Case Report

Acanthamoeba encephalitis in immunocompetent hosts: A report of two cases

Sohini Das[1], Karthik Gunasekaran[1], Sitara S. R. Ajjampur[2], Dilip Abraham[2], Tina George[1], M. Asisha Janeela[1], Ramya Iyadurai[1]

[1]Department of Medicine, Christian Medical College, [2]The Wellcome Trust Research Laboratory, Division of Gastrointestinal Sciences, Christian Medical College, Vellore, Tamil Nadu, India

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, meningoencephalitis, 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.

Address for correspondence: Dr. Sohini Das, Department of Medicine, Christian Medical College, Vellore - 632 004, Tamil Nadu, India.
E-mail: sohinidas@hotmail.com

Received: 14-11-2019 **Revised:** 22-12-2019
Accepted: 27-12-2019 **Published:** 28-02-2020

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_1010_19

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

How to cite this article: Das S, Gunasekaran K, Ajjampur SS, Abraham D, George T, Janeela MA, *et al*. Acanthamoeba encephalitis in immunocompetent hosts: A report of two cases. J Family Med Prim Care 2020;9:1240-3.

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.

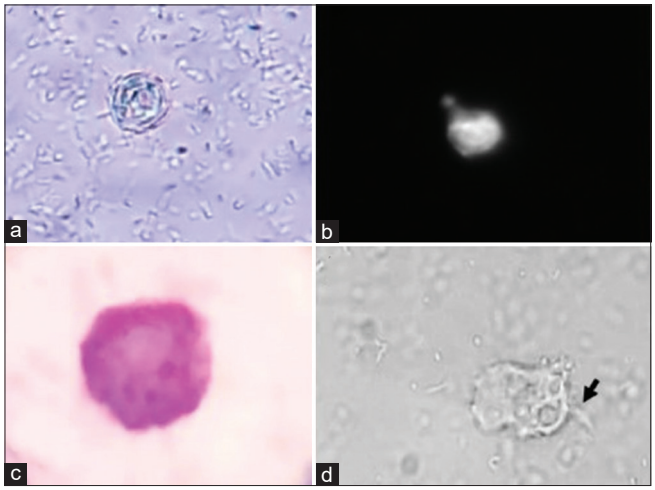

Figure 1: Acanthamoeba cyst and trophozoite stages in CSF cultures from reported cases: (a) wet mount (400×) (b) calcofluor stain (400×) and (c) Giemsa stain (1000×) cyst in patient 1 and (d) trophozoites (400×) with acanthopodia (black arrow) in patient 2

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.[12] Regions of brain involved include frontal, temporal, and parietal lobes, cerebellum, and corticomedullary junction.[13] Brain autopsy specimens show necrotizing vasculitis.[3] On microscopy, venulitis, trophozoites/cysts in perivascular spaces, meningoencephalitis with lymphocytic/histiocytic infiltrate, and granulomatous

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

First Author; Year of Publication	Age/ gender*	Immunocompromised state/risk factors-Yes/No	Clinical features	Diagnostic test	Imaging features	Treatment	Follow-up after treatment completion
Sahly *et al.*[18]; 2017	38/M	Yes (HIV infection)	Headache	amebic 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.*[16]; 2012	38/M	No	Tinnitus, seizures	Brain biopsy H and E stain and PCR	Temporal lobe lesion	Surgical excision; voriconazole, miltefosine; 3 months	3 years
Lackner *et al.*[19];2010	17/M	No	NM**	CSF	NM	meropenem, linezolid, moxifloxacin, fluconazole	NM
Sheng *et al.*[20]; 2009	63/M	Yes (h/o falling into ditch and aspirating water)	Headache, vomiting	CSF Wet-mount smear and Giemsa-trophozoites; CSF PCR	Cerebral lesions; leptomeningeal enhancement	Amphotericin B, rifampicin; 4 weeks	NM
Aichelburg *et al.*[21]; 2008	25/M	No	Fever, ataxia, cutaneous ulcers	CSF Acanthamoeba PCR	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.*[22]; 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.*[23]; 2006	64/F	Yes (Diabetes mellitus, mid-facial fracture)	Headache	CSF culture	Pneumatocele	fluconazole, rifampin, metronidazole, sulfadiazine; 14 days.	1 month
Hamide *et al.*[24]; 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.[3,5,14] Though immunocompromised state is a risk factor, there are reports of severe disease in immunocompetent patients.[15-17]

Our first patient had history of fall into a freshwater body which may have led to the entry of *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 Acanthamoeba CNS infections from 1999 to 2019 indexed in Pubmed [Table 1]. 50% (4/8) were immunocompetent with no contact with water sources. However, *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.

Calcium-channel modulators and statins are being studied to look for anti-amoebic effects.[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 Acanthamoeba infections. Family medicine practitioners are often the first medical contact for such patients. 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.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Marciano-Cabral F, Cabral G. *Acanthamoeba* spp. as agents of disease in humans. Clin Microbiol Rev 2003;16:273-307.
2. Bunsuwansakul C, Mahboob T, Hounkong K, Laohaprapanon S, Chitapornpan S, Jawjit S, *et al. Acanthamoeba* in Southeast Asia – Overview and challenges. Korean J Parasitol 2019;57:341-57.
3. Siddiqui R, Khan NA. Biology and pathogenesis of *Acanthamoeba*. Parasit Vectors 2012;5:1-13.
4. Lazuana T, Astuty H, Sari IP. Effect of cellulase enzyme treatment on cyst wall degradation of Acanthamoeba sp. J Parasitol Res 2019;2019:16.
5. Chandra SR, Adwani S, Mahadevan A. *Acanthamoeba* meningoencephalitis. Ann Indian Acad Neurol 2014;17:108-12
6. Khanna V, Khanna R, Mukhopadhayay C, Shastri B, Anusha G. *Acanthamoeba* meningoencephalitis in immunocompetent: A case report and review of literature. Trop Parasitol 2014;4:115.
7. Król-Turmińska K, Olender A. Human infections caused by free-living amoebae. Ann Agric Environ Med 2017;24:254-60.
8. Orosz E, Kriskó D, Shi L, Sándor GL, Kiss HJ, Seitz B, *et al.* Clinical course of *Acanthamoeba* keratitis by genotypes T4 and T8 in hungary. Acta Microbiol Immunol Hung. 2019;66:289-300.
9. Diaz JH. Behavioral and recreational risk factors for free-living amebic infections. J Travel Med 2011;18:130-7.
10. Megha K, Sehgal R, Khurana S. Genotyping of *Acanthamoeba* spp. isolated from patients with granulomatous amoebic encephalitis. Indian J Med Res 2018;148:456-9.
11. Das S, Saha R, Rani M, Goyal R, Shah D, Asish JK. Central nervous system infection due to *Acanthamoeba*: A case series. Trop Parasitol 2016;6:88-91.
12. Khan NA. *Acanthamoeba* and the blood-brain barrier: The breakthrough. J Med Microbiol 2008;57:1051-7.
13. Ong TYY, Khan NA, Siddiqui R. Brain-eating amoebae: Predilection sites in the brain and disease outcome. J Clin Microbiol 2017;55:1989-97.
14. Thamtam VK, Uppin MS, Pyal A, Kaul S, Jyostna Rani Y, Sundaram C. Fatal granulomatous amoebic encephalitis caused by *Acanthamoeba* in a newly diagnosed patient with systemic lupus erythematosus. Neurol India 2016;64:101-4.
15. Binesh F, Karimi M, Navabii H. Unexpected postmortem diagnosis of *Acanthamoeba* meningoencephalitis in an immunocompetent child. BMJ Case Rep 2011;2011. pii: bcr0320113954. doi: 10.1136/bcr. 03.2011.3954.
16. Webster D, Umar I, Kolyvas G, Bilbao J, Guiot MC, Duplisea K, *et al.* Case report: Treatment of granulomatous amoebic encephalitis with voriconazole and miltefosine in an immunocompetent soldier. Am J Trop Med Hyg 2012;87:715-8.
17. Ghadage DP, Choure AC, Wankhade AB, Bhore AV. Opportunistic free: Living amoeba now becoming a usual pathogen? Indian J Pathol Microbiol 2017;60:601-3.
18. El Sahly H, Udayamurthy M, Parkerson G, Hasbun R. Survival of an AIDS patient after infection with *Acanthamoeba* sp. of the central nervous system. Infection 2017;45:715-8.
19. Lackner P, Beer R, Broessner G, Helbok R, Pfausler B, Brenneis C, *et al.* Acute granulomatous *Acanthamoeba* encephalitis in an immunocompetent patient. Neurocrit Care 2010;12:91-4.

20. Sheng WH, Hung CC, Huang HH, Liang SY, Cheng YJ, Ji DD, *et al*. First case of granulomatous amebic encephalitis caused by *Acanthamoeba* castellanii in Taiwan. Am J Trop Med Hyg 2009;81:277-9.
21. Aichelburg AC, Walochnik J, Assadian O, Prosch H, Steuer A, Perneczky G, *et al*. Successful treatment of disseminated *Acanthamoeba* sp. infection with miltefosine. Emerg Infect Dis 2008;14:1743-6.
22. Fung KT, Dhillon AP, McLaughlin JE, Lucas SB, Davidson B, Rolles K, *et al*. Cure of *Acanthamoeba* cerebral abscess in a liver transplant patient. Liver Transpl 2008;14:308-12.
23. Petry F, Torzewski M, Bohl J, Wilhelm-Schwenkmezger T, Scheid P, Walochnik J, *et al*. Early diagnosis of *Acanthamoeba* infection during routine cytological examination of cerebrospinal fluid. J Clin Microbiol 2006;44:1903-4.
24. Hamide A, Sarkar E, Kumar N, Das AK, Narayan SK, Parija SC. Acanthameba meningoencephalitis: A case report. Neurol India 2002;50:484-6.
25. Martín-Navarro CM, Lorenzo-Morales J, Machin RP, López-Arencibia A, García-Castellano JM, De Fuentes I, *et al*. Inhibition of 3-hydroxy-3-methylglutaryl-coenzyme a reductase and application of statins as a novel effective therapeutic approach against *Acanthamoeba* infections. Antimicrob Agents Chemother 2013;57:375-81.
26. Sifaoui I, Martín-Navarro C, López-Arencibia A, Reyes-Batlle M, Valladares B, Pinero J, *et al*. Optimized combinations of statins and azoles against *Acanthamoeba* trophozoites and cysts *in vitro*. Asian Pac J Trop Med 2019;12:283-7.