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

Ju Yeon Lee¹, In Kyu Yu¹, Seong Min Kim², Joo Heon Kim³, and Ha Youn Kim¹

Departments of ¹Radiology, ²Neurosurgery, and ³Pathology, Eulji University Hospital, Eulji University College of Medicine, Daejeon, Korea.

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 amebic 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.¹⁶

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

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.]
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*. 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*. 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. In 2019, Kum, et al. 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-
like enhancement. In our case, however, there were two additional features. First, unlike GAE, which has a chronic prolonged clinical course, our patient showed 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 lesion.

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. 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.

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.

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-neoplastic 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.

ORCID iDs

Ju Yeon Lee https://orcid.org/0000-0002-8054-124X
In Kyu Yu https://orcid.org/0000-0003-1587-2840
Seong Min Kim https://orcid.org/0000-0001-7161-0226
Joo Heon Kim https://orcid.org/0000-0001-7592-0985
Ha Youn Kim https://orcid.org/0000-0002-7139-8410

REFERENCES

1. Jung S, Schelper RL, Visvesvara GS, Chang HT. Balamuthia mandrillaris meningoencephalitis in an immunocompetent patient: an unusual clinical course and a favorable outcome. Arch Pathol Lab Med 2004;128:466-8.
2. Shih RV, Koeller KK. Bacterial, fungal, and parasitic infections of the central nervous system: radiologic-pathologic correlation and
historical perspectives: from the radiologic pathology archives. Radiographics 2015;35:1141-69.
3. Singh P, Kochhar R, Vashishta RK, Khandelwal N, Prabhakar S, Mohindra S, et al. Amebic meningoencephalitis: spectrum of imaging findings. AJNR Am J Neuroradiol 2006;27:1217-21.
4. Martínez DY, Seas C, Bravo F, Legua P, Ramos C, Cabello AM, et al. Successful treatment of Balamuthia mandrillaris amoebic infection with extensive neurological and cutaneous involvement. Clin Infect Dis 2010;51:e7-11.
5. Cary LC, Maul E, Potter C, Wong P, Nelson PT, Given C 2nd, et al. Balamuthia mandrillaris meningoencephalitis: survival of a pediatric patient. Pediatrics 2010;125:e699-703.
6. Visvesvara GS, Moura H, Schuster FL. Pathogenic and opportunistic free-living amoebae: Acanthamoeba spp., Balamuthia mandrillaris, Naegleria fowleri, and Sappinia diploidea. FEMS Immunol Med Microbiol 2007;50:1-26.
7. Jamieson A, Anderson K. Letter: primary amoebic meningoencephalitis. Lancet 1974;1:261.
8. van der Beek NA, van Tienen C, de Haan JE, Roelfsema J, Wismans PJ, van Genderen PJ, et al. Fatal Balamuthia mandrillaris meningoencephalitis in the Netherlands after travel to the Gambia. Emerg Infect Dis 2015;21:896-8.
9. Kum SJ, Lee HW, Jung HR, Choe M, Kim SP. Amoebic encephalitis caused by Balamuthia mandrillaris. J Pathol Transl Med 2019;53:327-31.
10. Chong-Han CH, Cortez SC, Tung GA. Diffusion-weighted MRI of cerebral Toxoplasma abscess. AJR Am J Roentgenol 2003;181:1711-4.