

# Cephalosporin-resistant typhoid

SAGE Open Medical Case Reports  
Volume 8: 1–3  
© The Author(s) 2020  
Article reuse guidelines:  
sagepub.com/journals-permissions  
DOI: 10.1177/2050313X20917835  
journals.sagepub.com/home/sco



Noella Maria Delia Pereira<sup>ID</sup> and Ira Shah

## Abstract

Typhoid fever is endemic in developing countries like India. An increasing prevalence of resistance to cephalosporins and fluoroquinolones by *Salmonella* isolates is seen. We present an 8-month-old boy with invasive *Salmonella typhi* disease. Blood culture showed *S. typhi* sensitive to ampicillin–sulbactam and cotrimoxazole but resistant to fluoroquinolones and third-generation cephalosporins. Cerebrospinal fluid examination revealed an aseptic meningitic picture. He was treated with intravenous meropenem and azithromycin following which his condition improved. This case highlights the need for improvement in environment sanitation and hygiene combined with early vaccination against typhoid fever and antimicrobial stewardship to help reduce the emerging resistance to cephalosporins and fluoroquinolones.

## Keywords

Typhoid, infancy, early vaccination, fluoroquinolone resistance

Date received: 29 July 2019; accepted: 28 February 2020

## Introduction

Ceftriaxone resistance in non-typhoidal *Salmonella* isolates has been reported in Taiwan,<sup>1</sup> and an increasing prevalence of resistance to third-generation cephalosporins in human non-typhoid *Salmonella enterica* has been reported in England and Wales.<sup>2</sup> Multidrug resistant (MDR) strains of *S. typhi* (resistance to first-line antimicrobials such as ampicillin, chloramphenicol and cotrimoxazole) had emerged in the 1970s and 1980s leading to the use of third-generation cephalosporins and fluoroquinolones as advised by the World Health Organization (WHO).<sup>3,4</sup> But indiscriminate use of fluoroquinolones has led to decreased susceptibility to ciprofloxacin in South East Asia.<sup>5</sup> We describe a case with cephalosporin- and fluoroquinolone-resistant typhoid in an 8-month-old baby who presented at a tertiary hospital in Mumbai.

## Case report

An 8-month old baby boy presented with high-grade fever associated with chills and rigours for 15 days, abdominal distension for 5 days and diarrhoea for 5 days. He also had an erythematous rash over his face and back. On examination, his length was 73 cm (85th percentile) and weight was 7.3 kg (3rd percentile). He was afebrile, heart rate was 140/min, respiratory rate was 38/min and blood pressure was 102/74 mmHg. Abdominal examination revealed mild hepatomegaly. No neck stiffness or signs of meningeal irritation were seen.

Investigations revealed a haemoglobin of 7.2 gm/dL; total white cell count, 8300/mm<sup>3</sup> (neutrophils, 30%; lymphocytes, 69%; eosinophils, 0%; monocytes, 1%; basophils, 0%); and platelets, 81,000/mm<sup>3</sup>. Peripheral smear for malarial parasites was negative. Tests for dengue fever were negative. Widal test revealed the antibody titers to ‘O’ and ‘H’ antigens to be 1:160 each respectively. Liver function tests showed an elevation of the hepatic enzymes – alanine aminotransferase (ALT), 94 IU/L; aspartate aminotransferase (AST), 249 IU/L; and INR, 1.3. international normalized ratio (INR) Serum creatinine was 0.4 mg/dL. Urine examination and echocardiography were both normal. Ultrasound examination of the abdomen revealed mild hepatosplenomegaly with increased echogenicity of liver. Blood culture showed *S. typhi* sensitive to ampicillin–sulbactam and cotrimoxazole but resistant to fluoroquinolones and third-generation cephalosporins. The blood culture results were obtained on day 6 of admission. Cerebrospinal fluid (CSF) examination showed lymphocytic pleocytosis (14 leucocytes/mm<sup>3</sup> with 100% lymphocytes), 38 mg/dL of proteins and 74 mg/dL of glucose. CSF Gram stain, Zeil Neilson stain and culture were negative.

Department of Paediatrics, Bai Jerbai Wadia Hospital for Children, Mumbai, India

### Corresponding Author:

Noella Maria Delia Pereira, Department of Paediatrics, Bai Jerbai Wadia Hospital for Children, Parel, Mumbai 400012, India.  
Email: noella\_pereira@yahoo.com



The child was initially treated with IV ceftriaxone (100 mg/kg/day) for 5 days but had no response. Antibiotics were changed to IV aztreonam and oral azithromycin (20 mg/kg/day) which were given for 5 days but still the fever persisted. Hence, antibiotics were switched to IV meropenem (40 mg/kg/dose 8 hourly), and oral azithromycin was continued. The fever subsided in 13 days. IV meropenem was given for 14 days and oral azithromycin was given for 7 days.

## Discussion

*Salmonellae spp.* are motile (owing to peritrichous flagella), non-encapsulated, gram-negative bacilli and facultative anaerobes of the *Enterobacteriaceae* family. *Salmonella* serotype is defined by the serotype antigens, the flagellar (H) antigens and the virulence (Vi) antigen. H antigens can be either phase 1 (nonspecific) or phase 2 (specific).<sup>6</sup> Humans are the reservoir for *S. typhi*; infection implies direct or indirect contact with an infected person. Animal products transmit *S. typhi* if they are contaminated by infected humans during processing. The most common mode of transmission is food or water contaminated by human faeces. Waterborne typhoid fever epidemics are especially important.<sup>6</sup> Our patient consumed unboiled tap water. Boiling of tap water prior to consumption is advocated in India to avoid salmonellosis and other waterborne infections.

Garg and Krashak<sup>7</sup> in their study showed that the prevalence of typhoid fever below the age of 2 years was 13.1% of all cases in childhood. In view of a high prevalence of Multidrug Resistant *Salmonella Typhi* (MDRST) strains, therapy with cephazolin, cefotaxime and ceftriaxone is recommended. Aminoglycosides (gentamicin, amikacin) or nalidixic acid may be used as alternative drugs, with ciprofloxacin kept in reserve for those cases who do not respond to other drugs. In our patient too, ceftriaxone was initially used as the drug of choice for enteric fever and was later changed as the child did not respond to the same and the culture also showed resistance to cephalosporins and ciprofloxacin.

Increasing ceftriaxone resistance in non-typhoidal *Salmonella* appears to link to the spread of plasmid-mediated *ampC* or ESBL genes.<sup>2</sup> A study done in India by Jain and Das Chugh<sup>8</sup> found that an increasing rate of nalidixic acid, fluoroquinolone and azithromycin resistance among *S. enterica*, particularly in *S. Paratyphi A* strains, is of concern, as *S. Paratyphi A* is becoming increasingly common and is not prevented by current vaccinations. MICs for third-generation cephalosporins and susceptibility pattern must be closely monitored in view of this emerging resistance among *S. enterica*. Minimum inhibitory concentrations (MICs) A similar study done in Kolkata<sup>3</sup> found an increase in nalidixic acid resistant (NALR) strains of *S. typhi* showing decreased ciprofloxacin susceptible phenotype. Majority of these strains belonged to the H58 haplotype.<sup>3</sup> García-Fernández et al.<sup>9</sup> reported that 68% of *S. enterica* serovar Typhi strains isolated in Italy between 2011 and 2013 were resistant to

ciprofloxacin of which 12 were nalidixic acid–ciprofloxacin resistant. Cases of extensively drug-resistant *S. typhi* responding to carbapenems such as meropenem or azithromycin have been reported in Pakistan.<sup>10,11</sup> In view of the decreasing trend of MDR strains of *S. typhi* and increasing fluoroquinolone resistance, it may be prudent for clinicians to consider the use of first-line antimicrobials for typhoid fever.<sup>5,12</sup>

Antimicrobial resistance displayed by *Salmonella* is a growing public threat. Improvement in environment sanitation and hygiene combined with early vaccination and antimicrobial stewardship is necessary to reduce the emerging resistance to cephalosporins and fluoroquinolones.

## Acknowledgement

The authors would like to thank, Dr. Y. K. Amdekar, Medical Director, Bai Jerbai Wadia Hospital for Children, Parel, Mumbai – 400012.

## Author contributions

All authors were involved in patient management, preparation of manuscript and approving the final version.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Ethical approval

Ethical approval to report this case was obtained from “Bai Jerbai Wadia Hospital for Children” Ethics Committee or Institutional Review Board.

## Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

## Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

## ORCID iD

Noella Maria Delia Pereira  <https://orcid.org/0000-0002-5818-0791>

## References

1. Su LH, Wu TL, Chia JH, et al. Increasing ceftriaxone resistance in *Salmonella* isolates from a university hospital in Taiwan. *J Antimicrob Chemother* 2005; 55(6): 846–852.
2. Burke L, Hopkins KL, Meunier D, et al. Resistance to third-generation cephalosporins in human non-typhoidal *Salmonella enterica* isolates from England and Wales, 2010–12. *J Antimicrob Chemother* 2014; 69(4): 977–981.
3. Das S, Samajpati S, Ray U, et al. Antimicrobial resistance and molecular subtypes of *Salmonella enterica* serovar

- Typhi isolates from Kolkata, India over a 15 years period 1998–2012. *Int J Med Microbiol* 2017; 307: 28–36.
- World Health Organization (WHO). *Guidelines for the management of typhoid fever*. Geneva: WHO, 2011, <http://apps.who.int/medicinedocs/documents/s20994en/s20994en.pdf> (accessed 1 February 2020).
  - Chitnis S, Chitnis V, Hemvani N, et al. Ciprofloxacin therapy for typhoid fever needs reconsideration. *J Infect Chemother* 2006; 12(6): 402–404.
  - Ochoa T and Santisteban Ponce J. Salmonella. In: Cherry JD, Demmler-Harrison GJ, Kaplan SL, et al. (eds) *Feigin and Cherry's: Textbook of pediatric infectious diseases*. 7th ed. Philadelphia, PA: Saunders, 2014, pp. 1491–1509.
  - Garg RA and Krashak R. Typhoid fever before two years of age. *Indian Pediatr* 1993; 30(6): 805–808.
  - Jain S and Das Chugh T. Antimicrobial resistance among blood culture isolates of Salmonella enterica in New Delhi. *J Infect Dev Ctries* 2013; 7(11): 788–795.
  - García-Fernández A, Gallina S, Owczarek S, et al. Emergence of ciprofloxacin-resistant Salmonella enterica serovar Typhi in Italy. *PLoS ONE* 2015; 10(6): e0132065.
  - Petrin CE, Steele RW, Margolis EA, et al. Drug-resistant Salmonella typhi in Pakistan. *Clin Pediatr* 2020; 59(1): 31–33.
  - Bhatti JM, Memon Y, Sarfaraz S, et al. An unusual case of extensively drug resistant typhoid fever. *Cureus* 2019; 11(5): e4664.
  - Saragih RH and Purba GCF. Antimicrobial resistance problems in typhoid fever. *IOP Conf Ser: Earth Environ Sci* 2018; 125: 012091.