Recurrent meningitis caused by *Salmonella stanley* in an infant

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Introduction

Community-acquired bacterial meningitis is a severe infection that has a high mortality rate. A global investigation of bacterial meningitis in children showed that the mortality rate was around 20–40% in low- and middle-income countries and 5% in high-income countries (Lukšić et al, 2013). Permanent neurological sequelae were reported in around 27% of survivors (Svendsen et al, 2020). However, studies on meningitis caused by *Salmonella* spp. in children are rarely reported. This article reports an infant with recurrent *Salmonella* meningitis that was treated and discharged from hospital successfully.

Discussion

Salmonella is a Gram-negative, facultative anaerobe bacillus. Children under 5 years of age, older people and people with weakened immune systems are more likely to have severe *Salmonella* infection. This is usually caused by ingesting food containing *Salmonella* or indirect contact with reptiles or amphibians (Heaton et al, 2015). Invasive non-typhoidal *Salmonella* disease manifesting as bacteraemia and meningitis is endemic in some regions, such as sub-Saharan Africa (Gilchrist and MacLennan, 2019). Although

Case report

A 7-month-old girl presented with a 2-day history of high fever, drowsiness and poor feeding. She had been born at term by normal vaginal delivery with no congenital anomalies. She had a fever with a temperature of 38.8°C, heart rate 104/minute and respiratory rate 40/minute. On examination, a 1 cm x 1 cm bulging anterior fontanelle was noted; the rest of the examination was unremarkable. Blood, urine and CSF samples were collected for a definitive diagnosis, and she was then given meropenem combined with linezolid for empirical antimicrobial therapy.

Laboratory data included peripheral white blood cell count of 10.91×10^9/litre (normal range 5–14.2×10^9/litre) with 83% neutrophils (normal range 9–53%), absolute neutrophil count of 9.06×10^9/litre (normal range 0.8–6.1×10^9/litre), C-reactive protein level of 154 mg/litre, and CSF cell count of 152×10^6/litre with 65% polymorphonuclear cells, CSF glucose 1.2 mmol/litre (blood glucose 7.47 mmol/litre) and CSF protein 23.5 g/litre. CSF culture grew *Salmonella stanley* on day 5, that was susceptible to ampicillin, ceftazidime, ceftriaxone, chloramphenicol, gentamicin and meropenem, so linezolid was replaced by ceftriaxone. The patient improved markedly within 10 days. On day 14, ceftriaxone was stopped and intravenous meropenem was given for a total of 30 days. The CSF (day 10, day 15 and day 21), blood (day 6 and day 19), stool (day 7) and urine (day 15) cultures showed no bacterial growth. Unexpectedly, although brain magnetic resonance imaging revealed a subdural effusion on day 29, the girl's mother asked for her to be discharged from hospital. The source of infection could not be identified despite numerous discussions with parents of the patient.

The girl was readmitted with fever (39°C) on day 52. Her peripheral white blood cell count was 11.44×10^9/litre with 63% neutrophils, absolute neutrophil count of 7.19×10^9/litre, C-reactive protein level of 82 mg/litre, and CSF cell count of 339×10^6/litre with 26% polymorphonuclear cells. After multidisciplinary consultation, *Salmonella* was suspected to still be the pathogen, so ceftriaxone was given. CSF Gram stain and culture were both negative, but metagenomic sequencing assay revealed *Salmonella*. The girl defervesced on the third day of readmission. CSF was tested weekly. Laboratory investigations showed CSF cell count of 24×10^6/litre with 11% polymorphonuclear cells on day 20 of readmission. The girl was discharged from hospital with no neurological deficits on day 27 of readmission, with ceftriaxone given for a total of 4 weeks.

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Learning points

- Clinicians should be alert to the possibility of *Salmonella* meningitis in children.
- *Salmonella* meningitis has a high complication rate and may require treatment with intravenous antibiotics for at least 4 weeks.
- Third-generation cephalosporins, with or without fluoroquinolones, should be used.
- An interval lumbar puncture should be performed to guide the total duration of antibiotic therapy.
- Parents should be informed about the possibility of relapse weeks after an apparent satisfactory clinical response to antibiotics.

Salmonella meningitis is very rare, the acute complications include subdural effusion, cerebral infarction, ventriculitis and cranial nerve palsy, and often lead to a high prevalence of permanent adverse outcome, such as language disorder, motor disability, epilepsy or sensorineural hearing loss (Wu et al, 2011).

There is no consensus on the optimal treatment of *Salmonella* meningitis in children. Third-generation cephalosporins and fluoroquinolones are the most commonly used antibacterial agents in the treatment of *Salmonella* meningitis in children, with a high cure rate and low mortality rate (Anne et al, 2018; Ficara et al, 2019). However, in China fluoroquinolones are prohibited from use in children under the age of 18 years because of fears of arthropathy, so meropenem and ceftriaxone were used in this case after *Salmonella stanley* was confirmed.

The optimal duration of treatment is still uncertain. *Salmonella* spp. are facultative intracellular organisms that can persist in cells such as macrophages, so patients treated with antibiotics for less than 4 weeks have a high risk of relapse (Heaton et al, 2015). The American Academy of Paediatrics recommends that *Salmonella* meningitis should be treated for 4 weeks (Kimberlin et al, 2021), and the paediatric infectious diseases group of the Australasian Society of Infectious Diseases suggests 4–6 weeks treatment, particularly in young infants. If CSF remains culture-positive, repeat CSF should be tested after 48–72 hours with consideration of the addition of a fluoroquinolone, such as ciprofloxacin (Wen et al, 2017). The subspecialty group of neurology in the Society Paediatrics of the Chinese Medical Association suggests discontinuation of intravenous antibiotics in children with bacterial meningitis if the symptoms and signs have disappeared, the child has regular temperature for over 1 week, CSF cell count less than $20x10^6$/litre, normal CSF protein and glucose levels, CSF culture negative, and no neurological complications (Yi et al, 2019). Following those suggestions, the girl was discharged 4 weeks after the second admission. At 6-month follow up, the girl showed normal growth and development without neurological complications.

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