Salmonella meningitis with thrombotic microangiopathy in an exclusively breast-fed infant: Case report

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ABSTRACT

Salmonella species is now a leading cause of meningitis in the developing world. We report a 6-month-old fully vaccinated baby girl who presented with high-grade fever and seizures. Her CSF and blood cultures grew non-typable Salmonella strains. The child was treated with antibiotics and anti-epileptics and discharged home after 2 weeks of hospital stay. Children with salmonella meningitis may present with life-threatening manifestations in the absence of gastrointestinal symptoms.

Keywords: Meningitis/Bacterial; Infant/Newborn; Salmonella Infections; Cephalosporins

Introduction

Salmonella strains account for less than 1% of the confirmed cases of bacterial meningitis in neonates and infants1, but are often associated with a high complication rate, a high mortality rate and a greater potential for relapse than occurs with meningitis caused by the more common Gram-negative pathogen, Escherichia coli.2 If Salmonella spp. are grown from a site outside the central nervous system in any unwell child, especially under 6 months of age, consideration should be given to performance of a lumbar puncture.1

Case Report

A 6-month-old fully vaccinated, exclusively breast-fed baby girl, first born to non-consanguineous parents, with normal birth and development history, was brought to the Emergency Department with two days history of high-grade fever, lethargy and one brief episode of seizures. At admission, she was febrile 102 F, respiratory rates 70-80/min, blood pressure 80/60 mm Hg, heart rate 150-160/min with poor peripheral perfusion, severe hypoxemia (SpO2< 80% in room air), pin-point pupils and altered sensorium. Anterior fontanelle was flat, tone was increased in all 4 limbs and deep tendon reflexes were exaggerated. Anthropometry revealed length, weight and head circumference below the third centile for age. Blood gas showed hypoglycemia and metabolic acidosis. She was immediately intubated and fluid resuscitation was initiated, along with anti-seizure medications and was shifted to the Pediatric Intensive Care Unit (PICU). A provisional diagnosis of sepsis/ inborn error of metabolism was made and she was started on ceftriaxone and vancomycin after sending blood and urine cultures. In the PICU, her vitals continued to worsen with radiological and blood gas features of acute lung injury along with fluid refractory shock requiring inotropic support. CT brain was normal. Echocardiography revealed a moderate sized Atrial Septal Defect with good biventricular function. She continued to have persistent metabolic acidosis and recurrent episodes of hypoglycemia during the first 12 hours of hospital stay.

Initial laboratory investigations revealed total white blood cell count of 5620 cells/cu.mm with 47% polymorphs, 44% lymphocytes; hemoglobin (Hb) was within normal limits. Ammonia, lactate, pyruvate were all within normal limits. CSF showed turbidity with glucose 2mg/dl (blood glucose 56mg/dL), protein 252mg/dL and CSF total white cell count of 420 cells/cu.mm with 71% polymorphs. Gradually her vitals improved, ventilatory requirements reduced and all inotropes rapidly weaned over the next 24 hours. On day 3, the baby was noticed to have paucity of movements of her left upper and lower limbs with tonic posturing of the left side of the body on stimulation. MRI brain revealed...
bilateral frontotemporal subdural effusion and multiple infarcts in bilateral corona radiata. Subsequently, non-typable *Salmonella* species was identified in both blood as well as CSF cultures. Vancomycin was stopped. Workup for sickle-cell and immunodeficiency (immunoglobulin levels, T and B-cell markers, NBT) was done which revealed no significant abnormality. Simultaneously, she developed loose stools and was also noted to have a rapid drop in platelet count to 25000/cu.mm along with a fall in Hb to 8mg/dl and rise in total WBC count to 16,400 cells/cu.mm. Peripheral blood smear showed fragmented RBC with serum LDH 892 IU/L. Workup for Hemophagocytic Lympho-Histiocytosis was negative. Thrombotic microangiopathy (TMA) was suspected as the baby continued to have poor sensorium with focal deficits, and persistent fever despite repeat CSF being sterile with improvement in cell count and biochemistry. Hence, the baby was given cryo-poor plasma daily for 5 days, which resulted in improved mental status and platelets counts. She was successfully extubated on day 6 of PICU admission. She completed a 21-day course of β-lactams following which she was discharged home asymptomatic. Work up for IL-12 and DOCK8 mutations could not be done.

**Discussion**

*Salmonella* species are ubiquitous human and animal pathogens. They are motile, non-encapsulated Gram-negative bacilli of the *Enterobacteriaceae* family. *Salmonella* spp have the unique capability of causing a suppurative foci in any organ, particularly bone and meninges.

Infection is most often transmitted by the feco-oral route. The source of infection could not be ascertained in this infant. Young age, malnutrition, high fever, seizures, hypoglycorrhachia and loose stools are commonly reported features of Salmonella meningitis as in this patient. Further, children with immunodeficiency and sickle cell disease are more vulnerable to the complications of Salmonella infections. Though there have been reports of thrombotic microangiopathy associated with Pneumococcal infections, there have been no such reports in association with Salmonella.

Acute hydrocephalus, seizures, ventriculitis, abscess, subdural empyema and long-term neurological sequelae are known to occur in Salmonella meningitis. Neuroimaging studies have been recommended for every patient with Salmonella meningitis in view of the high percentage of abnormalities detected. This infant also had bilateral subdural effusion but did not have any neurological deficits at discharge.

In the past, chloramphenicol, ampicillin and co-trimoxazole have been widely used to treat Salmonellosis but due to the emergence of resistance to these agents, the American Academy of Pediatrics now recommends that treatment for *Salmonella* meningitis with cefotaxime or ceftriaxone should continue often for 4 weeks or more. Meningitis caused by *Salmonella* spp. resistant to cephalosporins is uncommon, although it has been reported occasionally. Optimal antibiotic regimen for Salmonella meningitis would include a third-generation cephalosporin or fluoroquinolones. Finally, even after an apparently satisfactory clinical response to antibiotics, staff and parents should be made aware that there is still a need for vigilance because of the possibility of relapse which can occur days or even weeks after apparently successful antibiotic treatment. Although not obvious in the early stages, progression of a relapse may be rapid.

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**References**

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