**CASE REPORT**

**Extended-Spectrum β-Lactamase Production in Shigella flexneri**

Abdul Sattar, Shahid Ahmed Abbasi, Javid Usman, Farah Faqir, Fatima Kaleem* and Faisal Hanif

**ABSTRACT**

Emergence of multidrug-resistant strains of Shigella is a growing concern across the globe. Third-generation cephalosporins are used for treating infections caused by multidrug-resistant Shigellae. However, resistance to these cephalosporin antibiotics due to extended-spectrum β-lactamases, has emerged as a new problem. So far extended-spectrum β-lactamases producing Shigella has not been reported from Pakistan. We report such a case in Shigella flexneri from an 8-year old girl with acute dysentery.

**Key words:** Extended-spectrum β-lactamases. Multidrug-resistant. Shigella flexneri.

**INTRODUCTION**

Shigellosis is an important public health problem, especially in developing countries. Isolates with resistance to the first line drugs (ampicillin, cotrimoxazole) have been reported throughout the world, thus making the third generation cephalosporins and quinolones as the mainstay of treatment. However, resistance to 3rd generation cephalosporins due to extended-spectrum β-lactamases (ESBLs) is rising worldwide. Although > 200 different ESBLs have been described worldwide in bacteria, only a few of them have been reported in Shigellae from different countries (like Argentina, South Korea, Turkey, Hong Kong, France, Czech Republic, Bangladesh and India). We report such a case in Shigella flexneri.

**CASE REPORT**

An 8-year old girl was admitted in the Children Ward of the Military Hospital, Rawalpindi, with 2 days history of high grade fever and loose motions mixed with blood and mucus, initially frank blood but later a streak of blood in stools. She has history of drinking boring water, there was no history of eating anything unusual or unhygienic. The child's family belonged to lower socio-economic status. She had been advised amoxicillin-clavulanate since 2 days before admission in the hospital but was not responding to it, which was omitted after hospital admission. On examination, she was pale and dehydrated (grade II). Her abdomen was soft with no hepato-splenomegaly. Chest was clinically clear. The temperature was 103.8°F, pulse rate 120/minute and a respiratory rate of 30/ minute.

Blood samples were obtained for culture, complete picture, Widal test, urea, creatinine and electrolytes. Stool was taken for routine examination and culture. She was started with oral rehydration salt 100 mL/loose stool, inj. ceftriaxone 750 mg I/V BD, and dextrose/water 1/2 saline 750 mg I/V over 12 hours and other supportive treatment. Her stool routine examination revealed pus cells 12-14/HPF and RBCs numerous/HPF. After 6 hours she was also started with syrup nalidixic acid 1 TSF x BD. Haemoglobin was 11.9 g/dL, TLC 12.9 x 10^9/L, platelet count 404 x 10^9/L; differential leukocyte count was neutrophils 79%, lymphocytes 16%, monocytes 2% and eosinophils 3%. Blood urea was 7.3 mmol/L, creatinine was 47 µmol/L, sodium was 139 mmol/L and potassium was 4.2 mmol/L. Widal test did not show any significant rise in titre.

The stool sample was inoculated on Mac Conkey (Oxoid) and salmonella-shigella agar (Oxoid). Her fever started settling down the next day and the same treatment was continued. Meanwhile blood was subcultured on Blood and Mac Conkey agar (Oxoid) and incubated at 37°C. Blood sample yielded no growth. The stool cultures yielded the growth of non-lactose fermenting colonies on Mac Conkey and salmonella-shigella agar. They were Gram negative rods, catalase positive, oxidase negative and were non-motile. The organism was tested biochemically using API 20E (bioMerieux) and antimicrobial testing was carried out on the Mueller-Hinton agar (Oxoid) using standard protocols as recommended by the CLSI. Next day the organism was identified as Shigella flexneri, this was confirmed by type specific antisera (Wellcome Diagnostics). The organism was sensitive to cotrimoxazole 25 µg (Oxoid), azithromycin 15 µg (Oxoid), nalidixic acid 30 µg (Oxoid ), ciprofloxacin 5 µg (Oxoid) and meropenem 10 µg (Oxoid) while resistant to ampicillin 10 µg (Oxoid), chloramphenicol 30 µg (Oxoid), tetracycline 30 µg (Oxoid), amoxicillin-clavulanate 20/10 µg (Oxoid) and ceftriaxone 30 µg (Oxoid). After the sensitivity report, inj. ceftriaxone was omitted and syrup nalidixic acid was continued along with supportive therapy.
Extended-spectrum β-lactamase production in *Shigella flexneri*

As this isolate was found resistant to ceftriaxone, ESBL production was determined by placing a susceptibility disk containing amoxicillin-clavulanate 20/10 µg (Oxoid) as the inhibitor of beta-lactamase in the center of the plate, ceftriaxone 30 µg (Oxoid) and aztreonam 30 µg (Oxoid) disks at 25 mm (center to center) from the amoxicillin-clavulanate disk. After 24 hours incubation at 37°C an enhancement of the zone of inhibition of the oxyimino-β-lactam was noticed establishing the isolate to be an ESBL producer. On the 3rd day of treatment the child was afebrile and symptom free and was discharged from the hospital with advice to continue oral nalidixic acid for 2 days. The child had fully recovered on follow-up examination.

**DISCUSSION**

*Shigella* species have managed to survive the antibiotic era via an ingenious mechanism of resistance, the production of β-lactamases. High rates of resistance to ampicillin among *Shigella* isolates are due to the production of β-lactamases similar to TEM-1 or OXA-1. In the past two decades both the isolation frequencies and the types of ESBLs have gradually increased. The ESBLs are detected most commonly in *Klebsiella pneumoniae* and *Escherichia coli* but have been noted in other members of the Enterobacteriaceae family as well. In *Shigella*, ESBL production is rare worldwide. In 1999, SHV-11 ESBL-producing *S. dysenteriae* strain was first time reported in India. Different ESBLs were identified from different countries like CTX-M-14-type from Korea, CTX-M-2-type from Argentina, SHV-2 and CTX-M-15 type from France, CTX-M-3-type from Turkey and CMY-2-type AmpC β-lactamase from Taiwan. Seven ESBL producing *Shigella* have been reported from Japan. A study conducted in Dhaka, Bangladesh during 2001–2002 of 160 *Shigella* isolates, three were class A type ESBLs and one AmpC-like β-lactamase.

These resistant bugs pose an important threat in the treatment of dysentery especially in children. Infections caused by MDR isolates which carry plasmid-borne genes for ESBLs should be considered as a warning message to limit irrational use of antibiotics. Recently, ciprofloxacin-resistant *S. dysenteriae* type 1 strains were reported from India and Bangladesh further complicating the treatment options. Like many other pathogens multiple antibiotic resistant *Shigella* have been on the rise. In countries like Pakistan the impact can be serious, due to the acute nature of illness in an infected population, spread of resistance to other enteric pathogens and also due to the non-availability of efficient and structured healthcare facilities to the public. Cephalosporin resistant *Shigella flexneri* was isolated in The Aga Khan University Hospital, Karachi, Pakistan in 2005, but it was not ESBL producer.

The ESBL producing *Shigella* has not yet been reported from Pakistan but an ESBL producing *Shigella sonnei* was isolated from a patient in United States who had recently traveled to Pakistan. Thus, this is the first reported case of ESBL producing *Shigella* from Pakistan. Most probably the problem is already with us but escapes detection due to limited awareness and facilities.

**REFERENCES**


