Fatal Granulomatous Amebic Encephalitis Due to *Balamuthia mandrillaris* in New Mexico: A Case Report

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***Balamuthia mandrillaris* is a free-living amoeba that can cause granulomatous amebic encephalitis (GAE). We report a case in an individual with a history of alcohol abuse, cocaine use, and ditch water exposure. This is the first reported case of GAE due to *B mandrillaris* in New Mexico.**

Keywords. ameba; *Balamuthia mandrillaris*; diagnosis; encephalitis; granulomatous amebic encephalitis.

CASE REPORT

A 56-year-old Hispanic man with chronic hepatitis C was found to have a sodium of 117 mmol/L and a temperature of 39.1°C when presenting for alcohol detoxification. Two weeks earlier, he had been mixing stucco using ditch water, drinking alcohol, and using intranasal cocaine. On physical exam, he responded to questions appropriately and cranial nerves II–XII were intact. Head computed tomography (CT) and magnetic resonance imaging (MRI) showed low attenuation areas in both frontal lobes with peripheral enhancement. Magnetic resonance imaging further showed small foci of restricted diffusion, especially around the ventricles. Computed tomography of the chest, abdomen, and pelvis was normal.

The patient developed progressive confusion, and an open brain biopsy was performed on the left frontal lesion. A grossly granulomatous-appearing, nonpurulent structure was removed. The patient became unresponsive, was intubated for airway protection, and was transferred to our facility.

On admission, he was mechanically ventilated but not sedated. Neurological exam was notable for lack of response to sternal rub or toenail pinching, and nonreactive, upward-gazing pupils. Gag reflex and patellar deep tendon reflexes were intact. His physical exam was otherwise unremarkable.

Vital signs, leukocyte count, hemoglobin, platelet count, electrolytes, and liver function tests were normal. Cerebrospinal fluid (CSF) analysis revealed 392 nucleated cells/mm^3 (lymphocytes 67%), 910 red blood cells/mm^3, >250 mg/dL protein, and 32 mg/dL glucose. Cerebrospinal fluid cytology and culture were negative. The biopsy specimen consisted of a 0.8 × 0.5 cm aggregate specimen with cautery artifact throughout. Hematoxylin and eosin (H&E)-stained sections revealed severe small vessel vasculitis with a mixed lymphoplasmacytic inflammatory infiltrate and no evidence of malignancy. No amebic organisms were identified in H&E, Gomori methenamine silver (GMS), and periodic acid-Schiff stains.

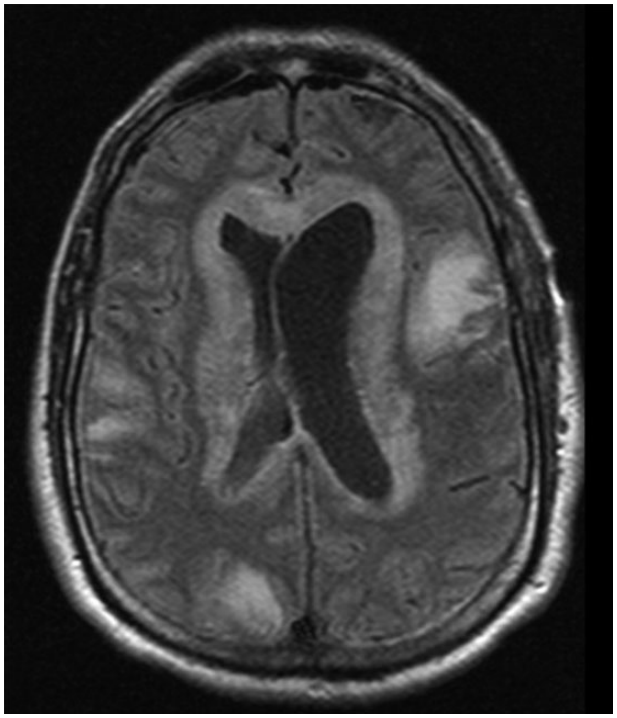

Figure 1. Magnetic resonance imaging 2 weeks later. Axial T2 FLAIR shows a thick rind of periventricular hyperintensity as well as focal right parietal and bilateral frontal lobe lesions.

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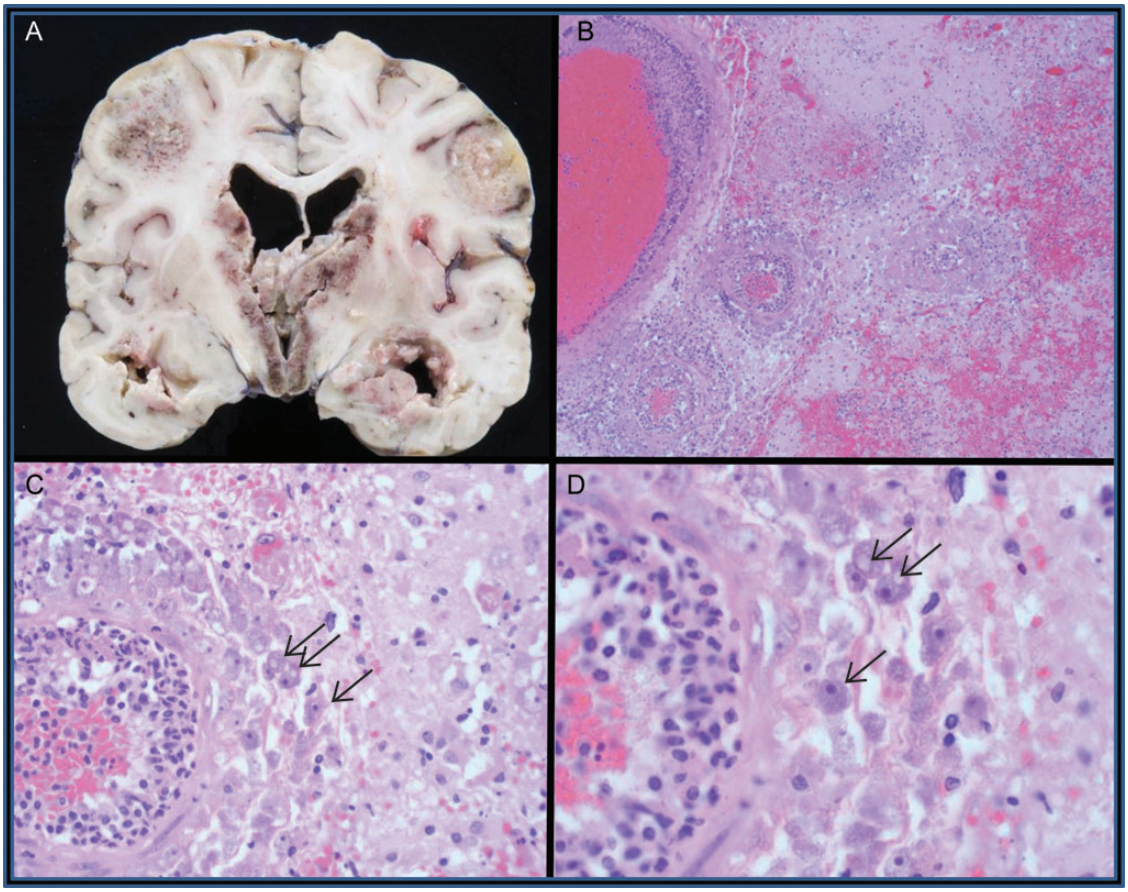

Figure 2. (A) Gross Photograph demonstrating multiple foci of necrosis and ventricular involvement; (B) 20×, hematoxylin and eosin (H&E) demonstrating vasculitis; (C) 40×, H&E representative of organisms and vasculitis; (D) 60× oil, H&E arrows point to trophozoites.

Cerebrospinal fluid polymerase chain reaction (PCR) test for herpes simplex virus and varicella zoster virus, CSF cryptococcal antigen, CSF serologies for *Listeria* and cysticercosis, CSF enterovirus PCR, CSF Venereal Disease Research Laboratory test, human immunodeficiency virus viral load and antibody, serum serologies for *Treponema pallidum*, hepatitis B, *Toxoplasma*, *Echinococcus*, and serum auto-antibody panel were all negative. Urine *Histoplasma* antigen was positive at 4.8, but serum serologies and immunodiffusion assays were negative. A serum *Coccidiodes* immunoglobulin (Ig)M antibody assay was positive, but IgG and immunodiffusion assays were negative. Cerebrospinal fluid culture and acid-fast bacteria smear and culture were negative, and GMS stain was negative for fungal elements.

Repeat MRI with and without gadolinium 20 days after initial presentation showed interval enlargement of the right superior frontal and right temporal lobe lesions (Figure 1), periventricular microhemorrhages, and restricted diffusion. The patient became hypotensive, requiring norepinephrine, and no brainstem reflexes could be elicited. Treatment was withdrawn and the patient died that day.

Autopsy revealed multiple hemorrhagic necrotic lesions in the bilateral frontal, temporal, and right occipital lobes (Figure 2). The cortical lesions extended to the internal capsule, bilateral deep grey nuclei, bilateral hippocampi, mammillary bodies, and thalamus. Extensive seeding of the ventricular system was present with abundant mucoid and necrotic material throughout.

Microscopically, numerous perivascular lymphoplasmacytic infiltrates, vasculitis, ventriculitis, meningitis, and choroid plexitis were present. Perivascular, large amebic organisms with abundant acidophilic, vacuolated cytoplasm, and eccentric small nuclei were numerous in viable areas. Organisms were best visualized on routine H&E staining (Figure 2), and speciation was confirmed by alkaline phosphatase immunohistochemical staining for *Balamuthia madrillaris* (positive) and *Acanthamoeba healyi* (negative). Polymerase chain reaction test was positive for *Balamuthia* and negative for *Naegeleria fowleri* and *Acanthamoeba*.

DISCUSSION

Balamuthia mandrillaris is a free-living ameba usually found in soil and dust. It can cause granulomatous amebic encephalitis

(GAE), which typically progresses over several weeks, leading to death [1]. It has been described in both immunocompromised and immunocompetent individuals [2]. Since first identified in 1986, approximately 200 cases have been reported worldwide [3]. However, the frequency of GAE due to *B mandrillaris* is thought to be underestimated because of the difficulty in diagnosis [3, 4]. Intranasal cocaine has not been described as a risk factor for GAE; however, in the setting of poor hygiene, alcoholism, and mixing stucco with ditch water, intranasal cocaine use may have increased the risk of GAE.

This case highlights the importance of imaging in the diagnosis of GAE. Although the brain biopsy was not diagnostic, CT and MRI were consistent with GAE. Most ring-enhancing brain lesions are not associated with rapid intralesional hemorrhagic conversion, and evidence of intralesional hemorrhage was reported as an important clue to the diagnosis [5]. Restricted diffusion was also an unusual feature, involving patchy, peripheral foci and a thick periventricular rind. The lack of trophozoites or cysts on initial biopsy may be due to tissue destruction during surgery caused by cautery artifact. Brain biopsies have been inconclusive in other reported cases of GAE, possibly because of inadequate sampling [4, 6–7].

Retrospective comparison of the biopsy to the autopsy sample revealed few key differences. Both samples demonstrated an inflammatory infiltrate consisting of lymphocytes, few plasmacytoid cells, and extensive necrosis out of proportion to the amount of vasculitis. However, only the autopsy specimen showed rare multinucleated giant cells with poorly formed granulomatous inflammation, and trophozoites. These striking differences reflect known potential limitations of brain biopsy in the diagnosis of *B mandrillaris* GAE [2].

Recent papers have focused on *B mandrillaris* as a public health concern secondary to an increasing incidence of reported cases [3]. This is the first reported case of GAE from New Mexico and the first reported case associated with intranasal cocaine use, illustrating the importance of early diagnosis and concomitant institution of treatment.

Acknowledgments

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