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Fatal Group A Streptococcal Meningitis Following Acute Otitis Media

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A 13-year-old girl presented to the emergency department (ED) with a 3-hour history of altered mental status (AMS), vomiting, and fever. One week prior, she had been seen at a local urgent care clinic with rhinorrhea, cough, and bilateral ear pain and had received a diagnosis of influenza A (via rapid point-of-care testing) and acute otitis media (AOM). She had received oseltamivir but not antibiotic therapy. Her symptoms initially had improved, but on the day of admission, she developed AMS. There was no history of head trauma, travel, or exposure to mosquitoes or ticks.

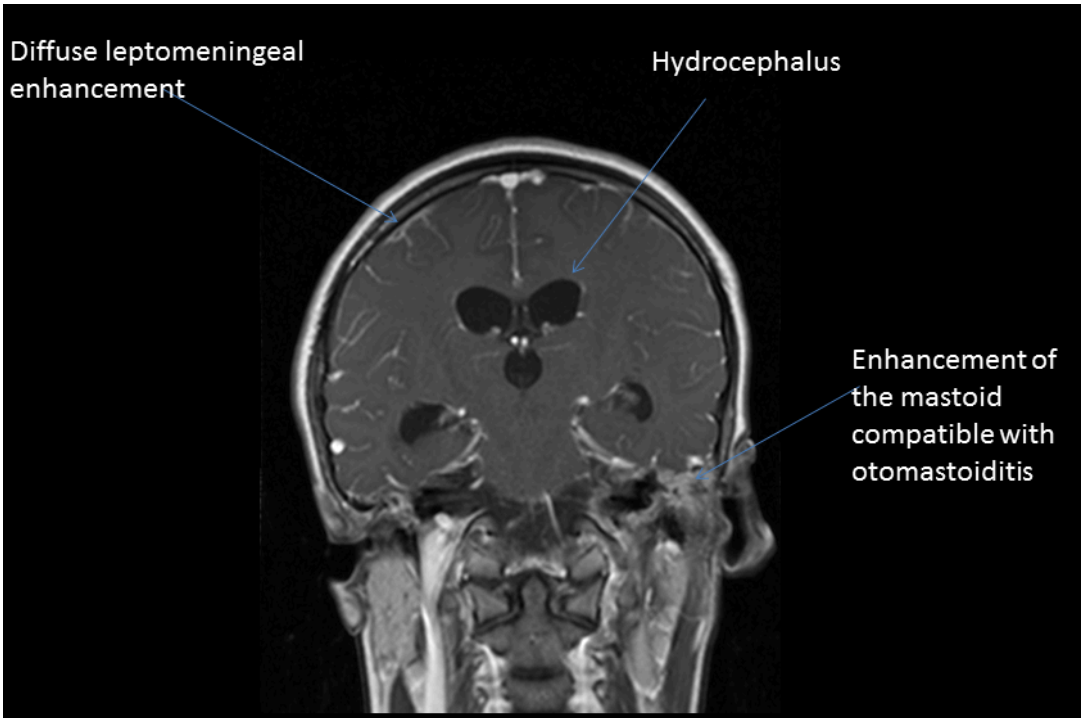
Physical examination. On admission, she was critically ill, with a temperature of 35.0°C, heart rate of 80 beats/min, respiratory rate of 26 breaths/min, blood pressure of 108/71 mm Hg, and a Glasgow Coma Score of 5. She had nonreactive pupils, a stiff neck, and bilateral purulent otorrhea.

Diagnostic tests. Lumbar puncture opening pressure was high (>55 cm H_2O); cerebrospinal fluid (CSF) showed a white blood cell (WBC) count of 462/μL (72% neutrophils), a glucose level of less than 20 mg/dL, and a protein level of 462 mg/dL. CSF histopathology showed gram-positive cocci in chains and pairs. A complete blood cell count showed a WBC count of 33,000/μL (83% neutrophils), a hemoglobin level of 11.0 g/dL, and a platelet count of 338 × 10^3/μL. Liver and renal function test results were normal. The serum lactate level was 2.6 mg/dL (reference value, <2.1 mg/dL). Urine drug screen results were negative.

After a blood culture was obtained, the patient received vancomycin, ceftriaxone, and acyclovir. She was intubated and admitted to the pediatric intensive care unit for critical care management.

Computed tomography (CT) scans of the head showed diffuse cerebral edema, hydrocephalus, and otomastoiditis. She was switched to vancomycin and meropenem for coverage of anaerobic bacterial infection. Tympanostomy tubes and an external ventricular drain were placed by the neurosurgery service.

Her condition worsened with acute neurologic deterioration, rising intracranial pressure, and the development of diabetes insipidus. Magnetic resonance imaging/angiography of the brain showed acute infarcts, cerebritis, hydrocephalus, and enhancement of leptomeninges (**Figure**). Despite aggressive critical care support, the girl died within 160 hours after presentation. Cultures from blood, CSF, and ear drainage grew group A streptococcus (GAS), sensitive to penicillin.



Discussion. Clinicians are often faced with decisions about antibiotic use in pediatric patients with AOM,[1] since early frequent antibiotic exposure can lead to colonization, treatment failure, and spread of resistant bacteria to close contacts.[2] Approximately 4% to 10% of children who receive antibiotics for AOM experience adverse effects.[3] Antibiotic overuse also has substantial financial cost.[4] In 2013, the American Academy of Pediatrics published clinical guidelines recommending observation off antibiotics in a subset of patients with uncomplicated AOM.[2]

Sequelae of AOM are relatively rare but include extracranial complications (eg, tympanic perforation, mastoiditis) and intracranial complications (eg, meningitis, empyema, venous thrombosis).[5] GAS meningitis is unusual in adults and children, accounting for less than 1% to 2% of cases of pyogenic meningitis.[6,7] In approximately two-thirds of childhood cases, a recognized focus of infection is noted, especially AOM.[7-9]

The precise pathophysiology of GAS meningitis following AOM is unclear, but the condition may result from direct extension of infection through the dura or other fistulized areas.[9,10] Although GAS represents less than 10% of all AOM cases,[11-13] the organism is virulent, particularly in younger children and older adults, likely related to immature and weak immune systems, respectively. The risk of development of mastoiditis/tympanic membrane perforation from GAS vs other pathogens was 11.6 per 1000 episodes compared with 2.2, 0.3, and 0 from *Streptococcus pneumoniae*, *Haemophilus influenzae,* and *Moraxella catarrhalis,* respectively.[11-13]

From 2005 to 2012, an estimated 10,649 to 13,434 cases of invasive GAS infections occurred annually in the United States, resulting in 1136 to 1607 deaths.[12] Neurologic sequelae are more common in children (46% in one series),[14] and mortality from GAS meningitis is higher (43%).[8] Streptococcal toxic shock syndrome (TSS) and certain GAS genotypes (*emm*1, *emm*3, cc28) associated with superantigen production are risk factors for mortality.[12,15]

In the setting of pyogenic meningitis associated with AOM and/or mastoiditis, antimicrobial therapy should target *S pneumoniae*, *Staphylococcus aureus* (including methicillin-resistant strains), gram-negative pathogens, and anaerobes. The drug of choice for GAS meningitis is high-dose intravenous penicillin, since GAS is universally susceptible to penicillin, and resistance to macrolides can occur.[14,16] The addition of clindamycin is recommended to suppress exotoxin production and facilitate the phagocytosis of GAS in cases of TSS-associated meningitis.[16,17]

The morbidity and mortality associated with GAS meningitis following AOM is substantial.[7-9,18-28] Brain abscess may also rarely complicate the clinical course.[29,30] Development of vaccines remains an important public health priority.[12] Testing asymptomatic household contacts for GAS colonization is not indicated. Targeted testing and chemoprophylaxis may be considered for contacts at risk for serious sequelae.[17]

Clinicians must be aware that GAS meningitis is a severe disease with a rapidly progressive fatal course and high mortality. Although rare, GAS meningitis may occur following AOM. Thus, if antibiotics are withheld in an older child with uncomplicated AOM, the patient must be reevaluated within 48 to 77 hours, at which time antibiotics should be started if there is no improvement or if symptoms worsen.[2]

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