

Relapsed Nosocomial Neonatal *Salmonella enterica* sv. Typhi Meningitis: A Case Report

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Citation

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Abstract

Salmonella enterica sv. Typhi (S typhi), the causative organism of enteric fever which is found mainly in the developing countries, is a severe systemic disease with a worldwide frequency estimated as 12-33 million cases per year. It is transmitted not only through contaminated food and beverages, but also via a vertical mechanism during the last trimester of pregnancy. *Salmonella enterica* sv. Typhi meningitis of the newborn is rare, but is important as its mortality, morbidity and relapse rates are high. The prognosis of salmonella meningitis is poor, even in the case of prompt diagnosis and adequate therapy. Third generation cephalosporines should be the first line drug of choice. However, cefotaxime used for 4 weeks could not prevent relapses. Meropenem and ciprofloxacin could be used alternatively. We report a neonatal nosocomial S typhi meningitis case relapsing in spite of cefotaxime usage for 4 weeks, which was then treated with ciprofloxacin.

INTRODUCTION

Salmonella enterica sv. Typhi is an important public health problem in the developing countries causing enteric fever, and its worldwide prevalence is 12-23 million cases per year (1). Classic S typhi infection starts 3 days after birth of a newborn and leads to undernutrition, vomiting, diarrhea, abdominal distention and variable fever. Extraintestinal infections like pneumonia, myocarditis, osteomyelitis, and meningitis are rare (2, 3). Clinically meningitis is important as its morbidity and mortality rate is high (4). *Salmonella typhi* meningitis of the newborn has been reported only as case reports or series consisting a few numbers of patients until nowadays and no nosocomial case has been reported in the literature. This is the first nosocomial *Salmonella enterica* sv. Typhi meningitis in the literature, which was transmitted from a patient who was *Salmonella enterica* sv. Typhi carrier.

A CASE REPORT

A boy, 14 days old who had been given birth with caesarean section, without any complication and whose birth weight was 3100 grams and who was breast fed, was referred to the out-patient clinic with history of undernutrition, fever and irritability. The patient had been kept in the hospital for two

days in the same room with a patient who had gastroenteritis and which we later learned that he was an S typhi carrier. The patient who had been mistakenly diagnosed with infantile colitis had been discharged from the hospital. He again was referred to our out-patient clinic with fever, undernutrition, and irritability eight days after he had been discharged from the hospital. The physical examination revealed a body temperature of 39.5°C, irritability and a pulsatile and tense anterior cranium.

The laboratory findings revealed a white blood cell count of 25500/ml, cerebrospinal fluid (CSF) was purulent, turbid, and its pressure was a slightly elevated. Gram staining of the CSF showed gram-negative cocci. CSF glucose level was 5 mg/dl (blood glucose level at the same time was 97 mg/dl), cell count was 1590 cells/ml (85% was PNL). Cefotaxime and ampicillin had been given empirically when meningitis was diagnosed. After one night of incubation, blood and CSF cultures yielded a non-lactose fermenting, gram-negative bacteria. The representative strains were identified using the API 20E system (following the manufacturer's instructions) and database profiling (bioMérieux La Balme, France). It was sensitive to cefotaxime. The patient whose serologic findings were salmonella negative was then treated

with cefotaxime for 4 weeks. At the 4th day of treatment, CSF and blood samples were obtained and no bacteria was isolated. There was not any complication except hydrocephalus.

The patient was examined once a week after discharge from the hospital and all clinical findings including head circumference were normal. Four weeks later, he was examined with a cranial CT and was found to be normal again. At the fifth week, he was referred again with fever, vomiting and undernutrition. The body temperature was 39.5°C, pulse rate was 178/minute, respiration rate was 40/minute, he was irritable, and there was a pulsatile and tense anterior cranium and neck stiffness. The laboratory findings revealed a white blood cell count of 39500/ml, CSF was purulent, turbid, and its pressure was a slightly elevated. Direct microscopically, there were abundant of gram-negative bacteria. CSF glucose was 6 mg/dl (blood glucose obtained at the same time was 81 mg/dl), and cell count was 1900 cells /ml (60% was PNL). Cefotaxime had been given empirically, and when the causative organism was isolated at culture and reported to be *Salmonella enterica* sv. Typhi, cefotaxime was stopped to prevent resistance and meropenem was initiated. At the second day of the meropenem therapy his convulsions started and status epilepticus pursued.

Convulsion was attributed to the adverse effect of meropenem and it was exchanged with ciprofloxacin, which the microorganism was susceptible. Although clinical healing was observed after the third day of ciprofloxacin therapy, bacterial eradication could be achieved only on the 15th day of therapy. At the same time hydrocephalus complication had evolved. After achieving bacterial eradication, at the 24th day of therapy ventriculoperitoneal shunt operation was performed. Treatment was completed to 6 weeks. The patient's motor development was normal and he had been monitored without any complication.

DISCUSSION

The only host of *Salmonella enterica* sv. Typhi is human being. Its incubation period varies between 5-21 days (5). The most important infection sources for newborn infection tend to be the mother and/or caregivers. The causative organisms for the reported nosocomial infections were salmonellas other than *Salmonella enterica* sv. Typhi and the sources of the infection were infected food and beverages (6, 7). In our case, there was not any reported infection in the

caregivers of the baby. Furthermore, the mother was screened for carrier by culture and serologically, but nothing significant was identified. At the fifth postnatal day of hospitalization, the patient residing in the same room was reported as the infection source. He had positive serological test result with 1/320 dilution by Grubel Widal test. Nevertheless the culture results were negative. For this reason, we could not perform genotyping analysis for identification the source of our microorganism.

Our patient is the first nosocomial meningitis case of the newborn with *Salmonella enterica* sv. Typhi as the causative agent. *Salmonella enterica* sv. Typhi meningitis is a devastating illness with a neurologic complication rate of 43% and a relapse rate of 64% with severe morbidity (7,8,9). Mortality rate is 94% when antibiotic therapy is initiated and this rate can decrease to 30-37% later (10).

Ampicillin, chloramphenicol and cotrimoxazole have been used for *S typhi* meningitis treatment as a single drug regimen or as various drug combinations and mortality rate has been high (10, 11). Aminoglycosides should not be used because of the possibility of high drug resistance. Thus, third generation cephalosporins should be the first drug of choice for *S typhi* meningitis of the newborn (12,13,14). However, precautions should be taken because of unsuccessful treatment and relapse. In our case, although 150 mg/kg/day cefotaxime had been used for four weeks, there was a relapse 5 weeks after the initiation of therapy. Meropenem had been used as another choice of treatment and there were successful results. Although the quinolone type of antibiotics that had been extensively used to treat adult salmonella infections were restricted because of adverse effects, it could be used safely for devastating gram-negative bacterial infections (12, 14). We used ciprofloxacin for six weeks for our case and the results were encouraging clinically and there was not any adverse effect.

As a result, it should be always kept in mind that (1) cefotaxime which is used for 4 weeks for *S typhi* meningitis treatment could not always prevent relapse and ciprofloxacin could be a good alternative although it has severe adverse effects, (2) infection control measures and isolation procedures are important for the control of nosocomial infections.

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