A 30 year old male with a seldom cause of Meningoencephalitis- Naegleria fowleri

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Abstract **- Primary Amebic Meningoencephalitis is a rare CNS infection caused by Thermophilic, freshwater parasite Naegleria fowleri. With almost 100% mortality this disease is a major concern in the field of Infectious diseases. Here we present a 30 year old male who had come with complaints of fever, headache and vomiting to us.On physical examination meningeal irritation signs were present and Lumbar puncture was done which revealed a picture of Bacterial Meningitis and empirical therapy was started. In the dew course of the hospital patient had raised Intracranial pressure and developed seizure. Later Giemsa wright stain revealed Naegleria fowleri and Amphotericin B was started but the patient didnot show any improvement and succumbed.Naegleria fowleri being a CNS infection of concern should be suspected in a rapidly deteriorating Meningitis and early treatment with Appropriate therapies is to considered. It is to noted that the water bodies for recreational activities have to be cholrinated and disinfected regularly and people should avoid exposure to such water bodies carrying risk of infection as prevention is the best medicine of all care.**

Keywords- **Naegleria fowleri, Primary Amebic Meningoencephalitis (PAM) ,Meningoencephalitis, Intracranial Pressure, Cerebrospinal Fluid (CSF) ,Amphotericin B , Brain Edema, Thermophilic Amoeba, PCR Diagnosis, Chlorination.**

INTRODUCTION

Naegleria fowleri is a virulent, thermophilic and free-living amoeba that can survive in soil and warm fresh water. It multiplies during summer when the high temperature is conducive for their growth. Found mostly in inadequately chlorinated domestic water supply or swimming pools. When humans are exposed to contaminated water, amoeba enters the nasal cavity of the host and travels through the nasal mucosa, followed by moving along the cribriform plate and olfactory nerve, finally reaching the olfactory bulbs. Consequently, it destroys the central nervous system (CNS), thereby causing primary amebic meningoencephalitis (PAM) (1, 2).

After few days of exposure to the organism the patients develop signs and symptoms of meningeal irritation like headache, fever, nausea, stiff neck, confusion, seizures, and hallucinations.It progresses rapidly, causing death within an average of 10 days from exposure. PAM can be diagnosed using microscopic methods, such as the wet film preparation of cerebrospinal fluid (CSF), CSF culture, and amebic antigen detection. In addition, the direct detection of parasite DNA by polymerase chain reaction (PCR) can be performed in CSF, biopsy, or tissue specimens.(2)

Case presentation

A 30 year old male , previously healthy and active presented with history of fever, headache, myalgia since 2 days for which he self medicated with acetaminophen but didnot get any better. He also had an episode of projectile vomiting on the day of admission.On examination Temperature was 39.3°C, Pulse rate - 110 bpm, Blood Pressure - 100/70 mmHg, Respiratory rate of 20cpm and oxygen saturation of 96% being maintained at Room air. Cardiovascular system, Respiratory system, Per abdominal examination was normal. But he had signs of meningeal irritation like Neck stiffness, Positive Kernig sign and Brudzinski sign. In view of all the above findings CT brain was done which revealed no abnormality and the patient was admitted to ICU , started on empirical antibiotic therapy suspecting bacterial meningitis (Ceftriaxone 2g IV BD, Vancomycin 1g IV BD). All routine investigations sent, Leukocytosis was present 11,400 cells/mm3. CSF analysis revealed opening pressure of more than 36cm of H2O, pleocytosis 1743cells/mm3 (87% being neutrophils) , glucose 36 mg/dL, protein 410mg/dL and cultures yielding no growth. The next day patient had altered mental status in the form of irritability and irrelevant talk. Patient had an episode of GTCS, right pupil being 5mm non reactive to light. Repeat CT done showed Diffuse cerebral edema with cerebral herniation. Immediately patient

was started on Mannitol, 3% NS, Dexamethasone, anti epileptics and sedation. Patient underwent External ventricular drain placement.

On further enquiry the attenders gave history of travel and swimming in an unnamed river/pond. This history made us suspect Primary amebic encephalitis and repeat CSF study for Naegleria fowleri sent and treatment changed to Amphotericin, Azithromycin, Rifampin, Flucanazole. Giemsa wright stain revealed trophozoites with pseudopodia and PCR showed the presence of Naegleria fowleri.

Despite the best efforts patient deteriorated and now the left pupil was also dilated and non reactive to light. Patient stayed in the ICU for 7 days and succumbed to the illness.

Amebic encephalitis

Discussion

Naegleria fowleri is distributed worldwide, but a majority of the reported cases are from the USA.(1) Incidence of PAM is low which says that all the exposures donot cause infection. But the mortality is high due to 2 reasons: underdiagnosis as the clinical features are similar to other known common types of meningoencephalitis and hence delayed diagnosis, treatment. PAM is rapidly progressive and causes raised Intracranial pressure and death. Secondly there are no specific proven treatment of the condition.(1)

The most common exposure types were swimming or diving(58%), bathing (16%), and water sports (10%).Previous case reports have also identified an association between PAM and prolonged water time in still water sources such as lakes, ponds, and reservoirs.(3) Avoiding jumping into the body of water, splashing, or submerging their heads under the fresh water during the summer season when the water temperature is high can reduce occurence of PAM. Individuals can use nose clips during the activities or rinse the nose and nasal passages with clean water immediately after such activities in order to avoid the infection. Currently Naegleria fowleri is highly sensitive to Amphotericin B in vitro and hence is the first choice drug(1)

The increased frequency of PAM cases has been associated with the rising temperature of domestic water during summer months and poor chlorination of potable water sources. Water stored in overhead tanks during summer months with negligible chlorine levels can facilitate the propagation of N. fowleri amebae which can lead to PAM cases.(2)Factors which increase the likelihood of PAM over Acute Bacterial Meningitis include: presenting during hot months of a year, male in gender, age under 40 years, and presentation with nausea and seizures.The average duration of illness with the onset of severe symptoms is 3 days for N. fowleri positive cases.(2)

This patient showed a rapid worsening and generalized brain edema with very high brain pressure and very high protein and blood cells in CSF. Difficulty in identification of N. fowleri on wet preparation may lead to delay in appropriate treatment and management of PAM cases.The PCR-based diagnosis of CSF is more sensitive than wet preparation examination and should be the method of choice for N. fowleri diagnosis.N. fowleri does not grow on standard culture medium, as it requires bacteria- enriched agar and is also not identified on Gram stain.(2)If the CSF sample showed changes similar to those of a bacterial infection and there was subarachnoid hemorrhage at the same time, PAM should be considered.(4) Nowadays metagenomic next-generation sequencing (mNGS) is used for diagnosis which is more accurate.(4)

The possible CT features in PAM are as follows follows: generalized brain edema or focal edema, hydrocephalus, small or absent ventricle, subarachnoid hemorrhage and erosion of the sphenoid sinus. Most PAM patients suffer from generalized brain edema. Considering the methods of invasion of Naegleria fowleri, the erosion of the sphenoid sinus may theoretically be an early marker of PAM and if the CT images illustrate focal edema, the outcome of PAM may be good. (4)

There are three morphological forms of Naegleria fowleri:trophozoite (amoeba), flagellate, and cyst. Generally, trophozoites are thought to be infectious forms of N. fowleri. In the cyst phase, even though it is unable to promote tissue degradation, this resistant form can enter the host and revert to the trophozoite form. If the patients were considered infected by amoebae, the fastest diagnostic tool seems to be microscopic examination of the CSF, but its positivity depends on the following factors: (a) fresh CSF samples at room temperature, which means that the CSF samples should be examined immediately after collection; (b) wet mounts of the

CSF, which can improve the percentage of positivity; and (c) experienced specialists. Thus, it is not a definitive diagnosis; other approaches, such as molecular investigation, should be used to confirm the identification. Another method for the definitive diagnosis of N. fowleri infection is the use of immunohistochemical staining of the brain tissue. This method requires a biopsy, which can be performed in few patients. The third method is polymerase chain reaction (PCR) testing. However, if not aware of the method to find pathogen mNGS can be done.(4) The dearth of information regarding PAM is concerning, given that the reported mortality rate ranges from 92% to 99%(3)

Empirical treatment of PAM include amphotericin B 1.5 mg/kg every 12 hours for 3 days with 1 mg/kg/day intravenous (IV) and 1.5 mg intrathecal, azithromycin 10 mg/kg once daily (OD), fluconazole 800 mg in 24 hours, rifampin 600 mg IV OD, chlorpromazine up to 2 gm/day, and miltefosine 150 mg/day.(2) The recommended therapy of CDC comprise of conventional amphotericin B administered intravenously at the dosages of 1.5mg/kg/day in 2 doses for 3 day, followed by 1 mg/kg/day for an additional 11 day. The intrathecal administration of conventional amphotericin B (1.5 mg/day for 2 day and 1 mg/day for an additional 8 day) can also be used in combination with intravenous amphotericin B.(1) Other drugs which could be effective in combination with conventional amphotericin B are Flucanazole, miconazole, miltefosine, Rifampin and Azithromycin.(1)

Recent studies have been devoted to new drugs targeting fatty acid oxidation, such as etomoxir, orlistat, perhexiline, thioridazine, and valproic acid.(4) It may be worthwhile to perform decompression in the early stages of PAM. It is argued that CRRT not only contributes to the clearance of inflammatory factors but also alleviates brain edema.(4)

Considering the unique invasive route of Naegleria fowleri, wearing a mask when working or applying protection to prevent dirty or fresh water from being inhaled into the nose during swimming is important.(4)

CONCLUSION

Rapid progressive meningoencephalitis in which the results of CSF analysis are similar to those during bacterial infection should be considered as a possible case of PAM. To facilitate earlier diagnosis and early initiation of correct therapy, clinicians should consider PAM as a potential cause of meningitis and encephalitis.As PAM presents during the summer months, there is a need for enhanced chlorination of domestic water supply to reduce the risk of ameobic growth.Public awareness needs to be raised regarding methods to reduce the risk of acquiring N. fowleri infection as prevention is the best medicine of all care.

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