

# Multidrug Resistant *Shigella flexneri* Infection Simulating Intestinal Intussusception

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## ABSTRACT

*Shigella* enteritis remains an important cause of mortality and morbidity in all age groups, in developing as well as developed countries. Owing to the emerging resistance to multiple antibiotics among *Shigella* spp., it has been recognized as a major global public health concern and warrants constant monitoring of its resistance pattern. We report a case of segmental ileitis caused by non-ESBL producing multidrug resistant *Shigella flexneri* in an infant clinically mimicking intussusception, which was effectively treated by ceftriaxone.

**Key words:** Bacillary dysentery, multidrug resistant, *Shigella flexneri*

## INTRODUCTION

Diarrhea is an important childhood infection globally, accounting for 2.5 million deaths in under-five children every year.<sup>[1]</sup> An intestinal infection caused by *Shigella* may have a wide range of clinical manifestations. Passage of blood and mucus in stool associated with high-grade fever, tenesmus, and intestinal cramps are common symptoms. Arthritis, conjunctivitis, parotitis, intussusception, rectal prolapse, and hemolytic uremic syndrome (HUS) may occur as complications, especially in the elderly, children, and immunocompromised patients.<sup>[2]</sup> Resistance to antibiotics such as ampicillin, co-trimoxazole, tetracycline, chloramphenicol, and aminoglycosides have become commonplace over decades.<sup>[3]</sup> Furthermore, resistance to third-generation cephalosporins, azithromycin, and fluoroquinolones are also on the rise.<sup>[4,5]</sup> This limits the antibiotic options available for empirical therapy, especially in children who also have a higher incidence of severe infections, complications, and mortality.<sup>[6]</sup> Here, we

describe a case of bloody diarrhea in an infant caused by multidrug resistant *Shigella flexneri*, presenting with the clinical features simulating intussusception. Although the rapid evaluation with emergency abdominal ultrasonography was imperative to rule out intussusception, treatment with appropriate antibiotic resulted in the resolution of acute bloody diarrhea.

## CASE REPORT

A 1-year-old male child was brought by parents to our hospital with several episodes of loose stools lasting 3 days with fever, vomiting, and abdominal pain. The stool was scanty in volume with mucus and blood. The fever was low-grade, not associated with chills and rigor. There was no history of similar episode of illness in the past. On examination, the baby was irritable and had moderate pallor and signs of mild

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dehydration. Abdominal examination revealed the soft abdomen with slight tenderness and mild hepatomegaly. Icterus, petechial rash, ecchymosis, splenomegaly, and joint tenderness were not detected. Emergency ultrasonography was done to rule out intussusception. It showed edematous loops of terminal ileum with few enlarged mesenteric lymph nodes and minimal free fluid in abdomen suggesting segmental ileitis. Hemogram showed hemoglobin 6.2 g/dl, total leukocyte count 15,300/cmm with 46% neutrophils, 50% lymphocytes, 3% monocytes, and 1% eosinophils. The platelet count, serum urea, creatinine, electrolytes, and bilirubin values were within normal range. Blood smear revealed normocytic/normochromic red blood cells (RBCs) without any acanthocytes, bite cells, and fragmented forms. Urine was normal in color and had no pus cells, RBCs, or hemoglobinuria. Intravenous (I.V.) rehydration therapy and antibiotics (ceftriaxone 350 mg I.V. 12 hourly) were started empirically. Packed cells transfusion was done to improve anemia on the same day. Although the frequency decreased, the child continued to pass loose mucoid greenish stools with streaks of blood. Further investigations were carried out to identify the etiology of bloody diarrhea. Urine and blood cultures were sterile. On microscopic examination, the stool was negative for ova, cyst, and trophozoites of intestinal parasites, and it showed 15–25 leukocytes and 10–15 RBCs per high-power field. A nonmotile, Gram-negative bacillus producing nonhemolytic colonies on blood agar and nonlactose fermenting colonies on MacConkey's agar was isolated from the stool. It was identified as *S. flexneri* based on biochemical reactions (catalase positive, indole negative, methyl red test positive, Voges-Proskauer test negative; citrate not utilized, urea not hydrolyzed; alkaline slant and acidic butt with no gas and no H<sub>2</sub>S production in triple sugar iron agar, glucose and mannitol fermented with acid only; lactose, sucrose and xylose not fermented; and lysine, arginine, and ornithine not decarboxylated). Serotyping confirmed it as *S. flexneri* 2a. The isolate showed susceptibility to ceftriaxone and gentamicin, but it was resistant to co-trimoxazole, chloramphenicol, tetracycline, ampicillin, furazolidone, nalidixic acid, and ciprofloxacin. Ceftriaxone (350 mg I.V. 12 hourly) was continued for 6 days along with intravenous fluids (for 2 days). It resulted in the resolution of symptoms of dysentery and general improvement of health. The baby was discharged on the 7<sup>th</sup> day with a plan to investigate the cause of anemia on subsequent visits. However, the patient was lost on follow-up.

## DISCUSSION

Diarrhea is an important cause of childhood morbidity and mortality. Invasive infections (i.e. *Shigella* sp.,

enterohemorrhagic *Escherichia coli* (EHEC), *Campylobacter jejuni*, *Yersinia enterocolitica*, *Aeromonas hydrophila*, *Entamoeba histiolytica*, and *Trichuris trichiura* infections) as well as noninfectious diseases such as inflammatory bowel disease (IBD), colitis associated with cow's milk, necrotizing enterocolitis, intussusception, and intestinal ischemia have been implicated in bloody diarrhea among children.<sup>[7]</sup> While abdominal ultrasonography and endoscopy are essential for the diagnosis of noninfectious causes, stool microscopy, and culture detect the pathogenic microorganism. Among these causes, shigellosis is, especially common in infants in developing countries.<sup>[7]</sup> In a study from North India, the most prevalent *Shigella* species among hospitalized children with diarrhea between 2001 and 2004 was *S. flexneri* (60%), followed by *Shigella sonnei* (23.8%), *Shigella dysenteriae* (9.8%), and *Shigella boydii* (5.7%).<sup>[8]</sup> *S. flexneri*, especially serotype 2a, was found to be the most common serotype among children in several other studies from the Indian subcontinent.<sup>[5]</sup> Grossly, bloody stools, dehydration, and seizures have been associated more frequently with *Shigella* species when compared with other intestinal bacterial pathogens.<sup>[9]</sup> Unlike *S. dysenteriae* type 1 and *S. flexneri* have been less frequently reported to cause severe extraintestinal as well as intestinal manifestations (i.e. intussusception and rectal prolapse).<sup>[2]</sup> In our case, abdominal cramp, vomiting, pallor, dehydration, and passage of bloody stool with mucus in the infant simulated the clinical picture of intussusception, mandating abdominal ultrasonography to rule it out. Surgical intervention for intussusception is indicated in case of bowel perforation and unsuccessful nonoperative reduction. As the baby was anemic, packed cells transfusion was given to prevent the complications of blood loss which might have occurred in the event of surgical reduction of intussusception. Since acute bloody diarrhea is unlikely to result in severe anemia, further investigations to rule out IBD, hook-worm infection, and other causes of severe anemia were scheduled during follow-up. However, the patient was lost during follow-up. HUS is a dreadful complication of *Shigella* and EHEC serotype O157:H7 infection, characterized by hemolytic anemia, thrombocytopenia, and acute renal failure.<sup>[10]</sup> In this patient, normal platelet counts, the absence of microangiopathic hemolytic anemia (acanthocytes, bite cells, and fragmented RBCs), and normal renal parameters were essential to rule out HUS.

Ampicillin, co-trimoxazole, and nalidixic acid were the treatment of choice for shigellosis in developing countries.<sup>[11]</sup> However, they have lost their clinical utility due to emerging antibiotic resistance. Hence, the third generation cephalosporins, azithromycin, and fluoroquinolones came up as alternatives.<sup>[12]</sup> Re-emergence of multidrug resistant *S. dysenteriae* type 1 strains during 2002 and *S. flexneri* type

2a since December 2003 with resultant year-wise increase in quinolone resistance from 15% in 2003 to 25% in 2004 have been reported from West Bengal.<sup>[8]</sup> Bhattacharya *et al.* have studied the trend of antimicrobial resistance in *Shigella* isolates from Andaman and Nicobar, which showed noticeable increase in resistance against ampicillin (72.7–100%), co-trimoxazole (57.6–80%), nalidixic acid (27.2–96%), ciprofloxacin (0 to 82%), and the third generation cephalosporins (0 to 12%) between 2000 and 2009.<sup>[3]</sup> Both plasmids-coded ESBLs of SHV-11 and CTX-M type and AmpC type beta-lactamases have been found in *Shigella* spp. to impart the third generation cephalosporin resistance.<sup>[5,12]</sup> In our case, although the *S. flexneri* isolate was multidrug resistant, it was not an ESBL producer. Therefore, prompt initiation of ceftriaxone along with good supportive care was effective in shortening the duration of symptoms and preventing complications.

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### Conflicts of interest

There are no conflicts of interest.

### REFERENCES

- Djie-Maletz A, Reither K, Danour S, Anyidoho L, Saad E, Danikuu F, *et al.* High rate of resistance to locally used antibiotics among enteric bacteria from children in Northern Ghana. *J Antimicrob Chemother* 2008;61:1315-8.
- Khan WA, Griffiths JK, Bennish ML. Gastrointestinal and extra-intestinal manifestations of childhood shigellosis in a region where all four species of *Shigella* are endemic. *PLoS One* 2013;8:e64097.
- Bhattacharya D, Sugunan AP, Bhattacharjee H, Thamizhmani R, Sayi DS, Thanasekaran K, *et al.* Antimicrobial resistance in *Shigella* – rapid increase and widening of spectrum in Andaman Islands, India. *Indian J Med Res* 2012;135:365-70.
- Nandy S, Mitra U, Rajendran K, Dutta P, Dutta S. Subtype prevalence, plasmid profiles and growing fluoroquinolone resistance in *Shigella* from Kolkata, India (2001-2007): A hospital-based study. *Trop Med Int Health* 2010;15:1499-507.
- Rahman M, Shoma S, Rashid H, El Arifeen S, Baqui AH, Siddique AK, *et al.* Increasing spectrum in antimicrobial resistance of *Shigella* isolates in Bangladesh: Resistance to azithromycin and ceftriaxone and decreased susceptibility to ciprofloxacin. *J Health Popul Nutr* 2007;25:158-67.
- Gu B, Ke X, Pan S, Cao Y, Zhuang L, Yu R, *et al.* Prevalence and trends of aminoglycoside resistance in *Shigella* worldwide, 1999-2010. *J Biomed Res* 2013;27:103-15.
- Murphy MS. Management of bloody diarrhoea in children in primary care. *BMJ* 2008;336:1010-5.
- Pazhani GP, Ramamurthy T, Mitra U, Bhattacharya SK, Niyogi SK. Species diversity and antimicrobial resistance of *Shigella* spp. isolated between 2001 and 2004 from hospitalized children with diarrhoea in Kolkata (Calcutta), India. *Epidemiol Infect* 2005;133:1089-95.
- Zaidi MB, Estrada-García T, Campos FD, Chim R, Arjona F, Leon M, *et al.* Incidence, clinical presentation, and antimicrobial resistance trends in *Salmonella* and *Shigella* infections from children in Yucatan, Mexico. *Front Microbiol* 2013;4:288.
- Özmert EN, Ince OT, Örün E, Yalçın S, Yurdakök K, Gür D. Clinical characteristics and antibiotic resistance of *Shigella* gastroenteritis in Ankara, Turkey between 2003 and 2009, and comparison with previous reports. *Int J Infect Dis* 2011;15:e849-53.
- World Health Organization. Guidelines for the Control of Shigellosis, Including Epidemics due to *Shigella* Dysenteriae Type 1. Geneva: World Health Organization; 2005. Available from: <http://www.who.int/publications/2005/9241592330.p>. [Last cited on 2014 Jan 12].
- Bhattacharya D, Bhattacharjee H, Ramanathan T, Sudharma SD, Singhanian M, Sugunan AP, *et al.* Third-generation cephalosporin resistance in clinical isolate of *Shigella sonnei* in Andaman and Nicobar Islands, India. *J Infect Dev Ctries* 2011;5:674-6.