Case Report
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Fulminant Disseminating Fatal Granulomatous Amebic Encephalitis: The First Case Report in an Immunocompetent Patient in South Korea

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Central nervous system infections caused by free-living amoeba are very rare, but often fatal. The typical image findings of amebic meningoencephalitis are non-specific, showing ring-like enhancement. We report the first case of fulminant disseminating fatal granulomatous amebic encephalitis caused by *Balamuthia mandrillaris* in an immunocompetent patient in South Korea. Our case exhibited two interesting features: one was the unusual clinical course and the other was additional image findings. Magnetic resonance imaging revealed a rim-enhancing lesion with intralesional blooming dark signal intensity on susceptibility weighted imaging and low signal intensity on diffusion weighted images and on apparent diffusion coefficient maps. Differential diagnosis was started from a tumor or non-tumorous lesion, and diagnosis was difficult due to the rarity of the disease. Following the clinical and diagnostic courses of our case, we recommend inspecting image findings of granulomatous amebic encephalitis for early diagnosis.

Key Words: Encephalitis, amoeba, *Balamuthia mandrillaris*

INTRODUCTION

Central nervous system infections caused by free-living amoeba are rare, but often fatal. Among free-living amoeba, *Acanthamoeba spp.* and *Balamuthia mandrillaris* are "opportunistic" pathogens causing fatal granulomatous amoebic encephalitis (GAE).[1] However, the imaging features of amebic meningoencephalitis are non-specific and have usually been described as focal or multifocal ring enhancing lesions in many previous case reports.[1-6]

Our report presents a short-term disseminating fatal case of amebic encephalitis in an immunocompetent 50-year-old man.

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CASE REPORT

A 50-year-old man presented with a headache for 3 days and abruptly started dizziness, dysarthria, and aphasia while he cleared away snow in the morning. Initial brain computed tomography (CT) revealed a hypoattenuated lesion with no demonstrable enhancement in the left parietal cortex and white matter area (Fig. 1A). T2-weighted axial magnetic resonance (MR) images exhibited a localized irregular marginated, low signal intensity lesion with surrounding edema at the left parietal cortex and white matter area (Fig. 1B). Dark signal intensity was seen in the lesion in susceptibility weighted imaging (SWI) (Fig. 1C). On gadolinium enhanced T1-weighted images, marginal, thin- rim enhancement of the lesion was observed (Fig. 1F). Diffusion weighted images (DWI) and apparent diffusion coefficient (ADC) maps also showed low signal intensity in the lesion surrounding edema, indicating a lack of diffusion restriction (Fig. 1D and E). However, because of this, the low DWI signal intensity was considered as a hemorrhage-related paramagnetic artifact. Perfusion MR showed relative ce-

rebral blood volume was not increased at the left parietal hemorrhagic lesion (Fig. 1H). MR spectroscopy also showed increased lactate peak (1.35 ppm), decreased N-acetyl aspartate peak (2.0 ppm), and no increased choline peak (3.2 ppm) (Fig. 1G). The first differential diagnosis was between hemorrhagic brain tumor and hemorrhagic non-tumorous lesion.

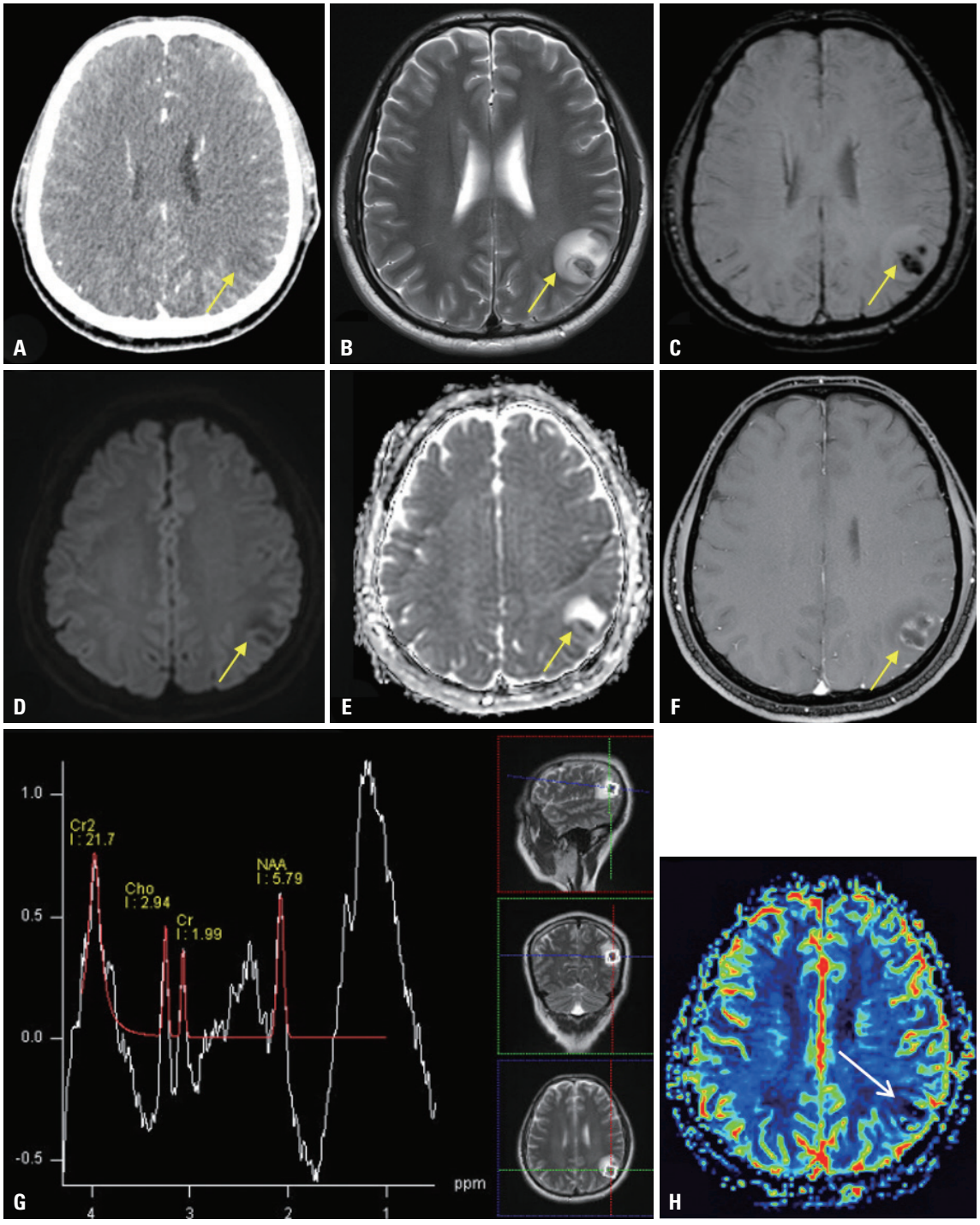

Fig. 1. Initial CT and MR. (A) Post-contrast CT image shows an ill-defined, hypoattenuated lesion (arrow) in the left parietal cortex and white matter area. (B) T2-weighted axial MR image shows a localized, irregular, marginated, low signal intensity lesion (arrow) with surrounding edema at the left parietal cortex and white matter area. (C) Susceptibility weighted imaging shows intralesional dark signal intensity (arrow). (D and E) Diffusion weighted image (D) and apparent diffusion coefficient map (E) show low signal intensity in the lesion (arrow) surrounding edema. (F) Gadolinium enhanced T1-weighted image shows marginal, thin rim enhancement of the lesion (arrow). (G) MR spectroscopy shows increased lactate peak (1.35 ppm), decreased N-acetyl aspartate peak (2.0 ppm) and no increased choline peak (3.2 ppm). (H) Perfusion MR shows relative cerebral blood volume was not increased at the left parietal hemorrhagic lesion (arrow). CT, computed tomography; MR, magnetic resonance.

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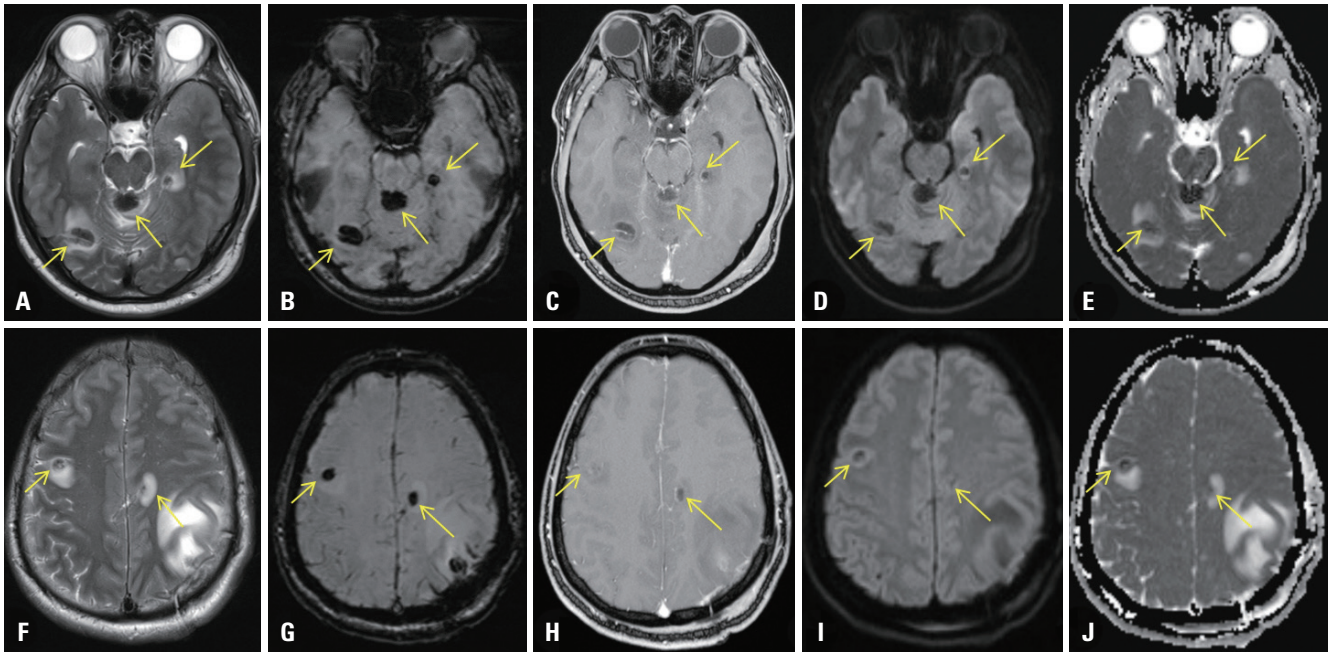

Fig. 2. Follow-up MR. A week after biopsy, follow-up MR shows newly developed multifocal lesions. (A and F) T2-weighted axial MR images show multifocal dark signal intensity lesions (arrows) with surrounding edema at the superior cerebellar vermis, left inferior basal ganglia, right occipital white matter (A), and both frontal cortex and white matter areas (F). (B and G) Susceptibility weighted imaging shows intralesional dark signal intensity of the lesions (arrows) at the superior cerebellar vermis, left inferior basal ganglia, right occipital white matter (B), and both the frontal cortex and white matter area (G). (C and H) Gadolinium-enhanced T1-weighted images show marginal, thin rim enhancement of the lesion (arrows). (D, E, I, and J) Diffusion weighted image (D and I) and apparent diffusion coefficient maps (E and J) show central low signal intensity with surrounding edema of the lesions (arrows). MR, magnetic resonance.

The patient underwent excision biopsy of the lesion, and hemorrhage in the surgical field was rare. A week after biopsy, follow-up MR images showed newly developed multifocal disseminated peripheral high T2 signal intensity, central dark signal intensity on SWI, and thin-rim-enhancing lesions at supratentorial and infratentorial areas with surrounding edema. Moreover, all of these new multiple nodules showed low signal intensity on DWI and ADC maps (Fig. 2).

The patient was negative for human immunodeficiency virus test and had no history of immunodeficient condition or disease. In serologic parasite-specific antibody tests, amoeba antibody was positive; other parasite-specific antibodies, including toxoplasmosis, were negative. In order to identify the primary source of the lesion, abdomen CT and chest CT were performed, although there was no evidence of infection, inflammation, or neoplasm.

A histopathologic examination of the surgical specimen revealed necrotizing vasculitis with infiltration of inflammatory cells surrounding vessels and amebic trophozoites infiltrating capillary walls (Fig. 3A). Another section of the specimen revealed necrotic material and periodic acid-Schiff-positive trophozoites (Fig. 3B). On real-time polymerase chain reaction, the trophozoites were confirmed as *Balamuthia mandrillaris*.

The patient was treated with antiamebiasis medications and dexamethasone. However, decompressive craniectomy was performed due to progressive brain swelling after biopsy. The patient suffered from septic condition and died 20 days later due to cardiac arrest. Informed consent was obtained from a legal surrogate of the patient regarding the publication of this case report.

DISCUSSION

Primary amebic meningoencephalitis (PAM) and GAE are two clinical central nervous system infections caused by free-living amoebae. Four genera of free-living amoebae have an association with human disease: *Acanthamoeba spp.*, *B. mandrillaris*, *Naegleria fowleri*, and *Sappinia diploidea*.[3,6] *Acanthamoeba spp.* and *B. mandrillaris* are "opportunistic" pathogens causing GAE in debilitated or immunocompromised patients. GAE has a chronic, prolonged, focal neurological symptom, unlike the rapid, fulminant clinical course of PAM which is caused by *N. fowleri*.[3,7] *B. mandrillaris* is present worldwide in soil and causes skin and central nervous system infections. About 200 cases of *B. mandrillaris* infections have been reported, mostly from South America.[4,8] In 2019, Kum, et al.[9] reported the first case of *B. mandrillaris* amoebic encephalitis with fatal progression in Korea: the patient had undergone continuous treatment with immunosuppressants due to rheumatic arthritis.

Numerous case reports describe GAE as single or multifocal lesions showing T2 hyperintensity and heterogeneous or ring-

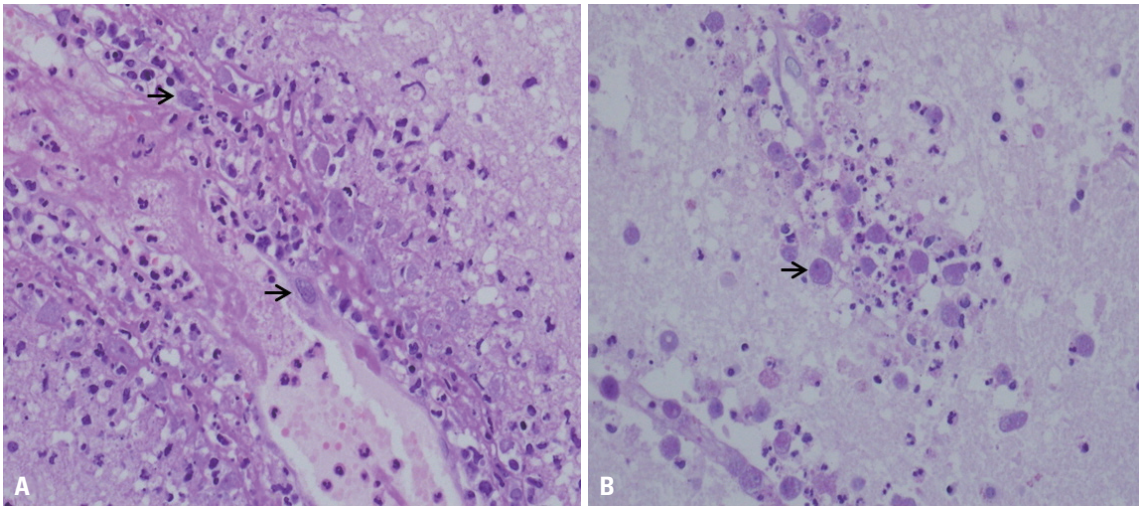

Fig. 3. Histopathologic examination of the surgical specimen. (A) Hematoxylin and eosin stain (HE) ×400, Amebic trophozoites (arrow) infiltrating vessel walls with diffuse infiltration of inflammatory cells around vessels, which are findings of vasculitis caused by trophozoites. (B) PAS ×400. Trophozoites (arrow) present PAS-positive staining. PAS, periodic acid-schiff.

like enhancement.[1-6] In our case, however, there were two additional features. First, unlike GAE, which has a chronic prolonged clinical course, our patient show rapidly disseminating central nervous system lesions with fulminant clinical progression, similar to that in PAM. Second, we observed intralesional blooming, dark SWI signal intensity, in addition to low signal intensity in DWI and ADC maps, in every single lesions.

Intralesional hemorrhage of GAE can be explained by necrotizing angitis that may damage the walls of small capillaries, arterioles, and venules by parasitism or immune-mediated vasculitis. Accordingly, this has been considered an important diagnostic feature by some authors.[3] The lesions of GAE are thought to represent focal areas of cerebritis or microabscess. Therefore, the differential diagnosis includes septic embolic infarct, abscess, toxoplasmosis granuloma, or neoplasm.[3]

A rim-enhancing brain mass can be caused by several reasons, including neoplasm and abscess. Markedly restricted diffusion is characteristic of a purulent abscess core, in contrast to increased diffusion in the center of a brain neoplasm. Cerebral toxoplasmosis may also show rim-enhancing masses, similar in appearance to a pyogenic abscess, although diffusion may not be restricted in the center of a *Toxoplasma abscess*.[10]

In our case, although necrotizing vasculitis resulted in dark SWI signal intensity, the short-term, sporadic disseminating pattern of the lesion and low DWI signal intensity helped to lower possibilities of neoplasm, but differential diagnosis was still difficult. Also, because hemorrhagic inflammation elicited edema, in addition to a paramagnetic artifact, the lesion with rim enhancement and low signal intensity on DWI was not supportive of a typical abscess.

In conclusion, we report the first case of fulminant disseminating GAE caused by *B. mandrillaris* in an immunocompetent patient in South Korea. Amebic encephalitis caused by *B. mandrillaris* presents dark SWI signal intensity with peripheral rim enhancement on MRI and may rapidly disseminate. Non-tumorous hemorrhagic lesions should be included in differential diagnosis, such as infectious necrotizing vasculitis, septic embolic infarct, abscess, and toxoplasmosis granuloma. However, a hemorrhagic tumor cannot be excluded easily. Diagnosis is made difficult by the rarity of the disease, so we report this case with unusual clinical course and image findings to raise awareness of this infectious disease.

AUTHOR CONTRIBUTIONS

Conceptualization: all authors. Data curation: Ju Yeon Lee, In Kyu Yu, Seong Min Kim, and Joo Heon Kim. Formal analysis: Ju Yeon Lee and In Kyu Yu. Investigation: Ju Yeon Lee and Ha Youn Kim. Methodology: Ju Yeon Lee and In Kyu Yu. Project administration: In Kyu Yu and Seong Min Kim. Resources: Ju Yeon Lee and Ha Youn Kim. Software: Ju Yeon Lee and Ha Youn Kim. Supervision: In Kyu Yu and Seong Min Kim. Validation: Ju Yeon Lee and Ha Youn Kim. Visualization: Ju Yeon Lee and In Kyu Yu. Writing—original draft: Ju Yeon Lee. Writing—review & editing: In Kyu Yu. Approval of final manuscript: all authors.

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