Salmonella enterica serotype arizonae: a rare entity in neonatal meningitis

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Abstract

Introduction
Salmonellosis is an important public health problem throughout the world. Salmonella meningitis is an unusual manifestation of salmonellosis and remains a threat to children below 2 years of age. Young children especially infants and immunocompromised adults are particularly at higher risk of acquiring this bacteria. The disease has a poor prognosis and is associated with significant morbidity and mortality. Salmonella enterica serotype Arizona is an uncommon human pathogen and a rarely encountered species in neonatal meningitis.

Case report
We here report a fatal case of neonatal meningitis due to Salmonella enterica serotype Arizona in a 7-day-old female neonate. Despite the prompt and aggressive treatment with broad-spectrum antibiotics, on sixth day of admission she succumbed to her infection.

Conclusion
Neonatal meningitis due to Salmonella is associated with very high mortality. Survival depends on the urgent prompt diagnosis and institution of appropriate therapy.

Introduction
Salmonellosis is a major cause of bacterial enteric illness and is an important public health problem throughout the world. Young children especially infants are more prone to infection and are at increased risk of severe complications like septicaemia and meningitis. Acute meningitis due to Salmonella species in infants is associated with significant mortality, and despite the appropriate antibiotic therapy, the chances of complications and relapse are very high. The overall case fatality rate of Salmonella meningitis is very high (73.5%) in all age groups and is even higher (92.5%) in neonates. Those who survive may have severe neurological complications like hydrocephalus, seizures, sensorineural hearing loss and developmental abnormalities. While such infections are relatively common in developing countries, they are rarely seen in developed ones. Salmonella enterica serotype Arizona causing neonatal meningitis is rare. A fatal case of neonatal meningitis due to Salmonella enterica serotype Arizona is reported herewith and to the best of our knowledge is a first case from Uttarakhand with this microbial aetiology.

Case report
A 7-day-old baby girl was brought to the paediatric emergency department with convulsions. She had a 2-day history of poor feeding, lethargy, abnormal body movements and fever. The baby was born at term by normal vaginal delivery with a birthweight of 1.9 kg. Her mother was a 21-year-old primigravida who was severely anaemic and had a poor socioeconomic status. On examination, the baby was febrile (101°F), pulse rate was 180 beats/min and respiratory rate was 50 breaths/min. She appeared pale, dehydrated and was icteric up to the thigh. Her anterior fontanel was full but non-bulging. On neurological examination, she had generalised increased tone, absent Moro reflex and a poor sucking reflex. Kernig’s and Brudzinski’s signs were negative, she was conscious and there was no neck stiffness. The rest of the systemic examination was unremarkable. A diagnosis of neonatal sepsis was made, and a full sepsis profile was requested. She was started empirically on intravenous (IV) ampicillin, gentamicin and phenobarbitone.

Laboratory investigations revealed haemoglobin 15.6 g/dl and total leucocyte count 14,600 cells/µl with differential count being 73% neutrophils, 17% lymphocytes, 7% monocytes and 3% eosinophils. The C-reactive protein was positive (175 mg/l). The serum electrolytes including calcium, liver function tests and renal function tests were normal. Lumbar puncture revealed turbid, xanthochromic cerebrospinal fluid (CSF) with 1,230 leukocytes/µl (81% neutrophils, 19% lymphocytes and few RBCs), protein 580 mg/dl and glucose 9 mg/dl (parallel blood glucose 95 mg/dl). The CSF findings were suggestive of meningitis. CSF gram staining showed many pus cells and few gram-negative bacilli (GNB). Latex agglutination test for Haemophilus influenzae type B, Neisseria meningitidis, Escherichia coli, Streptococcus pneumoniae and Streptococcus group B was negative. On the basis of CSF findings, ampicillin was omitted and ceftriaxone was added to the regime.

Both CSF and blood cultures collected at the time of admission were flagged positive after 12 h by Bactec 9120, an automated blood culture...
system (Becton Dickinson, USA). Subculture on 5% sheep blood agar and Mac Conkey agar (MA) was done, and growth on MA showed non-lactose fermenting colonies. The isolate, GNB was subjected to routine biochemical tests (triple-sugar iron agar; indole, mannitol, citrate, urea and motility), but the results were non-conclusive. However, extended biotyping eventually identified the organism as Salmonella enterica serotype Arizonae which was later confirmed by agglutination test (agglutinating serum, Remel Europe Ltd, Dartford, UK). Antibiotic susceptibility test by Kirby–Bauer disc diffusion method was done, and the isolate was found sensitive to ciprofloxacin, cotrimoxazole, ceftriaxone, meropenem and cefoperazone-sulbactam and was resistant to ampicillin, gentamicin, augmentin and chloramphenicol. At this point, gentamicin was omitted and cotrimoxazole was added to the regime. Subsequently, the mother gave a history of gastroenteritis 2 years back after having Katchmoli (a ritualistic preparation from the raw goat meat) from a stall in a Mela (a local village fest). The mother’s stool was cultured to rule out the carrier state and was found positive for Salmonella enterica serotype Arizonae with similar sensitivity pattern. Blood culture and Widal test were negative. The stool sample from the baby was negative. Despite the aggressive antimicrobial therapy, the patient remained critical throughout her hospitalisation and required intensive care. She had respiratory distress, frequent focal tonic seizures and alternating episodes of hypothermia and fever, regardless of the efforts to achieve thermoregulation. Seizures were characterised as focal tonic and in spite of phenobarbitone treatment up to two to three times per day. The baby had a progressive deterioration of mental status, and on sixth day of her admission she died. The mother was advised to take eradication treatment for carrier state with ciprofloxacin 750 mg twice daily for 4 weeks and repeat stool culture after treatment. Three subsequent stool samples from the mother were negative at the end of her course of eradication treatment.

**Discussion**

Salmonella organisms are gram-negative, flagellated, facultatively anaerobic bacilli which commonly cause food-borne illness. Salmonella strains are not a frequent cause of meningitis, but if intracranial infections occur, they are more common in paediatric age groups especially in neonates and young infants\(^1\). The prognosis and the course of Salmonella meningitis is different from that of other causes of meningitis and varies from patient to patient\(^2\). Neonatal meningitis due to Salmonella species is associated with high mortality, high treatment failure rates and the significant morbidities in the survivors\(^3\). The Salmonella serotypes most often reported to cause neonatal meningitis include Salmonella typhimurium, Salmonella paratyphi B and Salmonella typhi. However, Salmonella enterica serotype Arizonae is a rarely encountered species in neonatal meningitis.

Salmonella enterica serotype Arizonae is a common gut inhabitant of reptiles, with snakes as the most common reservoir with as many as 78.8% harbouring the organism\(^7,8\). This organism has also been responsible for severe outbreaks in turkeys and sheep. Later, it was also isolated from fowl, ducks and mammals, such as dogs, cats, monkeys and goats\(^8\). Salmonella enterica serotype Arizonae was first described by Caldwell and Ryerson in 1939, and the first report of human infection came in 1944\(^9,10\). Initially it was considered to be a reptile pathogen, but now it is established as a well-known pathogen in young children and in patients with underlying disease or impaired immunity. Most cases are in children less than 5 years of age; however, infants are at particularly higher risk\(^11\). A literature review by Mahajan et al. showed 17 documented cases of human infection by this organism, of which 11 were children and 4 were infants\(^6\). Neonates are known to be immunodeficient due to lack of foetal antigenic exposure and are generally less resistant to meningeal infection than older children and adults. The predominance of neonates with Salmonella meningitis may be due to increased permeability of blood–brain barrier, birth trauma, immaturity of cellular immunity or transmission of infection from an infected mother or nursing mate\(^4\). An organism that gains access to the circulation may localise to the central nervous system (CNS) to a greater degree in infants than in older age groups.

In our case, both the blood and the CSF cultures of the patient had grown Salmonella enterica serotype Arizonae. Also the same organism with similar antibiogram was grown from the mother’s stool sample demonstrating the carrier state. The possible routes of acquiring neonatal salmonellosis are by vertical transmission, feco–oral route, environmental transmission through contaminated top feeds, via breast milk and transplacental route\(^12,13\). In our case, the organism could have been transmitted through perineal contamination during delivery or through feco-oral route as the mother was a carrier. She might have got infected after consuming raw uncooked goat meat 2 years back and thereafter developed a carrier state. However, it was unclear how long the mother had been asymptomatically excreting Salmonella, as she only recalled the episode of gastroenteritis 2 years previously. She did not have a relevant travel history, her general health was normal and there were no occupational risks. A carrier state is not uncommon, and a recurrence of Salmonella enterica serotype Arizonae in immunocompromised
patients after 1 year has been reported previously. In our case also, the mother was somewhat immunocompromised as she was anaemic, was malnourished and had a poor socioeconomic status.

Our patient was treated empirically with broad-spectrum antibiotics, but there was no sign of improvement, and despite the aggressive antibiotic therapy, disease followed a rapidly progressive course with an unfortunate outcome. Treatment of *Salmonella* meningitis is known to be difficult and has not been well defined. Various studies have reported the use of different antibiotics like cephalosporins, ampicillin, gentamicin and fluoroquinolones. Although many authorities recommend the use of third-generation cephalosporins as good treatment, no standard treatment has emerged. Adjunctive dexamethasone may be recommended to attenuate the effects of the innate inflammatory response to the bacterial invasion within the CNS, although the benefit of steroids in meningitis seems to be controversial. *Salmonella* species are facultative intracellular microorganisms, and the ability to survive intracellularly protects the organism from the actions of extracellular antimicrobial agents, which may result in progression of infection of choice. *Salmonella enterica* serotype Arizona is a rare cause of neonatal meningitis and can manifest similar to meningitis caused by other *Salmonella* species. It should be included in the differential diagnosis of gram-negative bacillary meningitis especially in neonates. Young children (<5 years of age) particularly infants are at higher risk of acquiring such infections; therefore, proper history should be obtained in such cases.

**Consent**

Written informed consent was obtained from the patient for publication of this case study and the copy of same is available for review by the editor-in-chief of this journal.

**Abbreviations list**

CNS, central nervous system; CSF, cerebrospinal fluid; GNB, gram-negative bacilli; IV, intravenous; MA, MacConkey agar

**References**