Acanthamoeba encephalitis in immunocompetent hosts: A report of two cases

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ABSTRACT

Acanthamoeba are ubiquitous free-living amoeba. Acanthamoeba infections cause necrotizing vasculitis, resulting in vessel thrombosis and cerebral infarction. Acanthamoeba CNS infections, though uncommon, are associated with high mortality. Diagnosis is difficult and often delayed. Here, we present two immunocompetent hosts with Acanthamoeba encephalitis with good outcomes.

Keywords: Acanthamoeba CNS infections, Acanthamoeba encephalitis, granulomatous amoebic encephalitis

Introduction

Acanthamoeba are free-living protozoa found in soil, dust, and water.[1,2] Active trophozoites have acanthopodia and feed on bacteria, yeast, and algae. Dormant cysts are seen during unfavorable environmental conditions.[3] Cyst wall has strong glycosidic linkages that impart resistance to disinfection.[2,4]

Spectrum of disease includes keratitis, granulomatous encephalitis, meningocerebral encephalitis, sinusitis, and skin lesions.[5–8] Risk factors include Human Immunodeficiency Virus (HIV) infection, malignancy, immunosuppressant drugs, and history of organ transplant.[9] Acanthamoeba CNS infections are associated with high mortality.[10,11] Here, we describe two immunocompetent patients with Acanthamoeba encephalitis.

Case History

Patient 1

A 51-year-old woman with no preexisting illnesses presented with high-grade fever and right-sided weakness for 4 days. She had history of falling into a well one month ago. Neck stiffness, hemiplegia, exaggerated deep tendon reflexes, and extensor plantar response on the right side were seen. The initial diagnosis was meningoencephalitis and we worked her up for various etiologies. Magnetic resonance imaging (MRI) brain revealed left middle cerebral arterial territory infarcts. CSF opening pressure, leucocyte count, and protein were elevated (27 cm water, 340 cells with 80% lymphocytes, and 86 mg/dl, respectively). In view of possible aspiration, CSF microscopy and culture (on nonnutrient agar with E. coli overlay) for Acanthamoeba was done. This was positive for Acanthamoeba cysts on day 4 [Figure 1]. CSF GeneXpert polymerase chain reaction (PCR) and mycobacteria growth indicator tube (MGIT) for Mycobacterium tuberculosis, bacterial, and fungal CSF cultures were negative. After positive Acanthamoeba culture report, combination therapy with rifampicin, fluconazole, and trimethoprim-sulfamethoxazole was initiated and planned for treatment of Acanthamoeba encephalitis.
for 6 weeks. At follow-up after one month of treatment, she was afebrile with residual right-sided hemiparesis.

**Patient 2**
A 22-year-old student presented with holocranial headache for 3 weeks. There was no history of fever, seizures, nasal discharge, loss of weight/appetite or aquatic activities. He had bilateral papilledema, without other neurological deficits. In this patient, we considered differential diagnoses of chronic meningitis, cerebral venous thrombosis and idiopathic intracranial hypertension. MRI brain was normal. CSF opening pressure was 28 cm water. CSF analysis showed two lymphocytes, with normal glucose and protein. CSF culture for bacteria, Mycobacteria (MGIT and GeneXpert PCR test) and fungi were negative. At this point, the possibility of *Acanthamoeba* infection was considered. CSF *Acanthamoeba* culture was positive on day 7 [Figure 1]. This patient was managed with fluconazole, trimethoprim-sulfamethoxazole, metronidazole, rifampicin, miltefosine for 3 months. A decline in CSF opening pressure and resolution of headache were seen. He was well at follow-up 6 months after completion of therapy.

Both patients tested negative for HIV antibodies and had normal HbA1c levels.

**Discussion**

*Acanthamoeba* CNS infections are uncommon but frequently lethal. *Acanthamoeba* enter the body via inhalation/skin injuries followed by hematogenous dissemination and formation of cerebral ring-enhancing lesions.[2] Regions of brain involved include frontal, temporal, and parietal lobes, cerebellum, and corticomedullary junction.[13] Brain autopsy specimens show necrotizing vasculitis.[13] On microscopy, venulitis, trophozoites/cysts in perivascular spaces, meningoencephalitis with lymphocytic/histiocytic infiltrate, and granulomatous

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### Table 1: Selected Cases of Adult Survivors of Acanthamoeba Encephalitis in the last 20 years

| First Author | Year of Publication | Age/ gender | Immuno compromised state/risk factors | Clinical features | Diagnostic test | Imaging features | Treatment | Follow-up after treatment completion |
|--------------|---------------------|-------------|---------------------------------------|------------------|----------------|-----------------|-----------|-------------------------------------|
| Sahly et al,[3] 2017 | 38/M | Yes (HIV infection) | Headache, aemetic forms on H and E stain; positive CSF PCR | Ring-enhancing lesion on MRI | miltefosine, fluconazole, trimethoprim-sulfamethoxazole, flucytosine for 7 months | 5 months |
| Webster et al,[3], 2012 | 38/M | No | Tinnitus, seizures | Temporal lobe lesion | CSF | NM | Surgical excision; voriconazole, miltefosine; 3 months | 3 years |
| Lackner et al,[3]; 2010 | 17/M | No | NM** | CSF | NM | NM | | |
| Sheng et al,[3]; 2009 | 63/M | Yes (h/o falling into ditch and aspirating water) | Headache, vomiting, CSF wet-mount smear and Giemsa-trophozone/cysts; CSF PCR | Cerebral lesions; leptomeningeal enhancement | Amphotericin B, rifampicin; 4 weeks | NM |
| Aichelburg et al,[3]; 2008 | 25/M | No | Fever, ataxia, cutaneous ulcers | Multiple ring-enhancing lesions in cortex and brainstem | Trimethoprim-sulfamethoxazole changed to sulfadiazine, fluconazole, miltefosine, amikacin; excision of cerebellar abscess | 2 years |
| Fung et al,[3]; 2007 | 41/M | Yes (Liver transplant, diabetes mellitus) | Fever, seizures | Frontal lobectomy sample-cysts | Frontal lobe lesions | Surgical excision, rifampicin, trimethoprim-sulfamethoxazole; 3 months | 11 years |
| Petry et al,[3]; 2006 | 64/F | Yes (Diabetes mellitus, mid-facial fracture) | Headache | CSF culture | Pneumatocele | fluconazole, rifampin, metronidazole, sulfadiazine; 14 days. | 1 month |
| Hamide et al,[3]; 2002 | 45/F | No | Fever, signs of meningeal irritation | CSF wet mount and Giemsa | Normal | Rifampicin, fluconazole, trimethoprim-sulfamethoxazole, albendazole, ceftriaxone. | 1 year |

*M: Male; F: Female; **NM: Not mentioned
lesions have been noted.\textsuperscript{[3,5,14]} Though immunocompromised state is a risk factor, there are reports of severe disease in immunocompetent patients.\textsuperscript{[15‑17]}

Our first patient had history of fall into a freshwater body which may have led to the entry of \textit{Acanthamoeba}. However, our second patient did not have similar history and was immunocompetent. There is limited data regarding prognostic factors, especially in immunocompetent hosts. We reviewed published cases of adult survivors (>15 years of age) of \textit{Acanthamoeba} CNS infections from 1999 to 2019 indexed in Pubmed [Table 1]. 50% (4/8) were immunocompetent with no contact with water sources. However, \textit{Acanthamoeba} are ubiquitous and history of no contact with water would not rule out infection. All survivors (8/8) received combination therapy and excision of brain lesions was done in 37% (3/8). Fluconazole was given in 62% (5/8), trimethoprim-sulfamethoxazole in 50% (4/8), and miltefosine and rifampicin in 37% (3/8).

Challenges in management include reduced drug delivery across blood-brain barrier and lack of cysticidal action of drugs. Presenting features can mimic common diseases like cerebrovascular accident and tumors which makes early diagnosis difficult.

Caution-channel modulators and statins are being studied to look for anti-amoebic effects.\textsuperscript{[25,26]}

Patients with meningoencephalitis should be asked about history of aquatic activities. However, negative history of contact with water bodies does not rule out CNS \textit{Acanthamoeba} infections. Family medicine practitioners are often the first medical contact for such patients. \textit{Acanthamoeba} infection should be suspected in patients with meningoencephalitis in whom no etiological organism has been found and those with multiple cerebral lesions. High index of suspicion among family medicine physicians may lead to better outcomes as early diagnosis and prompt initiation of therapy are crucial aspects of management.

\textbf{Declaration of patient consent}

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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\textbf{Conflicts of interest}

There are no conflicts of interest.

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