ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

A REVIEW: AMOEBIC MENINGOENCEPHALITIS THE BRAIN - EATING AMOEBA

P. Dharani Prasad[1]*, G. Mounika Sree, G. Sreeya, G. Sushma, K. Chandana, K. Vanitha, K. Revathi

[1]Department of Pharmacology, MB School of Pharmaceutical Sciences, Mohan Babu University (Erstwhile: Sree Vidyanikethan College of Pharmacy) Tirupati-517102, Andhra Pradesh, India

*Corresponding author E-mail: dharani4prasadp@gmail.com

ARTICLE INFO

Key words:
Naegleria fowleri, Amoebic Meningoencephalitis, Infection.

ABSTRACT

Naegleria fowleri is an amoeba that is widely common in the environment. This pathogen reaches the brain of human while swimming through the nasal passage causing inflammation in brain tissue and cerebral membrane which is called Meningoencephalitis leading to death. Misdiagnosing *Naegleria fowleri* infection cases as tubercular meningitis or bacterial meningitis had occurred in many cases due to the limited information about this parasite. This review aimed to pay attention for its important and shows how to understand the effect of *Naegleria fowleri* infections on the health of human, its Pathophysiology, Clinical symptoms and the mechanisms that associate with the disease, as well as treatment and preventative ways.

INTRODUCTION

Naegleria fowleri is an ameboflagellate, known as "the brain-eating amoeba". It causes an acute, fulminant and rapidly fatal central nervous system (CNS) infection termed primary amoebic meningoencephalitis (PAM). The infection occurs from inhalation of trophozoites[(1)]. It enters the CNS, after insufflation of infected water, by attaching itself to the olfactory nerve, then migrating through the cribriform plate of the ethmoid bone along the fila olfactory and blood vessels, and into the anterior cerebral fossae. It feeds on nerve tissue and causes extensive inflammation, necrosis and haemorrhage leading to death[(2)]. *N. fowleri* is a thermophilic amoeba that grows well in tropical and subtropical climates. Raised temperature during hot summer months or warm water from power plants facilitates its growth[(3)].Infection occurs in healthy children and young adults with a recent history of exposure to warm fresh water (polluted water in ponds, swimming pools and man-made lakes). The amoeba has been also detected in artificially heated industrial watersources[(4)], and in domestic water supplies[(5)]. The number of reported cases of PAM has increased worldwide in recent years. The increased incidence may be due to greater awareness of the disease or due to the development of more rapid, highly sensitive and specific diagnostic assays such as PCR. In addition, changes in environmental conditions, thermal pollution of water from industry and the development of industrialized areas with nuclear power plants and cooling towers that allow for concomitant greater growth of amoeba and their bacterial food source may afford greater opportunities for infection[(6)].

Epidemiology: Human disease caused by free-living amoebae was first reported in 1965 by Fowler and Carter, who studied four patients with PAM in South Australia [(7)]. *N. fowleri* is pathogenic in human and has a tropism for the

CNS. It exists in three forms; the first is an invasive, reproductive trophozoite (ameboid-form) that is thermophilic and thrives best in temperatures from 35° to 46°C; the second is a flagellate pear-shaped motile form that is maintained at temperatures 27° to 37°C, while the third form is a spherical cyst that can survive in much lower temperatures and will convert to a trophozoite form in a suitable environment[8]. Trophozoites grow fast at around 42°C and proliferate by binary fission. In their free-living state, trophozoites feed on bacteria, while in tissues they phagocytose red and white blood cells and destroy tissue. A biflagellate form occurs when trophozoites are exposed to a change in ionic concentration such as placement in distilled water. Trophozoites encyst due to unfavorable conditions such as food deprivation, crowding, desiccation, accumulation of waste products and cold temperatures below 10°C[9]. More than 30 *Naegleria* species have been isolated from environmental sources with only *N. fowleri* known to cause human infections. Two other species, *N. australiensis* and *N. italica,* can cause infection in experimental animals but these species have never been identified in human infections**;** although they too are found in warm, stagnant bodies of water, and even chlorinated swimming pools, making contact with humans inevitable[10]. While a large number of animals also bathe, swim and frolic in thermally polluted waters, only one case of PAM has been described[11]in a South American tapir and another case in Holstein cattle[12]which was diagnosed by immunofluorescence in brain sections. Recently, an amoeba was isolated from the brain of an infected cow and identified as *N. fowleri* based on morphology[13]and sequencing of the internal transcribed spacers (ITS), including the 5.8S rRNA genes[14]. Until 2012, the 310 human cases reported worldwide were mostly from Australia, United States, Great Britain, Czechoslovakia, Thailand and Mexico. These cases typically occurred during the summer months in warm, humid climates presumably because of warmer water coupled with increased swimming activities. In North America, 111 human cases have been reported in the USA and nine cases in Mexico until 2008[15]. The majority of infections in Mexico occurred after swimming in water naturally heated by the sun, while in California, a few cases occurred after swimming in geothermal waters. In addition, PAM infections occurred in the USA by using tap water originating from warm groundwater and the amoeba was subsequently isolated from the well[16].

Pathophysiology of *N. fowleri* Infections

During human bathing or swimming, *Naegleria fowleri* enters forcefully the upper nasal passages developing an acute infection (Bright andGerba, 2017). In the beginning of infection the parasite attaches to the mucosa of the nose, movesthrough nerves, and finally reaches the olfactory bulbs through the cribriform plate inside the central nervous system (Heggie, 2010). PAM opportunity is very high in children and adult with a porous cribriform plate (Heggie and Küpper, 2017). The recent study showed that Naegleria fowleri could infect human only when entering the nasal passage and does not make any infection when entering the oral passage during drinking contaminated water (Shakeel *et al.,* 2016). Certain circumstances can lead to the disease such as the ability of Trophozoites in attaching the mucosa of the nose, chemotactic response to nerve cell components and the speed of the locomotion (Naqvi *et al.,* 2016). Invasion could be detected by several clinical features such as smell ability change, respiratory system infection by neural tissue and olfactory epithelium invasion (Visvesvara *et al.,* 2007). The signs and symptoms of PAM patient do not contain bleeding, nasal pain during inflammation, tenderness of the nose Bridg and Rhinorrhea before Meningitis signs (Naqvi *et al.,* 2016). Even Destruction of the mucous and olfactory bulb "which would be surrounded by purulent exudate", the Hemorrhagic and necrosis are usually occur (Visvesvara *et al.,* 2005). Hemorrhage of the brain cortex and adjacent areas were also observed after infection with pam, while a destruction of non-olfactory mucosa in the nose was not-recorded

(Baig *et al.,* 2016). A cisternae of subarachnoid space and midbrain may appear during CT scans over the cerebral hemispheres. Many lesions could appear around the temporal and orbitofrontal lobes, hypothalamus, midbrain, medulla oblongata, pons, brain base and the upper part of the spinal cord (Morales *et al*., 2006). A fibrino-purulent leptomeningeal excretion (macrophages, lymphocytes, eosinophils and predominantly PMNs) could be examined microscopically filling the brain stem, cerebral hemispheres, and upper part in the spinal cord and cerebellum (Baig *et al.,* 2016).

Clinical symptoms: When polluted water with *Naegleria fowleri* is forcing into human nasal passage by diving, skiing swimming and other activities, PAM begins in approximately 5 - 7 days, and may even begin in 24 hrs (Fowler and Carter, 1965). It is important to get "12 week" past history of the patient to know if there is any fresh water contact "such as hot springs and swimming pools, "To determine whether the infection is bacterial meningoencephalitis or from *Naegleria fowleri* because of the similarities in the clinical symptoms in both infections (Jones *et al.,* 2009).*Naegleria fowleri* symptoms begins first with abifrontal headache, fever, nausea, restlessness, irritability and vomiting, the infection of the olfactory nerve at the beginning of the disease could led to a smell and taste alterations also. In the clinical course, Photophobia may occur late then neurological changes such as lethargy, seizures, confusion, coma, diplopia or bizarre behaviour, leading to death within a week. Brain oedema may cause a Cranial nerve palsy in the third, fourth, and sixth cranial nerves, myocardial necrosis and abnormalities of the Cardiac rhythm have been occur (Jones *et al.,*2009). Death may occur in about 7 - 10 days post infection because of the necrotic haemorrhagic that follows infection of the CNS.

Treatment: Systemic amphotericin B with or without miconazole, sulfisoxazole and rifampinis was the best treatments of PAM because *Naegleria fowleri* is very sensitive for that medication *in vitro* (Schuster and Visvesvara, 2004). A serious acute reactions after the infusion was detected including shaking, headache, nausea, chills, dyspnoea, tachypnoea and fever (Proffitt *et al.,* 1991). Fluconazole was effective treatment in reducing the dysfunction of the infected organs by increasing neutrophils numbers and due to its ability in penetration the blood-brain barrier(Jacobs *et al*., 2003). For experimental PAM in mice, Azithromycin was a good treatment, Phenothiazine compounds had the ability to inhibit *Naegleria fowleri in vitro* because it can accumulate in the CNS (Schuster and Visvesvara,2004). Fluconazole, Amphotericin B and oral Rifampicin were recorded as the best medicationsfor PAM infected patient during the early diagnosis (Vargas - Zepeda *et al*., 2005). Also theeffect of antibacterial agents such as Neomycin, Roxithromycin, Clarithromycin, Rokitamycin, Zeocin, Hygromycin and Erythromycin all were tested in both *in vitro* and *in vivo* showing *Naegleria fowleri* inhabitation, Chlorpromazine was recorded as a rapid and strong treatment for *Naegleria fowleri* Trophozoites more than Fluconazole and Amphotericin (Tiewcharoen *etal.,* 2011).

Prevention and Control

Naegleria fowleri prefers reproduction in water with a temperature above 30 °C because it is a thermophilic amoeba, therefore it is not surprising to see cases of PAM in areas where it had not been recorded before with the recent global warming (Cogo *et al*., 2004). *Naegleriafowleri* can be controlled in swimming pools during hot months by using Chlorinated water to prevent reproduction, furthermore in the recreational water areas where the infection chance of PAM is high, people should not immerse their heads in non-chlorinated water, also purified water should be used in nasal cleansing process (Schuster and Visvesvara, 2004).

Conclusion

Naegleriafowleri is a dangerous parasite that is responsible for primary amoebic meningoencephalitis with a death rate approximately 95 % in human. It is a wide

spread in the countries where summer months are very hot. The parasite cause the disease when human is in contact with polluted water. The infection begins with the entrance of the infective stage "Trophozoites" to the nasal passage, reaches the brain, causing the infection to the central nervous system and finally death in 3 – 7 days. Even there is a medication this serious infection such as Amphotericin B but it is still killing. Finally, it could be concluded that it is important to make further studied about this parasite and how to protect the immune system by controlling this pathogen.

Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Gyori E. 19-year-old male with febrile illness after jetski accident. Brain Pathol; 2003, 13: 237–9.
2. Centers for Disease Control and Prevention (CDC). Primary amebic meningoencephalitis-Arizona, Florida, and Texas, 2007. MMWR Morb Mortal Wkly Rep; 2008, 57: 573-7.
3. Martinez AJ, Visvesvara GS. Free-living, amphizoic and opportunistic amoebae. Brain Pathol; 1997, 7: 583–98.
4. Huizinga HW, McLaughlin GL. Thermal ecology of *Naegleria fowleri* from a power plant cooling reservoir. Appl Environ Microbiol; 1990, 56:2200–5.
5. Marciano-Cabral F, MacLean RC, Mensah AH, La-Pat L. Identification of *Naegleria fowleri* in domestic water sources by nested PCR. Appl Environ Microbiol; 2003, 69:5864–9.
6. Marciano-Cabral F, Cabral GA. The immune response to *Naegleria fowleri* amebae and pathogenesis of infection. FEMS Immunol Med Microbiol; 2007, 51(2): 243-59.
7. **7.**Fowler M, Carter RF. Acute pyogenic meningoencephalitis probably due to *Acanthamnoeba spp.*: A preliminary report. Br Med J; 1965**,** 3:740-2.
8. Jones K, Singhatiraj E, MacDougall R, Beaver TR, Nugent K. A 22-year-old man with headache and stiff neck after a water skiing fall. Chest; 2009, 135(1):225-7.
9. Marciano-Cabral F. Biology of *Naegleria* spp. Microbiol Rev; 1988, 52:114–33.
10. De Jonchheere JF. Molecular definition and the ubiquity of species in the genus *Naegleria.* Protist; 2004, 155: 89–103.
11. Lozano-Alarcon F, Bradley GA, Houser BS, Visvesvara GS. Primary amebic meningoencephalitis due to *Naegleria fowleri* in a South American tapir. Vet. Pathol; 1997, 34**:** 239-43.
12. Daft B, Kinde H, Read D, Visvesvara GS. *Naegleria fowleri* meningoencephalitis in Holstein cattle associated with drinking surface water. Proceedings of the 42nd Meeting of American Association of Veterinary Laboratory Diagnosticians, San Diego, California; 1999, p. 59.
13. Visvesvara GS, De Jonckheere JF, Sriram R, Daft B. Isolation and molecular typing of *Naegleria fowleri* from the brain of a cow that died of primary amebic meningoencephalitis. J Clin Microbiol; 2005**,** 43(8): 4203–4.
14. Morales JA, Chavez AJ, Visvesvara GS, Dubey JP. *Naegleria fowleri*-associated encephalitis in a cow from Costa Rica. Vet Parasitol; 2006, 139: 221-3.
15. Yoder JS, Eddy BA, Visvesvara GS, Capewell L, Beach MJ. The epidemiology of primary amoebic meningoencephlitis in the USA, 1962–2008. Epidemiol. Infect; 2010, 138: 968–75.
16. Bennett WM, Nespral JF, Rosson MW, McEvoy KM. Use of organs for transplantation from a donor with primary meningoencephalitis due to *Naegleria fowleri*. Am J Transplant; 2008, 8: 1334–5.