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June 26, 1992 / 41(25);437-440

## Primary Amebic Meningoencephalitis -- North Carolina, 1991

During September 1991, two children in North Carolina died from primary amebic meningoencephalitis (PAM), a rare and often fatal illness resulting from infection with *Naegleria fowleri*. This report summarizes clinical and epidemiologic information about these two cases and characterizes *N. fowleri* infection. Patient 1

In September 1991, a previously healthy 3-year-old girl was evaluated by her physician for a 36-hour history of headache and fever; she was lethargic without focal neurologic or meningeal signs. Four hours after evaluation, she became disoriented and did not recognize her parents. When examined at a local emergency department, she was unresponsive to painful stimuli and had fever of 101.8 F (38.8 C). Subsequently, she had a generalized seizure, followed by posturing movements; she was treated with anticonvulsants and tracheally intubated.

Ceftriaxone was initiated for suspected meningitis. She was transferred to a children's hospital, where she responded only to painful stimuli by flexion withdrawal. Computed tomography (CT) of the head without contrast was normal. No organisms were seen on Gram or acid-fast stains of cerebrospinal fluid (CSF); CSF antigen-detection tests were negative for *Haemophilus influenzae* type b, group B *Streptococcus*, *S. pneumoniae*, *Neisseria meningitidis*, and *Escherichia coli* K1. CSF red blood cell count (RBC) was 1800 per mm<sup>3</sup>; white blood cell count (WBC), 8000 per mm<sup>3</sup>; glucose, 41 mg/dL; and protein, 950 mg/dL.

Fourteen hours after admission, the patient developed primary central hyperventilation and anisocoria. Head CT with contrast revealed generalized meningeal enhancement most prominent in the basilar cisterns, with mild hydrocephalus and no brain swelling. Initial bacterial cultures of blood, CSF, and urine were negative.

On the second hospital day, further history revealed that the family, including the patient, had been swimming in a freshwater pond 7 days before the patient's hospitalization. A second CSF specimen obtained 38 hours after admission was xanthochromic with 17 mg/dL glucose, 3200 mg/dL protein, 500 RBC per mm<sup>3</sup>, and 2400 WBC per mm<sup>3</sup>. No amebae were seen on Giemsa stain. There was no evidence of brain stem function; brain death was diagnosed on hospital day 4.

Autopsy findings revealed acute PAM caused by *N. fowleri*. Cerebral and spinal cord edema were severe. Sections of the cribriform plate revealed inflammatory infiltration of the nasal mucosa, submucosa, olfactory nerves and dura mater overlying the frontal cortex at the base of the brain.

Additional history during a postmortem conference indicated that 5 days before illness the patient had been learning to swim at the freshwater pond. She stayed primarily in shallow areas and had repeatedly inhaled and swallowed quantities of water. Patient 2

In September 1991, a previously healthy 4-year-old boy was admitted to a community hospital with a 3-day history of fever to 102 F (38.9 C) and headache. The child had vomited during the 2 days before admission but had remained alert and intermittently playful. On evaluation he was febrile with neck stiffness and positive Kernig's and Brudzinski's signs. CSF contained 77 mg/dL glucose and 150 mg/dL protein, with 123 RBC per mm<sup>3</sup> and 1830 WBC per mm<sup>3</sup>. On admission, blood, urine, and CSF cultures were obtained; ceftriaxone was initiated intravenously. Four hours after admission, the patient had brief generalized tonic-clonic seizures. Although anticonvulsant therapy was initiated, he had another brief generalized seizure, after which he remained agitated and intermittently disoriented. He was then transferred to a university medical center.

On admission, additional history revealed that the patient swam in a grassy marsh 18 days before becoming ill. He was afebrile but he remained intermittently disoriented; respiratory distress developed shortly after admission, and a chest radiograph was consistent with aspiration pneumonia. His respiratory status deteriorated, and he was tracheally intubated. Five hours after admission he developed anisocoria. Head CT showed massive brain swelling. Treatment included hyperventilation, placement of a ventriculostomy, and parenteral dexamethasone.

Despite these efforts, the patient continued to deteriorate. He developed fixed and dilated pupils bilaterally. Spontaneous respirations ceased, and there was no response to painful stimuli. Brain death was diagnosed. Cerebellar brain cuttings during autopsy revealed *N. fowleri* in the subarachnoid space.

Additional history indicated that the patient had been swimming in a freshwater lake 5 days before hospital admission.

Reported by: I Fiordalisi, MD, J Christie, MD, Greenville; C Moffitt, MD, Durham, North Carolina. Div of Parasitic Diseases, National Center for Infectious Diseases, CDC.

## Editorial Note

Editorial Note: *N. fowleri* is an ameboflagellate from the family Vahlkampfiidae, whose members can transform from amebae to flagellates; either form can cause disease. Although infection with *N. fowleri* is rare, cases have been reported throughout the world (e.g., in Australia, Belgium, Czechoslovakia, Great Britain, India, Ireland, New Zealand, Nigeria, Panama, Puerto Rico, Uganda, and Venezuela). During 1991, in the United States, four patients were reported to have had fatal PAM. *N. fowleri* is most frequently isolated from natural and manmade bodies of warm fresh water. Most cases of PAM occur in previously healthy nonimmunocompromised children or young adults and have been traced to water-related activities during hot summer months.

Amebae invade the central nervous system through the cribriform plate and can be found in the subarachnoid and perivascular spaces. Disease characteristics include inflammation of the olfactory bulbs, progressing rapidly to the cerebral hemispheres, brain stem, posterior fossa, and spinal cord. Symptoms occur within 7 days of exposure, are indistinguishable from fulminant bacterial meningitis, and can include headache, fever, anorexia, vomiting, signs of meningeal

inflammation, altered mental status, and coma. Signs of brain stem compression and seizures may ensue. Death typically occurs within 72 hours of onset of symptoms.

CSF findings mimic those of bacterial meningitis, with a predominantly polymorphonuclear leukocytosis and increased protein and decreased glucose concentrations. Occasionally, amebae may be seen on Gram-stained smears. Typically, however, PAM is diagnosed at autopsy. The key to diagnosis during life rests on clinical suspicion based on history. PAM should be suspected in a previously healthy patient with history of exposure to fresh, warm water within 7 days of onset of illness and who has clinical findings characteristic of bacterial meningitis and predominantly basilar distribution of exudate by head CT.

If PAM is suspected, a fresh nonrefrigerated specimen of CSF must be brought directly to the laboratory. If lumbar puncture has already been done and another cannot be performed, inspection of the high-velocity centrifuged preparation made for determination of CSF cell count may be helpful, especially if "atypical mononuclear cells" are reported; such cells actually may be amebae. Although culture of the organism on an agar slant or plate containing *E. coli* or *Enterobacter aerogenes* is possible, most laboratories are not prepared to perform such cultures. Thus, diagnosis depends on microscopic examination of CSF. CSF should be examined in wet-mount preparation as well as with fixation and staining. Dilution of 1 drop of CSF with 1 mL of distilled water will allow transformation of the organism within 1-20 hours from the ameboid to the biflagellate form. For permanently stained preparations, Masson's trichrome stain is optimal as it is generally available and readily demonstrates the ameba's typical nuclear morphology consisting of a prominent central nucleolus without any chromatin lining the nuclear membrane (1-4).

Three survivors of PAM have been documented (5-7). Successful therapy in these cases appeared related to early diagnosis and administration of intravenous and intrathecal or intraventricular amphotericin B along with intensive supportive care. One surviving patient received miconazole intravenously and intrathecally and rifampin orally (7).

In nearly all instances of infection in the United States, several other persons swam in the same water at the same time but did not become ill. The specific behavioral, physiologic, or anatomic risk factors for disease are unknown. More aggressive diagnosis and reporting of disease may assist in clarifying risk factors and in improving therapeutic interventions and possible strategies for prevention.

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This page last reviewed 5/2/01