

Extended Spectrum Beta Lactamase Producing *Shigella Flexneri*: A Therapeutic Concern?

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ABSTRACT

Shigella flexneri is the most commonly isolated species in the developing world. Prompt and appropriate therapy is necessary in shortening the duration of clinical symptoms, as well as to prevent transmission of infection to close contacts. Emerging multidrug resistant strain of *Shigella* is a growing concern across the globe and in India. Herein we report a case of dysentery in a child caused by an

extended spectrum beta lactamase (ESBL) producing and multidrug resistant (MDR) *S. flexneri* so as to alert the clinicians, microbiologists and epidemiologists regarding the emergence of resistance in *Shigella* spp. An outbreak of shigellosis by such resistant strains in overcrowded communities will be a tough challenge in the containment of the disease.

Keywords: Multidrug resistant shigella, *Shigella flexneri*, Shigellosis

CASE REPORT

A 2 ½ year-old- boy presented to the Emergency Department of C.S.S.Hospital (associated with Subharti Medical College, Meerut) with three days history of fever, loose bloody stools (10-12 times /day) and crying before defecation. There was past history of birth asphyxia and delayed milestones of developments, for which he was on a regular follow up in a private hospital. The child was treated earlier by a local doctor with metronidazole and co-trimoxazole syrup. As there was no clinical improvement, he was referred to us. On clinical examination, the child was conscious and oriented but signs of dehydration were present. He was admitted immediately and started on intravenous fluid with antibiotics (ceftriaxone and amikacin). Stool sample from the child was collected and sent to clinical microbiology laboratory for culture and sensitivity. The stool sample obtained in the laboratory showed the presence of blood and mucus, which when plated onto MacConkey agar and Xylose lysine deoxychocolate agar (Himedia, Mumbai, India) plates showed the presence of a few non-lactose fermenting colonies along with pink colonies. The pale colonies were biochemically identified as *Shigella* spp. by the standard biochemical tests [1], and confirmed to be *S. flexneri* by serotyping using type-specific antiserum (Denka-Seiken Antisera, Tokyo, Japan). Identification was also performed with the automated Vitek-2 C (bioMerieux, France) which gave an excellent confidence level for identification of *S. flexneri*. Antibiotic susceptibility was determined by the Kirby-Bauer method as per Clinical Laboratory Standards Institute (CLSI) guidelines [2], which showed that this isolate was resistant to more than three antibiotics, including

ampicillin, nalidixic acid, cefixime, cefoxitin, ceftriaxone, amikacin, tetracycline, co-trimoxazole and ciprofloxacin but was sensitive only to imipenem and meropenem. Using the CLSI approved phenotypic confirmatory test (PCT) *S. flexneri* isolated was identified as an ESBL producer. Following the susceptibility report, ceftriaxone and amikacin was replaced and the patient was administered an eight hourly dose of meropenem 1g in 100 ml as an infusion in normal saline which was continued for five days. The child started showing clinical improvement. A repeated stool sample culture on the 3rd day of treatment did not grow *Shigella* spp. He was finally discharged from the hospital in a stable condition.

DISCUSSION

Shigellosis is a major cause of morbidity and mortality among children in the developing countries [3]. *S. flexneri* is the most commonly isolated species in the developing world [4]. Prompt and appropriate antibiotic therapy is necessary in shortening the duration of clinical symptoms. Emerging multidrug resistant strain is a growing concern across the globe [5] and in India [6,7] and MDR in *Shigella* has made selection of drugs complicated. Third generation cephalosporin was the mainstay of treatment in MDR cases [8]. However, with the emergence of ESBL producing strains even cephalosporins are ineffective, drastically limiting treatment options. Such MDR strains can arise as an important threat in the treatment of dysentery [5-7,9]. ESBL / AmpC producing *S. flexneri* has been reported from other part of Indian subcontinent [6,7]. However, we are unaware of the resistance pattern of *Shigella* spp. from Western Uttar Pradesh due to lack of

published cases. In fact a recent Indian study has highlighted that screening for ESBL / AmpC must be considered upon isolation of *Salmonella* / *Shigella* isolates, which would help in reducing the morbidity and mortality associated with the disease for better patient outcome [8]. One of the mechanisms of resistance to third generation cephalosporin is mediated by ESBL. Isolation of MDR and ESBL producing bacteria with the persistence of symptoms made carbapenems the drug of choice in this case. However, in a country like India where shigellosis is a common infection of the under privileged society, treatment only by carbapenems will pose a serious economic as well as therapeutic challenge. Studies have reported that alternative drug such as azithromycin (rather than ceftriaxone) should be used as an empiric antibiotic for cases of severe dysentery prior to susceptibility reports to minimize the morbidity associated with the disease [7,10]. It is known that infections due to ESBL producers are predominantly hospital acquired. Our case being a case of delayed milestone of development had been in a regular contact with hospital setting for treatment and follow up. This may explain this ESBL positive *S. flexneri* being isolated from him. Though molecular detection of various genes are the gold standard for identifying ESBL/AmpC or carbapenemase gene, not many laboratories in our country can offer this tests as a daily diagnostic tool for identification of these resistance mechanisms. Therefore in such areas if available Vitek 2C is an acceptable alternative [5]. In the present case also we reconfirmed our isolate as ESBL positive *S. flexneri* using Vitek 2C system.

CONCLUSION

MDR *Shigella* is a matter of therapeutic concern. An outbreak of shigellosis by such resistant strains in overcrowded communities will be a tough challenge in the containment of the disease.

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