



Meningitis Due to *Streptococcus pneumoniae* Serotype 24A in a Child Vaccinated with 13-valent Pneumococcal Conjugate Vaccine*

13 Valanlı Konjuge Pnömonokok Aşısı ile Aşılanmış Bir Çocuk Olguda *Streptococcus pneumoniae* Serotip 24A'ya Bağlı Gelişen Menenjit

Hacer Aktürk¹, Handan Ayhan Akoğlu², Lütfiye Öksüz³, Nezahat Gürler³, Emek Uyar Yalçın⁴, Nilüfer Eldeş Hacıfazlıoğlu⁴, Nihan Uygur Külcü², Feyza Mediha Yıldız²

¹ Clinic of Pediatric Infectious Diseases, Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital, Istanbul, Turkey

² Clinic of Pediatric, Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital, Istanbul, Turkey

³ Department of Microbiology, Istanbul University Istanbul School of Medicine, Istanbul, Turkey

⁴ Clinic of Pediatric Norology, Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital, Istanbul, Turkey

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Abstract

The introduction of conjugated pneumococcal vaccines into routine vaccination schedules resulted in a reduction in invasive pneumococcal disease due to vaccine strains. However, invasive pneumococcal diseases caused by non-vaccine strains have increased. Here, we present a fully vaccinated child with 13-valent pneumococcal conjugate vaccine, who suffered from meningitis caused by *Streptococcus pneumoniae* serotype 24A, a non-vaccine and very rare serotype. Longitudinal pneumococcal surveillance is important in monitorization of vaccine coverage and effectiveness and guidance for future vaccination programmes.

Keywords: Meningitis, PCV13, *Streptococcus pneumoniae* serotype 24A

Öz

Konjuge pnömonokok aşısının rutin aşı takvimlerine girmesiyle aşı suşlarına bağlı invaziv pnömonokok hastalıklarında azalma kaydedilmiştir. Ancak aşı dışı suşlara bağlı ampiyem, menenjit gibi hastalıklar görülmeye devam etmektedir. Bu yazıda, daha önce 13 valanlı konjuge pnömonokok aşısı ile aşılanmış bir çocuk olguda, çok nadir görülen bir serotip olan *Streptococcus pneumoniae* tip 24A'nın etken olarak saptandığı menenjit gelişiminden bahsedilmiştir. İnvaziv pnömonokok hastalıklarının sürveyans çalışmalarının devamı, aşı ile birlikte değişen serotip dağılımlarının saptanmasında ve geleceğe yönelik aşı programlarının planlanmasında önemlidir.

Anahtar Kelimeler: Menenjit, PCV13, *Streptococcus pneumoniae* tip 24A

Correspondence Address / Yazışma Adresi

Hacer Aktürk

Tophanelioğlu Cad. Güzelyalı Sitesi
A Blok Daire 12 34662 Üsküdar,
İstanbul-Türkiye

E-mail: hacergunakturk@gmail.com

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Introduction

Invasive pneumococcal diseases (meningitis, bacteremia, pneumonia) caused by *Streptococcus pneumoniae* still constitute a major health problem worldwide. Pneumococcal meningitis is of particular importance due to its high case-fatality rates and substantial long term morbidity (1).

There are pneumococcal conjugate and polysaccharide vaccines targeted at the microorganism's polysaccharide capsule, which has different antigenic structures forming the basis for the serotype classification. More than 90 serotypes have been defined so far, however, a limited number of capsular types have been associated with majority of the invasive diseases (2). Introduction of pneumococcal conjugate vaccines into routine immunization schedules broadly reduced the incidence of invasive and noninvasive pneumococcal diseases caused by vaccine serotypes (1,3). As the incidence of invasive pneumococcal diseases caused by vaccine serotypes has decreased, that of non-vaccine serotypes has increased, a phenomenon known as serotype replacement (3). Here, we present a fully vaccinated child with 13-valent pneumococcal conjugate vaccine (PCV13), who suffered from pneumococcal meningitis caused by a non-vaccine and very rare serotype.

Case Report

A previously healthy 6 years old girl was admitted to the hospital with 1-day history of fever, and the complaints of headache, vomiting and drowsiness, which have developed on the same day. On physical examination, she appeared ill and pale. The body temperature, heart rate and blood pressure were 39.4°C, 128 beats/minute and 100/64 mmHg, respectively. Neurologically, she was drowsy, irritable and barely cooperated. Nuchal rigidity was present. The findings of other systemic examinations were unremarkable. On routine laboratory tests, total blood leukocyte count was 17.100/mm³ with a differential of 88% polymorphonuclear leucocytes and C-reactive protein was 16.4 mg/dL (normal range 0.1-0.5 mg/dL). Intravenous ceftriaxone was administered with the initial diagnosis of meningitis. Cranial CT scan was performed and reported as normal. Examination of cerebrospinal fluid (CSF) sample obtained by lumbar puncture revealed neutrophilic pleocytosis, high protein (227 mg/dL) and low glucose (< 5g/dL) levels. Intravenous vancomycin was added to antibiotherapy. On the second day of treatment, clinical status of the patient improved and frequency of febrile episodes decreased. CSF culture yielded *S. pneumoniae*. Serogrouping was performed with the latex particle agglutination and serotyping was made with the conventional Quellung reaction using commercial type-specific antisera (Statens Serum Institute, Copenhagen, Denmark) in the Medical Microbiology Department of Istanbul Medical Faculty. It was determined

that the isolate belonged to serotype 24A. The antibiotic resistance profile was determined by gradient test (E-test, bio-Merieux, France) for penicillin and ceftriaxone. The isolate was found to be susceptible to both penicillin (minimal inhibitory concentration: 0.064 µg/mL), and ceftriaxone (minimal inhibitory concentration: 0.094 µg/mL), therefore vancomycin was discontinued. On the fourth day of treatment -after an afebrile period of one day, the patient suffered from fever, headache and vomiting. To rule out intracranial complications, cranial MRI was performed and reported to be normal. Symptomatic therapy was given and the symptoms cleared within one day. Control CSF examination, taken on the 13th day of treatment, revealed a protein level of 22.5 mg/dL, a glucose level of 52 mg/dL, and no pleocytosis. Control CSF culture remained sterile. Treatment was completed after 14 days of antibiotic therapy and the patient was discharged without any sequelae. Inspection of the patient's vaccination card disclosed that she had been vaccinated with 4-dose PCV13 series.

Discussion

Serotype distribution of *S. pneumoniae* causing invasive disease may vary across time due to a variety of factors, one of which is widespread use of pneumococcal vaccination. In this report, we presented a rarely defined pneumococcal serotype -serotype 24A- as the causative agent of a purulent meningitis in a properly vaccinated child.

Serotype 24A is seldomly reported in epidemiological studies searching for serotype distribution. Gant et al collected 285 *S. pneumoniae* strains causing invasive disease throughout 2009-2010 in Spain and serotype 24A was determined only in one case (4). A study from Algeria, which evaluated serotype distribution of *S. pneumoniae* isolated from children disclosed only one noninvasive pneumococcal disease (lower respiratory tract infection) caused by serotype 24A (5). Our literature search revealed no other report indicating serotype 24A as the etiologic agent. However, other subgroups of serotype 24, especially 24F, have been reported as causative agents of invasive pneumococcal diseases. Pantosti et al published three adult patients who had meningitis due to multiple drug resistant serotype 24F (6). The authors noted that this novel strain had probably arose through transformation of a serotype 14 strain with type 24F capsular biosynthetic operon sequences (6). They claimed that increased levels of antibody to a commonly occurring serotype could select for variants that express a nonvaccine serotype capsule (6). Capsular gene cassette transformation may lead to a change in capsule specificity and make the serotype escape from vaccine protection (7). Serotype 24F was also reported to be one of the dominating non-PCV13 serotypes causing pneumococcal meningitis in 2012 in a study including a large series of pneumococcal meningitis cases from France (8).

The prevalence of pneumococcal meningitis and other invasive pneumococcal diseases among children has been found to be decreased significantly in the post-vaccination period (1,8). This decrease has also been observed in older children and adults indicating the effect of the vaccination on the herd immunity (1). Introduction of PCV13 induced a decline in the frequency of non-PCV7 serotypes covered by PCV13 (1). Recently, reports have started to disclose that, as with PCV7, there is an increasing frequency of non-PCV13 serotypes among invasive pneumococcal diseases (8,9). For the present, it seems that there is no dominating serotype among non-PCV13 invasive pneumococcal diseases (10). Rather, a broad range of serotypes have been detected so far (9). However, it should be taken into consideration that a relatively short period of time has passed since the implementation of PCV13. There is a need for a longer period of surveillance to reach a comprehensive evaluation about serotype replacement following PCV13.

In conclusion, pneumococcal meningitis due to rare and non-vaccine serotypes may be seen in previously healthy and older children, who were properly vaccinated by PCV13, as in our case. To our knowledge, this is the first report of pneumococcal meningitis caused by serotype 24A. Continuation of longitudinal pneumococcal surveillance is important in monitoring of vaccine coverage and effectiveness and guidance for future vaccination programmes.

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