms of mountain sickness, to produce symptomatic oedema.

One other similar case has been reported.[6] A climber taking oral acetazolamide developed high-altitude pulmonary oedema, blurred vision and myopia without other neurological symptoms at 4 700 m. Both visual and pulmonary symptoms resolved with descent. The findings on subsequent eye examination were normal. We speculate that, as in our case, carbonic anhydrase inhibition of the endothelium may have been the mechanism of visual impairment.

Fast ascent can cause acute mountain sickness and high-altitude cerebral or pulmonary oedema, symptoms of which may mask coexistent corneal oedema. As most high mountains are in remote, sparsely populated ranges, visual abnormalities may resolve by the time climbers descend to a large hospital to obtain a formal examination. Kilimanjaro, a volcano, is a large freestanding mountain rising above a well-populated plain. The fortuitous combination of a nearby specialist hospital, a very rapid descent and the absence of other high-altitude symptoms allowed for this condition to be diagnosed. Symptomatic high-altitude corneal oedema may therefore be more common than is realised, but resolve before examination takes place, or the symptoms may erroneously be attributed to one of the high-altitude syndromes.

Myopia and endothelial dysfunction are rare adverse reactions to acetazolamide. Since oral acetazolamide is typically taken as prophylaxis before and during a rapid ascent, these side-effects could coincide with altitude gain. While the current report cannot demonstrate whether the association with ascent was causal or simply contemporaneous, acetazolamide-related complications may therefore occur during climbing.

Given the frequent use of acetazolamide to facilitate rapid climbs, the major increase in adventure tourism, and the life-threatening consequences of visual impairment on high mountains, this unusual complication should be recognised. If visual changes occur at altitude, the climber should stop taking acetazolamide and consider immediate descent.

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