



CASE DESCRIPTION

Acanthamoeba meningoencephalitis in an immunocompetent patient

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Introduction

Acanthamoeba spp. are free living amoeba capable of causing granulomatous amoebic encephalitis (GAE). It is also an important cause of severe keratitis among contact lens wearers and may also cause cutaneous lesions, particularly in immunocompromised individuals. Species known to infect humans include *A. byersi*, *A. castellani*, *A. culbertsoni*, *A. hatchetti*, *A. healyi*, *A. astroonyxix*, *A. divionensis*, *A. polyphaga*.

Acanthamoeba spp. are ubiquitous in the environment and have been found in a variety of sites, including soil, fresh, brackish and sea water; field grown vegetables, sewage, swimming pools, contact lens supplies, medicinal pools, dental treatment units, dialysis machines; heating, ventilating and air conditioning systems; tap water, mammalian cell cultures and vegetables.

Clinical presentation of *Acanthamoeba* infections:

1. GAE is of chronic onset and progressively worsens over a period of weeks to months. The signs and symptoms are typical of meningoencephalitis and encephalitis with varying degree of neurological involvement. See Table 1 for cases reported in India.

2. *Acanthamoeba* keratitis is associated with the use of contact lens. Corneal ulceration and scarring become apparent if not treated. See Table 2 for cases reported in India.

3. Rarely it can cause cutaneous acanthamoebiasis, which presents as a single/disseminated chronic skin lesions, initially appear as reddish nodules and later it is crusted or ulcerated. These may occur with or without concurrent CNS disease.

4. It also can cause disseminated infection that typically causes inflammation of lungs or sinuses and/or skin infections but has the potential to spread to brain.

Patient description

A 19-years old female patient complained of fever (102°F/38.9°C), vomiting, headache for 2 weeks and episodic abnormal neurological manifestations and disorientation for a period of 1 week.

On physical examination, she showed abnormal behaviour in the form of agitation and her Glasgow coma score (GCS) was 13/15 with E4V3M5 although other vital parameters were normal. A lumbar puncture showed clear cerebrospinal fluid (CSF) and wet-mount examination showed 6-8 lymphocytes and



three sluggishly motile structures in two different high power microscopic fields (Fig. 2). Motile structures were producing spinous protrusions in random directions suggestive of free-living amoeba (FLA). Microbiological culture of CSF for FLA, bacteria, fungi and *Mycobacterium tuberculosis* were all negative besides blood culture for bacteria and fungi. Multiplex bacterial PCR assay for *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae* type b was negative. Serological assay against Hepatitis C virus (HCV), HIV 1 & 2, Hepatitis B virus surface antigen (HBsAg) and autoimmune encephalitis panel were all negative.

We also investigated the patient for haematological parameters. Total leukocyte count (TLC) of the patient was 9500/cubic millimetres of blood with neutrophils 62%, lymphocytes 31%,

monocytes 4%, eosinophils 3%, All the parameters were within normal limits.

CSF was subjected to conventional PCR assay which showed an amplified product of 180 bp corresponding with that of genus *Acanthamoeba* (Fig. 1). All imaging findings were insignificant. Cytological and biochemical analysis of CSF depicted total cells of 35 with 100% being lymphocytes, protein of 1500 mg/dl, glucose of 46 mg/dl, ADA (adenosine deaminase) of 15.1 U/L. There was no history of exposure to fresh water bodies and swimming. A diagnosis of infection due to *Acanthamoeba* species was made.

Treatment

The patient was treated with fluconazole, miltefosine, metronidazole and ceftriaxone, however she died after 12 days of admission.

Table 1. Granulomatous amoebic encephalitis cases reported in India since 1990.

SI No.	Patient details	Sample taken	<i>Acanthamoeba</i> species/genotype identified	Treatment given	Patient outcome	Ref.
01	Immunocompetent young adult 19y/female	CSF (postmortem)	<i>Acanthamoeba castellanii</i> / T4	-	Patient died	[1]
02	Child acute on chronic malnutrition 3 y/male	CSF (antemortem)	<i>Acanthamoeba castellanii</i> / T4	-	Patient survived	[1]



03	Immunocompetent child 10 y/male	CSF (antemortem)	<i>Acanthamoeba hatchetti</i> / T11	-	Survived but CT after 2 months still showed persistence of mass-like lesion. Final outcome not known	[1]
04	Immunocompetent young adult 22 y/male	CSF (postmortem)	<i>Acanthamoeba hatchetti</i> / T11	-	Patient died	[1]
05	Patient with AML 22 y/male	Brain abscess (antemortem)	<i>Acanthamoeba culbertsoni</i> /T10	-	Patient died after 6 months	[1]
06	Immunocompetent child 2 y/male	CSF	<i>Acanthamoeba</i> spp.	Inj. vancomycin, ceftriaxone and dexamethasone	Patient responded well to therapy	[2]
07	Patient with SLE 28 y/male	Brain examination (postmortem)	<i>Acanthamoeba</i> spp.	-	Patient was dead	[3]
08	Immunocompetent patient 20 y/male	CSF	<i>Acanthamoeba</i> spp.	Rifampicin 600 mg once daily, Trimethoprim-sulfamethoxazole 960 mg twice-a-day and fluconazole 400 mg once daily for 2 weeks.	Patient responded well to therapy	[4]
09	Immunocompetent patient 16 y/male	Brain autopsy	<i>Acanthamoeba</i> spp.	-	Patient died	[5]
10	Immunocompetent child 3 y/male	CSF	<i>Acanthamoeba</i> spp.	Co-trimoxazole, rifampicin and ketoconazole	Patient responded well to therapy	[6]
11	Immunocompetent patient 38 y/male	Brain autopsy	<i>Acanthamoeba</i> spp.	-	Patient died	[7]
12	Immunocompetent patient 25 y/male	Fronto-temporal craniotomy done and cystic lesion was noted	<i>Acanthamoeba</i> spp.	Rifampicin, Trimethoprim-sulfamethoxazole, and fluconazole	Patient responded well to therapy	[8]



13	Patient with ALL 14y/male	CSF	<i>Acanthamoeba</i> spp.	Ketoconazole (5 mg/kg/d) and Trimethoprim- sulfamethoxazole (15 mg/ kg/d of the Trimethoprim component)	Patient did not respond well to treatment	[9]
14	Patient hypertensive for last past 20 years 63 y/female	CSF	<i>Acanthamoeba</i> spp.	Amphotericin B 30 mg, rifampicin 450 mg once a day and co-trimoxazole. Later two drugs withdrawn after a week. Inj. fluconazole 100 mg intravenously twice a day.	Patients died after 4 months	[10]
15	Patient with SLE and autoimmune haemolytic anaemia 24 y/female	Brain tissue sections	<i>Acanthamoeba</i> spp.	-	-	[11]
16	Immunocompetent patient 26 y/male	Brain biopsy	<i>Acanthamoeba</i> spp.	-	Patient died	[12]
17	Immunocompetent patient 45 y/female	CSF	<i>Acanthamoeba</i> spp.	Rifampicin 600 mg once daily, co-trimoxazole 960 mg twice daily orally and fluconazole 200 mg once daily intravenously for 1 week. Intravenous ceftriaxone was added (2 g 12 hourly) and carbamazepine 200 mg three times a day, was introduced to control seizures	No organism observed in CSF sample after treatment.	[13]



18	Post COVID 32 y/male	Brain biopsy	<i>Acanthamoeba</i> spp.	Liposomal amphotericin B (3 mg/kg/day), TMP-SMX (160 mg/800 mg/day), fluconazole (800 mg/day), albendazole (400 mg/day), azithromycin (500 mg/day), rifampicin (600 mg/day), Miltefosine (50 mg thrice daily for 4 weeks).	Patient survived [14]
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Table 2. Acanthamoeba keratitis reported in India since 1990.

Sl. No	Patient details	Sample taken	<i>Acanthamoeba</i> species/genotype identified	Treatment given	Patient outcome	Ref.
01	300 clinically suspected Acanthamoeba keratitis (AK) cases	Corneal scraping, contact lens	<i>Acanthamoeba</i> spp. (11)	Poly-hexamethylene biguanide eye drops (0.02%)	Complete healing in 7 (63.6%) patients	[14]
02	14 clinically suspected Acanthamoeba keratitis (AK) cases; non-contact lens wearer	Corneal scraping	<i>Acanthamoeba</i> spp. (T4 type)	Poly-hexamethylene biguanide, chlorhexidine digluconate eye drops (0.02%) - 9 patients, surgical intervention (5 patients)	Healed in 9 (75%) patients	[15]
03	Clinically suspected Acanthamoeba keratitis (AK) case; contact lens wearer	Contact lens	<i>Acanthamoeba culbertsoni</i>	Keratoplasty followed by local itraconazole and neomycin	Vision restored	[16]



04	183 clinically suspected Acanthamoeba keratitis (AK) cases.	Corneal scraping	<i>Acanthamoeba</i> spp. (T4 type)-80% <i>Acanthamoeba</i> spp. (T4 type)-20% <i>Acanthamoeba</i> spp. (unassigned genotypes)	-	-	[17]
05	30 culture confirmed patients with Acanthamoeba keratitis	-	<i>Acanthamoeba</i> spp. (T4 type)-86.7% <i>Acanthamoeba</i> spp. (T12 type)-10% <i>Acanthamoeba</i> spp. (T11 type)-3.3%	Poly-hexamethylene biguanide, chlorhexidine digluconate eye drops (0.02%)- 23 patients, surgical intervention (7 patients)	Healed in 21 patients	[18]
06	9 clinically suspected Acanthamoeba keratitis (AK) cases; non-contact lens wearer	Corneal scraping	<i>A. castellani</i> (2), <i>A. polyphaga</i> (2), <i>A. culbertsoni</i> (1), <i>Acanthamoeba</i> spp. (4)	Topical Neomycin-polymyxin B- bacitracin drops alone or in combination with either miconazole nitrate or ketoconazole drops	Healed in 5 patients	[19]
07	55-year-old woman with yellow plaque like lesion on cornea surrounded by infiltrate with history of trauma	Corneal scraping	<i>Acanthamoeba</i> spp.	Poly-hexamethylene biguanide eye drops (0.02%)	Restoration of vision after 8 weeks	[20]
08	53 clinically suspected Acanthamoeba keratitis (AK) cases; non-contact lens wearer	Corneal scraping	<i>Acanthamoeba</i> spp. (10)	Poly-hexamethylene biguanide eye drops (0.02%)-7 patients Surgical intervention – 3 patients	Healed in all patients	[21]

09	13 culture confirmed patients with <i>Acanthamoeba</i> keratitis	Corneal scraping	<i>A. culbertsoni</i> (6) <i>A. polyphaga</i> (4) <i>A. triangularis</i> (3) Genotype T4 (12) Genotype T12 (1)	Poly-hexamethylene biguanide eye drops (0.02%)-8 patients Surgical intervention- 5 patients	Healed in 10 patients	[22]
10	9-year-old boy presented with dense anterior corneal stromal infiltration.	Corneal scraping	<i>A. jacobsi</i>	Poly-hexamethylene biguanide, chlorhexidine digluconate eye drops (0.02%)	Restoration of vision	[23]
11	42 clinically suspected <i>Acanthamoeba</i> keratitis (AK) cases	Corneal scraping	<i>Acanthamoeba</i> spp. (5)	-	-	[24]
12	15 <i>Acanthamoeba</i> isolates from cornea of suspected <i>Acanthamoeba</i> keratitis (AK) cases	Corneal scraping	<i>Acanthamoeba</i> spp. [T4 genotype-15]	Poly-hexamethylene biguanide, chlorhexidine digluconate eye drops (0.02%)	Restoration of vision	[25]
13	59-year-old-female presented with corneal ulcer with history of trauma	Corneal scraping	<i>Acanthamoeba</i> spp.	Chlorhexidine digluconate eye drops (0.02%)	Restoration of vision	[26]

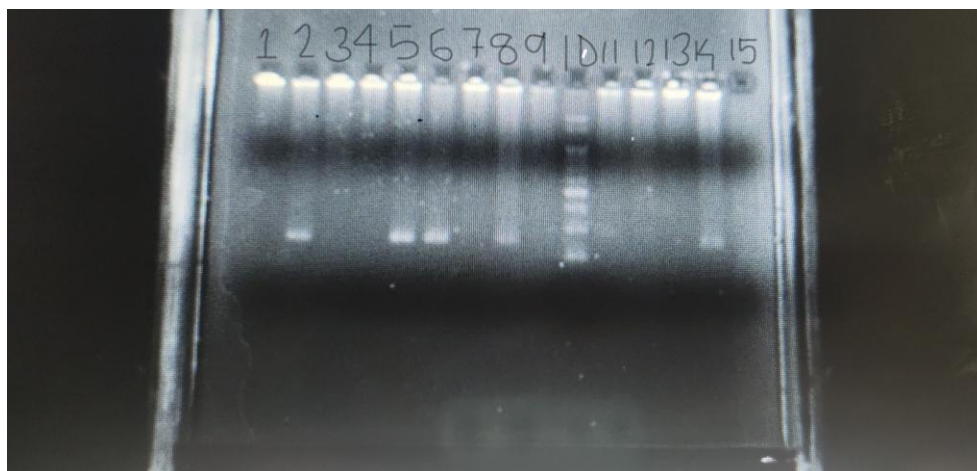


Figure 1. 1.5% agarose gel electrophoresis showing 180 bp band corresponding to that of *Acanthamoeba* genus.

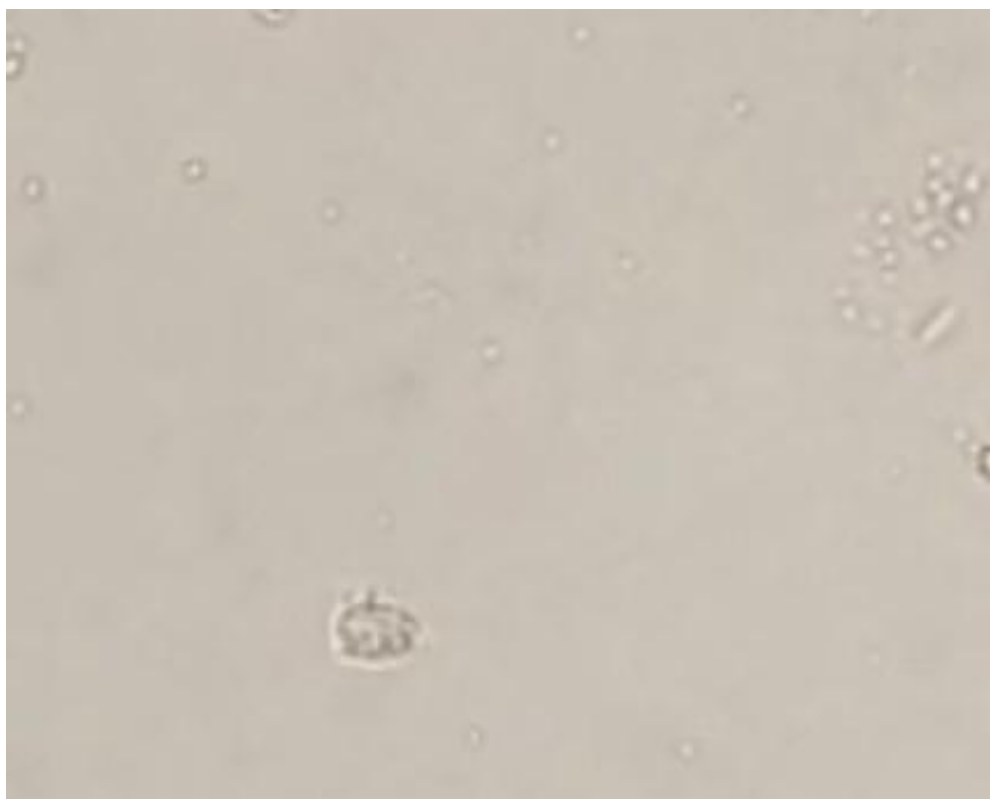


Figure 2. Wet mount examination of CSF on light microscope showed sluggishly motile structures with spine like projections.

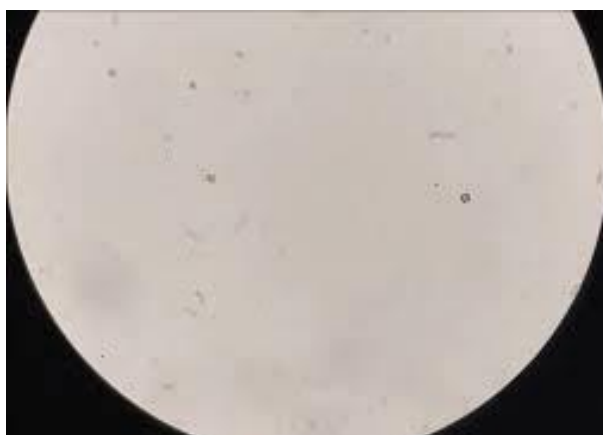


Figure 3. Still shot from the film showing wet mount examination of CSF under the light microscope with 6-8 lymphocytes per high power field and sluggishly motile structures with spine like projections. Published on the official WJOMI YouTube channel: <https://youtu.be/zLcNHLe0Gpk>



Conclusion

Considering his illness, two other panel of markers were used to exclude auto-immune encephalitis, if at all. Following auto immune encephalitis marker panel was found to be negative

- a) NMOSD (Neuromyelitis optica spectrum disorder) and MOG (Myelin oligodendrocyte glycoprotein) with NMO Aquaporin 4 Ab+ MOG antibodies (Immunofluorescence);
- b) Auto-immune encephalitis mosaic (NMDA, VGKC, AMPA 1&2, GABA: Immunofluorescence).

No other immune disorders were detected in this apparently healthy patient.

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Conflict of interest: none declared.

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