Case Report / *Olgu Sunumu*

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A 21-day-old Term Newborn Diagnosed with non-Typhoidal *Salmonella* Sepsis and Meningitis: A Rare Case

Tifo Dışı *Salmonella* Sepsis ve Menenjit Tanısı Alan 21 Günlük Term Yenidoğan: Nadir Bir Olgu

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Abstract

A 21-day-old baby boy was presented with complaints of decreased feeding and fever. The patient's physical examination revealed no features other than lethargy and hypotonia. *Salmonella* growth was observed in the blood and cerebrospinal fluid (CSF) culture of the patient, whose acute phase reactants were high, and antibiotic treatment was adjusted to cefotaxime, and this treatment was continued for four weeks after the patient's CSF culture became negative. Additionally, the patient's neuroimaging results were determined to be compatible with areas of ischemia in the brain. As a result, magnetic resonance imaging angiography scanning was performed, and low molecular weight heparin treatment was started upon detection of thrombosis. During the clinical follow-up of the patient, he had focal seizures, and the patient was started on phenobarbital and levatiracetam treatments, respectively, and his seizures were controlled with this treatment regimen. After the treatment, the patient's neurological findings improved, and the patient started to feed per oral. Mortality and morbidity rates are high in *Salmonella* sepsis and meningitis due to neurological complications such as severe brain abscess, hydrocephalus, subdural effusion and thrombosis, and therefore early diagnosis and treatment are crucial. In this case report, it is emphasized that *Salmonella* may be the causative agent of meningitis in cases with prominent neurological findings and that detecting rare complications such as ischemia and thrombosis in these cases by detailed neuroimaging is important for early intervention.

Keywords: Newborn, sepsis, *Salmonealla* menengitis, seizure, thrombosis

Öz

Yirmi bir günlük erkek bebek beslenmede azalma ve ateş şikayetleriyle kliniğe getirildi. Hastanın fizik muayenesinde letarji ve hipotoni dışında özellik saptanmadı. Akut faz reaktanları yüksek olan hastanın kan ve beyin omurilik sıvı (BOS) kültüründe *Salmonella* üremesi görülmüş ve antibiyotik tedavisi sefotaksime ayarlanmış, hastanın BOS kültürü negatifleştikten sonra bu tedaviye dört hafta devam edilmiştir. Ayrıca hastanın nörogörüntüleme sonuçları beyinde iskemi alanları ile uyumlu olarak tespit edilmiştir. Sonuç olarak hastaya manyetik rezonans görüntüleme anjiyografi taraması yapıldı ve tromboz saptanması üzerine düşük molekül ağırlıklı heparin tedavisi başlandı. Hastanın klinik takibi sırasında fokal nöbetleri için sırasıyla fenobarbital ve levatirasetam tedavileri başlandı ve bu tedavi rejimiyle nöbetleri kontrol altına alındı. Tedavi sonrası hastanın nörolojik bulguları düzeldi ve hasta ağızdan beslenmeye başladı. *Salmonella* sepsisi ve menenjitinde ciddi beyin apsesi, hidrosefali, subdural efüzyon ve tromboz gibi nörolojik komplikasyonlar nedeniyle mortalite ve morbidite oranları yüksektir ve bu nedenle erken tanı ve tedavi çok önemlidir. Bu olgu sunumunda, belirgin nörolojik bulguları olan olgularda menenjit etkeninin *Salmonella* olabileceği ve bu olgularda iskemi ve tromboz gibi nadir komplikasyonların ayrıntılı nörogörüntüleme ile tespit edilmesinin erken müdahale için önemli olduğu vurgulanmıştır.

Anahtar Kelimeler: Yenidoğan, sepsis, *Salmonella* menenjiti, nöbet, tromboz

Introduction

Salmonella spp. gram-negative, facultative anaerobic flagellated bacillus primarily found in contaminated foods. Invasive infections due to non-typhoidal *Salmonella* (NTS) infection occur in every region of the world, but their prevalence varies by geographic location. Although it causes intestinal diseases, NTS bacteremia is common in HIV

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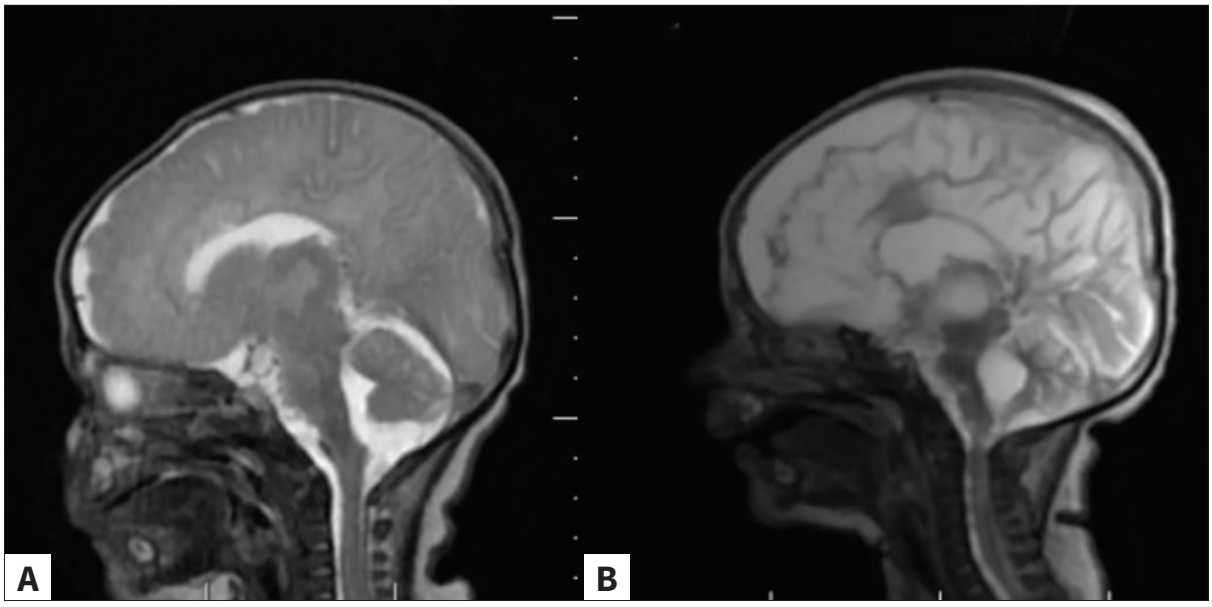

Figure 1. A. Extracerebral fluid increase with a thickness of approximately 6 mm in the bifrontal, temporal and parietal areas on the right, and an appearance evaluated in favor of an ischemic area in the left frontal region. **B.** Heterogeneous slightly intense appearances were observed in the T1 secant in the frontoparietal regions on the left in the frontoparietal regions in the periventricular white matter areas, in the convexity plane in the periventricular white matter areas, intense in the T2 sequence.

patients, malaria, anemia, and malnutrition in infants and young children with low immunity (1). NTS species causes bacteriemia, and can be fatal, especially in newborns with low immunity, causing meningitis, brain abscess, hydrocephalus and thrombosis (2).

Case

The patient, who was brought to our emergency department with complaints of fever and decreased feeding for two days, was admitted to the neonatal intensive care unit with the preliminary diagnosis of sepsis and meningitis. In the patient's first examination, lethargy and decreased tone were detected, but other system examinations, including fontanel bulge, were normal. The patient had been feeding with formula and had no signs of diarrhea. At the first blood evaluation of the case, C-reactive protein (CRP) was= 138 mg/L, white blood cell count was= 6.220 u/mm^3, neutrophil count= 4.710 u/mm^3, hemoglobin= 11.4 g/dL and platelet count= 260.000 u/mm^3 and coagulation evaluation was found to be the normal range. The family did not accept to give consent for lumbar puncture (LP). Therefore, ampicillin and cefotaxime treatment was started at the meningitis dose, and blood and urine cultures were taken. The transfontanel ultrasound performed on the first day of hospitalization was reported as "diffuse echogenicity increase in the brain parenchyma, thickening and increased echogenicity in the dura, septa-containing free fluid in the subdural space, and these findings are significant in terms of meningitis". Abdominal ultrasound performed at the same time was found to be unremarkable. Echocardiography (ECHO) revealed an increase in left ventricular muscle mass.

During the follow-up, as the patient continued to be lethargic and had a focal seizure, a cranial-contrast, and diffusion magnetic resonance imaging (MRI) was performed, and it was reported as "extracerebral fluid increase with a thickness of approximately 6 mm in the bifrontal, temporal and parietal areas on the right, and an appearance evaluated in favor of an ischemic area in the left frontal region" (Figure 1A). With the preliminary diagnosis of meningitis and encephalitis, vancomycin, meropenem, and acyclovir treatment was started at the meningitis dose. In addition, thrombosis was observed on the patient's MRI angiography, and low molecular weight heparin treatment (LMWH) was started. As *Salmonella* species grew in the patient's blood culture, the family was contacted again, and consent was obtained for LP. It was also learned from the detailed history taken that the family consumed their own produced cheese, but none of the family members had any symptoms of the disease. Another suspicious history of the patient was that many guests came to the house to visit the baby. After LP, the cerebrospinal fluid (CSF) was seen to be transparent, the pressure was low, and only enough CSF quantity could be taken for culture. It was observed that the same microorganism was grown in the CSF culture as in the blood culture, and according to the antibiogram examination of the growing microorganism, antibiotic treatment continued with cefotaxime, and acyclovir treatment was stopped. His seizures were controlled with phenobarbital and levetiracetam on the seventh day of his hospitalization, and

the treatment was continued after discharge. The patient's urine and stool cultures resulted as normal, and during follow-up, CRP gradually decreased and was found to become negative on the 18th day of antibiotic treatment. There was no growth in the CSF and blood culture were taken for control purposes on the fourth day of single cefotaxime treatment. The patient was evaluated for immunodeficiency, and IgG, A, M, and lymphocyte subgroups were normal.

The patient was followed up multi-disciplinarily with pediatric neurology, neurosurgery, pediatric infection, pediatric allergy immunology, pediatric hematology, and pediatric cardiology. During the follow-up, the patient's lethargic state decreased, and oral feeding started. On the 14th day of treatment, ECHO was repeated, and it was observed that left ventricular hypertrophy disappeared. Control MRI-angiography was performed on the 24th day of the treatment. It was concluded that "heterogeneous slightly intense appearances were observed in the T1 secant in the frontoparietal regions on the left in the frontoparietal regions in the periventricular white matter areas, in the convexity plane in the periventricular white matter areas, intense in the T2 sequence, and heterogeneous hypointense appearances in the FLAIR sequence were observed, and no thrombosis was observed" (Figure 1). As a result of this MRI result, the patient's LMWH treatment was changed to a single prophylaxis dose. As projectile vomiting occurred after the 20th day of treatment, abdominal ultrasonography was performed for pyloric stenosis, brain computed tomography imaging was performed for hydrocephalus, and no significant pathology requiring surgery was detected. Therefore, anti-reflux treatment and two-hourly feeding were initiated, and the patient was discharged on oral nutrition after four weeks of cefotaxime treatment.

Discussion

Salmonella meningitis is a rare, fatal form of bacterial meningitis caused by *Salmonella* bacteria; a gram-negative, facultative anaerobic flagellated bacillus primarily found in contaminated foods. *Salmonella* meningitis can range from less than 1% of cases in developed countries to up to 13% in developing countries. It is challenging to treat and has a high complication rate (3). In a recent systemic review, the worldwide frequency of NTS infection was reported to be 7.5/100.000 (4). The majority of these cases occur in sub-Saharan Africa. The association was mostly found in newborns, early childhood, malnutrition, anemia, and malaria. Recurrent infection and mortality are more common in the presence of HIV infection (5). Our case was in the neonatal period, but no other facilitating factor, such as immunodeficiency, was detected. Although this rate drops below one percent in developed countries, it still maintains its importance because it causes severe meningitis, especially in children under the age of two (6,7). Previous studies have reported the complication rate in *Salmonella* meningitis as 50-90% and the mortality rate as 50-70% (3,5). In a retrospective study, possible neurological complications in *Salmonella* meningitis have been reported as convulsion, hydrocephalus, subdural collection, cerebral infarction, ventriculitis, empyema, intracranial abscess, and cranial nerve damage (8,9). In these cases, the benefit of early MRI has been reported, and it has been shown that complications can be detected early and appropriate treatment can be administered (9). Therefore, timely and appropriate treatment is essential to prevent mortality and morbidity. In our case, convulsions were observed in the early period, intracranial abscess and infarction were detected by cranial MRI, and mortality was prevented with timely and appropriate treatment. Additionally, MRI angiography was performed in our case, and LMWH treatment was applied upon detection of thrombosis.

Medical treatment of meningitis caused by *Salmonella* is complicated and not standardized. In 2003, Owosu-Ofori et al. described two cases of *Salmonella* meningitis and suggested that conventional antibiotics (ampicillin, chloramphenicol, and cotrimoxazole) had a minimal role in the treatment of *Salmonella* meningitis (in which the cure rate was 41.2%, the recurrence rate was 11.8%, and the associated mortality was 44.7%). One of the problems with chloramphenicol is that it is bacteriostatic against *Salmonella*. Optimum treatment of bacterial meningitis requires antibiotic(s) with bactericidal effect (10). Fluoroquinolones (ciprofloxacin) showed a cure rate of 88.9%, while third-generation cephalosporins (cefotaxime or ceftriaxone) had a cure rate of 84.6%. One of the main concerns with the use of ciprofloxacin is potential joint toxicity and cartilage destruction in children. Fluoroquinolones have many positive aspects: High bioavailability (close to 100%) following oral administration, excellent penetration into many tissues (including CSF and brain), and good intracellular diffusion. The American Academy of Pediatrics recommends treatment of *Salmonella* meningitis with cefotaxime or ceftriaxone with or without fluoroquinolone for four weeks or longer. However, cases of relapse have been reported following four weeks of treatment. The combination of ciprofloxacin and ceftriaxone or cefotaxime has been recommended, especially for treating cerebral abscesses caused by *Salmonella* spp. (11,12). We describe a rare case of NTS infection in an immunocompetent patient living in an industrialized country. The baby developed meningitis as a complication of systemic infection, probably due to his early age.

In conclusion, in our experience, early diagnosis based on recognizing acute neurological signs and laboratory findings associated with prompt and appropriate antibiotic therapy for at least four to six weeks can improve patient outcomes and reduce the risk of neurological sequelae. Neuroimaging

follow-up, along with accurate neurological clinical examination, is necessary to prevent and reduce the high risk of complications.

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the author.

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