Primary Amoebic Meningoencephalitis – A Case Review

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Abstract: Primary amoebic meningoencephalitis (PAM) is a rare but fatal Central Nervous system infection caused by *Naegleria fowleri.* It is a free-living amoeba that lives in soil and warm fresh water like lakes, rivers, streams, hot springs, unchlorinated swimming pools and ponds. Patients with PAM typically have a history of swimming, diving, bathing, surfing or playing in warm, generally stagnant freshwater. Symptoms are like meningitis and include headache, fever, nausea, vomiting, a stiff neck, confusion, changes in mental status, hallucinations and seizures. Onset of symptoms begins one to twelve days following exposure with *Naegleria fowleri*. PAM develops in healthy young individuals exposed to warm freshwater. This infection is almost uniformly fatal with only few reported survivors globally. Here we review a 23year-old male patient who presented with severe head ache, fever, myalgia and vomiting and PAM was diagnosed following a comprehensive checkup.

Keywords: Primary amoebic meningoencephalitis, Naegleria fowleri, Meningitis

INTRODUCTION:

Naegleria fowleri infections are rare and devastating. Primary Amoebic Meningoencephalitis (PAM) is caused by *Naegleria fowleri,* a thermophilic, free-living amoeba also known as "brain-eating amoeba." This lives in temperatures above 30^0 C and can tolerate temperatures up to 45^0C. It is typically found in freshwater, lakes, pond and rivers. PAM have occurred when people go swimming in warm fresh water or rinse their sinuses or nasal passages with water containing *Naegleria fowleri.* Symptoms typically start about 5 days after a person is exposed to *Naegleria fowleri and* early symptoms are headache, nausea, vomiting and fever. The infection can progress rapidly, causing death within ten days and the mortality rate is above 90%, despite antimicrobial therapy. An infection from *Naegleria fowleri* cannot be spread from one person to another.

DEFINITION:

Primary Amoebic Meningoencephalitis is an acute, fulminant and fatal central nervous system infection caused by *Naegleria fowleri*.

SYNONYMS:

Amoebic meningitis

Amoebic encephalitis

Naegleriasis

INCIDENCE AND PREVALENCE:

In recent years, the number of cases reported have raised, likely as a result of greater awareness of disease or due to development of more rapid, highly sensitive and specific diagnostic tests. About 300 cases have been reported up to now with high case fatality rate of around 95%. On August 8, 2024, Kerala has stated 15 cases of amoebic meningoencephalitis (PAM), since January 2024, with five deaths. The cases have been reported from various parts of the state, including Thiruvananthapuram, Malappuram, Kozhikode, Kannur, and Thrissur. The majority of cases have been in adolescents, with a male-to-female ratio of 3:2 Only 11 survivors of confirmed PAM have been documented in the literature.

ETIOLOGY/ RISK FACTORS:

PAM caused by Naegleria fowleri, commonly occur after someone goes swimming or diving in a lake, river, pond or other fresh water during summer months. A few infections have occurred when people used tap water that contaminated by Naegleria fowleri to rinse their sinuses or cleanse their nasal passages. You cannot get PAM from swallowing / drinking water containing *Naegleria fowleri.*

PATHOPHYSIOLOGY:

PAM occurs in healthy young individuals brought in to contact with warm freshwater. *Naegleria fowleri* infects susceptible individuals when contaminated water enters the body through the nose. Trophozoites (the vegetative or feeding stage of the amoeba and is the infective form) penetrate the olfactory mucosa, cross the cribriform plates, and ultimately reach the olfactory bulb. As

a result of an amplified host immune response causing an exaggerated inflammatory reaction, necrotizing encephalitis and subsequent parenchymal damage.

Clinical Stage I: Nasal Stage (Pre-Cerebral Stage)

N. fowleri gains entry into the human host via the nose and proceeds the nasal passage. The introduction of water deep into the nasal orifice causes the protist to encounter the nasal mucosa, leading likely to infection.

Clinical Stage II: Olfactory stage

In certain cases, N. fowleri advances from nasal mucosa to olfactory mucosa and bulb. The involvement of the olfactory mucosa and olfactory bulb is a transient stage before the involvement of the brain. This stage is heralded by changes in the olfactory perception (parosmia).

Clinical Stage III: Meningoencephalitic stage

N. fowleri causes neuronal injury, both through direct cell damage, and by the release of cytotoxic proteins. Cellular debris and these proteins lead to an inflammatory response involving cytokine release, which mediates further tissue damage. The final stage in the pathogenesis of N. fowleri infection is rapidly progressing meningo-encephalitis. The patient presents in this stage after 1 to 2 days from the olfactory stage described above. Herniation and cerebral edema occur due to a severe inflammatory response.

SIGNS AND SYMPTOMS:

The clinical presentation of PAM is often similar to bacterial meningitis with headache, fever, nausea and vomiting. Symptoms can be mild at first, but they worsen quickly. Usually start about 5 days after infection (but can range from 1 to 12 days) • The earliest symptoms are sudden onset of bifrontal or bitemporal headaches, high fever, nausea, or vomiting • Nuchal rigidity usually occurs with positive Kernig and Brudzinski signs. Alterations in taste and smell may occur initially because of involvement of the olfactory nerve. Photophobia may occur late in the clinical course, followed by neurological abnormalities, including lethargy, seizures, confusion, coma, diplopia or bizarre behaviour. The disease progresses rapidly with increased intracranial pressure leading to uncal herniation and death. PAM causes death within about 5 days (but can range from 1 to 18 days).

DIAGNOSTIC FINDINGS:

Clinicians should have a high index of suspicion for PAM in the setting of acute meningoencephalitis with negative results for bacteria and common viruses, which should prompt the search for amoebae in the CSF. A history of exposure increases the likelihood of PAM, but it is not always obtained. In the current Kerala context, any person with an epidemiological link should be immediately suspected of having PAM. The diagnosis of PAM is generally established via observation of motile trophozoites on examination of a CSF wet mount preparation immediately after obtaining the sample. A polymerase chain reaction (PCR) from the CSF facilitates rapid detection. Serology is not useful for diagnosis.

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are nonspecific. Brain edema, basilar meningeal enhancement, hydrocephalus, and areas of cerebral infarction have been described. Brain tissue can be examined for trophozoites, and brain sections can be stained with immunofluorescent anti-N. fowleri antibodies.

Differential diagnosis

PAM must be distinguished from acute bacterial meningitis. The clinical manifestations and CSF findings of these two entities are similar. Epidemiological exposure may be useful in differentiating the two conditions.

MANAGEMENT:

The optimal approach to treatment of PAM due to N. fowleri is uncertain; no studies evaluating the potency of single-drug or combination-drug regimens have been performed. The rarity of the disease, delay in diagnosis, fulminant clinical course, and the difficulties in making a rapid diagnosis have hindered the evaluation of drug regimens. In theory, the best drug regimen should include an amoebicidal drug (or a combination of drugs) with good in vitro activity that is capable of crossing the blood-brain barrier. considering the fulminant course of the disease and high mortality rates, a combination of drugs is generally used. Reports include the use of amphotericin in addition to rifampicin, fluconazole, miltefosine, and azithromycin.

- Conventional amphotericin B (1.5 mg/kg/day intravenously [IV] +/- intrathecally)
- Rifampicin (rifampicin; 10 mg/kg/day orally in three divided doses or every 24 hours)
- Fluconazole (10 mg/kg/day IV or orally).

Supportive treatment

Supportive therapy aimed at reducing intracranial pressure is equally important. In the survivors, along with antimicrobials, aggressive treatment for cerebral edema and the resulting elevated intracranial pressure with dexamethasone, CSF drainage via an external ventricular drain, hyperosmolar therapy with mannitol and 3% saline, moderate hyperventilation ($PaCO_2$ 30-35 mm Hg), and induced hypothermia (32–34°C) etc. were implemented.

PREVENTION:

Measures to prevent primary amoebic meningoencephalitis include the following:

- Avoidance of diving and jumping into stagnant freshwater.
- Consider using nose plugs for unavoidable exposures or pinching your nose shut when diving or swimming in freshwater.
- Keep your head above water when swimming in freshwater, hot springs, and other untreated thermal bodies of water.
- When participating in water-related activities, avoid digging, or stirring up the sediment.
- Use boiled, filtered, or sterile water for nasal or sinus irrigation, not tap water.
- Wading pools should be emptied each day
- Swimming pools/water theme parks and spas should be kept clean, chlorinated and maintained correctly
- keep sprinklers and hoses away from noses.
- Flush still water from hoses before letting children play with them

CDC's *Naegleria fowleri* Program provides 24/7 diagnostic assistance, specimen collection guidance, shipping instructions, and treatment recommendations.

PROGNOSIS:

PAM is associated with an extremely high mortality rate. Studies have reported a case-fatality rate of as high as 99%. The mean time from onset of symptoms to death was 5.3 days (range from 1 to 12 days). However, in July 2024, a 14-year-old boy from Kozhikode recovered from PAM after a comprehensive treatment at Baby Memorial Hospital.

CASE REPORT:

The present report investigates the journey of the patient with PAM, through identification and management by discussion of health history, investigations and current management of the clinical problems. The report is intended to create awareness among health care providers regarding the condition to be competent to deliver comprehensive nursing care and supportfor the patient as well as family.

CASE PRESENTATION:

A 23-year-old man came to a tertiary care hospital in Kerala on August 2, 2024, with initial symptoms of fever for two days, severe headache, myalgia and vomiting for one day. No history of seizures / altered sensorium. He had h/o swimming and bathing in a pond along with his brother, who died one week ago due to Amoebic encephalitis. He swims in the pool regularly that's also a popular spot for animals. On examination patient was conscious and oriented, vitals were stable. He had stiffness of neck and bilateral down going planters. He got admitted in MICU for comprehensive management.

PAST HISTORY:

No relevant past history of Amoebic meningitis or any other infections

FAMILY HISTORY:

There is a relevant family history of Amoebic meningitis, his brother died due to Amoebic meningitis.

INVESTIGATIONS:

Laboratory results revealed leucocytosis. CSF sample sent for microscopic examination, chemical testing, and bacterial culture. CSF sample was slightly turbid, and test results showed high levels of protein and glucose. A wet mount of the CSF showed trophozoite forms of an amoeba. ECG was done for cardiac evaluation and it was normal. CT Brain (plain) result revealed no significant MLS, no diffuse brain edema and no gross intra cerebral bleed.

CURRENT HEALTH STATUS:

Patient is conscious and oriented. Vitals are stable. Now patient has mild headache and neck rigidity. He has no fresh complaints.

MANAGEMENT:

The patient received intravenous Amphotericin B Deoxycholate 50 mg in 500 ml of 5% Dextrose over 10 hrs followed by Inj. Amphotericin B Deoxy cholate 50 mg in 500 ml of 5% Dextrose over 10hrs followed by 500 ml NS infusion. He was managed with combination therapy such as Inj. Azithromycin 500mg IV OD, Inj. Fluconazole 600mg IV OD, Inj. Rifampicin 600 mg IV OD, Inj. Dexamethasone 8 mg IV, Inj. Mannitol 20% 100 ml BD, Inj. Pantoprazole 40 mg IV OD, T. Miltefosine 50 mg thrice a day.

DISCUSSION:

As mentioned earlier, PAM has been infrequently reported in Indian medical literature. The index patient is a noticeable case of PAM because the patient shows classic manifestations of PAM such as headache, fever, nausea, vomiting, and stiff neck. Laboratory test, CSF analysis and imaging studies were carried out to diagnose the case. Now the patient is getting the combination therapy as well as supportive treatments. The survival of the index case could be multifactorial: firstly, a high index of suspicion brought about an early diagnosis within 24 hours from seeking care to ICU admission; secondly, he received a combination of antimicrobial drugs, including miltefosine, amphotericin B, rifampicin, and azithromycin, administered within 2 hours of diagnosis and within 48 hours after onset of symptoms.

CONCLUSION:

Primary Amoebic Meningoencephalitis is a rare but fatal disease. A high index of suspicion, early diagnosis, and aggressive combination therapy can help to prevent death and long-term illness.

REFERENCE:

1. Maciver SK, Pinero JE, Lorenzo-Morales J. Is Naegleria fowleri an Emerging Parasite. Trends Parasitol. 2020 Jan;36(1):19-28. [PubMed]
2. Epidemiology and Clinical Characteristics of Primary Amoebic Meningoencephalitis Caused by Naegleria fowleri: A Global Review Radhika Gharpure, John Bliton, Alexandra Goodman, Ibne Karim M. Ali, Jonathan Yoder, and Jennifer R. Cope: Clinical Infectious Diseases · May 2020.
3. https://www.cdc.gov/parasites/naegleria/health_professionals.html
4. Ahmed Mujadid Khan Burki, Luqman Satti, Saira Mahboob, Syed Onaiz Zulfiqar Anwar, Mahwash Bizanjo, Muhammad Rafique, and Najia Karim Ghanchi Successful Treatment of Confirmed *Naegleria fowleri* Primary Amebic Meningoencephalitis. EID Journal. Volume 30, Number 4;April 2024.
5. *Chelsea Marie, William A. Petri, Jr* . Amoebic Brain Infection: Primary Amoebic Meningoencephalitis. *University of Virginia School of Medicine; Reviewed/Revised Mar 2023*.

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