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Case Presentation
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Salmonella Meningitis

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Abstract

We report the case of 7 weeks-old male infant who presented with fever of 38.1ºC, lethargy, poor feeding, decreased level of activity and irritability for 4 days. He had bulging anterior fontanelle but no nuchal rigidity on examination. Full septic work up was done and Investigations showed high CRP; U/S neonatal brain showed thickening and increased echogenicity of the cortical sulci of both cerebral hemispheres raising the possibility of meningitis. CSF analysis showed leukocytosis with neutrophilia, high protein and low glucose. CSF, blood and stool cultures grew: *Salmonella*, non-typhi. Urine culture showed no growth. MRI brain showed pyogenic ventriculitis. No brain abscess or extra-axial empyema.

Keywords: Meningitis; *Salmonella*; Shigella; Non-typhoid *salmonella*

Introduction

Salmonella is an enteric gram-negative bacillus, motile, Hydrogen Sulfide (H_2S) producing, non-spore-forming, facultative anaerobic bacteria. It produces colonies similar to *E. coli* but do not ferment lactose [1]. It is classified under *Enterobacteriaceae* group along with other enteric organisms like (*Escherichia, Shigella, Enterobacter, Klebsiella, Serratia, Proteus*, and other). Their natural habitat is the intestinal tract of humans and animals, but *Salmonella* and *shigella* are mainly pathogenic for humans [2,3]. However, *Salmonella* can be also seen in mammals, reptiles, birds, and insects.

Salmonellae can be classified by their serotype like: *Salmonella* Typhi, *Salmonella* Para typhi A, *Salmonella Choleraesuis, Salmonella Typhimurium* and *Salmonella Enteritidis*. They can be further classified as "typhoidal" and "non-typhoidal". Typhoidal *Salmonella* are those serotypes that cause typhoid ("enteric") fever, for example: Typhi, Para typhi A, Para typhi B, and Para typhi C. Non-typhoidal *Salmonella* refers to all other serotypes. The non-typhoidal *Salmonella* serotypes: Enteritidis and Typhimurium are the two most common serotypes reported in the United States [1].

It is well known that non-typhoidal *Salmonella* serotypes are the leading cause of community acquired gastroenteritis worldwide. *Salmonella* transmitted mainly by fecal-oral route typically *via* consumption of contaminated water or food from animals and animal products to humans. Foodborne outbreaks, consumption of raw or undercooked poultry, egg, or meat, consumption of unpasteurized milk or dairy products, consumptions of fresh fruits, vegetables and sprouts, swimming in or drinking untreated fresh water, all these exposures are main ways for *Salmonella* transmission [4,5].

According to the CDC, an estimated 1.2 million cases of foodborne salmonellosis occur annually in the United States [4,6]. Incidence of non-typhoidal *Salmonella* human infection has significantly increased over the past decades in many countries, worldwide [7]. Non-typhoidal *Salmonella bacteremia* and vascular infections accounts for 8% and meningitis, septic arthritis, and osteomyelitis have been reported as a complication of *Salmonella bacteremia* but are exceedingly rare events.

Salmonella infection can present in many different clinical scenarios like enteritis, systemic infection, and enteric fever; however, asymptomatic colonization may also occur [3]. Invasive *salmonella* infection is seen mostly in immunocompromised infants, but in our patient, who developed NTS meningitis and he is an immunocompetant infant and born in developed country, growing of non-typhoidal *salmonella* in CSF, stool and blood is rare and there are few similar cases reports. In 2016, United Kingdom of Saudi Arabia has published a case report about *salmonella* meningitis presenting with multiple micro-abscesses in the brain in a 4 months immunocompetant infant [4].

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When a physician suspects *Salmonella* infection, history is very important tool to identify the source of the infection as it can be acquired from farm animals and pets or environment or even from the mother if she was a carrier. For example, asking about history of contact with young poultry, cattle, cats, dogs, rodents, turtles, parrots and reptiles, ingestion of infected breast milk of mothers infected with *salmonella*, and having contact with stools of *salmonella* carrier mothers [1,4]. Human salmonellosis associated with exposure to pet animals is a recurring public health problem in the United States, and individual cases or even small outbreaks have been reported. It caused about 1.2 million human illnesses, 23,000 hospitalizations, and 450 deaths each year in the United States [6].

Invasive Non-typhoidal *salmonella* infection can be seen in patients with comorbidities (immunosuppression), sickle cell anemia and HIV infection, in infants and elderly. A systematic review of scientific databases and grey literature that was published in 2019 showed that 535,000 cases of non-typhoidal *Salmonella* invasive disease occurred in 2017, with the highest incidence in sub-Saharan Africa (34.5% cases per 100 000 person-years) and in children younger than 5 years (34.3% cases per 100,000 person-years). Mean all-age case fatality was 14.5%, with higher estimates among children younger than 5 years 13.5%, and elderly people 51.2%, people with HIV infection 41.8%, and in areas of low sociodemographic development 15.8% in sub-Saharan Africa [5].

Case Presentation

A 7 weeks old male infant, part of twins, previously healthy, received birth vaccine, developed fever for duration of 4 days. Fever was measured at home by auricular thermometer and it reached 38.6°C. It was responding to paracetamol and sponging as the lowest temperature recorded was 37.8°C. He also had irritability, poor feeding, lethargy with decreased level of activity, diarrhea 8 times a day, yellow color stool, non-bloody. He was crying every time mother will pick him up.

There were no URTI symptoms, no rash, no vomiting and no change in number of wet diapers. No sick contacts, no travel history and no history of contact with COVID-19 patients. As for the perinatal history, there were no maternal comorbidities during pregnancy. He was born at 37 weeks + 2 days by C-section because of malpositioning, birth weight was 2,930 gram. No PROM, GBS status was unknown; mother did not require antibiotics before, during or after delivery. No maternal fever as well. He cried after birth and breastfed immediately. In his neonatal period, he developed neonatal jaundice but did not require treatment; he was discharged after 3 days of birth. No previous hospital admissions. His vaccination is up-to-date. His nutrition is from mother breast milk and topped up with formula milk with bottle.

There is turtle and hamster in the grandmother house where they usually go and visit her. They also have cat in their house. They have housemaid who play with all these animals and she takes care of the baby as well.

On examination in the ER, he was looking ill and irritable, his vital signs were as follow: Temperature: 38.1°C, respiratory rate: 40 breaths/min, pulse rate 138 beat/min, O_2 saturation 98%. Regarding his growth chart: Weight: 5.2 kg, length: 61 cm, Head circumference: 40 cm.

He had full and bulging pulsatile anterior fontanelle. Good pulses equal in all extremities, Normal peripheral perfusion. He was admitted and required active isolation. Quantifiable lab results are summarized in Table 1. Blood tests showed: Normal white blood cells, high CRP 117. Blood culture and sensitivity, CSF culture were sent and results came back with CSF analysis suggestive of non-typhoidal *Salmonella* meningitis, high WBC 18,759 cells, high protein 4.82 g/L and low glucose less than 0.11 mmol/L.

U/S neonatal brain showed thickening and increased echogenicity of the cortical sulci of both cerebral hemispheres raising the possibility of meningitis. No bleeding or dilated ventricles could be identified. No midline shift. Urinalysis was unremarkable and urine culture showed no growth.

Culture results are summarized in Table 2. First Blood culture taken on admission was reported as Gram Negative *Coccobacilli* at first and later identified as *Salmonella*, non-typhi, and was pan-sensitive to ampicillin, cefotaxime, ertapenem, meropenem, trimethoprim/sulphamethaxozole and ciprofloxacin. Stool culture came positive for non-typhi *Salmonella* on admission then became negative on 3rd day of admission. Our final impression was *Salmonella* sepsis as CSF, blood and stool cultures were positive.

First LP on admission was bloody tap and sent for culture only, reported as gram negative rods. Second LP which done later, on same day of admission is also reported as gram negative rods with further identification. CSF cultures grew *Salmonella* species, non-typhi. Culture repeated and showed No growth after 5 days enrichment

Table 1: Lab reports.

Lab test	Result
CRP	117.91 mg/L
WBC	12.08 × 10^9/L
CSF analysis	
Protein	4.82 g/L
WBC	18,759 × 10^6/L with 86% neutrophils
Glucose	<0.11 mmol/L

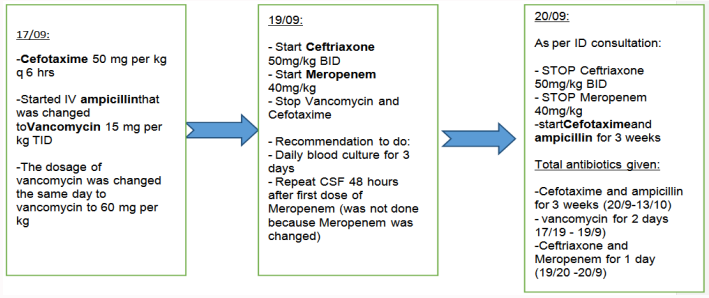

Figure 1: Site of culture reports.

Table 2: Site of culture on different dates.

Site of culture	17/09/2020	18/09/2020	19/09/2020	20/09/2020	21/09/2020	23/09/2020	25/09/2020	28/09/2020
CSF	Bloody, clotted No organisms seen.	For gram stain: No organisms seen.	salmonella species , non typi,	salmonella species , non typi , sensitivity result was out: Pansensitive	salmonella species , non typi,	No organisms seen	No growth at 48 hours	No growth after 5 days
Blood	-	Presumptive Gram Negative Coccobacilli seen	Salmonella species (not Salmonella Typhi)	-	Salmonella species (not Salmonella Typhi)	-	No growth at 5 days	
Stool	-	-	salmonella, non typi,	salmonella, non typi,	-	No Salmonella, Shigella, Campylobacter or Enterohaemorrhagic Esch. coli isolated.	-	-
Urine	-	No growth	-		-	-	-	-

culture. He had total of 3 taps done: One on admission (17/09) and was bloody, repeated one next day (18/09), and 3rd one (23/09) (Figure 1).

He was initially treated as bacterial meningitis and started empirically on: IV cefotaxime 50 mg/kg and Vancomycin 15 mg/kg q6h. The primary nurse was asked to measure his Vital signs and GSC q2h. Infectious disease consultant was consulted regarding starting dexamethasone and the recommendation was that there is no indication if the baby is less than 6 weeks and since our patient is 7 weeks we can give, but because the patient completed 24 h since the antibiotics started, the recommendation was to not start dexamethasone as it will not help.

After we got the result of CSF cultures and that the *Salmonella* was pan-sensitive, we de-escalated antibiotics to Cefotaxime and Ampicillin for 3 weeks from first negative CSF culture (23/09). Infectious diseases recommendation was to do blood culture daily for 3 days and to repeat CSF after 48 h of starting Ceftriaxone and Meropenem. Blood culture and stool culture were repeated as well after changing the antibiotics and both came back negative. See graph 1 for our center management.

He continued to have fever until 5th day of admission (21/09), and then he became a febrile. MRI brain done in 4th day of admission and showed Mild diffuse smooth pial enhancement suggestive meningitis. It also showed pyogenic ventriculitis. No brain abscess or extra-axial empyema. He had ultrasound for neonatal spine and it ruled out any port of entry.

Patient was discharged after 3 weeks of Cefotaxime and ampicillin. He was doing well, returned to his baseline, and upon discharge he was given appointment with audiology for hearing assessment and follow up with general pediatrics.

Discussion

Meningitis caused by *Salmonella* species is considered to be relatively rare clinical entity. It accounts for <1% of the confirmed cases in neonatal and infantile age groups. Despite being an uncommon form of infection, it's associated with higher rates of complications, mortality, and relapses when compared to other forms of gram-negative rods meningitis. Its mood of transmission is mainly fecal-oral, and the common infection resources are contaminated foods or carriers [8]. Non-typhoid *Salmonella* species are known to cause asymptomatic infections, uncomplicated gastroenteritis that rarely require an antibiotic treatment. However, invasive forms of infections such as bacteremia, meningitis, and osteomyelitis have been also reported [9]. The most commonly isolated serotypes from different cultures such as blood or stools are *Salmonella enteritidis* and *typhimurium* [10].

It has been reported that, *Salmonella* meningitis is highly associated with contact with reptiles, contact with stools of mothers who are *Salmonella* carriers, and ingestion of infected breast milk of mothers who are infected with *Salmonella* [11]. In our case, the infant has been switched to formula feeding one week prior to his presentation to the emergency room with fever and diarrhea. Hence, it withdrawn was unclear whether the formula is the source of the bug, as his other twin experienced no similar symptoms on the same formula.

In addition, the patient was taken to his grandparents' house on many occasions, where they have pets and turtles. Turtle-associated meningitis and septicemia has been strongly described in the literature. Most of the patients with *Salmonella* meningitis present initially with gastrointestinal symptoms. This can occur following blood stream invasion *via Salmonella* that passes through the intestinal mucosa and lymphatic barriers [8]. However, the literature presented one case in which the patient had invasive *Salmonella* infection without gastrointestinal symptoms [12]. Our patient showed positive stool, blood and CSF cultures. Also, his first presentation was more with loose stools and fever.

Given the seriousness and the severity of the infection, *Salmonella* meningitis and septicemia requires rapid initiation of intravenous antibiotics. Unfortunately, there are no enough controlled trials or consensus guidelines to consider the right antibiotic approach. Hence, the management is more based on the information provided by case report or series and expert recommendation [13].

Historically; ampicillin, chloramphenicol, and cotrimoxazole were used individually or in combination, but the outcomes were not always successful, the reported mortality rates were up 30% with ampicillin and/or chloramphenicol [14].

With the emergence of third-generation cephalosporin's and their use in treating *Salmonella* meningitis, the relapses rates were decreased significantly, as did the mortality rates. This can be explained by the uncommon resistance strains. Although, general resistance of *Salmonella* to different antimicrobials is becoming a global public health problem [15]. The current recommendation for the American Academy of Pediatrics is the use of Cefotaxime or Ceftriaxone for at least four weeks, as previous studies showed higher risk of relapses with shorter duration [16].

Gentamicin has not shown to be a very effective option for treating *Salmonella* meningitis. The organism is facultative intracellular and

gentamicin has poor cellular and blood brain barrier penetration. No sufficient evidence has been seen with the use of carbapenems, although adequate results can be explained at individual bases [17].

Our patient had different courses of different antibiotics. His initial septic coverage was Cefotaxime and ampicillin, which were given for two days and one day, respectively. When his LP was suggestive of bacterial meningitis, his ampicillin was replaced by vancomycin on the same day 17/09/2020. Further cultures and sensitive's showed non-typhoid *Salmonella* strains that are pan sensitive. The patient was placed on meropenem and ceftriaxone for one day. Later switched to Cefotaxime and Ampicillin for 3 weeks as per ID recommendation.

Considering our literature review, we believe that the patient should have been kept on antibiotics for at least four weeks, as the data showed higher risk of relapse on shorter period of treatment [16]. We also noted rapid changes of different antibiotics which would put the child at risk of developing resistance to these antimicrobials. We strongly recommend further studies and discussions about the right management approach and the antibiotics of choice in such cases.

References

1. Shane AL, Mody RK, Crump JA, Tar PI, Steiner TS, Kotloff K, et al. Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea. Clin Infect Dis. 2017;65(12):e45-80.
2. Walters MS, Simmons L, Anderson TC, DeMent J, Zile KV, Matthias LP, et al. Outbreaks of salmonellosis from small turtles. Pediatrics. 2016;137(1):e20151735.
3. Carroll KC, Hobden J, Miller S. Jawetz, Melnick & Adelberg's medical microbiology. New York: Mcgraw-Hill Education; 2016.
4. Ahmed B, Jarallah AE, Asin A, Hanash AA, Maely AA, Organ H, et al. *Salmonella* meningitis presenting with multiple microabscesses in the brain in a young infant: A case report. Int J Clin Pediatr. 2016;5(1):13-4.
5. GBD 2017 non-typhoidal salmonella invasive disease collaborators. The global burden of non-typhoidal salmonella invasive disease: A systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2019;19(12):1312-24.
6. Bosch S, Tauxe R, Behravesh CB. Turtle-associated salmonellosis, United States, 2006-2014. Emerg Infect Dis. 2016;22(7):1149-55.
7. Zhao J, Hua C, Zhou M, Wang H, Xie Y, Wang G. A case report of *Salmonella* meningitis in three Chinese children and a literature review. Res Square. 2020;1(1):63494.
8. MacLennan CA, Msefula CL, Gondwe EN, Gilchrist JJ, Pensulo P, Mandala WL, et al. Presentation of life-threatening invasive nontyphoidal Salmonella disease in Malawian children: A prospective observational study. PLoS Negl Trop Dis. 2017;11(12):e0006027.
9. Barrios P, Badía F, Misa V, Mota MI, Martinez A, Mariño H, et al. A five-year experience with zoonotic *Salmonella* at a pediatric reference centre. Rev Chilena Infectol. 2017;34(4):359-64.
10. Wen SC, Best E, Nourse C. Non-typhoidal *Salmonella* infections in children: Review of literature and recommendations for management. J Paediatr Child Health. 2017;53(10):936-41.
11. Ricard C, Mellentin J, Chabchoub RBA, Kingbede P, Heuclin T, Ramdame A, et al. *Salmonella* meningitis in an infant due to a pet turtle. Arch Pediatr. 2015;22(6):605-7.
12. Brent AJ, Oundo JO, Mwangi I, Ochola L, Lowe B, Berkley JA. *Salmonella bacteremia* in Kenyan Children. Pediatr Infect Dis J. 2006;25(3):230-6.
13. Owusu-Ofori A, Scheld WM. Treatment of *Salmonella* meningitis: Two case reports and a review of the literature. Int J Infect Dis. 2003;7(1):53-60.
14. Rowe SY, Rocourt JR, Shiferaw B, Kassenborg HD, Segler SD, Marcus R, et al. Breast-feeding decreases the risk of sporadic salmonellosis among infants in FoodNet sites. Clin Infect Dis. 2004;38(Suppl 3):S262-70.
15. Fomda BA, Charoo BA, Bhat JA, Reyaz N, Maroof P, Naik MI. Recurrent meningitis due to *Salmonella enteritidis*: A case report from Kashmir India. Indian J Med Microbiol. 2012;30(4):474-6.
16. Price EH, de Louvois J, Workman MR. Antibiotics for *Salmonella* meningitis in children. J Antimicrob Chemother. 2000;46(5):653-5.
17. Koç E, Turkyilmaz C, Atalay Y, Sen E. Imipenem for treatment of relapsing *Salmonella* meningitis in a newborn infant. Acta Paediatr Jpn. 1997;39(5):624-5.