Case Report

Amebic encephalitis

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Abstract

**Background:** Amebic encephalitis (granulomatous amebic encephalitis, GAE) an extremely rare disease occurring in immunocompromised patients. Presentation and early imaging findings are nonspecific. In GAE, enhancement may or may not be seen on imaging studies despite the presence of an aggressive, necrotizing, parasitic infection.

**Case Description:** The patient was a 79-year-old man with ill-defined autoimmune hepatitis. He was on mild immunosuppression with 6-MP and low-dose prednisone. He presented with an acute febrile illness and obtundation. Imaging revealed a nonenhancing mass lesion of the frontal lobe. The patient briefly improved on high-dose steroids, then deteriorated again, with repeat imaging showing enlargement of the edematous brain lesion and herniation. The patient underwent craniotomy for evacuation of a necrotic brain lesion. His condition did not improve. Frozen section revealed only necrosis. Permanent pathology revealed GAE caused by *Acanthamoeba*.

**Conclusion:** Neurosurgeons should remain aware of this rare disease. Imaging is variable and may not show enhancement or necrosis despite large areas of parasitic infection.

**Key Words:** *Acanthamoeba*, Ameba, encephalitis, granulomatous amebic encephalitis

INTRODUCTION

Amebic encephalitis is a rare neurosurgical problem. Amebic infection in the central nervous system (CNS) can take the form of the following two distinct clinical entities: meningoencephalitis and granulomatous amebic encephalitis (GAE). The former is more common and is seen in immunocompetent patients following swimming in fresh water, with parasites entering the CNS through the olfactory epithelium. The latter disease, GAE, is extremely rare. It occurs in immunocompromised patients, usually from hematogenous spread. Clinical presentation and imaging studies are nonspecific. Patients may require neurosurgical attention.

CASE REPORT

**History**

The patient was a 79-year-old man who presented with hepatosplenomegaly, thrombocytopenia, and pancytopenia approximately nine months before admission. Liver and bone marrow biopsies were most consistent with autoimmune hepatitis. The patient had been under treatment with 6-mercaptopurine and low-
dose prednisone for 4 months. Prednisone had recently been weaned from 15 to 10 mg daily.

The patient had experienced subtle personality change, flattened affect, and shuffling gait for as much as a year before admission. For two weeks before admission, all symptoms were worsening, with falls, lethargy, and fatigue. On the day of admission, the patient had profound lethargy and fever to 103.7°F (39.8°C). He was brought to the emergency department.

Additional medical history was positive for non-insulin-dependent diabetes mellitus, hypertension, gastroesophageal reflux disease (GERD), colectomy in the 1970s for benign tumor, cholecystectomy, and small bowel obstruction requiring lysis of adhesions.

Medications were prednisone, 6-MP, sitagliptin, calcium, potassium, esomeprazole, amiodipine, duloxetine, aspirin, glyburide, and metformin.

The patient did not smoke cigarettes nor drink alcohol. There was no unusual environmental exposure nor history of trauma. He had not been swimming in the past year. There was no travel outside the country.

Family history was notable for a malignant brain tumor in the patient’s father who died in the 1960’s.

On initial examination, temperature was 103.7°F (39.8°C); heart rate, 118; blood pressure, 152/86; and room air oxygen saturation, 96%. The patient was lethargic and awake, with psychomotor slowing. Glasgow coma scale was 14, with no focal neurologic deficit. There were multiple petechiae and ecchymoses throughout the skin, with a few small areas of skin opening.

Laboratory data showed a white blood count, 3.4; hemoglobin, 12.9; and platelet count, 50 000. Complete metabolic profile was normal except for mildly elevated blood glucose at 129. Chest x-ray showed mild prominence of the pulmonary hilum.

Diagnostic studies on admission included computerized tomography (CT) of the head without contrast [Figure 1] and magnetic resonance imaging (MRI) with and without contrast [Figures 2 and 3]. These revealed a nonenhancing mass lesion of the right frontal lobe. The primary radiographic diagnosis was low-grade glioma.

**Early hospital course**

It was not at first clear that the lesion seen on imaging was the dominant problem. The films were suggestive of a possibly benign process, such as low-grade glioma, and the history seemed to be one of mild progressive psychomotor decline for a year, with acute worsening over two weeks. The patient’s lethargy improved on higher doses of steroids. However, he developed a significant ileus, with question of Ogilvie’s syndrome or obstruction. Internal medicine, infectious disease, and gastroenterology were consulted. Abdominal films and further blood work were nonspecific. He remained afebrile for several days. On the fourth hospital day, his level of consciousness declined markedly coincident with
another fever to 101.9°F (38.8°C). A repeat head CT was performed [Figure 4] revealing increase in cerebral edema with mass effect and shift. The patient was taken for emergency surgery for anticipated brain biopsy and tissue cultures, and possible decompressive craniectomy.

**Operation**
No antibiotics were given preoperatively so that cultures would not be inadvertently sterilized if an infectious process were encountered. A right frontal craniotomy was performed, and a large area of necrotic brain was identified and evacuated. Several frozen sections were sent revealing necrotic brain tissue and acute inflammatory cells, but no apparent neoplasm or infection was observed. Gram stains and stains for acid fast bacilli and fungi were negative. The diagnosis of tumefactive demyelination was considered.

**Postoperative course**
The patient did not improve neurologically postoperatively, and remained deeply comatose for the remainder of the hospital stay. Daily CT scans showed progressively severe brain edema and herniation. The diagnosis was elusive and no antimicrobial agents were utilized at first. Pathology eventually showed ameba, that is, GAE [Figure 5]. The organism was further identified as *Acanthamoeba*, without further speciation. Based on limited available information in the literature, an aggressive regimen of intravenous pentamidine, voriconazole and azithromycin was initiated, with no improvement noted. Decision was made to withdraw care.

**DISCUSSION**
There are three main pathologic free-living Amoeba (not including the gastrointestinal parasite *Entamoeba histolytica*) which are as follows: *Naegleria fowleri*, *Acanthamoeba* species, and *Balamuthia mandrillaris*. *Naegleria* are associated with primary amebic meningoencephalitis, a rapidly fatal hemorrhagic encephalitis typically occurring in healthy children or young adults and usually following recent fresh water swimming. *Acanthamoeba* and *Balamuthia* both can cause the syndrome of GAE, which our patient had, an insidious and almost uniformly fatal encephalitic process.[5,6] *Acanthamoeba* is also associated with keratitis in otherwise healthy individuals, typically contact lens wearers who use homemade solutions to clean lenses or wear lenses while swimming in fresh water, and with chronic skin ulcers.[5,6]

*Acanthamoeba* are found worldwide in a variety of habitats, including freshwater, soil, air, and sewage.[2] They have also been isolated from the nasopharyngeal passages of healthy persons and may be considered normal flora.[16] Serologic surveys have detected serum antibodies against *Acanthamoeba* in healthy individuals.[2]

Despite the ubiquitous nature of the organism and common exposure, the incidence of human disease from *Acanthamoeba* is low. GAE from *Acanthamoeba* occurs almost exclusively in immunocompromised hosts or debilitated patients. HIV disease, systemic lupus erythematosus, diabetes, chronic liver disease, chemotherapy, prolonged steroid, and organ and marrow transplantation have all been described as potential associations.[2,6,8-10] *Acanthamoeba* encephalitis has also been reported in immunocompetent hosts, although much less commonly.[17] Recently, a case of *Acanthamoeba* encephalitis was reported in a patient who received rituximab for cryoglobulinemia.[10] The patient also received plasmapheresis, but steroids were being tapered at the time of disease occurrence. Our patient had an ill-defined chronic liver disease with no cirrhosis on biopsy, was on a low and tapering dose of steroids for a short period of time, and was taking 6-MP.

![Figure 4: Head CT with contrast, hospital day 4](image)

*Figure 5: Edematous brain parenchyma with inflammation, infarction, and reactive astrocytes. Within the necrotic tissue and perivascular areas are polygonal structures with bright red intracytoplasmic structures consistent with amoeba (arrows) (H and E, ×400)*
The portal of entry of cases of *Naegleria* meningoencephalitis is usually through the olfactory neuroepithelium. Although *Acanthamoeba* more commonly gain access to the CNS hematogenously either through the respiratory tract or skin, organisms can also enter through the olfactory route. The frontal location of the infection in our patient suggests an olfactory site of entry. However, our patient demonstrated ecchymotic skin lesions, one or more of which could have represented a site of entry.

The diagnosis in our patient was not certain until brain biopsy was performed as is typical. It is possible that if the diagnosis had been considered and the treatment initiated sooner, the patient could have had a better outcome. The febrile nature of the illness was a clue to the diagnosis, but this was not considered because of the unusual imaging and the intercurrent gastrointestinal illness. The immunosuppression, though considered “mild,” could also have alerted the medical team to the presence of an unusual or opportunistic infection. The initial imaging, which demonstrated no enhancement on MRI, suggested relatively benign entities, such as low-grade glioma and tumefactive demyelination, rather than an inflammatory process. However, in GAE, enhancement may or may not be seen on imaging studies despite the presence of an aggressive necrotizing parasitic infection. 

Although GAE is not new to the international medical literature, it is nonetheless exceptionally rare.

Treatment options for GAE are not well-defined as the majority of cases are diagnosed postmortem. Although our patient did not improve with aggressive surgical and medical treatment, there have been reports of successful treatment. Despite many anecdotal antimicrobial regimens in the literature, no regimen is universally accepted or effective.

**CONCLUSION**

Amebic brain abscess should be considered in patients presenting with a clinical triad of edematous brain lesions, immunosuppression, and fever. Brain imaging may or may not show contrast enhancement despite an aggressive, necrotizing lesion. Early diagnosis and treatment is essential.

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