CASE REPORT

A case study of symptomatic urinary tract infection by *Shigella sonnei* in adult female and a short review on drug-resistant *Shigella* species

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ABSTRACT

Shigella species belong to family *Enterobacteriaceae* and are causative agents of bacillary dysentery. The whole spectrum of disease caused by *Shigella* species is called Shigellosis. *Shigella* has four major subgroups: *Shigella dysenteriae*, *Shigella flexneri*, *Shigella boydii,* and *Shigella sonnei*. *S. sonnei* causes the mildest form of bacillary dysentery, and in many cases, it causes only mild diarrhea. It is the most common Shigellosis in developed countries. There are few reported cases of asymptomatic bacteriuria due to *S. sonnei* both in adults and pediatric patients. Few cases of symptomatic urinary tract infection (UTI) are also reported. In pediatric patients, the common risk factor for UTI is found to be vesicoureteric reflux, especially in females. Recent studies done in various countries show an alarming increase in resistance of *Shigella* species to commonly used antibiotics such as chloramphenicol, ampicillin, co-trimoxazole, nalidixic acid, fluoroquinolones, macrolides, and cephalosporins. Many outbreaks of Shigellosis by multidrug-resistant (MDR) strains have also been reported. *Shigella* rarely causes extraintestinal manifestations such as hemolytic uremic syndrome, hyponatremia, reactive arthritis, altered neurologic state, bacteremia, UTI, and vulvovaginitis. UTI is a rare complication of Shigella infection. Here, we report a case of UTI due to *S. sonnei* in an adult female with diabetes mellitus (DM). We have also done a short review of increasing antibiotic resistance among *Shigella* species. The Institutional Ethics Committee approval was obtained to publish this case study. A 64-year female presented to an outpatient clinic with symptoms of UTI. Urine culture was done by the semiquantitative method in blood agar plate and MacConkey agar. A Gram-negative bacilli were isolated with a significant colony count of >100,000 cfu/ml. Antibiotic sensitivity was done by both disc diffusion method and minimum inhibitory concentration. Stool culture was also done after 4 days. In this case study, *S. sonnei* was isolated from urine, but stool culture done after 4 days of treatment with antibiotic was negative. The patient was newly diagnosed with type 2 DM. Hence, DM could be a risk factor for *S. sonnei* UTI in the elderly. Taking into consideration the emergence of antibiotic resistance among *S. sonnei* isolates, knowledge of antibiotic sensitivity pattern is crucial in the treatment of such infections. In our study, the isolate was not MDR. It was sensitive to ampicillin, cefixime, cefotaxime, ciprofloxacin, nitrofurantoin, and norfloxacin and azithromycin and resistant to co-trimoxazole and nalidixic acid.

KEY WORDS: *Shigella sonnei*; Urinary Tract Infection; Drug Resistance

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INTRODUCTION

Shigella species belonging to family *Enterobacteriaceae* are causative agents of bacillary dysentery. The term Shigellosis has been used to include the whole spectrum of disease caused by *Shigella* species. *Shigella* has four major subgroups: *Shigella dysenteriae*, *Shigella flexneri*,

Shigella boydii, and *Shigella sonnei*. Infection occurs by contaminated food and water through fecal-oral route. The number of bacteria needed to initiate infection is low. They are able to survive better than other bacteria in acidic pH of the stomach. The natural habitat of these bacteria is the intestine of human beings and primates. Recent studies reveal the dominance of *S. sonnei* as the causative agent of dysentery.[1] *S. sonnei* was first described by Sonne in Denmark. *S. sonnei* causes the mildest form of bacillary dysentery. In many cases, it causes only mild diarrhea. In developed countries, it is the main cause of Shigellosis. The mucosal epithelial cells are invaded by the bacteria, and then they multiply and spread to adjacent cells and also penetrate inside the lamina propria. Inflammatory reaction develops with capillary thrombosis leading to necrosis of patches of epithelium which slough off leaving behind transverse superficial ulcers.[2] The symptoms vary from asymptomatic infection to severe dysentery. The incubation period is short (1–7 days). The main symptoms are the frequent passage of loose small volume feces containing blood and mucus with abdominal cramps and tenesmus. Fever and vomiting may be present. Complications are more common in *S. dysenteriae*.

Shigella is usually confined to colonic mucosa, and it rarely causes extraintestinal manifestations such as hemolytic uremic syndrome, hyponatremia, reactive arthritis, altered neurologic state, bacteremia, urinary tract infection (UTI), and vulvovaginitis. *Shigella* bacteremia is more common in malnourished children and infection with *S. dysenteriae* serotype 1. In AIDS patients, shigellosis is severe and causes severe infection with bacteremia. In children, surgical complications such as appendicitis, perforation of colon, intestinal obstruction, and intra-abdominal abscess have been reported.[3]

The four *Shigella* species differ in their geographical distribution. *S. boydii* infections are limited to Indian subcontinent. In the past, many epidemics of dysentery were caused by *S. dysenteriae*. However, there is a decline in cases due to *S. dysenteriae* due to measures taken to improve sanitation and availability of antibiotics. Now *S. flexneri* is common in developing countries, whereas *S. sonnei* is predominant species in developed countries. Recently, *S. sonnei* has become the common species replacing *S. flexneri*[1] The symptoms vary from asymptomatic infection to severe dysentery. *Shigella* rarely causes extraintestinal manifestations such as hemolytic uremic syndrome, hyponatremia, reactive arthritis, altered neurologic state, bacteremia, UTI, and vulvovaginitis. UTI is a rare complication of Shigella infection.

Here, we report a case of UTI due to *S. sonnei* in an adult female with diabetes mellitus (DM). The resistance of *Shigella* species to commonly used agents is increasing. *Shigella* species were earlier susceptible to antibiotics such as ampicillin, chloramphenicol, nalidixic acid, and co-trimoxazole but recent studies show the emergence of resistance to fluoroquinolones, macrolides, and cephalosporins. We have also done a short review of antimicrobial resistance among *Shigella* species.

CASE REPORT

A 64-year-old female presented to the outpatient clinic with a history of abdominal pain, fever with chills, frequency of micturition and burning micturition for 5 days. On examination, the patient's vitals are as follows: Temperature 100°F, pulse rate 92/min, and blood pressure 110/70 mm Hg. Table 1 shows the laboratory workup done for the patient.

Urine analysis was done and it revealed Albumin: +++, Sugar: +++, and Pus cells: Plenty. Other significant laboratory findings were blood sugar fasting: 108 mg/dl, blood sugar postprandial: 198 mg/dl, HbA1C: 7.4. Gram stain of urine showed few pus cells, occasional epithelial cells, and Gram-negative bacilli.

Urine culture was done by the semiquantitative method in blood agar plate and MacConkey agar. A Gram-negative bacilli were isolated with a significant colony count of >100,000 cfu/ml. The organism was identified as *S. sonnei* by Vitek 2 compact (BioMerieux). Antibiotic susceptibility was done both by disc diffusion method and minimum inhibitory concentration (Vitek 2 compact).[4] Table 2 shows the antibiotic susceptibility pattern of the organism. The isolate was sensitive to ampicillin, cefixime, cefotaxime, ciprofloxacin, nitrofurantoin and norfloxacin, and azithromycin. It was resistant to co-trimoxazole and nalidixic acid.

Table 1: Laboratory investigations

Test	Result
Urine analysis	Albumin: +++, Sugar: ++++, RBCs: Nil, Pus cells: Plenty, Epithelial cells: Occasional
Total count	10800 cells/cmm
Differential count	Neutrophil: 71, Lymphocyte: 25, Monocyte: 2, Eosinophil: 2
Hemoglobin	13.0 g/dl
Urea	22 mg/dl
Creatinine	0.5 mg/dl
Blood sugar (fasting)	108 mg/dl
Blood sugar (post prandial)	198 mg/dl
Glycosylated Hemoglobin (HbA1C)	7.4 mg/dl
Urine gram stain	Few pus cells, occasional epithelial cells, and Gram-negative bacilli
Urine culture	*Shigella* sonnei with count >100,000 cfu/ml

The patient came for review after 3 days. On further inquiry patient revealed a history of loose stools for 2 days (four episodes) before symptoms of UTI started. Stool culture done after 3 days of treatment with antibiotic was negative for *Shigella*. Ultrasound abdomen and pelvis were also done and the following findings were observed – mild hepatomegaly with Grade 1 fatty liver, cholelithiasis, diffusely thickened and irregular urinary bladder wall suggestive of cystitis and uterine fibroid.

The patient was treated as an outpatient with tablet ciprofloxacin 500 mg BD for 3 days and had a gradual resolution of urinary symptoms. The patient was newly diagnosed with Type 2 DM.

DISCUSSION

The case which we are reporting is that of a 64-year-old female who is newly diagnosed with type 2 DM with symptoms of lower UTI and mild diarrhea. *S. sonnei* was isolated from urine, and it was found to be sensitive to ampicillin, cefixime, cefotaxime, ciprofloxacin, nitrofurantoin and norfloxacin, and azithromycin and resistant to co-trimoxazole and nalidixic acid. Stool culture done after 4 days of treatment with antibiotic was negative. At first visit, the patient complained only about symptoms of UTI. Since *S. sonnei* was isolated from urine, the patient was enquired about complaints of loose stools and patient revealed mild diarrhea before the onset of urinary symptoms. Since stool culture done after 4 days course of antibiotics was negative for *S. sonnei*, we could not confirm the source of UTI. The patient was diagnosed with type 2 DM at that time.

UTI due to *S. sonnei* is very rare. There are few reported cases of asymptomatic bacteriuria due to *S. sonnei*[5-7] both in adults and pediatric patients. Table 3 gives details of published articles. Few cases of symptomatic UTI are also reported.[8-11] In pediatric patients, the common risk factor for UTI is found to be vesicoureteral reflux[8,9] especially in females. In a retrospective study done in Turkey, six cases of UTI caused by *Shigella* species were reported.[12] *Shigella* species were distributed as follows: *S. boydii* (four), *S. dysenteriae* (one), and *S. flexneri* (one) in the above study. All six patients were diabetic. DM is the most known risk factor for UTIs[13]

In a study done on surveillance data from cases of shigellosis, urine was the most common site from which *Shigella* species were isolated.[14] Shigellosis incidence was higher in children and in elderly and children, the infection was more invasive in nature.[15]

Antimicrobial resistance has become a threat to modern medical technologies, which is addressed seriously by the global health community. Treatment of UTI with proper antibiotics reduces the disease duration, but the resistance of *Shigella* to common antibiotics is on an increasing level. *Shigella* species were earlier susceptible to antibiotics such as ampicillin, chloramphenicol, nalidixic acid, and co-trimoxazole but recent antibiogram patterns published from various parts of the world show resistance to fluoroquinolones, macrolides, and cephalosporins. There have been many outbreaks of Shigellosis caused by multidrug-resistant (MDR) strains.[16]

Chung *et al.* have done a study in which South Asia has been described as a reservoir from which *S. sonnei* resistant to fluoroquinolones have spread globally.[17] In a study done in North India, *S. flexneri* was the common isolate and it showed resistance to most commonly-used drugs, such as ampicillin and fluoroquinolones chloramphenicol.[18] In a similar study in China, *Shigella* isolates showed resistance to common antibiotics such as penicillins and tetracyclines. Fluoroquinolones and cephalosporins were routinely used for treating dysentery empirically. However, in the above study, *Shigella* isolates resistant to both quinolones and cephalosporins were reported.[19] The high-level of MDR frequency threaten the effectiveness of treatment in infections caused by *Shigella* species. In a study conducted among Jewish community increased prevalence of MDR *S. sonnei* was reported.[20]

Table 2: Antimicrobial susceptibility pattern of *Shigella sonnei*

Antibiotics	Sensitivity
Ampicillin	Sensitive
Cefotaxime	Sensitive
Cefixime	Sensitive
Ciprofloxacin	Sensitive
Norfloxacin	Sensitive
Nalidixic acid	Resistant
Co-trimoxazole	Resistant
Nitrofurantoin	Sensitive
Azithromycin	Sensitive

Table 3: Reported cases of *Shigella sonnei* urinary tract infection

Year	Reference	Patient group	Predisposing factors
2013	Baka, *et al*.[11]	31-year pregnant female	Nil
2003	Anatoliotaki, *et al*.[8]	6-year-ld girl	vesicoureteral reflux
1995	Papasian, *et al*.[10]	45-year female	Nil
1990	Awadalla, *et al*.[9]	3-year-old girl	Vesicoureteral reflux
1987	Narchi and Beattie[7]	Pediatric	Nil
1984	Ekwall, *et al*.[6]	74-year male	Nil
1963	Jao, *et al*.[5]	Adult	Nil

Resistant to macrolides have also been reported.[21] A study done in Bangladesh showed the emergence of MDR *S. sonnei* replacing other *Shigella* species in prevalence. In the above study co-trimoxazole and nalidixic acid showed maximum sensitivity above 80%. Many strains were resistant to ciprofloxacin and ampicillin. All the isolates were sensitive to the cephalosporin group of drugs. *S. flexneri* is a predominant species in Bangladesh. Recent studies show the emergence of *S. sonnei* as the second most common species in this country.[22]

In one African country, MDR strains of *S. flexneri* and *S. sonnei* have been reported.[23] In a study done in Indian city of Bangalore, majority of *Shigella* isolates were resistant to two or more drugs. Fluoroquinolone resistance has also increased.[24]

In this case study, stool culture done after 4 days course of antibiotics was negative for *S. sonnei*. Hence, we could not confirm the source of UTI. This is a limitation of the above case study. The patient was diagnosed with type 2 DM at that time. Hence, DM could be a risk factor for *S. sonnei* UTI in the elderly. In elderly patients with comorbidities like DM *Shigella* should be kept in mind as a causative agent of UTI. It is not clear how *Shigella* sps enter the urinary tract. The organism may gain access to urinary tract both in patients with clinical infection and asymptomatic carriers by ascending the retrograde route. In immunosuppressed patients, neonates and elderly *Shigella* bacteremia may occur and then cause urinary infection.

CONCLUSION

Taking into consideration the emergence of antibiotic resistance among *S. sonnei* isolates, knowledge of antibiotic sensitivity pattern is crucial in the treatment of such infections. In our study, the isolate was not MDR. It was sensitive to ampicillin, cefixime, cefotaxime, ciprofloxacin, nitrofurantoin and norfloxacin, and azithromycin and resistant to co-trimoxazole and nalidixic acid. Such reported case studies will create awareness among clinicians about *S. sonnei* UTI and guide them in the treatment of patients with appropriate antibiotics.

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