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Pneumococcal Meningitis with Serotype 7 Who Develops 12. Nerve Paralysis

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Abstract

Meningitis is an inflammatory disease of the leptomeninges surrounding the spinal cord and brain. *Streptococcus pneumoniae (S. pneumoniae)* is the most common cause of bacterial meningitis in infants and children older than one month. In this report, we present a 13-month-old infant who, after receiving three doses of the 13-valent conjugated pneumococcal vaccine, had nervus hypoglossus paralysis as a result of serotype 7 *S. pneumoniae* meningitis. She was admitted into our center with complaints of high fever for 2 days, apathy that started in the last 24 hours, and a tendency for sleeping. Penicillin and ceftriaxone susceptible *S. pneumoniae* grew in cerebrospinal fluid culture. Antibiotic treatment was completed in six weeks as she had a millimetric abscess in MR imaging. Considering common variable immunodeficiency in the patient who was examined for immunodeficiency, intravenous immunoglobulin treatment was started. The physical examination results of the patient were entirely improved. In conclusion, meningitis is a pediatric emergency with a high mortality and complication rate. If meningitis is managed on time and correctly it can heal without sequelae. Vaccination is crucial for prevention. Despite vaccination, although rare, infection with vaccine strains may occur. Patients infected with vaccine strains may require evaluation in terms of immunodeficiency.

Keywords: *Streptococcus pneumoniae*, meningitis, nervus hypoglossus paralysis

Introduction

Meningitis is an inflammatory disease of the leptomeninges surrounding the spinal cord and brain. *Streptococcus pneumoniae* (*S. pneumoniae)* is the most common cause of bacterial meningitis in infants and children older than one month. The incidence of pneumococcal meningitis decreased after the initiation of routine vaccination against *Pneumococci*.[1] 13-valent pneumococcal conjugate vaccination (PCV13) in Turkey. It includes serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. Despite this, pneumococcal meningitis continues to be a major factor in the morbidity and mortality of children.[1] So far, 100 different serotypes have been defined for *Pneumococci*.[2] As the frequency of invasive pneumococcal diseases caused by vaccine serotypes decreases, the rate of unvaccinated serotypes increases.[1] Pneumococcal vaccines have been developed to provide effective vaccination protection, particularly in young infants. These vaccines are effective in reducing transmission and are protective against invasive disease.[3] However, the disease can also be seen with the

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serotypes contained in the vaccine strains. In this report, we describe a 13-month-old child who developed nervus hypoglossus paralysis due to serotype 7 *S. pneumoniae* meningitis after receiving three doses of the 13-valent conjugated pneumococcal vaccine (PCV13).

Case Report

A 13-month-old female patient with no prior history of any disease was admitted to our center with complaints of high fever for 2 days, apathy that started in the last 24 hours, and a tendency for sleeping. She received the 3rd dose of 13-valent conjugated pneumococcal vaccine 23 days ago. She had a lower respiratory tract infection 1 month ago and used antibiotics for 1 week. It was one week before the pneumococcal vaccine. On physical examination of the patient, the fever was 38.9 ˚C. She was throwing her head back and she had neck stiffness. The fontanel was 1x0.5 cm open, with normal camber. Other system examinations were normal. In the blood tests, C-reactive protein: 209 mg/L, procalcitonin: 89.6 ng/mL, white blood cell (WBC): 15700/mm³, hemoglobin: 9.2 g/dL, thrombocyte: 299000/mcL. In fundus examination papillae stasis was not observed. Brain computerized tomography imaging was normal. Cerebrospinal fluid (CSF) was examined by lumbar puncture. CSF glucose was 2 mg/dL and protein was 148 mg/dL, concomitant blood sugar was 110 mg/dL. CSF direct examination of thoma slide showed 70 WBC/mm³, they were neutrophils and Gram-positive diplococci were observed in gram staining. Vancomycin (60 mg/kg/day), ceftriaxone (100 mg/kg/day), acyclovir and dexamethasone treatments were started. Fever continued for 2 more days. *S. pneumoniae* signal was seen in CSF culture on day 2. Acyclovir treatment was stopped. She took the dexamethasone treatment for 48 hours. Consciousness and general condition improved. On the fifth day her tongue was deviated to the right inside the mouth (**Figure 1**) to the left outside the mouth (**Figure 2**), nervus hypoglossus palsy was considered. Brain magnetic resonance imaging (MRI) revealed increased contrast enhancement in leptomeningeal structures and an appearance consistent with millimetric abscess in the left frontal region. There was not an infarct shown in brain MRI. We did not perform any other brain imaging for infarction. In her daily examination, the deviation of the tongue to the right decreased and completely resolved within 1 month. Penicillin and ceftriaxone susceptible *S. pneumoniae grew* in CSF culture. Chocolate agar method was used and the minimum inhibitory concentration (MIC) of penicillin was 0.25. The serotyping result was type 7 (type 7 subtype could not be determined). Antibiotic treatment was completed for 6 weeks as she had a millimetric abscess in MRI. Although there was no history of frequent illness it was speculated that there might be a common variable immunodeficiency (CVID) or combined immunodeficiency (CID). Despite 3 doses of pneumococcal vaccine, she developed pneumococcal meningitis. Serum immunglobulin G: 9.3 g/L, immunglobulin: 0.69 g/L, immunglobulin A: 0.6 g/L were normal for her age. CD3: 22.6%, CD4: 16.3%, CD8: 5.9% and CD16 + CD56: 2.1% were low for her age. Intravenous immunoglobulin (IVIG) treatment was started, genetic testing was sent for CVID and CID, there are no test results yet. The patient's physical examination findings improved completely. MRI findings regressed. Hearing test and eye examinations were normal. The patient's follow-up continues in the polyclinic.

Discussion

S. pneumoniae, Neisseria meningitidis and *Haemophilus influenzae* constitutes the primary etiology of bacterial meningitis.[4] An association has been reported with pneumococcal meningitis and pneumonia in 15-25% of cases, with pneumococcal meningitis and acute otitis media in 30% of cases.[5] Our case also had a history of lower respiratory tract infection 1 month ago. The incidence of pneumococcal meningitis decreased significantly after the addition of the heptavalent conjugated pneumococcal vaccine (PCV7) to the infant immunization program.[1] With the licensing of expanded PCV10 and PCV13 conjugate vaccines in 2009 and 2010, diseases caused by vaccine serotypes have decreased by more than 90 percent, but overall disease

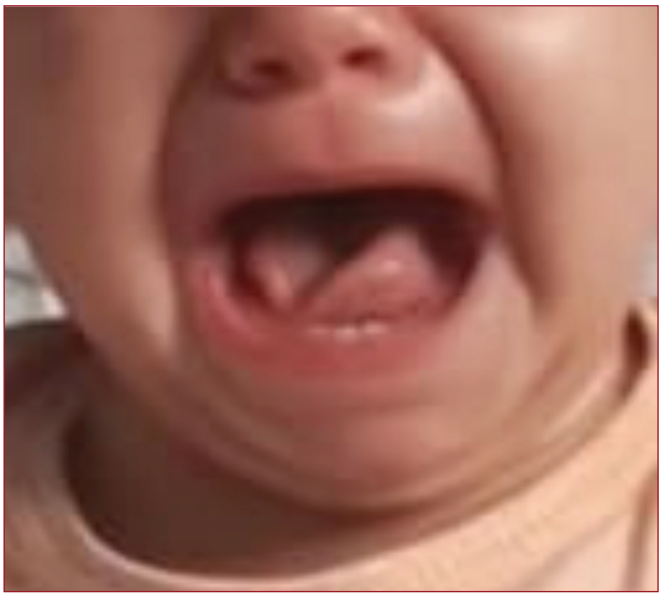

Figure 1. Her tongue was deviated to the right inside the mouth

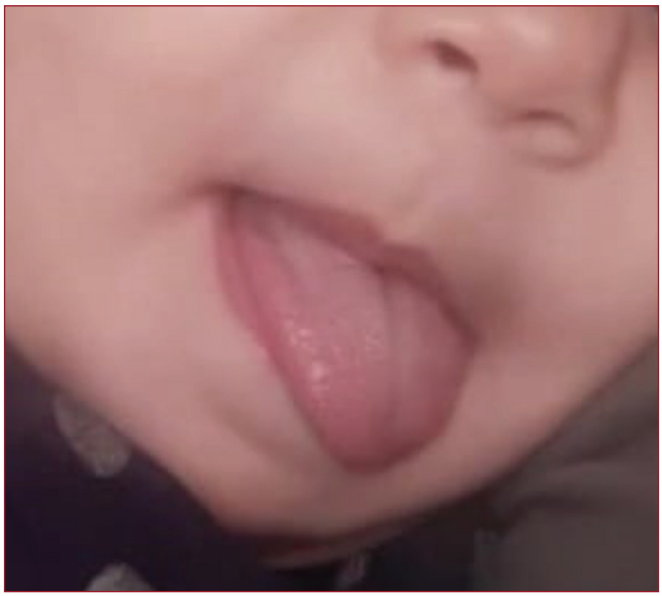

Figure 2. Her tongue was deviated to the left outside the mouth

rates remain high with serotype change.[6] Although it is reported that vaccine failure is rare, cases that become infected despite vaccination are reported. In a study of 161 pediatric cases vaccinated with PCV13 in the United Kingdom, vaccine failure was found to be 0.66/100,000.[7] The reasons for vaccine failure may be related to the patient, the vaccine, and the vaccine administration methods. The patient's immunodeficiency status, age, and eating disorder are important factors in vaccine failure.[3] In Turkey, infection rates were found to be 25% between 2008 and 2014 despite vaccination.[8] Our case's 13 valences pneumococcal vaccination was completed. It was determined that she was infected with type 7, one of the strains included in this vaccine. A poor response to vaccines is seen in common variable immunodeficiency. According to studies, presentation with meningitis has been reported in 25% of CVID patients. An immunological deficiency that renders the host defense inadequate against potential bacterial pathogens may facilitate hematogenous spread. In the literature, pneumococcal meningitis has been reported in a 22-year-old female patient with CVID.[9] The CVID genetic result of our patient has not been revealed yet, but due to the test results, IVIG treatment was started by considering CVID. Bacterial meningitis has fever and present with signs of meningeal irritation. Meningeal irritation findings can be seen such as nuchal rigidity, irritability, confusion or change in mental status, headache, photophobia, nausea, vomiting.[10] Our case had high fever, nuchal rigidity, and neck hyperextension. Pneumococcal meningitis requires detection of S. pneumoniae in CSF by techniques such as culture, gram stain and polymerase chain reaction (PCR). A positive blood culture is also diagnostic in a patient with CSF pleocytosis. Gram staining is positive in approximately 90 percent of children with pneumococcal meningitis.[11] In our case, Gram-positive diplococci were observed in gram staining and *S. pneumoniae* was grown in its culture. While penicillins were the first choice in treatment, in 1974 penicillin-resistant *Streptococcus pneumoniae* meningitis has been described. Over the years, multi-antibiotic resistance has also developed widely. As in our case, it is recommended to start vancomycin and ceftriaxone or cefotaxime in empirical treatment.[12,13] Treatment should be revised according to culture - antibiogram sensitivity.[12] The benefits and harms of dexamethasone in children with suspected pneumococcal meningitis are uncertain and should be evaluated on a patient basis.[14] A decrease in antibiotic resistance has been observed after vaccination applications all over the world. However, ongoing studies have shown that non-vaccine serotypes have increased and that these serotypes have increased in the rate of antibiotic resistance. Data on serotype distribution and antibiotic resistance after KPA13 application in Turkey are limited. In the USA, after KPA7, penicillin-resistant *Pneumococci* decreased by 81%, especially under the age of two. In a study involving eight hospitals in the USA, ceftriaxone resistance in pneumococcal meningitis decreased from 13% to 3% after KPA13. According to the review in which four studies performed after KPA7 application in Europe were examined, it was reported that penicillin resistance decreased from 48% to 29% in children under the age of five, and cephalosporin resistance decreased by 10%.[15]

When the penicillin MIC values of isolates obtained from children under the age of five with meningitis were examined in a single-center study conducted in our country and published in 2021, it was determined that 38.8% of the isolates were resistant.[15] A wide variety of complications can be seen due to pneumococcal meningitis. Cerebral edema and increased intracranial pressure, convulsions, hearing loss, cranial nerve palsies, hemiparesis, quadriparesis, ataxia, cerebrovascular abnormalities, subdural effusion or emphysema, hydrocephalus, brain abscess, behavioral and developmental disorders can be seen among the complications.[14] In our case, brain abscess and transient 12th cranial nerve palsy developed. Cranial nerve palsies are well-known complications of basal meningitis, particularly in patients with tuberculous meningitis.

Conclusion

Meningitis is a pediatric emergency with a high mortality and complication rate. If managed on time and correctly can heal without sequelae. Vaccination is very important in prevention. Despite vaccination, although rare, infection with vaccine strains may occur. Patients with vaccine strain infections may need to be assessed for immunodeficiency, as was the reported case.

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Informed Consent: The written informed consent was obtained from the parents of the patient for publication.

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