

A Review on Global Distribution of Primary Amoebic Meningoencephalitis (PAM) Caused By Naegleria Fowleri- The Brain Eating Amoeba

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INTRODUCTION

Naegleria fowleri, a free living thermophilic brain eating amoeba, also known as N. aerobia or N. invades that belongs to Heterolobosea group. It causes a dreadful and fatal condition of Central Nervous system known as Primary Amoebic

ABSTRACT

Naegleria fowleri is thermophilic, free living amoeba commonly known as "Brain eater". The habitats are in fresh water reservoirs and soil at a temperature of 46°C. It is capable of invading CNS via the nose in humans, causing fatal condition known as Primary Amoebic Meningoencephalitis (PAM). The symptoms initially present like bacterial meningitis and ultimately death within 5-7 days. So differential diagnosis done by withdrawing the sample of CSF from the patient to confirm the presence of amoeboid trophozoites. Other molecular test is Polymerase Chain Reaction but it is less favorable because of time consumption. The treatment protocol reported as combination therapy, which includes amphotericin B, miconazole, fluconazole, miltefosine depending upon the early diagnosis and condition of the patient. A vast study revealed approximately 260 cases throughout the world since 1962-2014 which are from Pakistan, 17 cases, United States 132, Venezuela 7, Mexico 9, In Australia 19, 9 from New Zealand. India 11, Nigeria 4. 1 case in Namibia, Iran, Costa Rica, New Guinea, South Africa and Madagascar. 5 cases from Thailand and Belgium. In the Czech Republic, 16 cases and in United Kingdom 2 cases were reported. It is the rapidly replicating and lethal condition having more than 95% fatality rate with only 11 survivals throughout the world.

Meningoencephalitis (PAM) that was first discovered in 1965 by Fowler and Carter [1].

Its replication initiates during a hot season at a temperature ranges up to 46°C, and it is distributed in fresh water lakes, rivers, ponds, disinfected swimming pools, domestic water

supplies, thermally polluted water, sewage and soil [2, 3].

The life cycle of *N. fowleri* appears in 3 forms. The first form is amoeboid trophozoite (10-35 μm long) survive best in 35°- 46°C and it is the only stage which is pathogenic or infectious in humans. The second stage is pear-shaped flagellate form (10-16 μm long), exist at 27°-37°C. The third is a spherical shaped cyst form that persist in lower temperature. At an appropriate environment the cyst is converted into a trophozoite form[4].

Trophozoites invade into the nasal cavity of victims during aquatic events and penetrate in nasal mucosa from where it enters into the cribriform plate by the olfactory bulbs and finally propagate into the CNS predominantly at the base of the brain, brain stem and cerebellum where it triggers massive inflammation, necrosis and hemorrhagic state. The adhesion of this organism is due to the presence of carbohydrates residues in the outer surface of the plasma membrane, pore-forming proteins (Naegleria pores) and glycoconjugates that contain α -D-mannose, α -D-glucose and terminal α -L-Fucose. It also secretes proteases, phospholipases, acid hydrolases, neuraminidases, glycolipid and phospholipolytic enzymes that destroy sphingomyelin ultimately results in neurological deficit indications [4].

The severity of the disease reflected by the symptoms included headache, high-grade fever, neck rigidity along with nausea, vomiting, restlessness, photophobia, variation in taste and smell due to the involvement of olfactory nerve. Neurological deviation includes brain edema, agitation, confusion, seizures, lethargy, hallucinations, coma ultimately leads to death within 5-7 days [4, 5].

PAM is diagnosed by lumbar puncture of the patient in which the sample of cerebro-spinal fluid is withdraw and mounted on a wet slide. It is examined under 10x and 40x lens of

compound and light microscope that shows trophozoites nuclei, single large, rounded refringent nucleolus, and the organism's nucleus is surrounded by numerous cytoplasmic vacuoles and pseudopodia may be identified projecting away from the cells[5, 6].

The treatment protocol provided by giving drugs either by monotherapy of miltefosine or combination therapy of amphotericin B along with rifampin, miconazole, fluconazole, doxycycline depending upon the early diagnosis and the condition of the patient [1, 2, 7, 8,9].

Materials:

A google scholar search was done using "Naegleria fowleri", combined with "Primary Amoebic Meningoencephalitis", "Global distribution of PAM", "Biology of N.fowleri", "Pathogenesis", "Treatment", "Prevention", "Case studies of PAM" in addition we also consulted reviewed and published articles from Centers for Disease control and Prevention (CDC), Journal of Pakistan Medical Association (JPMA), PLOS, Canadian Journal of Emergency Medicine, American College of Chest physician and PUJ. Most of the cases have been reported from US because they are so much involved in swimming activity but as far as Pakistan is concerned, mostly cases reported are of males rather than females due to ritual rinsing of nose and ablution [11,12]. The no. of cases reported of PAM throughout the world since 1962-2014 are 260 out of them only 11 survived. The survival rate of this disease is very less because it requires early diagnosis and immediate treatment to cure the disease otherwise death occur within a week or approx 5-7 days.

RESULTS

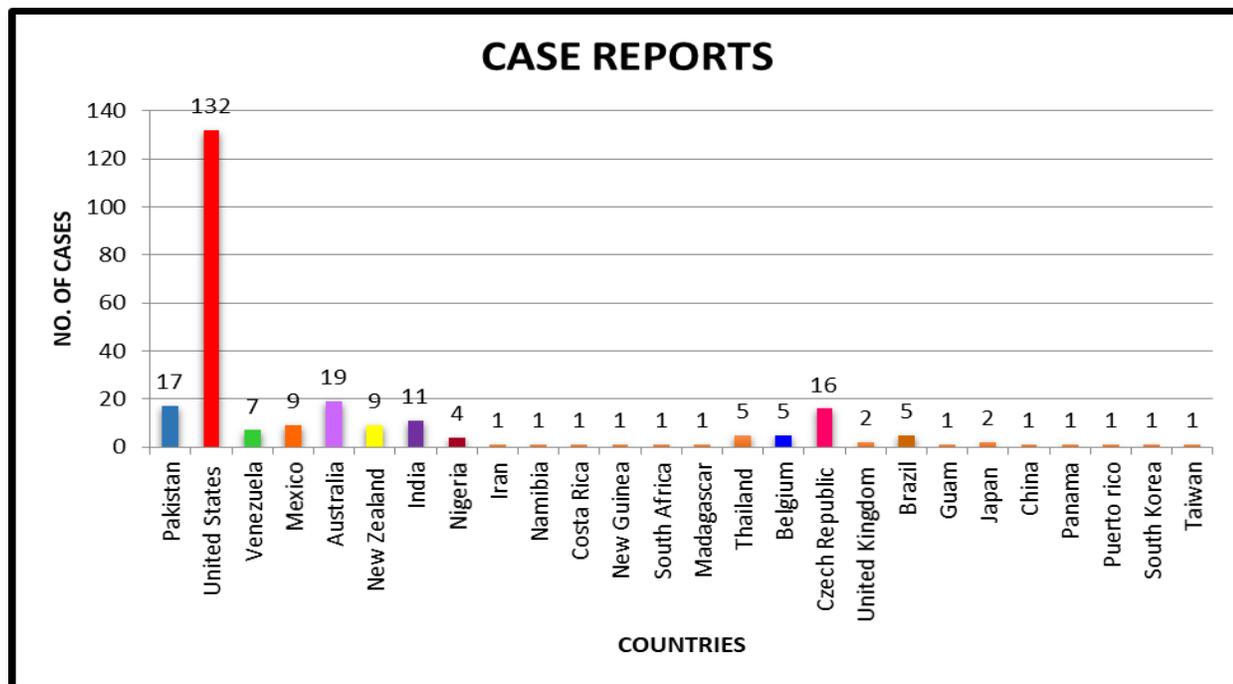


Figure 1: Cases reported of PAM from all over the world

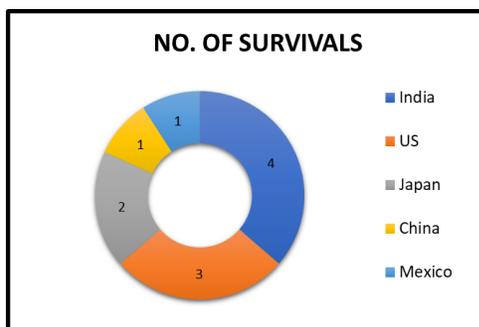


Figure 2: No. of patients who were survived from PAM

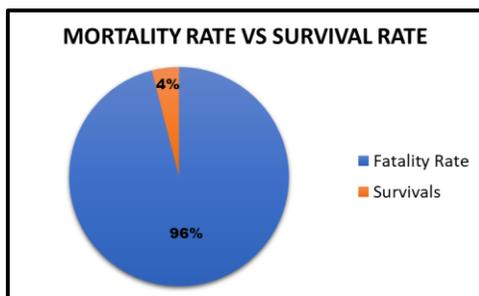


Figure 3: interprets the survival rate and the fatality rate after PAM

Discussion

Naegleria fowleri is a thermophilic rapidly dividing amoeba that causes lethal or fatal neurological disorder known as PAM. It invades in the human body by swimming or by ritual nasal rinsing and abluion. Initially the symptoms appear are severe headache, fever, neck rigidity and CNS disabilities like seizures, hallucinations, confusion, coma which leads to death within a week. Due to these symptoms PAM is usually confused with bacterial meningitis so differential diagnosis have to be performed by smearing the CSF sample of the patient on the wet mount slide and observed under the microscope, which shows the presence of motile amoeboid trophozoite of N.fowleri indicated by the elevated numbers of polymorphonuclear leukocytes (PMNs) which is a major evidence of PAM, other lab findings include high levels of protein and neutrophils with low levels of sugars [10]. Another diagnostic tool is Polymerase Chain Reaction (PCR) used to detect amoebic DNA, but it is less prefer due to time consuming. The reported articles suggested that amphotericin B

(1-1.5mg/kg/day) is a drug of choice for treating PAM administered intravenously or intrathecally in combination with Chloramphenicol (100mg/kg/day) and oral rifampicin (20mg/kg/day) or tetracycline, fluconazole, miconazole, dexamethasone. In some cases miltefosine is also recommended but early diagnosis and treatment is immediately required within 30-36 hours for the survival of patients as it is ultimately damaging the neuronal cells. The no. of individuals who survived is mostly received a combination of amphotericin B with rifampin with the hospitalization of up to one month but the time period of hospitalization can be increased up to 2-3months for full recovery [8]. Certain self-preventive measures can be implemented to reduce the risk of PAM such as chlorination of water in swimming pools (one part per million) which adequately controlled the replication of the organism and use of nose clips during swimming. The Government of Health Ministries should monitor the natural reservoirs such as lakes, ponds, rivers and streams, especially during summer seasons as it is impossible to chlorinate.

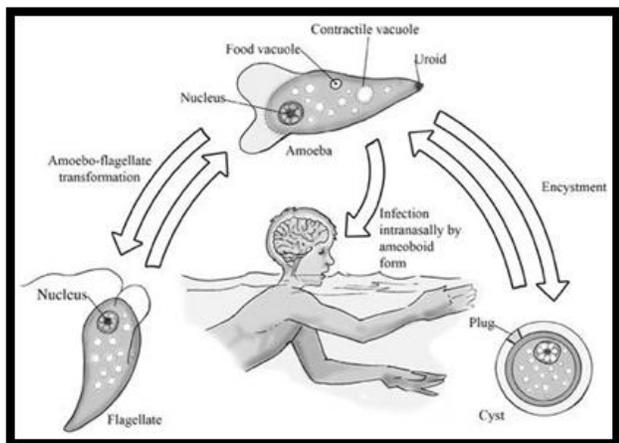


Figure 4: Life cycle of Naegleria fowleri

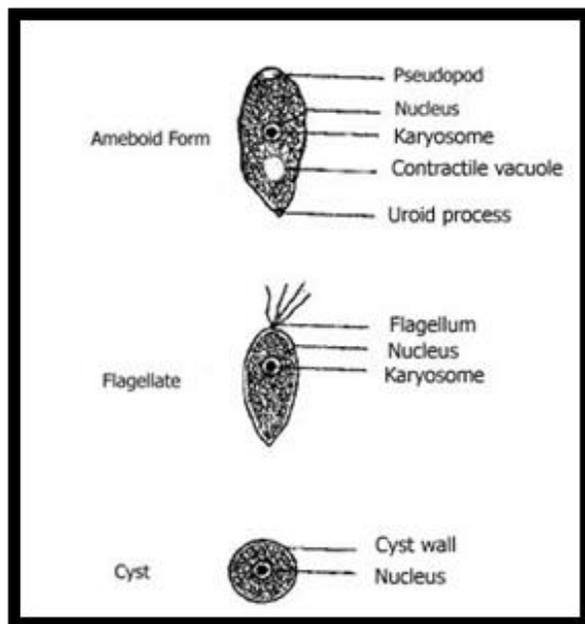


Figure 5: Phases of Naegleria fowleri

CONCLUSION

PAM is a rapidly fatal condition and most of the cases have been reported from US because they are so much involved in swimming activity, but as far as Pakistan is concerned, mostly cases reported are of males rather than females due to ritual rinsing of the nose and ablution. The number of cases reported of PAM throughout the world since 1962-2014 are 260, and out of them only 11 survived. The survival rate of this disease is very less because it requires early diagnosis and immediate treatment to cure the disease, otherwise death occurs within a week or approx 5-7 days.

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