Case Report

Granulomatous amoebic encephalitis in an immunocompetent young female: A rare case with microbiological confirmation and survival

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ABSTRACT

Granulomatous amoebic encephalitis (GAE) is an uncommon but life-threatening central nervous system infection caused by *Acanthamoeba* species. It predominantly affects immunocompromised individuals, although cases in immunocompetent hosts are increasingly reported. We present the case of a 23-year-old previously healthy female who developed fever, severe headache, diplopia, vomiting, and altered sensorium. Magnetic resonance imaging showed mild cerebral atrophy, and cerebrospinal fluid (CSF) analysis revealed markedly elevated leukocyte count with mildly raised protein. CSF wet mount and Giemsa stain demonstrated trophozoites of *Acanthamoeba* with acanthopodia. Culture and other routine CSF tests were negative. The patient was treated with a combination of fluconazole, cotrimoxazole, rifampicin, and miltefosine and showed a significant improvement. She was discharged in stable condition. This case underscores the importance of clinical suspicion, timely diagnosis using microscopy, and the effectiveness of multidrug therapy in managing this otherwise fatal condition.

Key words: *Acanthamoeba*, Central nervous system, Encephalitis, Granulomatous, Miltefosine, Trophozoites

Granulomatous amoebic encephalitis (GAE) is a rare and often fatal central nervous system (CNS) infection caused by *Acanthamoeba* species, free-living amoebae that are widely distributed in soil, freshwater sources, contaminated contact lens solutions, and air-conditioning units. The organism primarily infects immunocompromised individuals but can occasionally affect immunocompetent hosts. Clinical manifestations are non-specific and may mimic other forms of chronic meningitis or encephalitis, making early diagnosis challenging. A high index of suspicion and early microscopic identification of the trophozoites in cerebrospinal fluid (CSF) are essential for prompt treatment and better outcomes. GAE is exceptionally rare, with approximately 75 *Acanthamoeba*-associated cases reported worldwide since 1990, nearly half of which originate from India [1,2]. In the United States, the incidence is estimated at <30 cases annually, with mortality rates ranging above 90% [3-6].

This case is reported for its rarity, confirmed microbiological diagnosis in an immunocompetent host, and successful outcome following combination antimicrobial therapy.

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CASE REPORT

A 23-year-old woman, previously healthy and well-functioning, was brought to the emergency department of a hospital in Eastern India with a constellation of alarming symptoms: high-grade fever, excruciating headache, persistent vomiting, double vision, and an altered mental state. Just days earlier, she had been functioning normally, with no signs of any underlying illness. The patient had initially visited multiple peripheral hospitals over 10 days for fever, headache, and vomiting, with diplopia for the past 5 days, before presenting to our center on December 11, 2023, with altered sensorium, where the diagnosis was confirmed and treatment initiated within 24 h. There was no significant past medical history, no immunocompromising condition, and no recent hospital admissions or surgeries. What stood out, however, was her casual mention, almost an afterthought, of frequently bathing in the local ponds near her home.

On admission, vitals were: temperature 39°C, pulse 102/min, blood pressure 110/60 mmHg, respiratory rate 18/min, SpO_2 92% on room air. Within hours of admission, her condition deteriorated dramatically. She slipped into a comatose state, forcing clinicians to act swiftly. A magnetic resonance imaging scan was

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performed, revealing mild cerebral atrophy without focal enhancing lesions or mass effect. No hydrocephalus or midline shift was noted. With a provisional diagnosis of meningitis, CSF was urgently obtained via lumbar puncture and sent for comprehensive microbiological analysis.

The initial CSF profile showed a markedly elevated white blood cell count of 2200 cells/mm^3, predominantly neutrophils, a mildly elevated protein concentration, and near-normal glucose levels. Despite the inflammatory profile, routine microbiological investigations revealed nothing. Gram stain was negative for organisms. Ziehl–Neelsen (ZN) and modified ZN stains failed to show acid-fast bacilli. India ink preparation yielded no encapsulated organisms. Culture for bacteria and fungi was sterile, and GeneXpert testing for *Mycobacterium tuberculosis* was also negative. The diagnostic trail had gone cold.

It was during this window of uncertainty, as the clinical team grappled with possibilities ranging from viral encephalitis to autoimmune disease, that a wet mount saline preparation of the CSF was examined under the microscope. What emerged under high-power illumination was unexpected, motile trophozoites with thorn-like projections, the characteristic acanthopodia (Fig. 1a). The discovery was confirmed with Giemsa staining, which vividly highlighted the amoeboid forms of *Acanthamoeba* (Fig. 1b).

A diagnosis of GAE was made, a rare and often fatal infection, especially in immunocompetent individuals like her. The diagnosis was met with urgency and cautious optimism. A combination antimicrobial regimen was initiated immediately, comprising fluconazole, cotrimoxazole (trimethoprim-sulfamethoxazole), rifampicin, and miltefosine drugs with *in vitro* and anecdotal clinical success against *Acanthamoeba*.

Over the next few days, the patient's response was nothing short of remarkable. From the abyss of unconsciousness, she gradually began to show signs of neurological recovery. Her fever subsided, sensorium improved, and by the end of the 2nd week, she was fully awake and communicative. After 3 weeks of hospitalization, she was discharged in stable condition with instructions for follow-up and long-term monitoring.

Since discharge, the patient has been on regular outpatient follow-up and remains neurologically intact with no residual deficits.

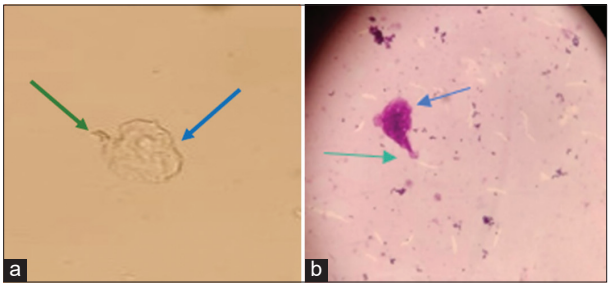

Figure 1: Microscopic visualization of *Acanthamoeba* trophozoites in cerebrospinal fluid. (a) Direct saline wet mount showing a motile trophozoite of *Acanthamoeba* with central nucleus (blue arrow) and characteristic spine-like projections known as acanthopodia (green arrow). (×400 magnification); (b) Giemsa-stained smear of cerebrospinal fluid (CSF) highlighting the trophozoite (blue arrow) with prominent acanthopodia (green arrow) in better contrast against the stained background. These findings confirm the presence of *Acanthamoeba* in CSF and are diagnostic of granulomatous amoebic encephalitis. (×1000 oil immersion)

DISCUSSION

Acanthamoeba spp. are free-living amoebae known to cause three major forms of human disease: keratitis, disseminated systemic infections, and GAE. While GAE is classically associated with immunocompromised states such as acquired immunodeficiency syndrome, hematological malignancies, or post-transplant immunosuppression, a growing body of literature, along with the current case, demonstrates that even immunocompetent individuals can develop fulminant CNS involvement, often triggered by environmental exposure to contaminated freshwater.

The clinical course of GAE is typically insidious in onset but rapidly progressive, making early recognition particularly challenging. Initial symptoms such as headache, vomiting, altered mental status, or cranial nerve deficits are non-specific and frequently mimic more common CNS infections such as tubercular meningitis, viral encephalitis, or bacterial meningoencephalitis. In this case, the diagnosis was established through direct saline wet mount microscopy and confirmed by Giemsa staining, underscoring the continued relevance of basic parasitological techniques, especially in resource-limited settings where advanced diagnostics may not be readily available.

Granulomatous amoebic meningoencephalitis, caused by *Acanthamoeba* spp. or *Balamuthia mandrillaris*, is associated with devastating outcomes and high mortality. Although clinical experience is limited, case reports emphasize the role of early diagnosis, surgical intervention where feasible, and timely initiation of multidrug regimens.

Despite aggressive therapeutic efforts, reported survival rates remain dismally low [7-10]. Management strategies typically focus on early clinical recognition, surgical intervention to decompress or excise CNS lesions, and a prolonged, multidrug approach. The antimicrobial combinations commonly include miltefosine, voriconazole, albendazole, sulfamethoxazole-trimethoprim (cotrimoxazole), azithromycin, and, in some cases, fluconazole [7,8,11-13].

This case further illustrates that a high index of clinical suspicion, prompt identification of the amoebic trophozoites, and timely initiation of combination antimicrobial therapy may significantly alter outcomes, even in otherwise fatal conditions. However, the rarity of such cases, lack of standardized guidelines, and absence of randomized trials emphasize the need for enhanced clinician awareness and global collaboration to develop evidence-based protocols for managing this formidable infection.

Although standardized guidelines are lacking, an increasing number of case reports and systematic

Table 1: Diagnostic and therapeutic strategies in GAE

Aspect	Modality/approach	Details/comments
Diagnostic modalities	Clinical suspicion	Based on subacute meningoencephalitis symptoms, especially in immunocompromised or freshwater-exposed individuals
	Neuroimaging (MRI/CT)	May show cerebral edema, enhancing lesions, hydrocephalus, or cerebral atrophy; findings are non-specific
	CSF analysis	Elevated WBC count (neutrophilic or lymphocytic), elevated protein, near-normal glucose; helps exclude other causes
	Wet mount microscopy (saline)	Detects motile trophozoites with acanthopodia; quick, low-cost, essential in early diagnosis
	Giemsa or trichrome staining	Enhances visualization of amoebic structures (trophozoites); useful in resource-limited settings
	Culture on non-nutrient agar with *Escherichia coli* overlay	Takes several days; rarely performed in acute clinical settings
	PCR and molecular testing	Species identification; highly specific and sensitive but limited to advanced centers
	Brain biopsy/histopathology	Confirms granulomatous inflammation; invasive, usually post-mortem or when diagnosis is unclear
Treatment approaches	Empirical combination therapy	Multidrug regimens are essential due to lack of standardized treatment. Commonly used agents: • Miltefosine • Voriconazole • Albendazole • Trimethoprim-Sulfamethoxazole (Cotrimoxazole) • Azithromycin • Fluconazole
	Duration of treatment	Prolonged therapy over several weeks to months; guided by clinical, radiological, and microbiological response
	Surgical intervention	Neurosurgical excision or decompression may be considered in patients with localized granulomas or raised intracranial pressure
	Supportive management	Includes management of raised intracranial pressure, seizure control, fluid-electrolyte balance, and intensive care support when required
	Adjunctive/experimental therapies	Investigational approaches include: • Drug repurposing (e.g., chlorpromazine, rifampicin) • Curcumin-gold conjugates • Nanoparticle-based delivery systems (currently experimental)
	Monitoring and follow-up	Survivors require long-term neurological, cognitive, and functional assessments; imaging may help assess resolution or recurrence.

GAE: Granulomatous amoebic encephalitis, MRI/CT: Magnetic resonance imaging/computed tomography, CSF: Cerebrospinal fluid, WBC: White blood cells, PCR: Polymerase chain reaction

reviews suggest that early surgical excision combined with multidrug regimens may offer survival benefits in select patients [8,11,13,14]. However, most individuals still experience a fulminant and ultimately fatal disease trajectory. Innovative therapeutic approaches, such as drug repurposing, curcumin-gold conjugates, and nanotechnology-based delivery systems, are currently under experimental exploration [15-17].

Overall, early diagnosis, aggressive medical management, and timely neurosurgical intervention offer the best, though still limited, chance of survival as outlined in Table 1. This underscores the critical need for greater awareness among clinicians, improved access to rapid diagnostics, and development of more targeted therapies for these often-overlooked and fatal infections [7-9].

CONCLUSION

GAE remains one of the most devastating CNS infections, with extremely high mortality despite advances in diagnostic and therapeutic approaches. This case underscores that even immunocompetent individuals are not immune to the disease, particularly following environmental exposure, and that timely microbiological diagnosis using simple wet mount and Giemsa staining can be lifesaving in resource-limited settings. The successful outcome highlights the importance of maintaining a high index of suspicion, initiating aggressive multidrug therapy without delay, and considering surgical intervention in selected cases. Greater clinician awareness, improved access to rapid diagnostics, and collaborative research are urgently needed to develop standardized treatment protocols for this often overlooked but fatal infection.

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