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NAEGLERIA FOWLERI INFECTIONS ARE BECOMING A BIGGER PUBLIC HEALTH PROBLEM, ESPECIALLY BECAUSE OF RECENT OUTBREAKS IN INDIA

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Abstract

Naegleria fowleri is a free-living amoeba that is a dangerous thermophilic pathogen. It is also known as the brain-eating amoeba. These bacteria may enter the central nervous system and produce a deadly brain illness called primary amoebic meningoencephalitis (PAM). Although the reported morbidity is lower, it has alarmingly shown a fatality rate of 95 to 98%, often resulting in death within two weeks after first exposure. This review offers an updated synthesis of the literature concerning the causative organism, the recent outbreak of N. fowleri in India, its mode of transmission, clinical manifestations, diagnostic protocols, and primarily, preventive strategies, aiming to disseminate this information to healthcare professionals.

Keyword: Naegleria fowleri, Primary Amebic Meningoencephalitis (PAM), Brain-eating amoeba, Amphotericin B, Freshwater infection

1. Introduction

The "brain-eating amoeba," or "Naegleria fowleri," is a single-celled protozoan that lives in warm freshwater environments such lakes, rivers, hot springs, and pools with low levels of chlorine. It can survive temperatures as high as 45 °C (yoder js et al., De Jonek here et al.) It grows best in places with the right circumstances, which is why it can live in tropical and subtropical climates all over the globe. Naegleria fowleri is the cause of deadly Primary amebic meningoencephalitis (PAM), which is an infection of the central nervous system (CNS) that kills more than 95% of those who have it (Pervin N. et al., Fowler M.). PAM is a potentially lethal condition that rapidly disseminates inside the central nervous system, resulting in significant cerebral edema and tissue degeneration. There are 47 identified species of Naegleria, but only N. fowleri causes PAM. (De Jonck et al. here). Even though it's not frequent, healthy kids and adults are more likely to get PAM after drinking contaminated water while doing something fun. When N. fowleri gets into the nose, it goes to the central nervous system via the olfactory nerves, where it produces extensive inflammation, necrosis, and a rapid loss in neurological function (Baig, 2016). Although very uncommon, PAM is a condition associated with a significant mortality risk (Ahmad Zamzuri et al.).

The name N. fowleri comes from Malcolm Fowler, who was the first person to describe a PAM infection in Australia (Fowler M et al.). It was first found in the US in 1937, although earlier investigations reveal that it wasn't very prevalent (Capewell LG). It usually does well in warm freshwater settings. N. fowleri was found in around 15 nations throughout the world, but not in Antarctica. The greatest rates were in warmer countries. The pathogen may also live and grow at warmer or higher temperatures (50–65°C) and salinities of 1.4–2.0% NaCl by eating bacteria, yeast, and algae.

Since most people don't know about the fatal infection, it's important to gather and organize the most current information about how it spreads, how to cure it, and how to avoid it. It is also very important to get and put together the most up-to-date information about its etiology, therapies, and ways to avoid getting it. Since diagnosis might be delayed, it is essential to enhance the knowledge of the efficacy of existing medications in traversing the blood-brain barrier. The current review integrates recent data regarding the nature and mechanism of pathogenesis, clinical presentation, diagnostic challenges, existing and novel treatment strategies, preventive measures, and international epidemiology. This synthesis addresses the knowledge gap and may serve as a foundation for future research on this topic and population health.

2. The Problem's Global Prevalence

From 1965 to 2018, the CDC and literature from across the globe documented 381 instances of PAM. From 1965 to 2016, the number of cases reported increased by 1.6% per year (Ghar pure R et al.). Prior studies indicate that ascertaining the true burden of N. fowleri will be difficult due to the underreporting of cases (Ahmad Zamzuri et al.). The majority of patients are male (75%), with an average age of 14. There are 16 instances in the US in 2018, 8 of which are males and 8 of which are women. In all of these situations, people died. A lot of people believe that PAME is really dangerous. From 1962 to 2022, there were 157 reported instances in the US, and just four people survived. (Kemble SK et al., Capewell LG et al., RKI et al.)

N fowleri was found in about 15 countries around the world, not including Antarctica. Significant number of the cases were raised in warmer areas (Matanocka et al.). Even though PAM cases were stayed same all year (0-8), a new out break in south korea is very worrying. As per the Korea Disease Control and Prevention Agency (KDCA), a new outbreak of brain-eating amoeba was first seen in South Korea on NaN Invalid Date N fowleri infection. Surprisingly it is very worrying that that there are not many good therapy options, though they were already seen. The US Centers for Disease Control and Prevention (CDC) say that in all over the world, new technologies are making the air hotter and may help diseases spread. Most of the PAM cases were reported in Pakistan, among adults between the ages of 26 and 45 [Philips et al.], while in the United States, most of the cases are in children under 14 [Online ET]. This clearly indicates that Pakistan might possess a genetically different strain. Most of the time, PAM cases are reported in the summer season. Since N. fowleri is spreading in Pakistan, scientists are now looking into climate change. As the climate become warms, summers gets longer, and the higher humidity makes water bodies the perfect place for amoebas to live.

Most of the recorded cases have occured in the United States (especially in the southern states like Florida and Texas), Pakistan, Australia, and Mexico. India, Thailand and some parts of Africa are also reported a good number of cases. There are cases reported in the southernmost state of india, kerala, too. The first cases were reported in kerala, was on May 21, 2024 and it was a five-year-old girl. The second case, which was reported on June 25, was about a 13-year-old girl. In July, two other cases were also reported, this time with two boys who were just fourteen years old. This made the total number of cases in Kerala this year four. Unfortunately, all four sick kids died (Online ET). Four days before, the five-year-old girl and four other kids had a bath in a nearby river (Philip et al.).

3. Clinical Presentation

After being injected, the amoeba gets into the central nervous system via the cribriform plate by going through the respiratory epithelium and olfactory mucosa (Pervin et al.). The olfactory bulb and cerebellum are the parts of the brain that are hurt the most. The result is a lot of bleeding in the cortex, tissue death, and swelling. Incubation may take anything from one to fourteen days. It might be hard to tell whether someone has N. fowleri PAM at first since its clinical signs can seem like those of bacterial meningitis. After being exposed, the first signs usually appear three to seven days later, but no later than fourteen days [Harris GR et al., Batra R et al.]. Symptoms manifest immediately and are rather severe. PAME is marked by a high temperature, headache, stiff neck, and acute nausea that leads to vomiting in the beginning of the illness phase (Shariq A et al., Gupta R et al.). The second phase is marked by pyogenic meningoencephalitis (the formation of pus) and coma (Baig et al., Harris et al., Nicholls et al.). Death occurs one week after the onset of symptoms. PAME mostly affects kids and young adults. So, PAME might be seen as a dangerous juvenile sickness, similar to malaria (Ghar pure et al.).

4. Diagnostic Procedures

Even though more people know about how dangerous PAM may be, it is still hard to identify since its early symptoms are not very clear and look like those of bacterial or viral meningitis. Some of the most common ways to diagnose include wet-mount microscopy, cerebrospinal fluid (CSF) staining, polymerase chain reaction (PCR), and next-generation sequencing (NGS).

The diagnosis should be considered in instances of meningitis or meningoencephalitis accompanied by a recent history of freshwater exposure. CSF examination shows low to normal glucose levels, high CSF pressures (up to 600 mmHg), and more protein and polymorph nuclear cells (Pervin et al.). The Gram staining and cultures may not be able to separate the organisms since they are usually killed during the fixation procedure. You can observe the organism well using wet mounts, hematoxylin and eosin (H&E), periodic acid Schiff (PAS), Giemsa-Wright staining, or modified trichrome stains (Pervin et al.). To achieve a final diagnosis, next-generation sequencing, polymerase chain reaction, indirect immunofluorescence, or immunohistochemistry (IHC) are utilized (Ahmad Zamzuri et al.).

5. Steps to Avoid

Regular health promotion campaigns in high-risk areas to teach people how to be safe around freshwater bodies assist to stop the problem. People should be reminded to pinch their nostrils or wear nose clips while they are in the water and to stay away from warm, still

water. They should be told to keep their heads above the surface of the water while swimming in freshwater and untreated thermal bodies of water. They should also be told not to plunge or leap into stagnant freshwater [1]. However, using nasal clips when swimming may greatly lower the danger. Also, preventative measures like proper water chlorination, public education, and not exposing the nose to warm freshwater are still very important for minimizing the number of people who become sick (Alanazi et al.,)

6. Management

There is currently no known cure for N.fowleri. The Centers for Disease Control and Prevention recommend high dosages of amphotericin B for therapy based on many laboratory and case investigations. Amphotericin B must be administered intrathecally [RKI et al.]. Many investigations looked into how people use more than one drug at the same time. Amphotericin B is one among the medications used to treat PAM. Other treatments that are regularly used include dexamethasone, fluconazole, rifampin, azithromycin, and miltefosine. These drugs were chosen because they are believed to work against Naegleria fowleri and because they have worked for those who have already been sick with it. But the success rate is poor, especially if the infection is found later.

Miltefosine is the newest drug on this list. Tests have demonstrated that it can kill free-living amoebae, such as Naegleria fowleri. A thorough comprehension of the biology and pathogenic mechanisms of the parasite will facilitate the identification of targets for the systematic development of treatment strategies. When the virulent amoebae in N. fowleri encyst, they change into the "avirulent" form, which stops the propagation of the illness. Cell surface receptors that leads to conformational changes which help make cysts. Any ligand that may stimulate encystation (other than an antibody or a spike in osmolarity) can also be used to change dangerous amoebae into their dormant state.

To cross the blood brain barrier and to cause encystation, and for the pathogenic amoebae turn into a dormant state, a chemical is necessary. The RNA-seq research findings regarding differential gene expression in additional protozoa following exposure to encystment medium will enhance the validity of this management regimen. Bioassay-guided testing of diverse chemical libraries, coupled with a comprehensive understanding of the composition, structure, and permeability of the Naegleria outer surface membrane, may aid in the formulation of an effective therapeutic strategy against brain-eating amoebae. But we need to do a lot more research to reach these goals.

There have also been a lot of new medications and therapies coming out recently. Many anti-inflammatory medicines are becoming less effective due to adverse side effects, making new types of pharmaceuticals more significant [99]. These include what are known as anti-heterocyclic chemicals. Making these active compounds has a lot of good effects. Making them isn't that pricey either. They also have a variety of various affects on the body. Studies have confirmed their antiviral, antibacterial, anticancer, and insecticidal properties.

7. Conclusion

N. fowleri infections may produce PAM, however this is not common. It happens everywhere in the globe and is quite likely to kill you. This study amalgamated the latest data from the preceding decade that included both epidemiology and clinical presentation. The findings corroborate the suggested probable case definition, which necessitates the sudden onset of fever, headache, and vomiting, accompanied by meningeal symptoms after 14 days of freshwater exposure. A wide clinical definition can let doctors suspect anything early on during a medical consultation, which will allow them to initiate diagnostic tests right away. It is possible to directly see the amoeba from CSF samples under a microscope, although this may lead to false-positive findings. It is recommended that molecular techniques be used for confirmatory testing. In the end, getting an early, accurate diagnosis is what makes it possible to set up an aggressive treatment strategy.

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