CASE

High-altitude cerebral edema or acute demyelinating encephalomyelitis in the Himalayas

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A healthy, nonacclimatized 56-year-old woman developed mood changes and general weakness followed by vomiting, sensory disturbances, and ultimately unconsciousness within hours during an ascent from 1,600 to 2,800 meters in the Himalayas, Nepal. She reported no headache, ataxia, or visual disturbances during and following the hike, as confirmed by fellow travelers. As high-altitude cerebral edema (HACE) was suspected, she received 8 mg of dexamethasone and was transferred to a hospital specializing in acute mountain sickness (AMS) located at 1,300 meters. During the transfer, she had a generalized seizure. The next morning, her consciousness was still clouded. She exhibited subtle, brief, involuntary muscle twitching in both arms and neck. Because she responded properly to stimuli, this was interpreted as myoclonus. Laboratory testing revealed serum hyponatremia (117 mmol/L), hyposmolarity, and urine hyperosmolality. These disturbances were associated with decreased urine volume, high positive fluid balance, anadipsia, and weight gain. Her history revealed multiple prior vaccinations but no infections.

PRACTICAL IMPLICATIONS

A high level of specialization may produce a diagnostic bias that hinders a physician's consideration of other possible differential diagnoses.

MRI performed 36 hours after symptom onset showed no brain edema or venous thrombosis. However, there were innumerous variably sized confluent and discrete nonenhancing T2 high signal intensity foci in subcortical and deep white matter (figure, A). The subcortical U-fibers were also affected. These hyperintense fluid-attenuated inversion recovery (FLAIR) foci were less than 20 mm in size and slightly hypointense at the T1 sequence. Two lesions were periventricular and none of the lesions affected the mesial temporal lobe or corpus callosum. The optic nerves were unremarkable. No spine MRI was performed.

Neurologists from Nepal and Germany (none experts in AMS) were involved in this case by happenstance. Because the circumstances and symptoms were atypical and rare for HACE (relatively low altitude, lack of headache and ataxia, myoclonus) and because of the MRI findings, the diagnoses of AMS and HACE were discarded and acute demyelinating encephalomyelitis (ADEM) was suspected.[1–4] Ultimately the patient was transferred to a neurologic hospital. A CSF analysis showed normal cell count, protein, and glucose levels. CSF testing was negative for herpes simplex, Japanese encephalitis, acid-fast bacilli, *Cryptococcus neoformans*, Gram stain, and culture. Further detailed CSF testing (e.g., aquaporin 4 immunoglobulin G) was not possible in Nepal. There was no evidence of autoimmune encephalitis.

The patient made a full recovery after a restriction of fluids and 1 g of IV methylprednisolone. Because a second MRI showed new lesions 6 days later, the methylprednisolone therapy was

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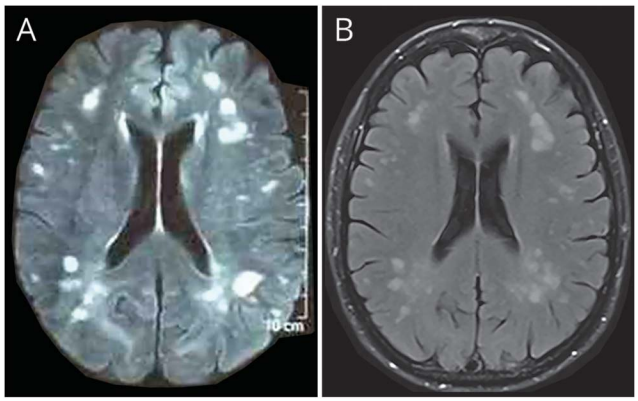
Figure Fluid-attenuated inversion recovery (FLAIR) MRI



(A) FLAIR MRI taken 36 hours after the onset of symptoms and before methylprednisolone therapy shows innumerous, asymmetric, patchy, and poorly marginated areas of increased signal intensity. (B) FLAIR MRI taken 2.5 months after the onset of symptoms shows residual lesions, but no new lesions.

extended for a total of 10 days. She had no neurologic deficits at the 5-month follow-up. A third MRI 2.5 months later showed residual lesions, but no new lesions (figure, B).

Discussion

The probability of a nonacclimatized young woman developing a severe case of AMS during a rapid ascent (<2 hours) to an altitude of 3,000 meters is less than 2%.[5] Furthermore, no symptoms of headache, ataxia, cerebral edema, or corpus callosum lesions on MRI are atypical for HACE[1,3,4,6] or exercise-induced hyponatremia.[7] Even though a headache has been proposed as the leading symptom required for a diagnosis of AMS or HACE according to the Lake Louise criteria,[3] there may be a few cases of HACE without headache.[4] Another hallmark of HACE is truncal ataxia.[4,6] This, however, was not observed in the patient. Perhaps due to specialized knowledge of AMS, these low-probability and atypical circumstances and symptoms were interpreted as compatible with a diagnosis of HACE. Since the circumstances and symptoms both have a low probability of supporting a diagnosis of HACE, their combined presence further reduces the epistemologic probability to an extremely low level. Furthermore, the presence of the lesions in the FLAIR MRI was regarded as a possible indication of other diagnostic considerations. This evokes the theory of the paradigm shift in science by T.S. Kuhn,[8] who postulated in 1962 that "Indeed those [phenomena] that will not fit in the box are often not seen at all." The final diagnosis of ADEM was made by recognizing the atypical symptoms as hints of an alternative diagnosis.

The electrolyte and fluid disturbances indicated a syndrome of inappropriate antidiuretic hormone secretion (SIADH). The innumerous cerebral lesions most probably provoked the SIADH; the linked hyponatremia might have caused the myoclonus,[9] clouded consciousness, and generalized seizure. ADEM and hyponatremia are often associated with one another.[10]

Author contributions

O. Hensel: idea and drafting of the manuscript. P. Niroul: acquisition of data and critical revision of manuscript for intellectual content. R. Paudel: acquisition of data and critical revision of manuscript for intellectual content. T. Sherpa: acquisition of data and critical revision of manuscript for intellectual content. T. Kraya: critical revision of manuscript for intellectual content. P. Presek: critical discussion of the case and revision of the manuscript. S. Zierz: critical revision of manuscript for intellectual content.

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Disclosure

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