

## Community-acquired meningoencephalitis due to concomitant infection caused by *Naegleria fowleri* and *Streptococcus pneumoniae* from Karachi, Pakistan: A Case Report

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### Abstract

*Naegleria fowleri* causes acute fatal primary amoebic meningoencephalitis in adults and children with a history of exposure to aquatic activities. However, several cases of Primary Amoebic Meningoencephalitis (PAM) have been reported from Karachi with no history of aquatic recreational activities suggesting the presence of *N. fowleri* in domestic water. This study reports a case of co-infection of *N. fowleri* with *Streptococcus pneumoniae* in an elderly hypertensive male.

**Keywords:** *Naegleria fowleri*. PAM, *Streptococcus pneumoniae*.

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### Introduction

Community acquired meningitis is a severe acute condition caused by several pathogens. There are reports of nosocomial superinfection in bacterial meningitis and of mixed bacterial and fungal infection. Co-infection in acute bacterial meningitis is usually seen in patients with neurosurgical events such as insertion of an external drainage device, surgical intervention, head or spinal injury and immunosuppression. These conditions might lead to infection of the central nervous system (CNS) with more than one organism.<sup>1</sup> Repeat cerebrospinal fluid (CSF) culture is mandatory to confirm the diagnosis as most of the implicated bacterial strains are resistant to common antibiotics. *Streptococcus pneumoniae* (*S. pneumoniae*) is a common cause of meningitis globally. Infection of the meninges occur either through the haematogenous route or by the direct extension of infection from the paranasal sinuses or from the middle ear through the mastoid.

Primary amoebic meningoencephalitis (PAM) due to

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*Naegleria fowleri* (*N. fowleri*) is a rare disease with high mortality. In recent years, several cases of PAM have been reported from Pakistan.<sup>2,3</sup> PAM occurs when *N. fowleri* enters the nose usually during swimming, and then migrates along the olfactory nerve through the cribriform plate to the brain. Symptoms start an average of five days after exposure and are indistinguishable from those of acute community-acquired bacterial meningitis. Symptoms include nausea, vomiting, headache, high grade fever, neck stiffness, progressing to altered mental status, seizures, coma, and death. *N. fowleri* infections occur primarily in young males and children.<sup>4,5</sup> This study reports an exceptionally rare case of concurrent central nervous system infection (CNS) with *N. fowleri* and *S. pneumoniae*.

### Case Report

A 75-year-old hypertensive male from Karachi presented with complaints of fever, headache, nasal congestion, neck stiffness, and altered consciousness for two days on October, 26, 2016 at Aga Khan University Hospital, Karachi. He experienced progressive weakness and confusion after falling at home. The patient was brought to the emergency room with Glasgow coma scale (GCS) of 13 and was started on IV Ceftriaxone, Acyclovir and Dexamethasone empirically. On day two, his neurologic status deteriorated, he was given Meropenem, Vancomycin, and Acyclovir, while Ceftriaxone was stopped to cover penicillin resistant *S. pneumoniae*. A lumbar puncture was performed and cerebrospinal fluid (CSF) was submitted to the laboratory for analysis and culture. CSF analysis was performed on day one of hospitalisation showing glucose 84 mg/dL (40-70 mg/dL), high protein level 393 mg/dL (15-40 mg/dL), red blood cells (RBCs) 40 cells/mm<sup>3</sup> (0 cells/mm<sup>3</sup>), and white blood cells (WBCs) 6000 cells/mm<sup>3</sup> with 10% lymphocytes and 90% neutrophils (0-5 cells/mm<sup>3</sup>). It was repeated again on day four showing similar glucose (84 mg/dL), and protein (390 mg/dL), levels but raised RBC (13000 cells/mm<sup>3</sup>), and WBCs (9300 cells/mm<sup>3</sup> with 10% lymphocytes and 90% neutrophils). Gram stain of the CSF revealed inflammatory cells with a few gram-positive lancet-shaped diplococci, suggestive of *S. pneumoniae*. Wet film preparation of unspun CSF was negative for trophozoites of *N. fowleri*. Due to summer in Karachi

(average temp 35°C) and presence of RBC in the CSF, it was also sent for polymerase chain reaction (PCR) based detection of *N. fowleri*. CSF tested positive for *N. fowleri* in two independent real-time PCR assays. The patient had no history of swimming in fresh water. PAM protocol was started immediately after PCR results and the patient was treated with amphotericin B 1.5 mg/kg every 12 hours for three days with 1mg/kg/day intravenous (IV) plus 1.5 mg Intrathecal, Azithromycin 10mg/kg once daily (OD), Fluconazole 800mg in 24hr, Rifampicin 600mg IV (OD), Chlorpromazine 2gm/day, and Miltefosine 150mg/day for PAM. Antibacterial therapy was also continued with no sign of improvement.

The patient died four days after admission. CSF and blood culture were reported as negative for fungal growth. Both CSF samples were reported positive for *S. pneumoniae* DNA using previously reported PCR method.

## Discussion

We report a rare case of concomitant CNS infection caused by *S. pneumoniae* and *N. fowleri*. Presence of both organisms in the CSF was confirmed by PCR.<sup>6,7</sup> Unfortunately, PAM remains clinically indistinguishable from acute bacterial meningitis and cases are often treated empirically for common bacterial meningitis. Detection of *N. fowleri* on routine microscopic examination of CSF is difficult, which leads to delayed diagnosis and initiation of appropriate PAM therapy causing irreversible damage to the brain. This can be one of the factors responsible for the high mortality associated with the disease.<sup>8</sup>

A study comparing acute bacterial meningitis and PAM showed no significant difference in clinical presentation such as headache, high-grade fever, and meningeal irritation along with indistinguishable haematological and CSF parameters.<sup>3</sup>

Super infection with acute bacterial meningitis in patients with surgical intervention is reported previously.<sup>9,10</sup> Similarly, few cases of meningeal co-infection with fungal pathogens and parasites are also reported in immune-compromised patients.<sup>11</sup>

In this rare case, a previously healthy male with no known co-morbid conditions or known immune-compromised status was revealed to be infected with two pathogens—*N. fowleri* and *S. pneumoniae*. Acquired on presentation, the patient was suspected of community pneumococcal meningitis and treated empirically. CSF gram stain revealed few *S. pneumoniae*. *S. pneumoniae* is a common pathogen causing meningitis with comparatively high case fatality rate in elderly population. Pneumococcal vaccination can be beneficial in elderly people. *N. fowleri* was not identified

on wet prep; however, PCR confirmed the presence of *N. fowleri*. In Karachi, local physicians are aware of PAM and often include investigation of *N. fowleri*, especially in summer.<sup>12</sup>

Considering the experience of the last eight years,<sup>2,8</sup> we anticipate that PAM cases are under-reported from Karachi and Sindh. This is due to lack of expertise, limited molecular testing facilities and lack of awareness among clinicians.<sup>13</sup> Nucleic acid amplification (PCR) based diagnosis is the gold standard and is more sensitive than wet prep examination for rapid detection of *N. fowleri*.

PAM cases, that have been reported worldwide, had a history of fresh water swimming or other aquatic recreational activities and nasal irrigation. Cases reported from Pakistan had a history of exposure to tap water used for ablution and bathing, suggesting the presence of *N. fowleri* in domestic water supply. Unchlorinated domestic water is the likely source of exposure to *N. fowleri* in this case as no swimming history was reported. There is a need for enhanced chlorination of domestic water supply and swimming pools should take stringent measures to reduce the risk of amoebic growth. Public awareness activities need to be organised to reduce the risk of *N. fowleri* infection, especially in areas where water quality is compromised.

## Conclusion

These challenging cases such as the presented one, require close communication between laboratory and treating physicians for timely diagnosis and management. We anticipate this report will create more awareness among clinicians about this fatal disease, available diagnostic and treatment options to improve outcomes. The limitation of the study was a considerable delay of 5.5 years in reporting the current study due to pandemic related responsibilities.

**Consent to participate:** Informed consent was obtained from the legal guardians. This study was approved by AKU-ERC (3603-Path-ERC-15).

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**Conflicts of interest:** None.

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