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Case Report

Salmonella typhimurium meningitis in an immunocompetent infant

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ABSTRACT

Meningitis due to *Salmonella* is rare and associated with high morbidity, mortality, and relapse rates despite adequate treatment. Here, we report a case of meningitis due to *Salmonella typhimurium* in an immunocompetent infant. The child was brought to the pediatric emergency department with complaints of high-grade fever, loose motions, vomiting, and irritability of 3-day duration. Cerebrospinal fluid (CSF) analysis was suggestive of acute bacterial meningitis, and the child was started on intravenous ceftriaxone. The CSF and blood cultures grew *S. typhimurium* and the treatment was accordingly modified. His serum immunoglobulin levels were normal, and enzyme-linked immunosorbent assay for HIV was negative. Clinical course, antibiotic treatment, and outcome of the case are discussed here.

Key words: *Salmonella typhimurium, Meningitis, Immunocompetent, Infant*

Acute bacterial meningitis in infancy is a medical emergency which requires prompt diagnosis and treatment. It is associated with significant morbidity and mortality despite advances in the treatment [1-3]. The common etiological agents of pyogenic meningitis reported from India include *Staphylococcus aureus* and *Streptococcus* species among Gram-positive bacilli and *Escherichia coli*, *Klebsiella pneumonia,* and *Pseudomonas aeruginosa* among the Gram-negative bacilli [2,3]. *Salmonella* is a rare cause of bacterial meningitis, and limited reports suggest high morbidity and mortality rates among infants [4-6]. We present a case of *Salmonella typhimurium* meningitis in an immunocompetent infant.

CASE REPORT

A 10-month-old male infant was brought to the pediatric emergency department of with complaints of fever with chills and loose motions for 3 days, vomiting, reduced oral acceptance and irritability of 1-day duration. There was no history of seizures or any abnormal movements. He was born by full-term normal vaginal delivery to a primigravida mother. His birth weight was 2.6 kg and cried immediately after delivery with no antenatal, intranatal, and postnatal complications. The child was exclusively breastfed, and complementary feedings were started at 6 months of age. He was immunized and had attained milestones as per age.

On initial examination, he was febrile (39.5°C) and had respiratory rate of 32/min, heart rate of 120 beats/min, blood pressure of 92/60 mmHg, capillary refill time of 2 s, and weight of 7.6 kg. The central nervous system examination revealed that the child was irritable, anterior fontanelle was full and had hypertonia with brisk deep tendon reflexes, neck rigidity and positive Kerning's and Brudzinski's sign. Bilateral symmetrical chest movements were present with no organomegaly and normal bowel sounds.

Initial blood investigations revealed anemia (hemoglobin [Hb]: 10 g/dL) with normal total and differential white blood cell (WBC) and platelet counts (Table 1). Liver and kidney function tests were normal and rapid test for malaria was negative. Samples were sent for blood culture and sensitivity testing. A lumbar puncture (LP) was done which revealed turbid cerebrospinal fluid (CSF) with total WBC count of 400 cells/mm^3 with 85% polymorphs. The CSF protein was elevated to 200 mg/dl, and sugar was reduced to 19 mg/dl. The child was started on IV ceftriaxone (100 mg/kg/day) along with intravenous fluids.

The CSF gram stain smear showed pus cells with a few Gram-negative bacilli. CSF culture grew *S. typhimurium*. The isolate was susceptible to ampicillin, ceftriaxone, imipenem, meropenem and ciprofloxacin by Kirby Bauer disc diffusion method, and minimum inhibitory concentrations (MICs) confirmed by Vitek II automated system. Blood culture also grew *S. typhimurium* with similar antibiogram. Other investigations including typhidot (immunoglobulin M), widal, and urine culture were negative. Further work-up for underlying immunodeficiency disorders was negative including normal immunoglobulin levels and negative enzyme-linked immunosorbent assay for HIV. His serum calcium was 7.1 mg/dl, and sickling test was negative. Ultrasonography (USG) of abdomen revealed mild hepatosplenomegaly.

Meanwhile, intravenous ciprofloxacin (15 mg/kg/day) was added after getting the culture reports. The child continued to have high-grade fever; although there was an improvement in irritability and meningeal signs over next 5 days. Repeat hemogram revealed

moderate anemia (Hb: 6.9 g/dL) and leukocytosis (total leukocyte count: 26,700/mm^3) with neutrophilia (polymorphs 78%). Blood cultures sent on day 5 of admission again grew *S. typhimurium*. A repeat LP was carried out on day 9 of admission (Table 2). Thereafter, intravenous ceftriaxone was discontinued, and intravenous meropenem was initiated (100 mg/kg/day q8h). The child became afebrile by day 14 of admission. Repeat blood, stool, and CSF cultures taken subsequently were sterile. An USG skull done on day 8 of admission revealed a normal study; however, a repeat study on day 47 of admission showed mild communicating hydrocephalus. Magnetic resonance imaging brain showed mild communicating hydrocephalus.

The child received antibiotics for duration of 7 weeks, and at discharge he was afebrile, having good oral acceptance, playful but carried sequelae in the form of mild communicating hydrocephalus. He is under close follow-up to assess for neurological sequelae and in view of high chances of relapse of the disease. All the family members were screened for carrier status by repeated stool cultures which were negative.

DISCUSSION

S. typhimurium is a rare cause of acute bacterial meningitis in immunocompetent infants worldwide including India [4-8]. In a report from South India, of 385 cases of pyogenic meningitis, *Streptococcus pneumonia* was the predominant pathogen [2]; whereas, in a series from North India, *S. aureus* was the most common pathogen among 403 culture-confirmed cases [3]. *Salmonella* as a causative organism of pyogenic meningitis was not reported in these two large series.

There are contentious issues regarding the management of *Salmonella* meningitis, i.e., choice of antibiotics, combinations in antibiotic therapy and the duration of treatment recommended. Antibiotics used previously either alone or in combination included chloramphenicol, co-trimoxazole, and ampicillin. Their use declined in view of changing resistance pattern and concern for toxicity profile. Subsequently, third-generation cephalosporin's were recommended for a minimum of 3 weeks [9,10]; however, reports of relapses emerged even after appropriate dose and duration of therapy with these agents [11,12]. Around the turn of the century, a combination of third-generation cephalosporin with ciprofloxacin was recommended to be used for a minimum of 3 weeks after the first sterile CSF [13]. Although there has been a concern of arthropathy due to use of ciprofloxacin in children, it is extremely uncommon, and it may be used in the treatment of serious pediatric infections where potential benefits outweigh the risks.

In this case, the child was put on a combination of ceftriaxone with ciprofloxacin once the CSF culture report was available.

Table 1: Routine hematological and biochemical parameters

Parameters	At admission	Day 5 of admission	Day 22 of admission
Hb (g/dL)	10	6.9	10.2
Total leucocyte counts (/mm^3)	10200	26700	6700
Differential leucocyte counts	N66 L31 M2E1	N78 L18 M4	N60 L30 M6E4
Platelet counts (10^9/L)	168	192	245
Urea (mg/dL)	28	30	22
Creatinine (mg/dL)	0.6	0.7	0.6
Calcium (mg/dL)	7.1	8.0	8.3
Phosphate (mg/dL)	2.5	2.4	2.5
Sodium (mEq/L)	138	138	140
Potassium (mEq/L)	3.8	3.9	4.2
Bilirubin (mg/dL)	1.1	0.9	0.9
Total protein (g/dL)	6.1	6	6.2
Albumin (g/dL)	3.5	3.2	3.4
Globulin (g/dL)	2.6	2.8	2.8
SGOT (IU/L)	25	37	34
SGPT (IU/L)	39	44	40

SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase, Hb: Hemoglobin

Table 2: Findings of serial CSF examinations during the illness

Day of admission	CSF TLC	CSF DLC	CSF proteins	CSF glucose	CSF culture	Clinical status	Antibiotics
Day 1	400 cells/mm^3	P85L15	200 mg/dl	19 mg/dl	*S. typhimurium*	Features of meningitis	D1-ceftriaxone D3-cipro floxacin added
Day 9	150 cells/mm^3	All lymphocytes	144 mg/dl	19 mg/dl	*S. typhimurium*	Partial response, high grade fever	Meropenem
Day 22	No cells	-	40 mg/dl	33 mg/dl	Sterile	Afebrile, no meningeal signs	Meropenem

CSF: Cerebrospinal fluid, TLC: Total leukocyte count, DLC: Differential leukocyte count

Salmonella meningitis resistant to cephalosporins, though uncommon, have been reported [13]. In a report of 4 cases from Vietnam, 2 patients required change of therapy from initial third generation cephalosporin combination to a combination of imipenem and ciprofloxacin due to slow clinical response [6]. Effectiveness of carbapenems in *Salmonella* meningitis has been shown in a few case reports [11,14]. Our patient had a response to the therapy of ceftriaxone and ciprofloxacin in terms of improvement in irritability and meningeal signs; however, he continued to have high-grade fever with leukocytosis. Despite 7 days of receiving these antibiotics to which isolate had shown MICs in susceptible range, blood culture was still positive. Therefore, his antibiotic was changed to meropenem as per the sensitivity report available. Our patient responded well to the change and fever subsided after 1 week and repeat cultures on day 22 (2 weeks after changing to meropenem) came out sterile. Meropenem was continued for another 5 weeks to prevent any relapse.

Salmonella meningitis in infants has a wide spectrum of morbidity including both acute complications and long-term neurological sequelae. Acute complications such as hydrocephalus, subdural collection, cerebral infarction, ventriculitis, and intracranial abscess were reported in a high proportion of patients by Wu et al. [5]. In long-term follow-up, language disorders (52%), motor disability (48%), intelligence quotient <80 (43%), epilepsy (33%), sensory neural hearing loss (17%), visual deficits (10%), microcephaly (5%), and hydrocephalus (5%) were reported in the same study [5]. The mortality rates are significant (13-18%) even in otherwise healthy infants [5,7]. Our patient developed mild non-communicating hydrocephalus despite otherwise favorable clinical response. He is under close follow-up to look for any long-term sequelae.

CONCLUSION

S. typhimurium meningitis is a rare illness, associated with high morbidity and mortality rates. The management is challenging and requires prolonged therapy with appropriate antibiotics. A follow-up plan for developmental assessment is essential.

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