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Case Report

A 30-day-old Infant with Meningitides due to Invasive Methicillin-sensitive *Staphylococcus aureus* Infections: A Case Report

İnvaziv Metisilin Duyarlı Staphylococcus aureus'un Neden Olduğu Menenjitli 30 Günlük İnfant: Olgu Sunumu

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ABSTRACT

One-month-old girl was referred to our hospital because of ongoing fever and methicillin-sensitive *Staphylococcus aureus (S. aureus)* (MSSA) positivity in blood cultures, despite the administration of antimicrobials for 14 days. Although there was, no immunodeficiency or underlying disease that could be a risk factor for infection, on the 14th day of the cefotaxime for MSSA meningitides, the persistence of leukocytosis in cerebrospinal fluid (CSF) analyses also was continued. After administration 30 days of treatment, the patient was discharged from the hospital with a normal CSF analysis and clinic. Central nervous system infections caused by *S. aureus* are uncommon in pediatric patients. The treatment of *S. aureus* meningitis is challenging because of the lack of established management guidelines, difficulty in achieving therapeutic drug concentrations in CSF, and presence of resistant strains. Therefore, it has a high clinical importance. This case is presented to emphasize that meningitis due to *S. aureus* difficulty in the treatment management, and need for further examination.

Keywords: *Staphylococcus aureus*, meningitides, cerebrospinal fluid culture

ÖZ

Dış merkeze ateş nedeni ile başvuran ve kan kültüründe metisiline duyarlı *Staphylococcus aureus (S. aureus)* (MSSA) üremesi saptanan 1 aylık kız hasta, 14 günlük antibiyograma uygun tedaviye rağmen klinik iyileşme olmaması ve kan kültürü pozitifliğinin devam etmesi üzerine hastanemize sevk edildi. Başvurusunda beyin omurilik sıvısı (BOS) kültüründe de MSSA saptanan ve altta yatan immün yetmezlik veya komorbiditesi olmayan hastanın, 14 gün süre ile antibiyograma uygun sefotaksim tedavisi sonucu BOS bakısında lökositozun sebat ettiği görüldü. Otuz günlük tedavinin ardından hastanın BOS bulguları ve klinik bulguları tamamen normal olarak taburcu edildi. Pediyatrik hastalarda *S. aureus*'un neden olduğu merkezi sinir sistemi enfeksiyonları nadirdir. *S. aureus* menenjitinin tedavisi, yayınlanmış rehberlerin olmaması, BOS'de terapötik ilaç konsantrasyonlarına ulaşmanın zorluğu ve dirençli suşların varlığı nedeniyle zordur. Bu nedenle klinik önemi yüksektir. Bu olgu, *S. aureus*'a bağlı menenjitin tedavi yönetiminde güçlüğü ve ileri tetkik gerekliliğini vurgulamak amacıyla sunulmuştur.

Anahtar kelimeler: *Staphylococcus aureus*, menenjit, beyin omurilik sıvısı kültürü

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INTRODUCTION

Invasive methicillin-sensitive *Staphylococcus aureus (S. aureus)* (MSSA) infections contribute significantly to public health burden and cause substantial morbidity and mortality [1]. Central nervous system (CNS) infections caused by *S. aureus* are uncommon in pediatric patients [2]. In Schlech et al.'s [3] study published about 20 years ago [3], the incidence of bacterial meningitis caused by *S. aureus* in children in the United States has been reported as less than one percent, while studies published in recent years have indicated an increase in its incidence [4,5]. Usually, these infections occur as a complication of invasive neurosurgical procedures or as a consequence of disseminated *S. aureus* infection [6]. In recent years, although the number of cases with CNS infections caused by *S. aureus* has increased, relevant large series have not been reported [2,4]. We presented an infant with long-term MSSA positivity in both blood and cerebrospinal fluid (CSF) cultures, despite administration of appropriate antibiotherapy.

CASE REPORT

A one-month-old girl was referred to our hospital for further evaluation due to recurrent MSSA positivity in blood cultures. Despite ampicillin and gentamicin antibiotherapies for 14 days in a tertiary healthcare center, she was referred to us with persistent fever. The patient was born at term without any history of chorioamnionitis or another maternal infectious disease. It was revealed that the patient, who had been hospitalized for five days in the postnatal period due to jaundice, had not undergone any additional invasive procedures.

She had been suffering from loss of appetite before her admission to the hospital physical examination revealed a lethargic infant with a suspect tense fontanel. Her weight and height were in the 75th percentile and head circumference was 38 cm (50-75th p). The remaining physical examination findings were within normal limits. Laboratory tests showed elevated white blood cell (WBC: 13,920/µL) count with lymphocytic predominance (6,770/µL; 48.6%), C-reactive protein (6.44 mg/dL; normal value: <5 mg/dL), and procalcitonin (0.27 ng/mL; normal value: <0.1 ng/mL), acetyl transferase (122 IU/L; normal range: 15-60 IU/L), alanine transaminase (76 IU/L; normal range: 13-45 IU/L) were elevated. Electrolytes, and the results of renal function and coagulation tests were within their normal ranges. Transfontanel imaging and lumbar puncture of the patient was performed, because of the findings of tense fontanel, signs of lethargy, and persistent MSSA positivity in blood cultures. The transfontanel ultrasonography scan was normal. CSF examination revealed leukocytosis with neutrophilic predominance, an elevated protein content (1,227 mg/dL; normal range: 20-80 mg/dL), low glucose levels (14 mg/dL; normal range 60-80 mg/dL). Any microorganism was not observed during microscopic examination of Gram stained specimens. After obtaining blood, urine, and CSF cultures, intravenous cefotaxime (300 mg/kg/day), ampicillin (300 mg/kg/day) and vancomycin (60 mg/kg/day) were initiated empirically. The fever persisted for only one day after hospitalization. Viral reverse transcription-polymerase chain reaction (PCR) tests performed in CSF samples were negative for herpes simplex virus 1-2, varicella zoster virus, enterovirus and paraechovirus. MSSA had been detected in both blood and CSF cultures obtained on admission. Antibiotherapy with clindamycin and cefotaxime was initiated based on antibacterial susceptibility test results which revealed *S. aureus* growth both in blood and CSF cultures. After detection of MSSA in blood and CSF, cranial magnetic resonance imaging and transthoracic echocardiography were performed, and any foci of metastatic infection was not found.

The patient developed neutropenia (absolute neutrophil count: 320/10^3 µL) during the follow-up and she was consulted to hematology and immunology departments. A follow-up protocol for neutropenia was recommended. An immunological screening was recommended in consideration of long-term reproduction of MSSA and the results of an evaluation of cellular immunity, humoral immunity, and complement levels. Although all immunological parameters evaluated were within normal limits, immunology recommended outpatient follow-up.

Results of the control analysis of the CSF at the 14th day of antibiotherapy were as follows: WBC: 120/mm^3, protein: 146.8 mg/dL, and glucose: 30 mg/dL. For differential diagnosis, tuberculosis tests, were also performed in addition to the culture obtained, due to the persistence of leukocytosis and high protein levels in the CSF. *Mycobacterium tuberculosis* was not detected in CSF based on Ehrlich-Ziehl-Neelsen staining a PCR assay and culture obtained. CSF and blood cultures were also negative for *Mycobacterium tuberculosis.*

Clindamycin was discontinued on the 14th day and cefotaxim was given for a total of 30 days. Lumbar puncture was performed again before the discontinuation of antibiotic treatment and CSF examination results were within normal limits. And she was discharged on the 32th day of hospitalization.

During a 6-month follow-up period, no sequela due to meningitis developed in the patient.

Consent was obtained from the patient during the formation of the case report.

DISCUSSION

Here we presented an infant with bacteremia and meningitis caused by MSSA. Although she previously received appropriate treatment for 14 days in a hospital she had been admitted, blood and CSF cultures were still positive for MSSA. There was no immunodeficiency or underlying disease that could be a risk factor for infection. Therefore, the patient's advanced imaging and immunological evaluations were performed, and her treatments were arranged according to the antimicrobial susceptibility test results. The treatment was continued for 30 days as a result of persistent leucocytosis in CSF. Since there is no clear information in the literature regarding the duration of treatment for *S. aureus*

meningitis and invasive infections, we maintained the treatment until both peripheral and CSF cultures were sterile and no cells were seen in CSF.

CNS infections caused by *S. aureus* are uncommon in previously healthy children [2]. Most cases of *S. aureus* meningitis occur in patients with a history of neurosurgical procedures, trauma and had CSF shunt devices implanted. Other important etiologic factors include hematogenous dissemination of *S. aureus* secondary to bacteremia, and presence of additional underlying diseases. In our case, blood culture was positive for MSSA. Similar to the literature, the case in our study was evaluated as meningitis due to hematogenous dissemination of *S. aureus* secondary to bacteremia.

The choice of antimicrobial agent for *S. aureus* meningitis should be determined by the susceptibility profile of the agent [7]. Any relevant large series and any established management guidelines for pediatric cases with *S. aureus* meningitis have not been reported so far [4]. The treatment is challenging because of difficulty in achieving therapeutic drug concentrations in CSF, and the presence of resistant strains. Usually, for the treatment of MSSA meningitis, a parenteral B-lactam antibiotic such as oxacillin, nafcillin, or cephalosporins is recommended [7]. Although the duration of treatment is controversial, the guidelines recommend the use of antibiotics for at least 2 weeks [2]. In an adult study by Aguilar et al. [4], the authors observed that CSF had been cleared of MSSA in a mean time of 7.7 days. In this case, on the 14th day of the cefotaxime and clindamycin treatments, CSF culture-negativity was achieved but cefotaxime treatment was maintained for one month due to the persistence of leukocytosis in CSF. Despite high mortality rates in infants with MSSA meningitis [8], our patient was discharged without sequelae.

MSSA should be considered as a causative agent in previously healthy patients whose clinical findings did not improve despite appropriate antibiotic therapy, and treatment should be managed according to the CSF findings and culture positivity.

Informed Consent: Consent was obtained from the patient during the formation of the case report.

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Author Contributions

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