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A REVIEW ON PRIMARY AMEBIC MENINGOENCEPHALITIS (PAM) CONTROL AND MANAGEMENT

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ABSTRACT

The severe and rare disease known as primary amoebic meningoencephalitis is caused by the free-living, thermophilic amoeba Naegleria fowleri, which inhabits freshwater systems. PAM is an infection of the brain that spreads quickly and is lethal. It destroys brain tissue, which ultimately results in death.

Primary amoebic meningoencephalitis (PAM) is a type of amoebic encephalitis.

PAM 's high death rate raises questions about its potential effects on world health. Numerous instances reported in Pakistan, particularly in Karachi, involve daily ablution with tap water but no history of contact to water for recreational purposes.

This study analyzed the physicochemical parameters, abundance of total and faecal coliforms, and detected Using ITS- and Naegleria primers, PCR was used to identify Naegleria species, including N. fowleri, were found in tap water samples from Karachi. High temperatures, low chlorine levels, and a high coliform presence were seen in nearly all samples. Eleven of the 39 samples contained N. fowleri and additional Naegleria species.N. fowleri was found in tap water from the Golimar and Lyari neighbourhoods of Karachi, according to sequence analysis, whereas the other nine samples contained other Naegleria species. This study suggests that the combination of high temperatures, insufficient chlorination, and the presence of coliforms may create favourable conditions for N. fowleri growth.

These features, however, are not unique to the Golimar and Lyari areas, suggesting that the occurrence of other environmental or infrastructure elements not included in this study might

have had an impact on fowleri in that specific area.

Naegleria fowleri is free living the thermophilic bacteria which occurs in warm fresh water swiming pool or in tap water, bacteria enter through nasal passage only after came in contact with polluted water, Although PAM is uncommon, 381 cases have been documented in medical literature as of 2018. It is also very lethal in 2024, and there have also been reports of unrelated diseases.

PAM remains an neglected disease but its pre-diagnosis and intensive combination therapy can manage this fatal infection.

- **INTRODUCTION**

PAM is a disease caused by naegleria fowleri, a microscopic amoeba commonly called a brain eating bacteria or amoeba.

In this brain tissue gets damaged which causes severe brain swelling and leads to death in many cases. It occurs in all age groups like healthy children's, teens and young adults. PAM occurs when peoples swim in bodies of warm fresh water or swimming pool which is not chlorinated where naegleria fowleri might be present, contact with contaminated water sources through nasal passage is main route of infection leading to purulent hemorrhagic inflammation and necrotic changes in olfactory bulb and brain tissue which causes CNS damage.

After the onset of PAM, the survival rate is extremely low (>95%mortality rate) since there are no effects, no medication available. The patient dies within 3 to 7 days.

Proper diagnosis and combinational therapy prevent infection but in early diagnosis.3 children, in Kerala have died since May 2024, a five year old girl from Malappuram, a 13 year girl According to reports, a 15-year-old boy from Payyoli, a 14 Year-old boy from Kozhikode, and a Kannur youngster are also getting treatment for the infection.

The main issue withPAM is the less information and awareness among people, as it is not known to many people even in major countries. Even if there is a patient who might have PAM that patient might get diagnosed with a different disease and get different medication. This results in severity of the symptoms and worsens the infection in the patient.

1. Transmission

Naegleria fowleri infects people with contaminated water, which enters the body through the nasal passage(nose), typically during swimming or diving in warm freshwater places. Naegleria fowleri infection is not contagious which means it cannot be spread from one person to another. The infection's actual "primary" location is the upper respiratory tract. Children and young adults who swim in lakes or rivers account for the majority of patients with Naegleria CNS infections. The cribriform plate allows N. fowleri to access the brain, where it infects the nasal mucosa before moving along the olfactory nerve. After reaching the brain, Naegleria fowleri usually infects people when contaminated water enters the body through the nose typically during swimming or diving in warm freshwater place.

2. Morphology & lifecycle

2.1 Morphology

Naegleria fowleri has 3 stages in its life cycle i.e, cyst, trophozoite, and cyst. Trophozoite:
The only stage of Naegleria fowleri that is infectious is trophozoites. Trophozoites have a single nucleus, a granular appearance, and a length of 10–35 µm. Cerebrospinal fluid (CSF) and tissue contain trophozoites of Naegleria fowleri.

Flagellate:
A reduction in food source is one example ofan unfavourable environmental shift that might cause trophozoites to transition into a transient, non-feeding, flagellated stage (10–16 µm in length). Sometimes CSF contains flagellated forms of Naegleria fowleri. They go back to the trophozoite stage when the right circumstances are present again.

Cyst:
The amoeba or flagellate will develop cyst if the conditions are unsuitable for further eating and development (for example, low temperatures, when food becomes limited). the spherical cyst type has a diameter of 7 to 15 um. It has a smooth wall with only one layer and a single nucleus. Cysts are environmentally resistant, which increases their chances of survival until better environmental conditions occur. Cysts are not seen in brain tissue.

3. Epidemiology

Naegleria fowleri is a free-living amoeba that causes a rare but deadly brain infection known as primary amoebic meningoencephalitis (PAM). Here's a brief overview of its epidemiology:

Global Occurrence: PAM cases have been reported worldwide, with the highest numbers in the United States, Pakistan, and Australia.

Exposure: The most common exposure associated with PAM is swimming or diving in warm fresh water environments such as lakes, ponds, and reservoirs. The amoeba enters the body through the nose and travels to the brain, causing infection.

Demographics: Patients are predominantly male (75%), with a median age of 14 years.

Case Numbers: There have been 488 PAM cases documented worldwide since 1962. Survival: The illness progresses quickly and is nearly always lethal. Nonetheless, several survivors have been reported.

Improved clinician awareness, early diagnosis, and treatment are crucial for increasing survival rates among PAM patients.

4. SIGNS AND SYMPTOMS

- **Naegleria fowleri** infection, also known as primary amoebic meningoencephalitis (PAM). have many symptoms that progress rapidly.
- The signs and symptoms of PAM occurs suddenly and are severe at the starting point This includes:

Early symptoms(1to9) days after exposure and late symptoms.

1. High Fever
2. Severe headache
3. Nausea and vomiting

Latesymptoms

1. Mental confusion
2. Trembling
3. Loss of balance
4. Seizures and hallucinations

Altered mental state, photophobia (sensitivity to light), coma and symptoms those of meningitis including a neck stiff, disease progress quickly and symptoms gets worse within few days.

5. **Risk Factors**

1. **Freshwater Exposure**: Swimming or diving in warm freshwater lakes, rivers, and hot springs.
2. **Water Treatment Issues**: Using untreated inadequately treated water specially during the summer months.
3. Occupying regions with a history of Naegleria fowleri infections.
4. Having open cuts or wounds that come into contact with contaminated warm freshwater.
5. **Disturbed sediments**:Activities that sediments warm freshwater environments may increase exposure of amoeba
6. **Nasal Exposure**: The amoeba enters through nasal passage so activities like diving, jumping and dunking in water must be avoided.
7. **Warm climate**: Naegleria fowleri occurs in warm water in regions with consistently warm temperature.

6. Management and prevention

There is no certain and fixed therapy for this disease it involves combination of drugs from various drugs from various classes which are (Antifungal, Antibiotics, Antiprotozoal).

A combination of medications is recommended for PAM these drugs have been used in PAM survivors, 5 documented survivors in North America.

6.1 Treatment

Medication	Dose	Route	Maximum Dose	Duration
Amphotericin $_B$*1	1.5mg/kg/day In 2 divided doses	IV	1.5mg/kg/day	3days
Then	1 mg/kg/day oncedaily	IV		11days
Amphotericin $_B$*1	1.5mgonce daily	Intrathecal	1.5mg/day	2days
Then	1 mg/day every otherday	Intrathecal		8days
Azithromycin[12]	10 mg/kg/dayonce daily	IV/PO	500mg/day	28days
Fluconazole[3]	10 mg/kg/dayonce daily	IV/PO	600mg/day	28days
Rifampin[1,3]	10 mg/kg/dayonce daily	IV/PO	600mg/day	28days
Miltefosine[13]	Weight < 45 kg: 50			

	mg BID			
	Weight > 45 kg: 50 mg TID	PO	2.5mg/kg/day	28days
Dexamethasone[3,24]	0.6mg/kg/day in 4 divided doses	IV	0.6mg/kg/day	4days

Fig. Recommended Treatment Regimen for *Naegleria fowleri* (PAM).

Classification

The treatment of primary amoebic meningoencephalitis (PAM) typically involves a combination of drugs from various classifications. Here are the main classifications of drugs used:

1. Antifungal Agents

Amphotericin B: This drug is often used as the primary treatment for PAM due to its effectiveness against Naegleria fowleri.

Fluconazole: Another antifungal that is sometimes used in combination with other

2. Antibiotics

The antibiotic azithromycin is frequently employed in treatment plans because of its broad-spectrum action. Another antibiotic used to treat PAM is rifampicin, which is taken in combination with other medications.

3. Antiprotozoal Agents

Miltefosine: This drug has shown effectiveness against free-living amoebae, including Naegleria fowleri, which is frequently combined with others.

4. Corticosteroids

Dexamethasone: This drug is used to reduce inflammation and swelling in the brain caused by the infection.

These drugs are typically used in combination to increase the chances of successful treatment.

6.2 Surgical Treatment

Surgical treatments for primary amoebic meningoencephalitis (PAM) are not commonly used, as the primary approach to managing the infection involves aggressive medical therapy. However, in some cases, surgical treatment may be considered to manage complications or support the overall treatment, here are some surgical treatments:

Intracranial Pressure Management: In cases where there is significant brain swelling (Cerebral edema) or increased intracranial pressure, surgical procedures such as decompressive craniectomy may be performed to relieve pressure on the brain.

Ventriculostomy: To lower intracranial pressure and drain extra cerebrospinal fluid (CSF), a hole is made in the brain's ventricles. It can help manage hydrocephalus, a condition where there is an accumulation of CSF in the brain.

Biopsy: In some cases, a brain biopsy maybe performed to obtain sample of brain tissue for diagnostic purposes. this can help confirm the presence of Naegleria fowleri and guide treatment decisions.

It's important to note that these surgical interventions are typically considered as supportive measures and are used in conjunction with aggressive combinational medical therapy.

7. Prevention

Preventing primary amoebic meningoencephalitis (PAM) involves reducing the risk of exposure to Naegleria fowleri. Here are some key prevention measures:

Avoid Warm Freshwater: Refrain from swimming, diving, or engaging in water sports in warm freshwater bodies, especially during hot weather when water temperatures are higher.

Use Nose Clips: If you do swim in warm freshwater, use nose clips or hold your nose shut to prevent water from entering your nasal passages.

Avoid Stirring Up Sediment: Try to avoid disturbing the sediment at the bottom of warm freshwater bodies, as the amoeba is more likely to be present in the sediment.

Proper Pool Maintenance: Ensure that swimming pools and hot tubs are properly chlorinated and maintained to kill any potential amoebae.

Use Safe Water for Nasal Irrigation: When using devices like neti pots for nasal irrigation, use only distilled, sterile, or previously boiled water. Tap water should be avoided unless it has been properly treated.

Stay Informed: Be aware of any local advisories or warnings about Naegleria fowleri in freshwater bodies.

8. Diagnosis

Diagnosing Naegleria fowleri infection, also known as primary amoebic meningoencephalitis (PAM), involves several laboratory tests.

Here are the key diagnostic methods:

Polymerase Chain Reaction (PCR): The presence of Naegleria fowleri in CSF or biopsy specimens canbe ascertained using molecular techniques. After being amplified using the polymerase chain reaction (PCR), the presence of a certain DNA sequence of this organism can be found.

Immunohistochemical (IHC)Testing and Indirect Immunofluorescent (IIF)Staining:

These tests use specific antibodies against Naegleria fowlerito detect the amoeba in CSF or tissue samples.

Direct Microscopic Analysis: Light microscopy in low light or phase-contrast microscopy for motile trophozoite (with a 40xobjective should be used to analyse small drops of CSF or tissue suspension in wet mounts on slides under coverslips. the preparation may contain motile Naegleria, which is actively motile at 22°C to 25°C. Giemsa Wright or a modified trichrome stain are two further stains that can be used to stain the amebae. Lumbar Puncture: In order to check for the presence of Naegleria fowleri, CSF is collected.

Amoeba Culture: Naegleria fowleri can be grown in culture by inoculating it into a growth plate containing the lawn culture of Escherichia coli or Klebsiella aerogenes (these bacteria Serve as a food source for Naegleria fowleri).to destroy any remaining free-living amebae, the growth plate is then incubated at 42°C.The development of amoeba tracks in the grass culture confirms the presence of thermophilic amebae, which could represent Naegleria. PCR or direct visualisation are then used to confirm the presence of Naegleria.

9. CONCLUSION

Known as the "brain-eating amoeba," Naegleria fowleri is still a dangerous infection because of its quick pathogenesis and high death rate from primary amoebic meningoencephalitis (PAM). This review emphasises the significant difficulties in identifying and managing N. fowleri infections, highlighting the necessity of increased awareness and cutting-edge diagnostic techniques to support early diagnosis. In the pathogenesis, the amoeba enters the nasal passages and travels to the brain, where it causes widespread necrosis and neuro

inflammation. The diagnostic process is complicated by the nonspecific early symptoms of PAM, which mimic bacterial meningitis, necessitating specific cerebrospinal fluid (CSF) examination and advanced laboratory techniques like PCR and immunofluorescence assays, Treatment strategies, though limited, have shown some promise. Amphotericin B remains the cornerstone of therapy, though its efficacy varies, and it is often accompanied by significant adverse effects. Combination therapies, including miltefosine, azithromycin, rifampicin and fluconazole, have shown synergistic effects and improved outcomes in some cases, but these treatments are not universally effective and are often hindered by problems including drug accessibility and blood-brain barrier penetration.

A14 year old boy from Thikkodi in Kozhikode district became the first Indian to survive the disease, and he was discharged from hospital, proper diagnosis and treatment can improve patient outcomes.

In conclusion, while significant progress has been made in understanding the pathogenesis, diagnosis, and treatment of N. fowleri infections, challenges remain. Improving patient outcomes requires early and accurate diagnosis, vigorous and combination treatment plans, and creative methods like vaccine development. In order to improve these tactics and boost treatment effectiveness and give hope for higher survival rates in the face of this deadly infection, more research and clinical trials are essential.

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