JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 2005, p. 5816–5818 Vol. 43, No. 11
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.11.5816–5818.2005

Group A Streptococcal Meningitis in a Pediatric Patient following Cochlear Implantation: Report of the First Case and Review of the Literature

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Received 4 March 2005/Returned for modification 13 May 2005/Accepted 17 August 2005

The Food and Drug Administration published a public health warning on the association of bacterial meningitis and cochlear implants in June 2002. This article reports the first case of group A streptococcal (GAS) meningitis in a cochlear-implanted patient, followed by a review on cochlear implantation and GAS meningitis.

CASE REPORT

A 4½-year-old white male presented to the emergency department in March 2004 with clinical features of meningitis. He had had a previous episode of pneumococcal meningitis associated with acute otitis media (AOM) in May 2000. The major complication was bilateral sensorineural hearing loss, for which he received a cochlear implant with electrode positioners (Clarion Platinum; Advanced Bionics). In the following months, he experienced another episode of pneumococcal AOM with tympanic perforation and suspected bacterial pneumonia. These recurrent invasive bacterial infections justified a complete immunologic workup. Measurement of serum immunoglobulins (immunoglobulin G [IgG], IgM, IgE, IgA, and subclass IgG2), components of the complement system (C3, C4, and CH100), and lymphocyte subsets were within normal values for age, as were phagocytic functions (opsonization and neutrophil activation). A single spleen was identified as appearing normal by abdominal ultrasound. The response to regular vaccines was documented by normal antibody levels against tetanus and diphtheria, and his immunization status was updated with vaccinations for *Streptococcus pneumoniae* and *Neisseria meningitidis*. In December 2003, he had purulent discharge from his right ear, which grew group A streptococcus, and received a 10-day course of cefprozil.

Three days prior to admission, he was diagnosed with acute otitis media and prescribed azithromycin. On arrival at the hospital, he was febrile and complaining of headache and an acute loss of hearing. He had altered mental status and positive signs of meningismus without any other neurological abnormalities. Physical examination, including the pharynx and tonsils, was otherwise normal.

Pertinent laboratory data included a white blood cell count of 36×10^9/liter with 89% segmented neutrophils. The cerebrospinal fluid was turbid and showed 3.8×10^6 white blood cells/liter with 60% polymorphonuclear cells, glucose of 1.8 mmol/liter, and protein of 0.93 g/liter. Cerebrospinal fluid (CSF) culture grew group A streptococcus sensitive to clindamycin, erythromycin, clarithromycin, penicillin, and vancomycin, while middle ear fluid, drawn during insertion of tympanostomy tubes after three doses of antibiotics, showed gram-positive cocci on a Gram stain but no growth of bacteria. Blood culture was negative. A computed tomography scan of the brain revealed increased density of tissues around the implant, and a gallium scan showed minor uptake of isotope at the right mastoid bone. Initially, given the clinical features consistent with bacterial meningitis, the patient received one dose of dexamethasone (0.15 mg/kg of body weight intravenously [i.v.]), ceftriaxone (1.5 g i.v.), and vancomycin (15 mg/kg i.v.) in the emergency department. Penicillin G (75,000 IU/kg/dose every 6 h i.v.) was then prescribed for a 2-week treatment course once results of the culture were available. The patient improved rapidly but had no recovery of hearing after 14 days of antibiotic therapy. In view of this persistent hearing loss and the presence of a foreign body and considering the lack of data available on treatment of group A streptococcal (GAS) meningitis in a patient with a cochlear implant, it was decided to administer 2 additional weeks of ceftriaxone (1.5 g i.v. daily). In the 9-month period following his second meningitis, he presented two other episodes of otitis media with right tympanic perforation and purulent discharge which once grew group A streptococcus and once *Pseudomonas aeruginosa*. He received topical and systemic antibiotics each time and had reinsertion of tympanostomy tubes. From the neurological standpoint, he presents an important language delay with loss of his milestones, to the point where he might have to learn sign language. This regression could be due to the GAS meningitis itself or secondary to the persistent dysfunction of the cochlear implant.

Cochlear implants are small electronic devices that transduce sound energy into coded electrical signals to bypass the dysfunctional cochlear hair cell and enable deaf individuals to access sound. The system consists of internal components in-

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serted in the inner ear that interact with an extrinsic microphone and speech processor. To facilitate transmission of the electrical signal by increasing the proximity of electrodes to the auditory nerves, a positioner was inserted next to the implanted electrode in some models (8). Implants have been available since the 1980s, and approximately 60,000 patients have received cochlear implants worldwide (11, 15). Since Food and Drug Administration (FDA) approval for pediatric use in 1990, children now account for about 50% of the implanted population in the United States and can receive implants at as young as 12 months of age (8).

The surgery for insertion of the implant exposes the patient to several potential risks, including bacterial meningitis, which can occur as soon as 24 h following surgery or as long as several years later. As of May 2003, the FDA was aware of 118 cases of bacterial meningitis in cochlear-implanted patients, resulting in 17 deaths. The patients ranged in age from 13 months to 81 years, the majority being younger than 5 years of age. CSF culture results were available in only 69 cases, and the organisms identified were *S. pneumoniae*, *Haemophilus influenzae*, *Escherichia coli*, viridans group streptococcus, and unspecified types of staphylococcus (7). A recent pediatric study, also conducted by the FDA, demonstrated that the incidence of pneumococcal meningitis in this population was 30 times that of a cohort of the same age in the general population (16). No case of GAS meningitis following cochlear implantation has ever been reported.

Group A streptococcal invasive disease has become increasingly common in recent years, usually involving soft tissues and occasionally progressing to bacteremia and toxic shock syndrome (14). Despite this increase, GAS bacterial meningitis remains uncommon and accounts for less than 0.2% of all cases of bacterial meningitis, with a total of 51 cases reported worldwide (5, 14, 18). In The Netherlands, a case series of 41 patients aged 16 years and older with GAS meningitis was published in 2002 (18). In this report, the mortality rate was 27%, which contrasts with data from the literature that describe a mortality rate of 5 to 10% (5, 14). In studies with children, Shetty et al. documented 30 cases of GAS meningitis over a 25-year period, from 1976 to 2001. Among these, 52% had a primary focus of infection in the ear, nose, and throat area and blood culture grew GAS in 59% of cases (17). Although GAS frequently colonizes the oropharynx, it does not usually invade the central nervous system directly and the pathogenesis of primary GAS meningitis remains unclear. In the presence of a positive CSF culture for GAS, penicillin is the antimicrobial agent of choice since antibiotic resistance among isolates of GAS is currently not a clinically significant problem (12, 18). In more-recent years, GAS meningitis has been associated with a lower mortality if treated promptly. Nevertheless, residual neurological damage, as seen in 46% of children with GAS meningitis, is more common than with *H. influenzae*, *N. meningitidis*, and *S. pneumoniae* meningitis (14, 17). Our patient also had neurological sequelae, mostly affecting language, which could be directly related to the GAS meningitis or secondary to his implant dysfunction.

The pathogenesis of meningitis among implant recipients remains uncertain. Some cases may be attributed to the procedure itself, justifying the use of perioperative antimicrobial prophylaxis targeting gram-positive skin flora and middle ear organisms by administration of a narrow- or expanded-spectrum cephalosporin (1). Based on the most commonly recovered organisms in the CSF (*S. pneumoniae* and *H. influenzae*), it is often assumed that the infection has taken the route of the middle ear through the cochlea to the meninges (1). Surprisingly, acute otitis media is evident in only a minority of cases and the incidence of AOM does not appear to increase following cochlear implantation (6, 8, 13). In the FDA's pediatric study, only 40% of the meningitis cases presenting more then 30 days after surgery occurred in patients with AOM. However, a history of AOM prior to implantation was identified as one of the risk factors for meningitis, along with ventriculoperitoneal-shunt placement, exposure to smoking in the household, inner ear malformation, incomplete insertion of the electrode, and a CSF leak through a fistula (16). All surgery-related factors should be documented at the time of insertion of the implant and reported to the child's health care provider and parents as potential risk factors for the development of subsequent bacterial meningitis. Among all risk factors listed previously, the presence of an implant with a positioner was the most significant: children wearing these types of implants had 4.5 times the risk of developing meningitis compared to those who had other types of implant (16). Because of this strong association, manufacturers have voluntarily withdrawn the positioner component of their devices since July 2002 (7). Our patient's only risk factors were the presence of a positioner, recurrent episodes of AOM, and a history of meningitis prior to implantation.

The clinical manifestations of meningitis in cochlear-implanted patients include fever, headache, stiff neck, nausea or vomiting, photophobia, and sleepiness or confusion. In addition to this classic presentation, meningitis in association with otitis media can present with signs and symptoms of labyrinthitis, including vertigo and transient or permanent sensorineural hearing loss (3). Parents of implanted children should be aware of this possible clinical presentation and seek medical attention as soon as there is a change in their child's hearing.

The accepted antibiotic regimen for empirical therapy of cochlear-implanted patients suspected of having meningitis does not deviate from the usual recommendations, the spectrum of organisms being similar for all types of meningitis. The current medical regimen should include vancomycin in combination with a broad-spectrum cephalosporin. In the presence of a perforated tympanic membrane or chronic otorrhea, ceftazidime, cefepime, or meropenem should be used to treat possible *P. aeruginosa* (1, 19). Once CSF infection is proven, antibiotics must be adjusted according to the microorganism identified but the duration of therapy can be variable as there is currently no consensus in the literature. Prompt insertion of tympanostomy tubes is also recommended in the case of otogenic meningitis. However, correlation between the cultures from the middle ear and the CSF is poor (4). Initial evaluation should be completed with imaging studies of the mastoid and middle ear region to guide further surgical intervention if necessary (1). According to Gower and McGuirt, more-extensive and urgent surgery is recommended for patients with coalescent mastoiditis or with worsening infectious and/or neurological manifestations 48 h after transtympanic drainage and appropriate antimicrobial therapy (9).

In addition to aggressive medical and surgical treatment,

efforts should be made to improve preventive measures. Recommendations concerning the management of children who are cochlear implant recipients or candidates for implantation have been published (2, 7, 20). Conjugate vaccines targeting *S. pneumoniae* and *H. influenzae* should be administered to all implanted patients while meningococcal vaccine is not routinely recommended. For children between 2 and 9 years of age, a combination of conjugate pneumococcal vaccination followed by a dose of the 23-valent pneumococcal polysaccharide vaccine is indicated. Clinicians should therefore carefully review the vaccination record to ensure that all recommended doses have been received (10, 20). Education of the patient's family and the primary care physician are of key importance for early recognition of meningitis after cochlear implantation. The patient's relatives should be taught how to recognize early signs of meningitis, so that antibiotic treatment can be started upon appearance of the first symptoms (1, 7). Education concerning AOM is also very important, considering the possibility of a bacterial progression from the middle ear to the meninges (1). Prompt recognition and aggressive treatment of each episode of AOM should be undertaken with tympanostomy tube placement and antimicrobial prophylaxis in children with cochlear implants who are otitis prone (2). Surveillance programs are currently in place to closely monitor cases of bacterial meningitis in implanted patients (7).

We report the first case of group A streptococcal meningitis in a pediatric cochlear-implanted patient who was completely vaccinated and immunocompetent. He developed important neurological sequelae, mostly affecting language. As the number of implanted children is growing rapidly, we wanted to highlight the association between cochlear implantation and bacterial meningitis. The incidence of this potentially life-threatening complication can be reduced by simple preventive measures. Primary care physicians need to review the patient's vaccination record, and current vaccination recommendations should be updated when necessary.

We thank Catherine Farrell for reviewing the manuscript.

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