CASE REPORT

Cephalosporin-resistant Typhoid Fever: A Report of Two Cases with a Unique Isolate from a Tertiary Care Hospital in Delhi

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Abstract

Typhoid fever is endemic in our country and is the commonest bacterial bloodstream infection in South Asia.[1] Multidrug-resistant typhoid fever (MDRTF) is defined as typhoid fever caused by *Salmonella enterica* serovar Typhi strains (*S.* Typhi), which are resistant to the first-line recommended drugs, i.e., chloramphenicol, ampicillin, and trimethoprim–sulfamethoxazole. Extensively drug-resistant typhoid fever (XDRTF) is defined as *Salmonella* Typhi/Paratyphi resistant to first line antibiotics (ampicillin, chloramphenicol and cotrimoxazole) and also to fluoroquinolone and ceftriaxone. Pakistan has an ongoing epidemic of extensively drug resistant (XDR) typhoid, which is a cause for alarm. Prior to this XDR typhoid epidemic, which started in 2016, only 17 cases of ceftriaxone resistance were reported in the world literature. Four out of these 17 were cases of XDR typhoid reported in Iraq, Bangladesh, India, and Pakistan.[2] We report two cases of cephalosporin resistant typhoid fever from North India in the pediatric age group and discuss the clinical presentation and treatment. These two isolates were resistant to four drugs (ampicillin, chloramphenicol, fluoroquinolone, and ceftriaxone) but sensitive to chloramphenicol.

Keywords: Blood culture, Drug-resistant typhoid, Enteric fever, Indian report.

Pediatric Infectious Disease (2019): 10.5005/jp-journals-10081-1205

Introduction

Lack of availability of clean water, sanitation, and poor personal hygiene contribute to the prevalence of typhoid fever. Multi drug resistant (MDR) strains, resistant to chloramphenicol, amoxicillin, and cotrimoxazole, appeared in the late 1980s and early 1990s. Fluoroquinolone resistance is almost universal now in India. Occasional reports of cephalosporin resistant typhoid have emerged in Western India. We report two such cases in siblings managed at a superspecialty hospital in Delhi.

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How to cite this article: Kukreja S, Gupta T. Cephalosporin-resistant Typhoid Fever: A Report of Two Cases with a Unique Isolate from a Tertiary Care Hospital in Delhi. Pediatr Inf Dis 2019;1(2):70–71.

Source of support: Nil

Conflict of interest: None

Case Description

Case 1

Fifteen years male presented with 6 days of intermittent high-grade fever (103–104°F) and poor oral intake. There were no localizing symptoms like rhinorrhea, rash, cough, or loose stools. On examination, he looked dull, but otherwise, there were no clinical findings.

The child was admitted and evaluated with complete blood count, C-reactive protein (CRP), liver function test (LFT), routine urine examination, and paired blood culture and sensitivity done by Bactalert 3D and VITEK 2 Compact System.

Initial reports were as follows-Hb-11.5/TLC-5000 cells/mm^3, N73, L25, E0, serum bilirubin was normal. Liver function test showed, raised liver enzymes—SGPT-92 and SGOT-80. C-reactive protein was 90 mg/dL and urine report was normal.

Clinical presentation (fever without localization) and initial reports were suggestive of enteric fever (normal TLC with eosinopenia, positive CRP, and mildly elevated liver enzymes). Child was started on inj. ceftriaxone and supportive treatment.

The child continued to have fever spikes, up to 103°F and 104°F.

Blood culture grew *Salmonella* Typhi resistant to ceftriaxone.

Antibiotics were changed to meropenem. Chloramphenicol and azithromycin were not used as the child had vomiting. Child became afebrile after 6 days of intravenous meropenem therapy and was given IV antibiotics for another 7 days. Child remained stable throughout the hospital stay and was discharged on day 13.

Case 2

A 10 years old female child, sibling of case 1 presented with a similar clinical picture. Her blood culture grew the same bacteria with a similar sensitivity pattern. Both the reports are attached herewith. She was also treated with intravenous meropenem, and defervescence occurred on day 5. She was treated for a total of 12 days.

Both children gave a history of eating out in a Delhi restaurant 2 weeks prior to presenting with fever. The water supply at home was filtered through the R-O system, and there was no history of recent travel.

Discussion

Pakistan, our neighboring country, has a large ongoing outbreak of XDR typhoid. This rapid emergence and spread of XDR typhoid is a

"sentinel event" in the evolution of antibiotic resistance in *S.* Typhi. It occurred in Sindh province, and data collected over 2 years from November 2016 to December 2018 and reported by the Provincial Disease Surveillance and Response Unit (PDSRU) revealed 5,274 cases of XDR typhoid out of 8,188 cases.[3] Sixty-nine percent of the cases were reported in Karachi, while twenty-seven percent were in Hyderabad district. Four percent of cases were found in other districts.[4] It was found that the circulating strain belonged to H58 haplotype common in Asia and Africa. In February 2018, British and Pakistani scientists identified the resistance genes in 300 XDR *Salmonella* isolates on a plasmid or a mobile piece of DNA. This plasmid has been theorized to have originated in *Escherichia coli*.

According to WHO, azithromycin is the only affordable first-line oral option for patients with XDR. However, many H58 haplotypes, especially in India, are resistant to azithromycin. Azithromycin resistance was seen in 7% of isolates of *S.* Typhi and in 24.3% isolates of *S.* Paratyphi A.[5] CDC recommends carbapenems. However, as experience is limited, clear cut guidelines are not available.[6] Our patients did well during the hospital stay and were followed up for 6 months. Stool culture at 6 months did not grow *Salmonella* Typhi.

Countries like India and Pakistan both have similar poor water, sanitation, and hygiene (WASH) infrastructure, hence, our country should be prepared for a potential spread of XDR typhoid to India. Antibiotic resistance may be controlled by not prescribing cephalosporins/azithromycin in viral infections. When indicated, subtherapeutic dosing should be avoided. Sending paired blood culture in appropriate volume in all cases of suspected enteric fever is absolutely essential. Molecular testing of resistant strains is also important for any XDR cases reported in our country.

Conclusion

We report two of the first few cases of cephalosporin-resistant typhoid fever in this country, which were successfully managed with carbapenem.

Patient A

Blood—Culture and Sensitivity

Parameter	*Result*
Comment	Fluoroquinolone-susceptible strains of *Salmonella* that test resistant to nalidixic acid may be associated with clinical failure or delayed response in fluoroquinolone-treated patients with extraintestinal salmonellosis
Organism isolated	*Salmonella* Typhi
Antibiotic	Susceptibility
Amox/K clav	Sensitive
Ampicillin	Resistant
Azithromycin	Sensitive
Cefixime	Resistant
Cefotaxime	Resistant
Ceftazidime	Resistant
Ceftriaxone	Resistant
Chloramphenicol	Sensitive
Ciprofloxacin	Resistant
Cotrimoxazole	Resistant

Contd…

Contd…

Parameter	*Result*
Levofloxacin	Resistant
Meropenem	Sensitive
Nalidixic acid	Resistant
Ofloxacin	Resistant

Patient B

Blood—Culture and Sensitivity

Parameter	*Result*
Comment	Fluoroquinolone-susceptible strains of *Salmonella* that test resistant to nalidixic acid may be associated with clinical failure or delayed response in fluoroquinolone-treated patients with extraintestinal salmonellosis
Organism isolated	*Salmonella* Typhi
Antibiotic	Susceptibility
Amox/K clav	Sensitive
Ampicillin	Resistant
Azithromycin	Sensitive
Cefixime	Resistant
Cefotaxime	Resistant
Ceftazidime	Resistant
Ceftriaxone	Resistant
Chloramphenicol	Sensitive
Ciprofloxacin	Resistant
Co-trimoxazole	Resistant
Levofloxacin	Resistant
Meropenem	Sensitive
Nalidixic acid	Resistant
Ofloxacin	Resistant

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