

Shigella Septicaemia in Adults: Report of Two Cases and Mini-Review

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Abstract

Introduction: We report 2 cases of *Shigella* septicaemia in adult patients. **Clinical Picture:** Two 57-year-old women presented with non-bloody diarrhoea and fever. The first patient was an inmate of a long-term care facility who was schizophrenic and the second patient was a diabetic who recently travelled to Medan, Indonesia. Both patients were febrile, hypotensive and dehydrated. The first patient was neutropenic, thrombocytopenic and had acute renal failure. Blood cultures yielded *Shigella flexneri* and stool cultures gave negative results for both patients. **Treatment:** Rehydration and intravenous ceftriaxone were instituted. **Outcome:** The patients' symptoms and hypotension resolved. **Conclusion:** Appropriate antibiotics can decrease the severity and duration of *Shigella* septicaemia.

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Introduction

Shigellosis is generally considered to be confined to the gastrointestinal tract. Septicaemic infections with *Shigella* species are extremely rare in adults.¹ A previous study suggests that *Shigella* septicaemia may occur more frequently with a higher case fatality in young malnourished children.²

In Singapore, there are 15 to 25 sporadic cases of shigellosis reported annually.³ In this report, we describe 2 cases of *Shigella* septicaemia in adult patients.

Case Reports

Case 1

A 57-year-old Chinese woman, an inmate of a long-term care facility, was admitted with five episodes of non-bloody diarrhoea and fever of one day's duration. She had a fall in the toilet and struck her right forehead. She was diagnosed as a schizophrenic on melleril, benzhexol and valium.

Physical examination revealed a moderately dehydrated, malnourished, drowsy patient with a temperature of 37.5°C, blood pressure of 95/65 mmHg and pulse rate of 90/min. There was a right frontal cephalhaematoma. The pupils were equal and reactive to light. The abdomen was soft and non-tender. No organomegaly was detected. Rectal

examination revealed brown stools. Neurological examination was normal. The rest of the examination was unremarkable.

The haemoglobin was 9.5 g/dL, the white cell count was 1200/mm³ (67.5% polymorphs, 30.7% lymphocytes) and the platelet count was 85,000/mm³. The serum urea was 26.7 mmol/L; serum potassium, 3.5 mmol/L; serum sodium, 129 mmol/L; and creatinine, 589 µmol/L. Computed tomographic (CT) scan of the head was normal. The liver function tests revealed hypoproteinaemia (49 g/L) and hypoalbuminaemia (20 g/L) and raised transaminases.

The initial diagnosis was gastroenteritis with septic shock and acute renal failure. She was initially treated with intravenous fluid replacement and oral ciprofloxacin 500 mg bd. The following day, her blood pressure dropped to 65/32 mmHg and she was started on inotropic support. The antibiotic regimen was changed to intravenous ceftriaxone 2 g daily and oral metronidazole 400 mg tid.

Stool microscopy revealed leukocytes but no ova, cysts or parasites. One of two sets of blood cultures yielded *Shigella flexneri* sensitive to cephalexin, ceftriaxone, gentamicin and ciprofloxacin but resistant to ampicillin, amoxicillin-clavulanate and chloramphenicol. Two stool cultures did not grow any pathogens. Widal test was negative.

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A bone marrow trephine biopsy on day 7 showed a hypercellular marrow with myeloid hyperplasia. Her diarrhoea resolved and the blood pressure normalised on day 6. Fever defervesced on day 3 but recurred on day 10. Her leukocyte count normalised on day 3 (white cell count $7900/\text{mm}^3$) and her thrombocytopenia resolved on day 8 (platelet count $246,000/\text{mm}^3$). Her serum creatinine on day 22 was $61 \mu\text{mol/L}$. On day 13, endoscopy and sigmoidoscopy were performed. There was atrophy with loss of rugosity of the mucosa of the body of stomach, and granular mucosa with pus in the distal sigmoid and rectum. No ulcers were seen. Colonic biopsies confirmed the presence of infective colitis.

The patient improved after 21 days on ceftriaxone. She was discharged 33 days after admission. She was well when last seen 6 weeks after discharge.

Case 2

A 57-year-old Malay woman was admitted with 6 episodes of diarrhoea over 2 days and constant abdominal pain plus fever and chills of one day's duration. There was no blood and mucus in her stools. She had been a mild diabetic on diet control for several years. She had returned from a tour of Medan, Indonesia 2 days before admission. Five members of the tour group had also developed diarrhoea.

On admission, she was dehydrated. Her temperature was 38°C and the blood pressure was 90/30 mmHg. She had mild pallor. No jaundice was detected. The abdomen was soft and non-tender with no organomegaly. Watery yellow stools was observed on rectal examination. The rest of the examination was unremarkable.

Investigations showed haemoglobin, 11.6 g/dL ; white cell count, $7700/\text{mm}^3$ (86% polymorphs); and platelet count of $178,000/\text{mm}^3$. The serum urea was 1.6 mmol/L ; creatinine, $63 \mu\text{mol/L}$; serum potassium, 3.4 mmol/L ; and glucose, 12.8 mmol/L . The initial diagnosis was infective gastroenteritis. She was initially treated with oral metronidazole 400 mg tid. Her blood pressure normalised with intravenous fluid rehydration.

Blood culture yielded *Shigella flexneri* sensitive to cephalexin, ceftriaxone, gentamicin and ciprofloxacin but resistant to ampicillin and chloramphenicol. Three stool cultures were negative. The antibiotic regimen was changed to intravenous ceftriaxone 2 g daily for 10 days.

Her diarrhoea resolved on the 7th day of hospitalisation and fever defervesced on the 4th day of hospitalisation. On the 7th hospital day, she developed mild thrombophlebitis which resolved with a course of oral cloxacillin for 1 week. The patient was discharged on the 14th day of hospitalisation. She was well when she was last seen 1 month after hospitalisation.

Discussion

Shigella species are a common cause of infectious enteritis in both children and adults. *Shigella* septicaemia seems to be a rare accompaniment of shigellosis. Reported prevalence rates of *Shigella* septicaemia in shigellosis range from 0.4% to 7.3%.^{1,2,4,5}

The single most important factor predisposing to the development of *Shigella* septicaemia is the age of the patient with a 6 to 1 ratio in the number of paediatric to adult cases.²

Several studies have shown that when *Shigella* septicaemia occurs in adults, it is usually associated with underlying diseases such as malnutrition, diabetes, leukaemia, sickle cell anaemia, malignancy, cirrhosis, immunosuppression and HIV infection.^{2,6,7} Case 1 was a schizophrenic patient from a long-term care facility, and whose personal hygiene may have been compromised. She was malnourished with hypoalbuminaemia, moderate dehydration and acute renal failure. Significantly, her initial leukopenia was associated with the *Shigella* sepsis.

The typical patient potentially at greatest risk of death from *Shigella* sepsis is malnourished, afebrile and severely dehydrated; develops leukopenia and is infected by ampicillin-resistant organisms.⁵ Bacteraemia is presumably a result of bacterial entry through the severely ulcerated colonic mucosa and diminished serum bactericidal activity in malnourished patients.² Case 1 is an example of a patient at high risk for *Shigella* septicaemia.

The presence of mild diabetes and overseas travel were the two possible risk factors that predisposed the second patient to shigellosis. Both patients had prolonged diarrhoea, and the first patient had colitis despite antimicrobial therapy. Although *Shigella* infection is commonly thought to produce the classic symptoms of bacillary dysentery, watery diarrhoea is the initial intestinal symptoms in most cases as demonstrated by our 2 patients.⁸

Virulence factors specific to each of the *Shigella* species may be responsible for the systemic spread of the organism. The significantly higher frequency of septicaemia infection with *Shigella dysenteriae* type 2 was observed in malnourished children by Struelens et al.² *Shigella sonnei* is the species most commonly isolated in the stools of patients with shigellosis in developed countries.⁹ *Shigella flexneri* causes more severe clinical disease and has been often cultured from the blood.^{7,10,11} *Shigella flexneri* is the commonest cause of endemic diarrhoeal disease in less developed countries.

In our 2 patients, *Shigella flexneri* was the organism responsible for the septicaemia. The fact that blood cultures are not a routine investigation in patients with dysentery,

may account for the apparently low incidence of bacteraemia in shigellosis. The negative stool cultures in both the patients were due to the collection of stool samples after commencement of antibiotics.

Shigella infections are usually restricted to the intestine. The organisms are locally invasive, probably due to the effects of an enterotoxin on epithelial cells. *Shigella* enterocolitis may lead to net exudative loss of immunoglobulins, complement and other plasma proteins required for lysis and opsonisation of invading gram-negative bacilli, and damage to the colonic mucosa, leading to overwhelming sepsis.² Koster et al¹² have shown that endotoxaemia during *Shigella* enterocolitis is followed by increased risk of coagulopathy, renal microangiopathy and haemolytic anaemia.

Once *Shigella* septicaemia is confirmed, early initiation of parenteral antimicrobial therapy and maintenance of intravascular volume by fluid or blood is required. Appropriate antibiotics can decrease the severity and duration of disease, and can reduce spread by rapidly eradicating the organism from the stools.¹³ The increasing worldwide emergence of antibiotic-resistant *Shigella* strains requires careful selection of antimicrobial agents such as ceftriaxone and fluoroquinolones for severe cases.¹⁴

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REFERENCES

1. Barret-Connor E, Connor J D. Extraintestinal manifestations of shigellosis. *Am J Gastroenterol* 1970; 53:234-45.
2. Struelens M J, Patte D, Kabir I, Salem A, Nath S K, Butler T. *Shigella* septicaemia: prevalence, presentation, risk factors and outcome. *J Infect Dis* 1985; 152:784-90.
3. Communicable Disease Surveillance in Singapore 1997 and 1998. Singapore: Quarantine and Epidemiology Department, Ministry of Environment, 1998 and 1999.
4. Haltalin K C, Nelson J D. Coliform septicaemia complicating shigellosis in children. *JAMA* 1965; 192:441-3.
5. Duncan B, Fulginitis V A, Sieber O F Jr, Ryan K J. *Shigella* sepsis. *Am J Dis Child* 1981; 135:151-4.
6. Morduchowicz G, Huminer D, Siegman-Igra Y, Drucker M, Block C S, Pitlik S D. *Shigella* bacteremia in adults. *Arch Intern Med* 1987; 147:2034-7.
7. Baskin D H, Lax J D, Barrenburg D. *Shigella* bacteremia in patients with acquired immune deficiency syndromes. *Am J Gastroenterol* 1987; 2:338-41.
8. Ronsmans C, Bennish M L, Wierzba T. Diagnosis and management of dysentery by community health workers. *Lancet* 1988; 2:552-5.
9. Centers for Disease Control. Shigellosis—USA, 1984. *MMWR Morb Mortal Wkly Rep* 1985; 34:600-2.
10. Martin T, Habbick B F, Nyssen J. Shigellosis with bacteremia: a report of two cases and a review of literature. *Pediatr Infect Dis* 1983; 2:21-6.
11. Trevelt A J, Ogunbanjo B O, Naraqi S, Igo J D. *Shigella* bacteremia in adults: *Postgrad Med J* 1993; 69:466-8.
12. Koster F, Levin J, Walker L, Tung K S K, Gilman R H, Rahaman M M, et al. Hemolytic-uremic syndrome after shigellosis: relation to endotoxemia and circulating immune complexes. *N Engl J Med* 1987; 298:927-3.
13. Haltalin K C, Nelson J D, Ring R, Sladoje M, Hinton L V. Double-blind treated study of shigellosis comparing ampicillin, sulfadiazine and placebo. *J Pediatr* 1967; 70:970-81.
14. Lopez E L, Prado-Jimenez V, O’Ryan-Gallardo M, Contrini M M. *Shigella* and Shiga toxin-producing *Escherichia coli* causing bloody diarrhea in Latin America. *Infect Dis Clin North Am* 2000; 14:41-65.