Naegleria Fowleri – Simple Facts About Brain Eating Amoeba

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Year after year, the inhabitants of Karachi have to face the fear and panic of Naegleria fowleri which can cause deadly disease called meningoencephalitis. A common citizen remains extremely wary of what to do and what not to do. The health authorities do come up with awareness campaigns mounted on large sized billboards, yet the simple facts remains eluded to even majority of health care personne[1].

It was in 1958 that Culbertson and his colleagues first described the concept that free living soil and water amoebae can cause disease in humans. Since then number of fatal cases of acute meningoencephalitis have been reported.[1] Naegleria is a free living amoeba, commonly found in warm freshwater for example, lakes, rivers, hot springs and soil. Only one of the specie of Naegleria known as Naegleria fowleri is pathogenic and infects humans. This parasite infects people when water containing the amoeba enters the body through the nose. This normally occurs when people swim or dive in warm freshwater places, like lakes and rivers. The amoeba then travels up the nose to the brain via olfactory nerve where it destroys the brain tissue.[2] As this amoeba can be found in warm freshwater, such as lakes and rivers, swimming pools that are poorly maintained, minimally chlorinated, and/or un-chlorinated, so the recreational water users should be aware that there will always be a low level risk of infection when entering these waters. Different behaviors associated with the infection include diving or jumping into the water, submerging the head under water or engaging in other water-related activities that cause water to go up the nose.[3]

Naegleria fowleri grows best at higher temperatures of up to 115°F (46°C). It occurs in three forms, a cyst, a trophozoite (amoeboid) and a flagellate. It is to be remembered that it does not form a cyst in human tissue. Only the amoeboid trophozoite stage exists in human tissue and actually is the pathogenic form. Trophozoites encyst due to unfavorable conditions. Factors that induce cyst formation include overcrowding, desiccation, accumulation of waste products, and cold temperatures. Naegleria fowleri has been found to encyst at temperatures below 10 °C/50°F. Trophozoite stage is reproductive stage of the protozoan organism, which transforms near 25 °C/77°F and grows fastest at around 42 °C/106.7°F proliferating by binary fission. The trophozoites are characterized by a nucleus and a surrounding halo. They travel by pseudopodia, temporary round processes which fill with granular cytoplasm. The pseudopodia form at different points along the cell, thus allowing the trophozoite to change directions. In their free-living state, trophozoites feed on bacteria. In tissues, they phagocytize red and white blood cells and destroy tissue.[2] Pathogenic form (trophozoite) is less likely to be found in the water as temperatures decline. While infections with Naegleria fowleri are rare, they occur mainly during the summer months of July, August, and September. Infections usually occur when it is hot for prolonged periods of time, which results in higher watertemperatures and lower water levels.[4,5]

Naegleria fowleri causes the disease Primary Amoebic Meningoencephalitis (PAM), a brain infection that leads to the destruction of brain tissue. In its early stages, symptoms of PAM may be similar to symptoms of bacterial meningitis. Initial symptoms of PAM start about 5 days (range 1 to 7 days) after infection. The initial symptoms may include headache, fever, nausea, or vomiting. Later symptoms can include stiff neck, confusion, lack of attention to people and surroundings, loss of balance, seizures, and hallucinations. After the start of symptoms, the disease progresses rapidly and usually causes death within about 5 days (range 1 to 12 days). The infection destroys brain tissue causing brain swelling and death.[2,6]

Currently, a great deal of work is being done to determine what factors specific to Naegleria fowleri makes it pathogenic and if these virulence factors could be targeted by drugs. One potential factor in motility of the "amoeba" is the protein coded by Nfa[1] gene. When the Nfa1 gene is expressed in non-pathogenic Naegleria gruberi and the amoebae are co-cultivated with target tissue cells, the protein is found to be located on the food cup which is responsible for ingestion of cells during feeding. Subsequen to those researches, Nfa1 gene expression knockdown experiments have been performed using RNA interference. In these experiments, double stranded RNA targeting the Nfa1 sequence was introduced and subsequently expression levels of the gene product dramatically decreased. This method could potentially be a technique applicable for knockdown of expression of pathogenicity factors in Naegleria fowleri trophozoites.[7]

The analysis of CSF of affected persons reveals decreased glucose, and increased protein concentrations. Leukocytes may range from several hundred to > 20,000 cells/mm^2.Gram stain and cultures of CSF are negative. The wet mount of CSF placed on a slide and covered with cover slip examined as soon as possible is observed for characteristic motile trophozoites. The amoeba can be grown in several kinds of liquid axenic media or on non-nutrient agar plates coated with bacteria. Escherichia coli can be used to overlay the non-nutrient agar plate and a drop of cerebrospinal fluid sediment is added to it. Plates are then incubated at 37 °C and checked daily for clearing of the agar in thin tracks, which indicate the trophozoites have fed on the bacteria. Detection in water is performed by centrifuging a water sample with E. coli added, then applying the pellet to a non-nutrient agar plate. After several days, the plate is microscopically inspected and

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Naegleria cysts are identified by their morphology. Final confirmation as regards the specie can be performed by various molecular or biochemical methods. Confirmation of Naegleria presence can be done by a so-called flagellation test, where the organism is exposed to a hypotonic environment (distilled water). Naegleria, in contrast to other amoebae, differentiates within two hours into the flagellate state. Pathogenicity can be further confirmed by exposure to high temperature (42 °C): Naegleria fowleri is able to grow at this temperature, but the nonpathogenic Naegleria gruberi is not.[2, 8]

As regards the treatment Amphotericin B is effective against Naegleria fowleri in vitro, but the prognosis remains poor for those who contract PAM, and survival remains less than 1%. On the basis of the in vitro evidence alone, the Center for Disease Control and Prevention (CDC) currently recommends treatment with Amphotericin B for primary amoebic meningoencephalitis, but unfortunately no evidence supports this treatment affecting outcome. Treatment combining miconazole, sulfadiazine, and tetracycline has shown limited success only when administered early in the course of an infection.[8, 9]

Prevention remains the only plausible solution to minimize the risk of acquisition of this parasite. Public awareness campaigns combined with adequate chlorination of water systems and swimming pools are recommended to prevent this infection. The swimmers are also advised to be careful not to allow water get up their nose. It is also advisable to be careful while cleansing the nose during religious practices when contaminated tap or faucet water is imminent. Naegleria fowleri can grow in pipes, hot water heaters, and water systems, including treated public drinking water systems. Hence public health authorities have to ensure the adequate chlorination of water at all times. Personal actions to reduce the risk of Naegleria fowleri infection should focus on limiting the amount of water going up the nose in all activities which involve contact with water.[2,10]

REFERENCES:

1. Schuster FL, Visvesvara GS. Free living amoebae as opportunistic and non –opportunistic pathogens of humans and animals. Int J Parasitol 2004; 34: 1001-27.
2. Garcia LS. Free living amoebae. In: Diagnostic Medical Microbiology. 5th Ed. ASM press;2007 p102-22
3. Phu NH, Hoang Mai NT, Nghia HD, Chau TT, Loc PP, Thai l H. Fatal consequences of freshwater pearl diving. Lancet. 2013; 381:176.
4. Gautam PL, Sharma S. A rare case of survival from primary amebic meningoencephalitis. Indian Crit Care Med 2012; 16:34-6.
5. Hebbar S, Bairy I .Fatal case of Naegleria fowleri meningo-encephalitis in an infant. Ann Trop Paediatr 2005; 25:223-6.
6. ShariqA, Afridi FI, Farooqi BJ, Ahmed S, Hussain A. Fatal primary meningoencephalitis caused by Naegleria fowleri. J Coll Physicians Surg Pak 2014; 24:523-5.
7. Kim JH, Yang AH, Sohn HJ, Kim D, Song KJ, Shin HJ. Immunodominant antigens in Naegleria fowleri excretory secretory proteins were potential pathogenic factors. Parasitol Res 2009; 105:1675-81.
8. Center for Disease Control and Prevention. Primary amoebic meningoencephalitis--Arizona, Florida, and Texas, 2007. MMWR Morb Mortal Wkly Rep. 2008; 57(21):573-7.
9. Vargas-Zepeda J, Gomez-Alcala AV, Vasquez-Morales JA, Licea-Amaya L, De Jonckheere JF, Lares-Villa F.Successful treatment of Naegleria fowleri meningoencephalitis by using intravenous amphotericin B, fluconazole and rifampicin. Arch Med Res 2005;36: 83-6
10. Shakoor S, Beg MA, Mahmood SF, Bandea R, Sriram R, Noman F. Primary amoebic meningoencephalitis caused by Naegleria fowleri, Karachi, Pakistan. Emerg Infect Dis. 2011; 17:258-61.