

Case study

Title: Successfully treated case of Non-Typhoidal Salmonella Meningitis in an otherwise healthy 5 month old infant: A case report.

Abstract

Acute bacterial meningitis in infants is a medical emergency requiring prompt diagnosis and early institution of empirical antibiotic therapy. Non-typhoidal salmonella (NTS) is a major cause of uncomplicated infectious diarrhoea worldwide; however NTS meningitis is extremely uncommon beyond the neonatal period with very few cases being reported in the literature and has been associated with increased mortality and morbidity with mortality rates of up to 40-70% reported in recent studies. NTS being a facultative intracellular organism does not respond to conventional antibiotic therapy and therefore failure and relapse rates are higher particularly with meningitis. We report a rare case of a five month old infant with non-typhoidal salmonella meningitis who was successfully treated with prolonged duration of antibiotic therapy.

Key words: Non-typhoidal salmonella, meningitis, infant

Introduction

Acute bacterial meningitis in infants is a medical emergency requiring prompt diagnosis and early institution of empirical antibiotic therapy [1]. Salmonella, a gram negative motile bacilli, has been recognized to cause diarrhoea, enteric fever, focal septic infections, bacteraemia and rarely osteomyelitis and meningitis [2]. They have been broadly classified in two types, Salmonella Typhi (which includes typhi and para-typhi species) and Salmonella Non-Typhi (with 80% of infections being caused by Salmonella Typhimurium and Salmonella Enteritidis. [3]. Non-typhoidal salmonella (NTS) is a major cause of uncomplicated infectious diarrhea worldwide; however NTS meningitis is extremely uncommon beyond the neonatal period with very few cases being reported in the literature. [1,3]. Complicated NTS infections and bacteremia typically occurs in infants having

26 phagocytic or T-cell dysfunction such as HIV, causing immune-suppression and other conditions such
27 as sickle cell disease causing salmonella osteomyelitis due to vaso-occlusive crises. [1,3].

28 Non-Typhoidal Salmonella meningitis, although a rare condition in infants of less than six months of
29 age has been associated with increased mortality and morbidity with mortality rates of up to 40-70%
30 reported in recent studies. [2, 4]. The common complications that have been reported in children
31 with this condition are seizures, hydrocephalus with recent case reports of infants presenting with
32 subdural empyema and brain abscess are found in the literature [5, 6]. A study also reported
33 significant developmental delay in 4 out of 9 children who presented with salmonella meningitis. [7].
34 NTS being a facultative intracellular organism does not respond to conventional antibiotic therapy
35 and therefore failure and relapse rates are higher particularly with meningitis. Hence prolonged
36 treatment of 4-6 weeks has been recommended in recent case series with antibiotics that has good
37 intracellular penetration such as third generation cephalosporins, fluoroquinolones and macrolides.
38 [1,3, 8, 9].

39 We report a case of 5 month old infant, with no other risk factors, that was found to have
40 Salmonella typhimurium meningitis on CSF examination.

41 **Presentation of Case**

42 A 5 months old baby boy presented to us with complaints of fever, cough and irritability for past 3
43 days and respiratory distress for 1 day. Fever was of low grade type, not-documented and not
44 associated with rigors and chills. Past history of the child was unremarkable. He was born by
45 caesarean section due to low-lying placenta, developmental milestones were according to his age
46 and he was exclusively breastfed. Parents had a non-consanguineous marriage and he had two elder
47 healthy brothers. On examination his weight was 6.7 kilograms, height 64 cm, and occipito-frontal
48 circumference (OFC) of 41cm. His vital signs on presentation were temperature of 38 degrees
49 centigrade, pulse of 181 beats/min, oxygen saturation of 94%, blood pressures of 100/54 mmHg and

50 respiratory rate of 80 breaths /min. On general physical examination he was pale, drowsy, sick
51 looking child with bulging anterior fontanelle. On systemic examination he had bilateral conducting
52 sounds with increased work of breathing. He was initially managed as upper respiratory tract
53 infection and was stabilized with back to back nebulisations and supportive oxygen via nasal prongs
54 which was then gradually weaned off. Chest Xray was done which showed no evidence of lower
55 respiratory tract infection (Figure 1).

56 Ultrasound head was done which showed no evidence of intra-ventricular haemorrhage or
57 hydrocephalus. Then computed tomography scan of head was done which was unremarkable
58 showing normal intra-cranial pressure (Figure 2). Lumbar puncture was done due to high suspicion
59 of meningitis, which showed murky cerebrospinal fluid (CSF) and when sent for detailed report
60 revealed a very low glucose (<5mg/dl) and high protein count (236 mg/dl) with a raised total
61 leukocyte count of 789/microlitre and 90% polymorphs. Moderate amount of pus cells were also
62 seen. Sample was sent for culture and sensitivity, and broad spectrum intravenous antibiotics that is
63 meropenem and vancomycin were started with a suspicion that the organism may be streptococcus
64 pneumonia which is a common organism in this age group. Blood culture was also sent which
65 revealed pan-sensitive Salmonella typhimurium. CSF culture also revealed pan-sensitive Salmonella
66 typhimurium. Therefore antibiotics were deescalated to intravenous ceftriaxone (100mg/kg/day)
67 and azithromycin (20mg/kg/day) considering the intracellular nature of the organism.

68 Lumbar puncture was repeated after 72 hours of antibiotic therapy and CSF sample sent for detailed
69 report revealed a decrease in total leukocyte count of 288/microlitre with 30% polymorphs, a
70 decrease in protein count to 144 mg/dl and few pus cells. Sample was sent for culture and sensitivity
71 which revealed no growth of organism. Patient remained afebrile, his symptoms improved, and he
72 was discharged from hospital on intravenous ceftriaxone which was continued for a total of 42 days
73 and oral azithromycin for a total of 14 days. He was followed up in clinic after 1 week and after 1

74 month of discharge and on both occasions he remained well without any signs and symptoms
75 achieving developmental milestones according to his age and compliant to antibiotic therapy.

76 **Discussion**

77 Salmonella Non-Typhi commonly causes asymptomatic infections, diarrhea, bacteremia and rarely
78 focal septic infections like osteomyelitis and meningitis [10]. The serotypes most frequently isolated
79 from blood and stool cultures are Salmonella typhimurium and enteritidis [3,10]. A recent study in
80 pediatric age group revealed that 24% of children having invasive NTS infections had risk factors
81 such as HIV infection, oncological diseases, malnutrition, pneumonia or low birth weight. [10].

82 Therefore it has been more commonly found in Africa, with a bimodal age distribution in which
83 children aged 6-36 months and elders in the fourth decade of life have been found to be at greatest
84 risk of invasive disease [11]. However a study involving five asian countries demonstrated Salmonella
85 typhi and para-typhi to be the most common organism being isolated [12]. Salmonella species both
86 typhi and non-typhi usually spread by feco-oral contamination. [1]. Therefore the presence of
87 invasive Salmonella non-typhi disease in a region where S.typhi strains are endemic was a cause for
88 concern as this patient also had no other risk factors and was also on exclusive breast feeding.

89 Acute bacterial meningitis, a medical emergency requires prompt treatment and early initiation of
90 intravenous antibiotic therapy is required even before the etiology is known. [1,2]. Only few case
91 reports have been reported in literature of Salmonella typhimurium causing meningitis in immuno-
92 competent infants especially from tropical countries.[1,2,6]. A recent case report from India
93 reported a case of acute pyogenic meningitis from Salmonella typhimurium leading to subdural
94 empyema and brain abscess [6]. Other case series have reported significant developmental delay in
95 infants presenting with salmonella typhimurium meningitis. [7,13]. Besides these, other
96 complications have been reported in literature in these infants including seizures, hydrocephalus,
97 paresis, athetosis and visual disturbances [2]. Therefore a high rate of mortality and morbidity in NTS

meningitis makes identification of this organism from cerebrospinal fluid absolutely necessary especially in tropical countries.

Salmonella typhimurium meningitis needs prolonged duration of antibiotics. A recent case reported by Anne et al revealed that *Salmonella typhimurium* meningitis in 5 month old infant treated with intravenous antibiotics for 14 days had a relapse after two weeks of discharge from hospital [1]. Also as it is a facultative intracellular organism and does not respond to conventional empirical antibiotic therapy therefore high rates of treatment failure have been reported with this organism [1,3]. Some studies have recommended a combination therapy of third generation cephalosporins and ciprofloxacin in meningitic doses for a prolonged duration of 4-6 weeks to ensure complete eradication of the organism and to prevent its relapse. [6,8,9]. A recent study by Wen et al also adds azithromycin to above regimen because of its effective intracellular penetration for treatment of invasive NTS infections. [3]. Also the current recommendation of American Academy of Pediatrics for invasive NTS infection is third generation cephalosporin for 4-6 weeks [14]. Therefore in our case we only continued intravenous ceftriaxone for 6 weeks and azithromycin for 2 weeks as the repeat culture was negative. Wen et al recommends a repeat CSF culture after 48-72 hours and if that is positive continuation of the second antibiotic is recommended for 6 week also. [3].

Conclusion

This case highlights the importance that clinicians should have low index of suspicion for NTS meningitis in patients presenting with acute bacterial meningitis and showing gram negative bacilli on gram stain. Also it is necessary to isolate the organism as NTS meningitis requires prolonged duration of antibiotics to prevent complications and relapse and a brain imaging is recommended to rule out any intracranial collection. Also the child should be followed regularly to look for any signs of developmental delay.

Competing Interest

122 The authors have no competing interests to declare.

123 **Source of Funding**

124 None

125 **Consent**

126 All authors declare that written informed consent was obtained from the patient's guardians for
127 publication of this case report and accompanying images. A copy of the written consent is available
128 for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

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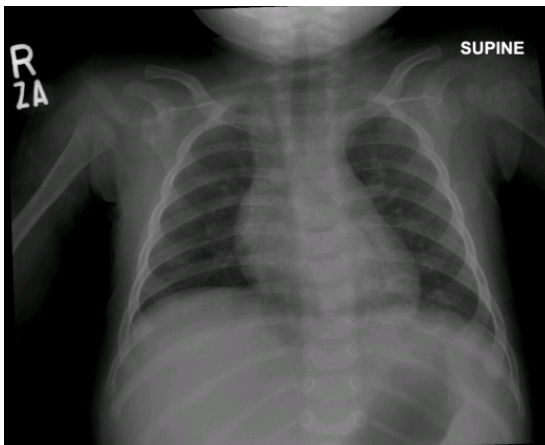
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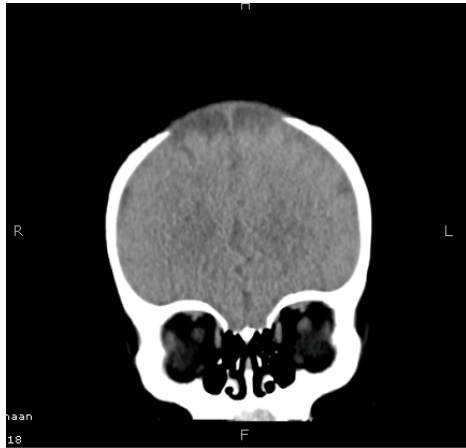
Figures

Figure 1. Chest Xray of the infant showing no evidence of lower respiratory tract infection



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190 Figure 2: CT scan of the infant showing bulging anterior fontanelle. No other gross abnormality is
191 identified. (A) Coronal view. (B) Sagittal view (C) Axial view with normal lateral and third ventricles,
192 no evidence of raised intracranial pressure.



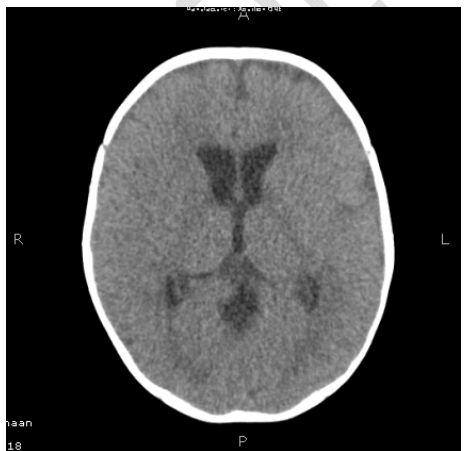
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(A)



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(B)



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(C).