An Acute Case of Granulomatous Amoebic Encephalitis—Balamuthia Mandrillaris Infection

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Abstract:
A 74-year-old woman who exhibited drowsiness was referred to our hospital. Enhanced head magnetic resonance imaging (MRI) revealed multiple ring-enhancing lesions and lesions showing partial mild hemorrhaging. The patient gradually progressed to a comatose condition with notable brain deterioration of unknown cause on follow-up MRI. On day nine, the patient inexplicably died, although brain herniation was suspected. Autopsy and histopathology revealed numerous amoebic trophozoites in the perivascular spaces and within the necrotic tissue. Brain immunostaining tested positive for Balamuthia mandrillaris. Infection due to free-living amoeba is rare in Japan; however, it may increase in the near future due to unknown reasons.

Key words: Granulomatous amoebic encephalitis, Balamuthia mandrillaris, CNS infection

Introduction
Similar to Naegleria fowleri and Acanthamoeba, Balamuthia mandrillaris is a free-living amoeba that causes fatal central nervous system (CNS) infections, with mortality rates of over 98% (1). More than 200 cases of B. mandrillaris infection have been reported worldwide since 1990. The highest prevalence of cases has been observed in temperate regions in the southern areas of North America and Latin America (2, 3). Nine cases of CNS infection due to B. mandrillaris have been reported in Japan (4, 5). Although only 3 cases were reported in the 23 years between 1986 and 2009 (the first case in 1986 was retrospectively diagnosed as a case of B. mandrillaris infection), infections have been reported almost every year since 2010.

We herein report a case of amoebic encephalitis caused by B. mandrillaris.

Case Report
In December 2015, a 74-year-old woman with a history of untreated diabetes mellitus (DM) and chronic hepatitis C virus infection (HCV) was referred to our hospital. Upon admission, the patient exhibited drowsiness that had persisted from the previous day. The patient had no dermatological disorders upon inspection. The test results on admission revealed mildly disturbed consciousness (Glasgow coma scale score of 13, E3V4M6); body temperature, 38.1°C; blood pressure, 108/67 mmHg; heart rate, 95 beats/min; white cell count, 10,060 cells/mm³ (neutrophil, 85%; eosinophil, 0%; basophil, 0%; monocyte, 4%; lymphocyte, 8%); hemoglobin, 13.0 g/dL; platelets, 21.7×10⁴ cells/mm³; erythrocyte sedimentation rate, 30 mm/h (1 hour); ferritin, 380 ng/mL; aspartate aminotransferase, 36 U/L; alanine transaminase, 69 U/L; blood urea nitrogen, 28.9 mg/dL; creatinine, 0.39 mg/dL; lactate dehydrogenase, 363 U/L; glucose, 254 mg/dL; glycated hemoglobin (national glycohemoglobin standardization program), 12.1%; and soluble interleukin-2 receptor, 553 U/mL. The patient tested negative for the presence of C-reactive protein, procalcitonin, antinuclear antibody, anti-treponemal antibody, Toxoplasma IgM/IgG antibody, Cysticercus cellulose-IgG antibody, human immunodeficiency virus, hepatitis B virus, and a wide...
revealed moderate pleocytosis (cell count, 130/mm³). The results were also normal. A cerebrospinal fluid (CSF) analysis revealed the range of tumor markers. Her interferon γ release assay results were also normal. A cerebrospinal fluid (CSF) analysis revealed moderate pleocytosis (cell count, 130/mm³); protein, 393 mg/dL; and glucose, 107 mg/dL; CSF tested negative for the presence of bacteria, Cryptococcus antigen, Aspergillus antigen, and β-D-glucan. The color of the CSF indicated xanthochromia. Enhanced head magnetic resonance imaging (MRI) revealed multiple necrotic lesions with hemorrhaging (Fig. 1A, 1B, 1C, 1D). Whole-body computed tomography (CT) and gallium-67 scintigraphy indicated the absence of abnormal lesions.

The patient's condition gradually progressed to a comatose state with notable brain deterioration on follow-up MRI performed six days after admission (Fig. 1E, 1F, 1G, 1H). On day 9 of admission, the patient died due to unexplained causes, although brain herniation was suspected. An autopsy performed six days after admission (Fig. 1E, 1F, 1G, 1H) Follow-up images on day 6 of admission showed deterioration. Locally, brain structures, especially around the lateral ventricle tissue, were destroyed, and there was a decrease rather than an increase in the gadolinium-enhanced oval lesions.

Discussion

The increasing number of observed cases of free-living amoebic infection may be due to the increasing availability of medical care, improvements in testing techniques, or other reasons. Immunocompromised hosts, including those with DM, are more susceptible than immunocompetent hosts to B. mandrillaris (1); indeed, our patient had untreated DM, HCV infection, and cirrhosis. In addition, the patient performed fieldwork and gardening throughout the year, which might have increased her risk of exposure. Typically, patients have ulcerated purple nodules at the site of skin lesions following percutaneous infection (6). Our patient, however, had no skin lesions.

Regarding the diagnosis of our patient, previous reports have described lymphocytic-predominant pleocytosis, ele-
deed, our patient progressed from presenting with develop-
ment included malignant lymphoma, metastatic brain tumor,
primary brain tumor-like diffuse glioma, toxoplasmosis, neu-
rocyticercosis, tuberculosis, brain abscess, and acute dis-
seminated encephalomyelitis. Few of these diseases aside
from bacterial infection present with day-by-day deteriora-
tion.

Generally, granulomatous amoebic encephalitis is reported
to have a prolonged or chronic course (1). However, some
patients have been reported to have an acute course (2).
Indeed, our patient progressed from presenting with develop-
ning symptoms to death in only nine days. Pathologically, our
patient demonstrated microhemorrhaging, diffuse invasion of
inflammatory cells, trophozoite accumulation in the perivas-
cular spaces that was more prominent than that in inflamma-
tory giant cells, fibrinoid necrosis, epithelioid cells, and vas-
cular cuffing. Such a case with a less granulomatous appear-
ance than most might reflect an acutely or sub-acutely pro-
ceeding amoebic CNS infection (7). Acutely proceeding
cases might be associated in some way with immunodefici-
cy; however, this link is still unclear.

Regrettably, our patient died before a diagnosis was con-
ferred; thus, antimicrobial therapy could not be initiated.
Regarding the treatment, past reports have suggested anti-
microbial therapy with flucytosine, pentamidine, flucnazole,
sulfadiazine, and a macrolide antibiotic; recently, miltefosine
has been suggested as a potential treatment for patients with
Balamuthia infection (8, 9). However, there is currently no
established treatment for this disease, and the survival of af-
licted patients is extremely rare (10). Considering the acute
progression of the disease in our patient, the outcome may
have been the same even if an attempt at treatment had been
initiated.

In conclusion, our patient presented with amoebic en-
cephalitis by B. mandrillaris. Clinicians should be aware of
such infections because of the difficulty of the diagnosis, the high mortality rate, and the rapid increase in the number of cases observed worldwide.

The authors state that they have no Conflict of Interest (COI).

References

1. Matin A., Siddiqui R., Jayasekera S., Khan N.A. Increasing importance of Balamuthia mandrillaris. Clin. Microbiol. Rev 21: 435-448, 2008.
2. Centers for Disease Control and Prevention. Balamuthia amebic encephalitis—California, 1999–2007. MMWR. Morb. Mortal. Wkly. Rep 18: 768-771, 2008.
3. Cabello-Vilchez A.M., Rodríguez-Zaragoza S., Piñero J., Valladares B., Lorenzo-Morales J. Balamuthia mandrillaris in South America: An emerging potential hidden pathogen in Perú. Exp. Parasitol 145: S10-S19, 2014.
4. Itoh K., Yagita K., Nozaki T., Katano H., Hasegawa H., Matsuo K., Hosokawa Y., Tando S., Fishiki S. An autopsy case of Balamuthia mandrillaris ameobic encephalitis, a rare emerging infectious disease, with a brief review of the cases reported in Japan. Neuropathology 35: 64-69, 2015.
5. Kobayashi S, Tsukada A, Kobayashi S, Izumiya S, Yoon HS. Amebic encephalitis in a farmer. Pathology 47: 720-722, 2015.
6. White J.M., Barker R.D., Salisbury J.R., Fife A.J., Lucas S.B., Warhurst D.C., E.M. Higgins. Granulomatous ameobic encephalitis. Lancet 364: 220, 2004.
7. Baig AM. Granulomatous ameobic encephalitis: ghost response of an immunocompromised host? J Med Microbiol 63: 1763-1766, 2014.
8. Deetz TR, Sawyer MH, Billman G, Schuster FL, Visvesvara GS. Successful treatment of Balamuthia ameobic encephalitis: presentation of 2 cases. Clin Infect Dis 15;37: 1304-1312, 2003.
9. Martínez DY, Seas C, Bravo F, Legua P, Ramos C, Cabello AM, Gotuzzo E. Successful treatment of Balamuthia mandrillaris amebic infection with extensive neurological and cutaneous involvement. Clin Infect Dis 15;51: e7-e11, 2010.
10. Kato H, Mitake S, Yuasa H, Hayashi S, Hara T, Matsukawa N. Successful treatment of granulomatous ameobic encephalitis with combination antimicrobial therapy. Intern Med 52: 1977-1981, 2013.