

Ceftriaxone Resistance in *Shigella flexneri* is a Worldwide Problem: Case of a Child from Turkey

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Abstract

Shigella is one of the causative agents of gastroenteritis and antimicrobial treatment in addition to hydration therapy can significantly reduce the mortality related to infection. Although seroprevalence of the *Shigella* infections varies between countries, *Shigella sonnei* is the first and *Shigella flexneri* the second most common isolated species in our country. A higher antibiotic resistance rate is reported in *S. flexneri* infections compared to other *Shigella* species. Herein, we report a case who presented with acute gastroenteritis due to ceftriaxone-resistant *S. flexneri*. This infection was complicated with severe dehydration, protein-losing enteropathy and was successfully treated with ciprofloxacin and meropenem.

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Introduction

Shigella seroprevalence varies between countries (1, 2). While *Shigella sonnei* is the most common serotype in developed countries, *Shigella flexneri* is more frequently seen in developing countries (3-6). Seroprevalence studies from Turkey indicate that *S. sonnei* is the most responsible serotype in *Shigella* infections in our country (3, 6). Recently, *S. flexneri* infections have been a serious problem especially in the central Asian countries because of antibiotic resistance (5, 7, 8). In these countries some mechanisms such as CTX-M, SHV and TEM type extended-spectrum beta-lactamase (ESBL) enzymes, OXA, AmpC and metallo-beta-lactamases are responsible from the resistance. Furthermore, multidrug-resistant and ciprofloxacin-resistant *Shigella* species have been reported in the most recent studies.

In this paper, we report a child diagnosed with ceftriaxone-resistant *S. flexneri* gastroenteritis, to draw attention to this problem. Severe

dehydration and protein-losing enteropathy occurred during follow-up and was successfully treated with ciprofloxacin and meropenem.

Case Report

A thirty one month-old boy was admitted to a local hospital with complaints of fever, vomiting and watery-bloodless diarrhea up to 20 times in a day. Ceftriaxone-resistant *S. flexneri* was detected in the stool culture, and then the patient was referred to our clinic before the single dose ceftriaxone treatment. Physical examination revealed blood pressure of 95/60 mmHg, pulse rate of 114/m, respiratory rate of 28/m and body temperature of 39.2°C. The patient was dehydrated with sunken eyes, dry lips and mouth, and poor skin turgor. Also, he had increased intestinal peristalsis. Laboratory findings revealed BUN: 1 mg/dL, creatinine 0.2 mg/dL, sodium 135 mmol/L, potassium 4.8 mmol/L, total proteins 4.9 g/dL, albumin 2.9 g/dL, SGPT 13 U/L, hemoglobin 10 g/dL, leuko-

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cyte 8900/mm³, platelet 311000/mm³, C-reactive protein 245 mg/L. Leukocytes and mucus were seen in the stool specimen by direct microscopic examination. We started intravenous ciprofloxacin treatment because of ceftriaxone resistance. On the first day of hospitalization, physical examination revealed a distended abdomen and marked bowel loops. Biochemical tests revealed serum sodium of 132 mmol/L and albumin of 1.7 g/dL on the second day of admission and required two albumin infusions. Intravenous meropenem was added to ciprofloxacin therapy because of progression of the diarrhea, deterioration of his general condition and significant distension of the bowel on the 3rd day of hospitalization. Blood and urine cultures remained sterile. Diarrhea significantly reduced and abdominal distension disappeared at the 24th hour of meropenem treatment. Stool culture sensitivity pattern of *S. flexneri* was determined by disc diffusion test according to Clinical and Laboratory Standards Institute (CLSI) proposals and confirmed by the Phoenix automated system. According to the culture antibiogram, the isolate was sensitive to ertapenem, imipenem, levofloxacin, piperacillin-tazobactam, cefoperazone-sulbactam, cefepime, ciprofloxacin and resistant to ampicillin, chloramphenicol, ceftriaxone, streptomycin, trimethoprim-sulfamethoxazole (TMP-SMX). He was discharged from the hospital on the 7th day of the admission completely recovered.

Discussion

While *S. sonnei* is the most commonly responsible serotype for shigellosis in developed countries, *S. flexneri* is the predominant species in the developing countries with low socioeconomic conditions (3-5). Likewise, it is reported that *S. sonnei* has been the most detected serotype in our country (3, 6). Due to the risk of transmission from infected or colonized persons, the World Health Organization recommends antimicrobial therapy for *Shigella* gastroenteritis. Quinolones, cephalosporins and azithromycin are often recommended regimens in children because of the occurrence of resistance to ampicillin and TMP-SMX in the recent years (1, 2, 6, 8, 9).

CTX-M, SHV and TEM type extended-spectrum beta-lactamase (ESBL) enzymes, OXA, AmpC and metallo-beta-lactamases in *Shigella* species are thought to be responsible for the resistance to cephalosporins (5). Antimicrobial susceptibilities of *Shigella* species vary geographically. Ceftriaxone is the most preferred antimicrobial agent due to resistance to ampicillin and TMP-SMX in the United States. Recently, 3rd generation cephalosporin resistance has been reported with increas-

ing frequency especially in the developing countries. It is reported that antibiotic resistance rate in these countries is highest for *S. flexneri* and *S. sonnei* isolates, respectively (1, 2, 5-9). Ceftriaxone resistance rate was 18.1% for *S. flexneri* isolates in a study which was conducted by Yang et al. (10). However, they have shown that all *S. flexneri* isolates were sensitive to imipenem in this study. Ceftriaxone resistance has been reported between 1.7% and 5.4% in various studies from Turkey (4, 6). Besides, a serious quinolone resistance has not been reported in our country, yet. Altun et al. (3) evaluated 605 *Shigella* isolates and noticed that cefotaxime resistance rate was 3.6% and all of the resistant isolates were *S. sonnei* (3). Although we did not find cephalosporin resistance in the study which was conducted in 1998 in our hospital, the current case report and recent papers from Turkey suggest that the importance of this problem will soon increase in our country (11).

By virtue of the increasing number of cephalosporin-resistant isolates, carbapenems and quinolones have become drugs of choice for treatment of these agents. On the other hand, multidrug-resistant and ciprofloxacin-resistant *Shigella* isolates have been reported with increasing frequency in recent years (5, 8, 9). Therefore antibiotic selection is restricted to a small number of antimicrobial agents.

Conclusion

Changing the treatment approach has come into question for shigellosis. Although ceftriaxone-resistance is common in some countries, this situation is very rare in Turkey. In resistant *Shigella* infections, effective therapy can be initiated only after the outcome of the culture-antibiogram. This issue may cause delays in appropriate treatment and prolong the severe course of the illness. Thus, knowledge of the antimicrobial resistance pattern of local *Shigella* strains is of critical importance. Although ceftriaxone-resistant *S. flexneri* isolates are currently quite rare in our country, it is possible that this problem will be important within a short period of time.

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