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Case Report

A Case Report of *Balamuthia mandrillaris* Encephalitis: Experience from Central China

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Abstract

Balamuthia mandrillaris is a free-living amoeba that can cause granulomatous amoebic encephalitis, a lethal neurological condition in humans. This pathogen infects not only immunocompromised hosts but, more commonly, immunocompetent individuals. *Balamuthia mandrillaris* mainly infects the skin and nervous system. When it affects the nervous system, it can manifest as *Balamuthia mandrillaris* encephalitis (BAE). This article presents a case of BAE in central China, diagnosed through next-generation sequencing and histopathology. The patient is a 64-year-old male who was admitted to the Department of Neurosurgery with a one-week history of headache. Magnetic resonance imaging scans revealed a mass in the right temporal-occipital region, and postoperative pathological examination confirmed that the lesion was BAE. We will detail the clinical course of this disease in this patient, aiming to enhance clinicians' understanding of *Balamuthia mandrillaris* infections.

Introduction

Balamuthia mandrillaris is a free-living amoeba that can cause granulomatous amoebic encephalitis, a lethal neurological condition. The encephalitis caused by *Balamuthia mandrillaris* is known as *Balamuthia mandrillaris* encephalitis (BAE), which was first identified in 1986 during a necropsy of a baboon brain at the San Diego Zoo in California, USA.[1–3] *Balamuthia mandrillaris* exists in two main forms: the trophozoite and the cyst. It is commonly found in water and soil, and it can invade humans through the respiratory tract or injured skin.[4] This pathogen infects not only immunocompromised hosts but more commonly affects immunocompetent individuals.[5] This article presents a case of BAE in central China, diagnosed through next-generation sequencing and histopathology. We will detail the clinical course of this disease, aiming to enhance clinicians' understanding of *Balamuthia mandrillaris* infections.

Case report

A 64-year-old male was admitted to the Department of Neurosurgery with a one-week history of headache. The patient developed a headache and right-eye tearing without any obvious triggering factors seven days before admission. A computed tomography (CT) scan was conducted on August 1, 2023, which revealed a mass in the right temporal-occipital region. The patient had no other significant symptoms and denied a history of hypertension, diabetes, heart disease, or special medication use. He had not traveled to any epidemic areas or pastoral regions. Upon physical examination, the patient's body temperature was 36.7°C, his pulse was 76 beats/m, respiratory rate was 20 breaths/m, and blood pressure was 140/87 mmHg. He was alert with a Glasgow Coma Scale score of 15 (E4V5M6). He could speak fluently and had normal orientation and calculation abilities. His pupils were equal and round, approximately 3 mm in diameter. There was no neck stiffness, and Brudzinski's and Kernig's signs were negative.

We conducted magnetic resonance imaging on August 29, 2023, which included plain, enhanced, magnetic resonance angiography, and magnetic resonance spectroscopy sequences (see Fig. 1). Plain and enhanced sequences and magnetic resonance angiography showed a mass in the right temporal-occipital lobe with a long T1 signal and multiple small blood vessels passing through it. Magnetic resonance spectroscopy indicated the mass with a reduced N-acetylaspartate peak, an increased choline peak, and an increased Cho/N-acetylaspartate ratio of 1.83 (the opposite side had a ratio of 0.17). These results suggested glioma with a small amount of hemorrhage. Pre-surgical investigations included a chest X-ray, which showed no abnormalities, and blood tests revealing normal white blood cell count, hemoglobin, and platelets. Further examination confirmed a possible diagnosis of right temporal glioma with intratumoral stroke.

Keywords: *Balamuthia mandrillaris*; Next-generation sequencing; NGS; Granulomatous amoebic encephalitis.

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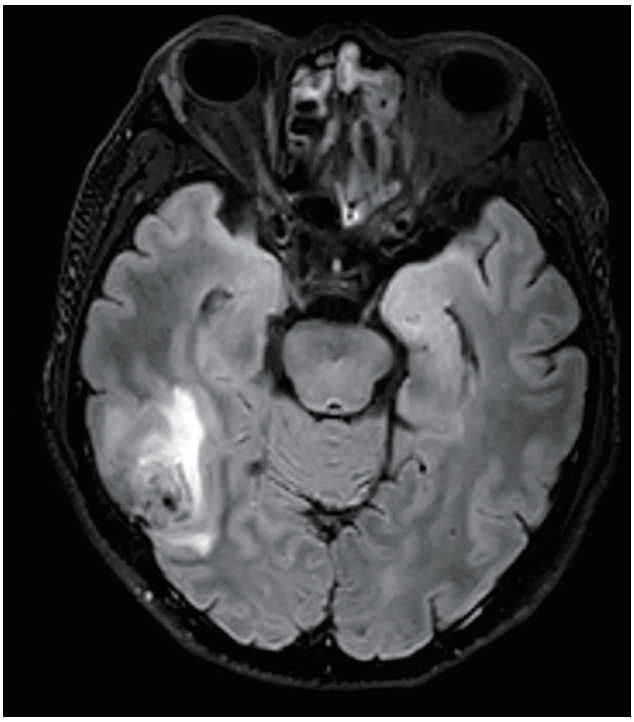

Fig. 1. The patient's preoperative magnetic resonance imaging examination showed a mass in the right temporal occipital lobe.

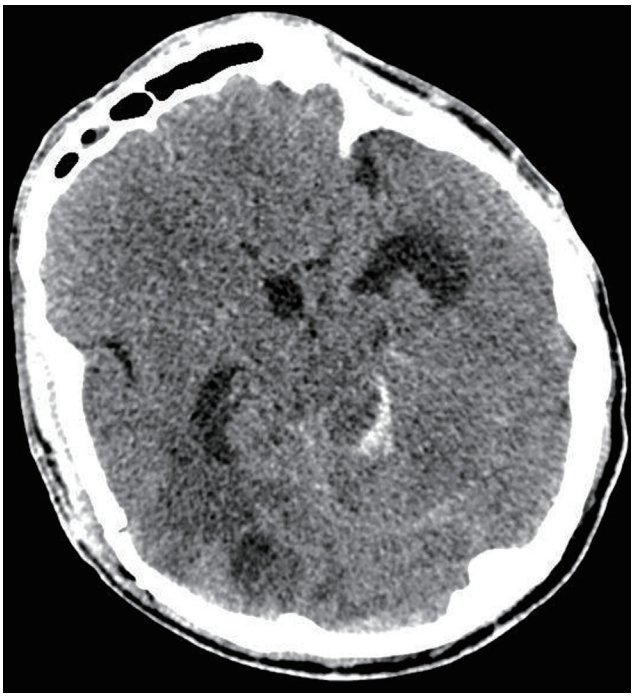

Fig. 2. The patient's postoperative computed tomography scan showed edema in the right temporal and occipital lobe brain tissue, along with intraventricular hemorrhage.

The patient underwent craniotomy on September 1, 2023. The surgically removed tissue was soft, grayish-red, and contained no pus. He had no fever or other symptoms after surgery. On September 8, 2023, histopathology of the surgically removed tissue revealed a brain abscess in the right temporal-occipital lobe. The patient received intravenous treatment with linezolid and meropenem. After three days of intravenous treatment, the patient developed a mild fever. A lumbar puncture revealed cerebrospinal fluid (CSF) with a slightly yellow appearance, weakly positive protein, no bacterial growth, and a white blood cell count of 252 × 10^6/L. The CSF sample had a normal glucose concentration of 3.02 mmol/L and a decreased chloride concentration of 114.8 mmol/L. On September 14, 2023, the patient developed a headache, and a follow-up CT scan revealed significant enlargement of the previously noted lesions. Dehydration and anti-cerebral edema treatments were intensified, and next-generation sequencing (NGS) was performed. On September 15, 2023, the patient suddenly fell into a coma, with a Glasgow Coma Scale score of 6 (E1V2M3). Emergency CT scans showed new areas of hemorrhage in the third and fourth ventricles, and results showed supratentorial ventriculomegaly (see Fig. 2). External ventricular drainage surgery was performed, and CSF was sent for pathogen NGS testing. After the drainage, the patient remained comatose, but his vital signs were stable, and he was transferred to the intensive care unit of neurosurgery. NGS tests on both blood and CSF identified sequences of *Balamuthia mandrillaris* and *Haemophilus parainfluenzae*, confirming a possible diagnosis of BAE. The patient was then treated with intravenous ornidazole. On September 16, 2023, the pathological sections of the surgically removed tissue were sent to the Parasitology Teaching and Research Section of Tongji Medical College, Huazhong University of Science and Technology. Microscopic examination revealed pathogenic free-living amebas around the tissue (see Fig. 3). The patient's diagnosis was consistent with BAE, but no specific antibiotic treatment was available. Ornidazole was replaced with amphotericin B for continued intravenous treatment. After four days, the patient suddenly developed dyspnea. Endotracheal intubation and ventilator-assisted breathing were initiated. The patient was trans-

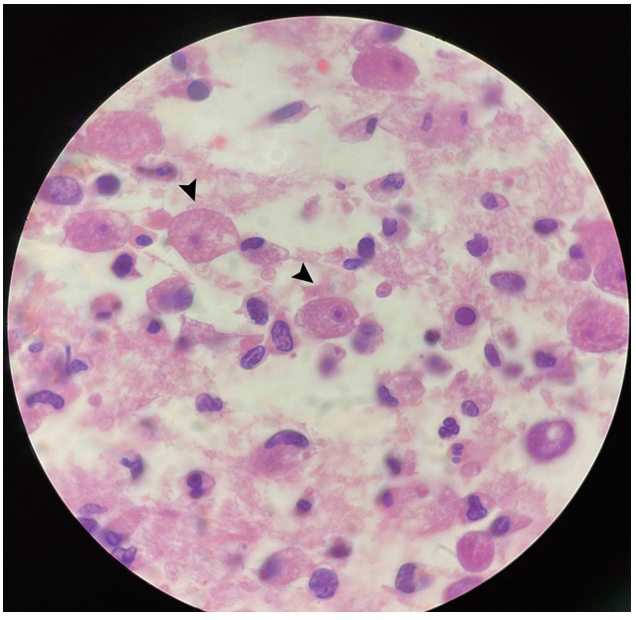

Fig. 3. Pathogenic free-living amoebas were found in the surgically removed tissue of the patient (Oil immersion lens, 1,500×).

ferred to a local hospital by his family for further treatment on September 21, 2023, and died of respiratory and cardiac arrest on September 22, 2023.

Discussion

Balamuthia mandrillaris infection predominantly affects the skin and nervous system. Skin lesions from the infection present as asymptomatic plaques with well-defined borders, mild elevation, and rare ulceration. The skin remains insensate.[6,7] Neurological symptoms are non-specific and may include headache, fever, nausea, vomiting, drowsiness, and altered consciousness.[8,9] The clinical course of *Balamuthia mandrillaris* infection varies, with some patients progressing rapidly to granulomatous encephalitis and death. Only 5% of patients infected with *Balamuthia mandrillaris* exhibit skin lesions, and in some cases, the skin lesions appear months to years before neurological symptoms develop.[2,6] In China, thirty-two cases of confirmed infection have been reported across 13 provinces,[5,6,10] with 56% of cases involving children, and 62% involving the central nervous system. Once the central nervous system is affected, the fatality rate reaches 95%.

In the patient reported in this article, the patient presented with a nonspecific headache and no skin lesions. Right-eye tearing may have been caused by ocular amoebic infection. The patient primarily presented with granulomatous encephalitis, and trophozoites were detected in the lesion. NGS confirmed *Balamuthia mandrillaris* infection, leading to a diagnosis of BAE. Unlike other amoebic infections, *Balamuthia mandrillaris* infections lack specific antibiotic treatments,[5] leading to a high mortality rate and poor prognosis. In 2011, Doyle *et al*.[11] reported a successful treatment case of BAE, where the patient recovered following surgical resection and a combination intravenous therapy of pentamidine, azithromycin, itraconazole, sulfadiazine, and 5-fluorocytosine. In another case from 2022, Cuoco *et al*.[12] successfully treated a patient with BAE using the novel antibiotic drug miltefosine, along with 5-fluorocytosine, sulfamethoxazole-trimethoprim, azithromycin, and fluconazole. Miltefosine was found to inhibit the growth of *Balamuthia mandrillaris* in vitro, although its in vivo efficacy remains uncertain.[5,12] With the advent of NGS for pathogen detection since 2014,[13] rare pathogens like *Balamuthia mandrillaris* have become more easily identifiable. However, the rapid progression and lack of effective treatments result in poor outcomes for BAE. In this case, despite early diagnosis through NGS, the patient's condition deteriorated due to the lack of effective medication. Given the nonspecific symptoms of BAE, serum tests, CSF tests, and NGS tests are valuable diagnostic tools. Further research on drug efficacy in treating *Balamuthia mandrillaris* infections is needed to improve patient prognosis.

Conclusions

This article presents a patient diagnosed with BAE in central China, with the diagnosis confirmed through NGS and histopathology. NGS is a highly effective diagnostic method for rare pathogen infections like *Balamuthia mandrillaris.* However, there is still a lack of effective drug treatments for *Balamuthia mandrillaris* infection, and further research is needed to investigate potential treatments for these infections.

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Conflict of interest

None declared.

Author contributions

WX and XY conceived the idea and wrote the article together. All authors have made a significant contribution to this study and have approved the final manuscript.

Ethical statement

The study was conducted in accordance with the ethical standards of the institutions to which we are affiliated and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for reporting the case and accompanying images.

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