Disseminated *Balamuthia mandrillaris* Amoeba Infection in an AIDS Patient from Brazil

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**Abstract.** This report describes a 32-year-old male AIDS patient. He presented with a clinical picture characterized by severe headache, blurred vision, and fever that had lasted for 10 days. At admission, no remarkable neurologic abnormalities were observed. Cranial tomography showed a ring-enhanced lesion with edema and a mass effect in the right occipital lobe. The initial diagnosis was toxoplasmosis, and treatment of this was administered. However, 5 days later, the patient’s clinical status worsened and he died. The necropsy showed necrotizing and hemorrhagic encephalitis, with trophozoites similar to an amoeba species. Furthermore, the kidneys, adrenal glands, thyroid gland, and liver were also involved. The amoeba *Balamuthia mandrillaris* was identified by an immunofluorescence test.

**INTRODUCTION**

Free-living amoebae have been recognized as uncommon human pathogens that involve the central nervous system (CNS). Classically, *Naegleria fowleri* causes primary amoebic meningoencephalitis in immunocompetent hosts, whereas *Acanthamoeba* spp. lead to granulomatous encephalitis mainly in immunodepressed hosts.¹ Today, nearly 100 cases of encephalitis caused by *Balamuthia mandrillaris* amoebae have already been described. Most of these cases have been in patients presenting immunocompromised states, including AIDS patients.²

This amoeba species is ubiquitous in nature and can be found in soil samples and probably in water sources.³,⁴ This organism infects the brain by hematogenous routes, after first infecting either the lungs after aspiration or the skin through cuts or abrasions. However, an olfactory nerve pathway into the CNS has recently been described.⁵ The clinical course of *B. mandrillaris* infection can be subacute or chronic, and the neurologic picture can be extremely variable.

Radiologic studies usually show one or more nonspecific enhancing lesions, but the gold standard diagnostic method is indirect immunofluorescence staining of brain tissue sections.⁶ In addition, immunofluorescence testing of serum can also be useful.⁷ Recently, a new tool for *B. mandrillaris* identification has been developed. The polymerase chain reaction (PCR) technique enables detection of mitochondrial 16S rRNA gene DNA from the amoeba in clinical specimens such as brain tissue and cerebrospinal fluid (CSF).⁸ However, amoebic meningoencephalitis diagnosis is rarely performed before death, and thus far only three such patients have survived. At present, no specific treatment is available, but if the infection is recognized early, empirical antimicrobial therapy can be offered.⁹,¹⁰

Dissemination of this amoeba species to organs other than the skin and CNS has rarely been described,¹¹ perhaps because in most places necropsy is rarely performed. The aim of this study was to present the first case of disseminated *B. mandrillaris* infection in a Brazilian AIDS patient.

**CASE REPORT**

A 32-year-old heterosexual man from Minas Gerais, Brazil, was admitted to the emergency room of the teaching hospital in 1998 with severe headache, blurred vision, scotomas, and fever that had lasted for 10 days. He had a past history of syphilis, gonorrhea, condyloma acuminata, hepatitis C, and tuberculosis. He had been a smoker and alcoholic since childhood and also presented with addiction to marijuana and intravenous drugs. He had been diagnosed with HIV infection 10 years earlier. During follow-ups, he was prescribed trimethoprim-sulfamethoxazole prophylaxis and antiretroviral therapy with zidovudine and didanosine on several occasions, but he always presented poor compliance.

At admission, he presented extreme cachexia, anemia, and dehydration. His blood pressure was 120/80 mm of Hg, his temperature was 37°C, and no remarkable neurologic abnormalities were observed. The laboratory test results were as follows: hemoglobin level, 8.8 g%; hematocrit, 29.3%; platelets, 69,000; white blood cells, 1700 cells – 4 bands; 81 neutrophils, 10 lymphocytes, and 5 monocytes; glucose level, 110 mg%; serum nitrogen level, 31 mg%; serum creatinine level, 1.1 mg%; cerebrospinal fluid analysis, 1 cell; glucose, 48 mg%; proteins, 108 mg%. Stains and cultures for bacteria, fungi, and acid-fast bacilli were negative. VDRL was negative, fluorescent treponemal antibody (FTA)-absorption (Abs) was positive, and *Toxoplasma gondii* IgG was 1:256. At that time, no CD4 count was available in the hospital.

A cranial computed tomography (CT) scan revealed a ring-enhanced lesion with edema and a mass effect in the right occipital lobe (Figure 1A). The initial diagnosis was toxoplasmosis, and therefore, sulfadiazine, pyrimethamine, and folic acid were administered. Over the first days, his clinical state remained unchanged, but on the fifth day his condition abruptly worsened and progressed to death.

The necropsy showed severe and generalized edema of the brain, with hemorrhagic foci measuring 0.2–2 cm (Figure 1B). The microscopic findings included multifocal necrotizing hemorrhagic encephalitis and great numbers of amoeba trophozoites clustered around the vessels (Figure 1C). These structures measured 15–25 μm and presented light nuclei and central nucleoli. No granulomatous reaction was noticed. Furthermore, the kidneys, adrenal glands, thyroid gland, and liver also showed the presence of amoeba trophozoites and cysts (Figure 1, D–G).

Brain sections from this case were sent to the Centers for
In clinical practice, AIDS patients who are not receiving antiretroviral therapy or antitoxoplasma prophylaxis and who present acute or subacute neurologic symptoms, *T. gondii* IgG antibodies and CT scans or MRI showing multiple ring-enhancing lesions are highly likely to have *Toxoplasma* encephalitis (positive predictive value of 80%). In most treatment centers using these criteria, empirical therapy with sulfadiazine plus pyrimethamine is begun and such patients often improve within 10–14 days. If no improvement is seen or there is clinical worsening after 3 days of therapy, other diseases such as lymphoma, viral encephalitis, nocardiosis, endemic mycosis, or less common infections like free-living amoebae must be considered. In such cases, lumbar puncture and/or brain biopsy are indicated.

Nevertheless, with few exceptions, *B. mandrillaris* has only been shown postmortem. Although immunofluorescence and PCR techniques are available for diagnoses on tissues and fluids; unfortunately, no reference laboratories are available in most places where this disease occurs.

The appearance of the structures seen in different organs makes it possible to suspect free-living amoeba infection, although absence of the characteristic cysts of *B. mandrillaris* hinders differentiation from *Acanthamoeba* spp. Otherwise, granulomatous encephalitis is the neuropathologic hallmark of both of these amoebic infections, although no granulomatus reaction was noticed in our case. Sometimes this may occur and it may be related to the intense lymphoid depletion that was observed in the spleen and lymph nodes. Despite the lack of CD4 count, this could explain the advanced immunodeficient state of our patient after long-duration HIV infection without therapy compliance.

In addition to the CNS involvement, *B. mandrillaris* dissemination to several organs was also shown. This feature has only rarely been described. Regrettably, necropsy is carried out less and less in teaching hospitals, which impedes better knowledge of the causes of mortality among AIDS patients and the real prevalence of free-living amoeba infection in these individuals.

Disease Control and Prevention (Atlanta, GA) where *B. mandrillaris* was identified by an immunofluorescence test (Figure 1H). In addition, esophageal candidiasis, aspiration bronchopneumonia, and septic foci on the skin, tongue and kidneys were seen.

**DISCUSSION**

Although the amoeba *B. mandrillaris* is found worldwide, most infections in humans and some mammals have been diagnosed in North and South America. The first human report was published in 1991: this was a case of granulomatous encephalitis caused by leptomyxid amoeba in New York. After this, several cases from different places were described. To our knowledge, this was the second Brazilian patient with meningoencephalitis caused by this amoeba species and the first associated with AIDS, because the other case was related to alcoholism. However, our patient presented clinical and radiologic features that were similar to previous cases, along with a delayed diagnosis that requires a high degree of suspicion.

**REFERENCES**

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