



Acute High-Altitude Cerebral Edema Presenting as Extensive Microbleeds along the Corpus Callosum without T2 Hyperintensity: A Case Report and Literature Review

T2 고신호강도가 동반되지 않은 뇌량의 광범위한 미세출혈의 형태로 나타난 고산병: 증례 보고 및 문헌 고찰

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High-altitude cerebral edema (HACE) is a potentially fatal neurological syndrome that develops in persons traveling to a high altitude. We report the case of a 49-year-old male who had traveled to a high altitude, and lost consciousness for a few hours. Susceptibility-weighted images revealed multiple, fine black pepper like microbleeds along the corpus callosum with several microbleeds in the left frontal and parietal subcortical white matter. The T2-weighted images did not show any abnormal signal intensities along the corpus callosum. The diffusion-weighted images revealed small nodular high signal intensities in the basal ganglia. This report describes the atypical radiologic findings of HACE showing multiple microbleeds along the corpus callosum, without abnormal high-signal intensity on T2-weighted images.

Index terms Altitude Sickness; Brain Edema; Cerebral Hemorrhage; Magnetic Resonance Imaging

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INTRODUCTION

High-altitude cerebral edema (HACE) is a potentially fatal neurologic syndrome that develops over hours or days in persons with acute mountain sickness or high-altitude pulmonary edema. The characteristic finding of HACE is increased signal intensity (SI) on T2-weighted images with diffusion restriction in the splenium of the corpus callosum, showing full recovery on follow-up (1). These findings reflect the pathophysiology of vasogenic and cytotoxic edema (2, 3). Recent studies have found that microbleeds in corpus callosum are another typical finding in patients with a history of HACE (4). We report a case of HACE showing fine black pepper like multiple microbleeds along corpus callosum without definite T2 hyperintensity.

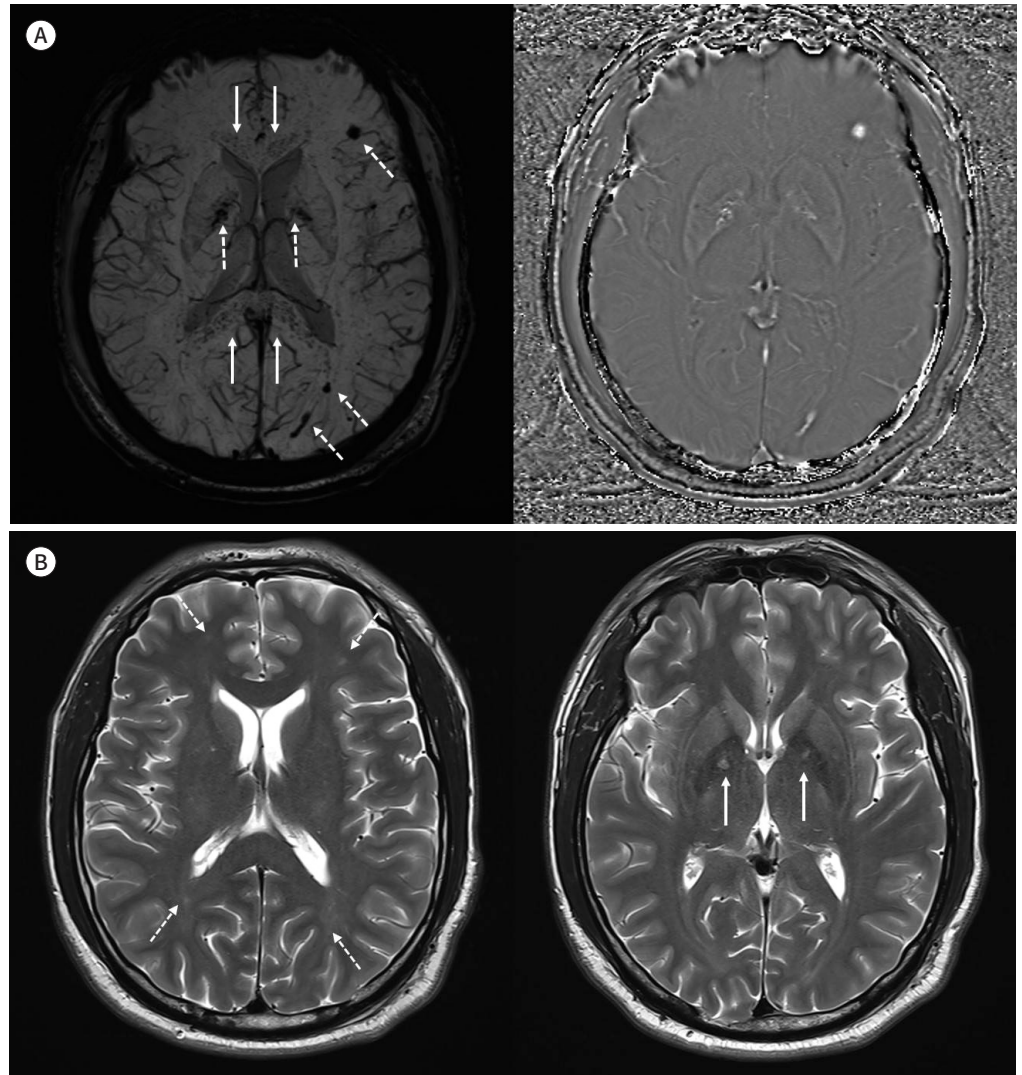
CASE REPORT

CLINICAL FINDINGS

A 49-year-old male experienced headache and sudden loss of consciousness while traveling to a high-altitude area in Nepal, 3400 m above sea level or higher. The patient had suffered from hypertension and coronary artery disease. He is taking aspirin. At the time of syncope, he fell down and became unconscious for 3 hours. After treatment for scalp laceration at local hospital, he returned to Korea immediately. When the patient was transferred to our clinic on 5 days after the onset of symptom, his conscious level was alert and Glasgow Coma Scale score was 15. He complained of subjective weakness in both legs and difficulty with gait and balancing. Neurological examination showed no focal deficit. He had no respiratory symptoms including dyspnea. On chest X-ray, no abnormalities were seen. Then 3 tesla MRI of brain was obtained. Susceptibility-weighted images (SWIs) demonstrated fine black pepper-like multiple microbleeds along both corpus callosum. Several microbleeds at left frontal and parietal subcortical white matter were also noted (Fig. 1A). There was no definite increase of signal along the corpus callosum on T2-weighted images. A few small nodular lesions with high SI on T2-weighted images were observed at bilateral frontoparietal white matter, which supposed underlying chronic small vessel disease. Diffusion-weighted images (DWIs) and apparent diffusion coefficient maps showed focal cytotoxic edema at both basal ganglia with focal high SI on T2-weighted images (Fig. 1B, C).

The patient was discharged from the hospital after five days of conservative treatment. After three months, he revisited the hospital due to aggravating gait disturbance. Neurological examination showed positive truncal ataxia, dysdiadochokinesia, and Romberg sign. Follow-up brain MRI showed persistent fine black pepper microbleeds along both corpus callosum without change of focal microbleeds at left frontal or left parietal subcortical white matter. Previously noted T2 high SI lesions in both basal ganglia decreased in size (Fig. 1D). A few small nodular T2 high SI lesions in bilateral frontoparietal white matter showed little interval change, suggestive of chronic small vessel disease. Other abnormal findings were not demonstrated.

Fig. 1. MRI of a 49-year-old male who had traveled to a high-altitude and lost consciousness for a few hours. **A.** Susceptibility-weighted images and filtered phase axial images reveal multiple microbleeds along the corpus callosum as fine black pepper like patterns (arrows) with multifocal hemorrhages at the bilateral basal ganglia, left frontal, and left parietal subcortical region (dashed arrows). **B.** T2-weighted axial images reveal small nodular high-signal intensity lesions in bilateral basal ganglia (arrows). In addition, there are no abnormal signal changes along the corpus callosum. A few nodular hyperintense lesions are visible on the bilateral frontoparietal white matter (dashed arrows).



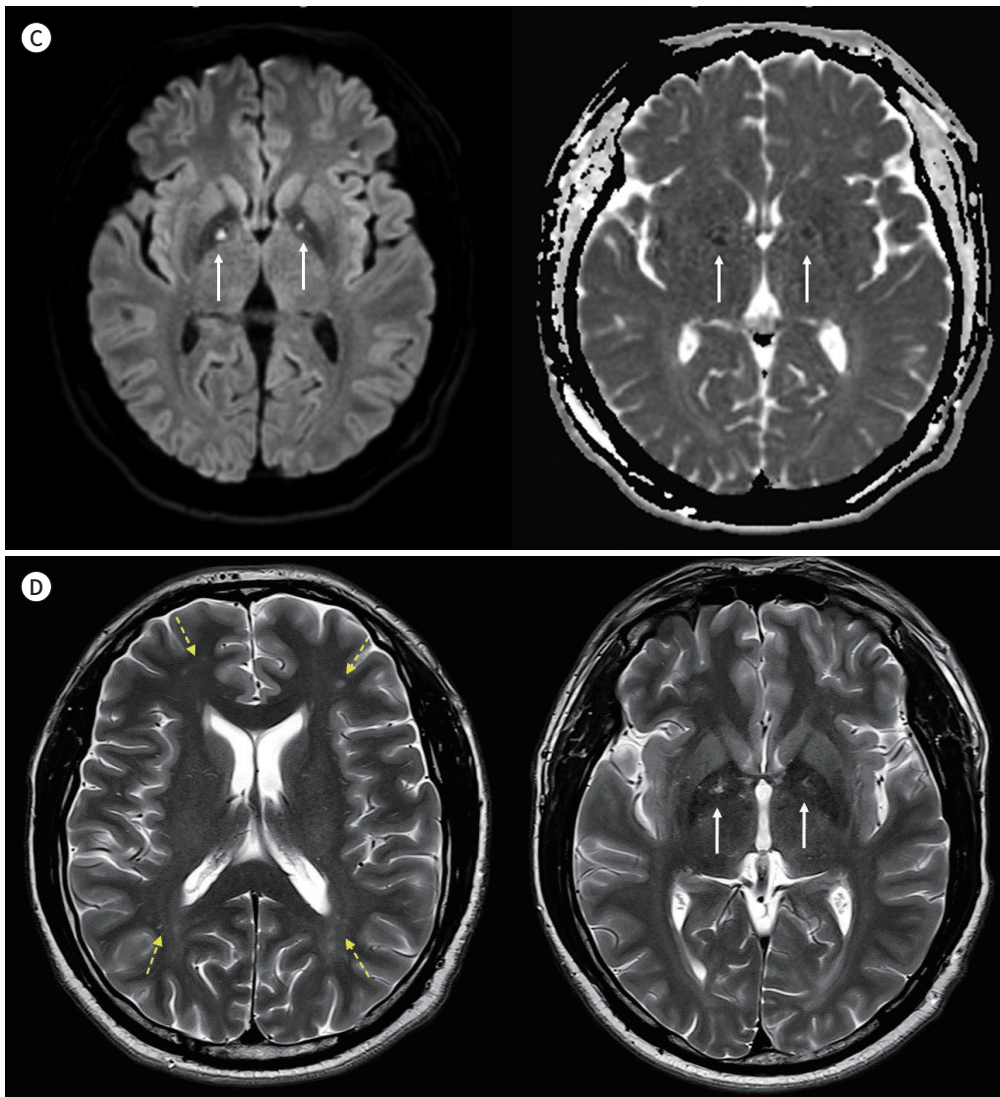
DISCUSSION

A typical MRI finding of HACE is transiently increased SI on fluid attenuated inversion recovery (FLAIR) and T2-weighted images with diffusion restriction in the corpus callosum, particularly the splenium. Other than that, microbleeds in the corpus callosum in patients with severe HACE have been recently noticed and reported (4, 5).

In this case, focal cytotoxic edema was revealed at bilateral globus pallidus on DWI with correlated T2 signal change and microbleeds. These findings were consistent with HACE (6). Another notable finding was the obvious fine black pepper-like microbleeds along both cor-

pus callosum without corresponding hyperintensity on FLAIR and T2 weighted images. It was a unusual finding. In most cases of HACE, typical microbleeds of corpus callosum and white matter were found with T2/FLAIR hyperintensity. Because the MRI was taken five days after the symptom developed, there was a possibility that the initial T2 signal change had reversed and normalized before the MRI was taken. However, this possibility is quite unlikely, considering that vasogenic edema is a process known to take several days for maximal accumulation of edema-triggering moieties (7). According to Hackett et al. (5), in the study analyzing temporal radiologic changes of HACE, all patients with repeat MRI within 10 days showed greater edema, rather than normalized.

Fig. 1. MRI of a 49-year-old male who had traveled to a high-altitude and lost consciousness for a few hours.
C. Diffusion-weighted images and apparent diffusion coefficient maps show focal cytotoxic edema in the basal ganglia (arrows).
D. Previously noted hyperintense T2 lesions in the basal ganglia decrease in size (arrows). A few nodular hyperintensities on the bilateral frontoparietal white matter show little interval change (dashed arrows), suggestive of an underlying chronic small vessel disease.



Imaging findings of T2/FLAIR hyperintensity and diffusion restriction were due to vasogenic edema and cytotoxic edema. On the other hand, microbleeds shown on SWI were attributed to endothelial dysfunction or changes in capillary permeability associated with aggravation of vasogenic edema. Recent studies have proposed that both mechanical factors (such as impaired autoregulation and excessive capillary hypertension) and permeability factors (such as vascular endothelial growth factor, reactive oxygen species, and other hypoxia induced factors) are related to the loss of white matter microvascular integrity (7). Therefore, in pathophysiologic point of view, it was rather interesting that prominent microbleeds without definite T2 hyperintensity were shown in our case.

It is convincing that even without vasogenic edema enough to be shown on T2/FLAIR image, permeability factors such as vascular endothelial growth factor work in a dominant fashion and consequently can induce microbleeds. Hackett et al. (5) have demonstrated that microbleeds do not appear to correlate with the degree of edema or restricted diffusion on the initial scan or with clinical severity. In this retrospective study, they found that extensive white matter microbleeds were already present on the initial MRI. The number and extent of microbleeds remained the same as time went by while white matter edema aggravated and improved (5).

In addition, aspirin that the patient is taking might have affected atypical radiologic findings of this case. Many studies have shown that the prevalence of microbleeds is higher in those with antiplatelet use and higher in those on aspirin than on other agents (8).

In conclusion, HACE is characterized with MRI of extensive fine black pepper microbleeds that can leave persistent imprint. HACE pathophysiology appears to involve reversible vasogenic and cytotoxic edema that progresses to microvascular disruption and microbleeds. As seen on our case, these microbleeds appeared without definite T2/FLAIR hyperintensity or pulmonary edema. Therefore, detection of typical microbleeds through SWI images may be critical for the diagnosis and management of HACE.

Author Contributions

Conceptualization, all authors; data curation, K.J.Y.; investigation, S.J.Y., K.J.Y.; project administration, K.J.Y.; resources, all authors; supervision, K.J.Y.; writing—original draft, S.J.Y.; and writing—review & editing, S.J.Y., K.J.Y.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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T2 고신호강도가 동반되지 않은 뇌량의 광범위한 미세출혈의 형태로 나타난 고산병: 증례 보고 및 문헌 고찰

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고소 뇌부종은 높은 지대를 여행하는 사람들에게서 발생하는, 잠재적 치명성을 갖는 신경학적 증후군이다. 본 증례는 높은 지대를 여행한 후 수 시간의 의식불명이 있었던 49세 남자에서 나타난 고소 뇌부종의 비전형적 영상 소견에 대한 보고이다. 환자의 자기공명영상 자기화율강조영상에서 미세한 점상의 다수의 미세출혈이 양쪽 뇌량을 따라 분포하고 있었고 몇 개의 미세출혈이 전두엽과 두정엽의 피질하 백질에서 관찰되었으나 T2 강조영상에서는 이에 상응하는 부위에 신호강도의 증가가 관찰되지 않았다. 확산강조영상에서는 양쪽 기저핵에서 작은 결절형의 고신호강도가 관찰되었다. 본 증례는 T2 강조영상에서 비정상적인 신호강도 없이 양쪽 뇌량에서 다수의 미세출혈을 보였던, 비전형적인 사례로서의 고소 뇌부종의 증례에 대해 문헌 고찰과 함께 보고하고자 한다.

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