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Review Article

Amoebic Meningoencephalitis: A Growing Concern

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Abstract

Amoebic meningoencephalitis is a rare but deadly brain infection caused by free-living amoebae, primarily *Naegleria fowleri*. It manifests as primary amoebic meningoencephalitis (PAM) or granulomatous amoebic encephalitis (GAE), with PAM being the more aggressive form. Infection occurs through nasal exposure to warm freshwater, leading to rapid onset of severe symptoms and high mortality. Diagnosis is challenging and involves imaging, cerebrospinal fluid analysis, and microbiological tests. Treatment options are limited but include repurposed antifungals and investigational drugs. Prevention focuses on avoiding contaminated water and proper pool maintenance. Enhanced awareness and early diagnosis are key to improving outcomes.

Keywords: Amoebic Meningoencephalitis; *Naegleria fowleri*; Granulomatous Amoebic Encephalitis

Introduction

Amoebic encephalitis is a rare yet deadly infection of the central nervous system, caused by free-living amoebae commonly found in freshwater sources like lakes and rivers. This infection manifests in two forms: primary amoebic meningoencephalitis (PAM) and granulomatous amoebic encephalitis (GAE). PAM, most often caused by the "brain-eating" amoeba *Naegleria fowleri*, is notorious for its aggressive destruction of brain tissue, leading to severe swelling and, in the majority of cases, death. Although it predominantly affects healthy children, teens, and young adults, PAM is particularly challenging to diagnose early, as its initial symptoms are similar to those of bacterial meningitis. GAE, on the other hand, can mimic a brain abscess, encephalitis, or meningitis, making both conditions extremely difficult to treat effectively [1]. Despite their rarity, cases of PAM and GAE have been documented worldwide, with the first known case of PAM reported in Australia in 1965. Since then, the disease has been observed more frequently in warmer climates, especially during spring and summer. Recently, Kerala has seen a concerning rise in amoebic meningoencephalitis, with 15 cases reported in 2024 alone, five of which were fatal, underscoring the devastating impact of this rare infection [2].

Etiology

Naegleria fowleri is a heat-loving amoeba found globally, particularly in warm freshwater like lakes, rivers, and hot springs. It thrives in water temperatures up to 115°F, especially during the summer months of July to September when prolonged heat raises water temperatures and lowers levels [3]. Although rare, infections typically occur when swimming or diving in warm freshwater. In some cases, infections have also been linked to using contaminated tap water for nasal irrigation. However, *Naegleria fowleri* cannot infect individuals by drinking contaminated water, swimming in properly maintained pools, or through person-to-person contact [3].

Pathophysiology

N. fowleri infection begins when the amoeba enters the nasal cavity through activities like diving or splashing in water. It then travels along the olfactory nerves, crossing the cribriform plate to reach the brain. The infection presents symptoms similar to meningitis, such as fever, headache, and stiff neck, and may include seizures. Known as the "brain-eating amoeba", *N. fowleri* destroys neurons and triggers an inflammatory response, leading to severe tissue damage. The amoeba employs mechanisms like protein secretion and immune evasion, resulting in acute necrotizing meningoencephalitis, which is often fatal due to increased intracranial pressure and brain herniation [4].an amoeba which resides in freshwater lakes and ponds and can survive in inadequately chlorinated pools (Lopez, C.; Budge, P.; Chen, J., et al. Primary amebic meningoencephalitis: a case report and literature review. Pediatr. Emerg. Care 2012, 28, 272–276

Life cycle of *N. fowleri*

The amoeba exists in three forms: cyst, trophozoite, and flagellated. The trophozoite stage is infectious, multiplying under favourable conditions Clinically, the infection manifests in two stages: early symptoms include headache, fever, nausea, and vomiting; as the infection progresses, it leads to severe neurological symptoms like stiff neck, confusion, seizures, and coma. The risk factors highlighted include swimming in contaminated water bodies and exposure to splashed tap water containing the amoeba [5].

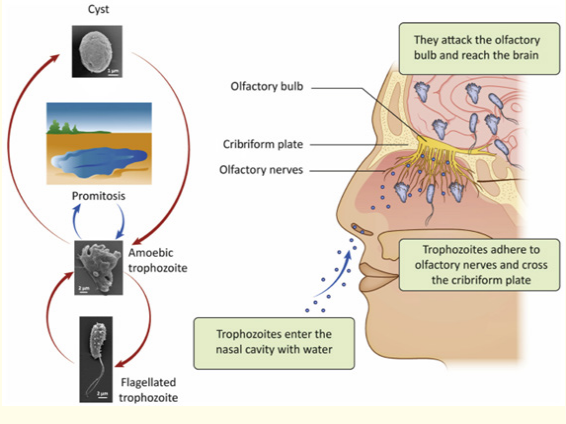

Figure 1: Life cycle of *N. fowleri* and pathophysiology.

Symptoms

PAM typically begin around five days after infection and start mildly but worsen rapidly. Early signs include headache, fever, nausea, and vomiting. As the disease progresses, more severe symptoms may appear, such as a stiff neck, confusion, lack of attention to surroundings, loss of balance, seizures, and hallucinations. Once symptoms manifest, the disease can quickly become fatal, often leading to death within five days. If someone experiences sudden fever, headache, stiff neck, and vomiting—especially if they have recently been in warm freshwater—they should seek immediate medical attention [3].

Diagnosis

Diagnosing amoebic meningoencephalitis is challenging due to its rarity and the non-specific nature of early symptoms. However, a high index of suspicion is crucial for timely diagnosis. The diagnostic process typically involves a combination of imaging studies, cerebrospinal fluid (CSF) analysis, and microbiological tests.

Imaging studies

Computed tomography (CT) scans and magnetic resonance imaging (MRI) can reveal brain abnormalities consistent with meningoencephalitis, such as brain edema or focal lesions. However, these findings are not specific to amoebic infections [4].

Cerebrospinal fluid (CSF) analysis

CSF analysis may show elevated white blood cell counts, increased protein levels, and decreased glucose levels. The presence of amoebae in the CSF, detected by wet mount microscopy, is a key diagnostic finding. Molecular techniques, such as polymerase chain reaction (PCR), can also be used to identify amoebic DNA in the CSF [6].

Microbiological tests

Culture techniques can isolate the amoebae from CSF or brain tissue samples, although this is time-consuming and often impractical in acute cases. Immunofluorescence assays and enzyme-linked immunosorbent assays (ELISA) can aid in the identification of specific amoebic antigens [6].

Treatment

Currently, there are no specific therapeutic drugs available for infections caused by Free-Living Amoebae (FLA). However, repurposed drugs, such as antifungal agents including amphotericin B, fluconazole, and miconazole, may offer potential treatment options. Additionally, antibiotics like paromomycin, polymyxin B, and sulfadiazine could be effective against Acanthamoeba infections. Due to the widespread presence of these parasites, eradicating them from the environment is challenging. Nevertheless, chlorinating water can help prevent infections during swimming [7]. South India, are creating ripples among medical and health administrations. Free-living amoebae (FLA

Miltefosine, available through the CDC as an investigational drug for treating primary amoebic meningoencephalitis (PAM), is an alkylphosphocholine initially developed as an antineoplastic agent and is now used to treat leishmaniasis. Although its precise mechanism of action against *Naegleria fowleri* is not fully understood, it is thought to affect cellular membranes by interacting with steroids and phospholipids, and it may also exert inhibitory effects on protein kinase B [4]. Another promising candidate is Nitroxoline, which has shown low micromolar activity against both trophozoite and cyst stages of *N. fowleri,* along with a favourable selectivity index, making it a strong candidate for alternative PAM treatment [8].

Prevention

Preventing amoebic meningoencephalitis is challenging due to the ubiquity of free-living amoebae in natural environments. However, certain preventive measures can reduce the risk of infection:

- **Avoiding Freshwater Exposure**: Individuals, particularly those in endemic areas, should avoid swimming in warm freshwater bodies, especially during periods of high-water temperature.
- **Nasal Protection**: When engaging in water activities, such as swimming, diving, or using neti pots, individuals should use nose clips or avoid submerging their heads to prevent water from entering the nasal passages.
- **Proper Pool Maintenance**: Swimming pools and hot tubs should be adequately chlorinated and maintained to prevent amoebic contamination.
- **Education and Awareness**: Public health campaigns can raise awareness about the risks of amoebic meningoencephalitis and encourage preventive measures, particularly in regions where the infection is more common.

Conclusion

Amoebic meningoencephalitis is a devastating and often fatal brain infection caused by free-living amoebae. While rare, the disease poses significant challenges due to its rapid progression, difficulty in diagnosis, and limited treatment options. Increased awareness, early diagnosis, and the development of more effective therapies are essential in improving outcomes for those affected by this deadly condition.

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