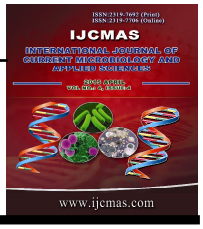
Int.J.Curr.Microbiol.App.Sci (2015) 4(4): 870-873

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 4 Number 4 (2015) pp. 870-873**
http://www.ijcmas.com



Case Study

Bacteremia due to *Shigella flexneri* in an adult

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Keywords

Shigella flexneri, sepsis, diarrhoea , multiple drug resistance

A B S T R A C T

Shigellosis continues to be an important public health problem since communication in the world has become more frequent. In addition, this disease is difficult to be prevented because only a small number of bacteria are required to cause infection, and it has exhibited steady trends towards multiple drug resistance. This report describes a 23-year-old female with *Shigella flexneri* sepsis presenting initially with a high fever, vomiting, watery diarrhoea and dry cough. She was successfully treated with meropenem. This case illustrates that *Shigella* should be included in the differential diagnosis of sepsis associated with diarrhoea.The choice of antimicrobial therapy and the optimal duration for treatment should be carefully evaluated because of the emergence of multidrug-resistant *Shigella flexneri*.

Introduction

Shigella species were discovered over 100 years ago by a Japanese microbiologist named Shiga, for whom the genus is named. *Shigella* organisms are a group of gram-negative, facultative intracellular pathogens. They were recognized as the etiologic agents of bacillary dysentery or shigellosis in the 1890s. These organisms are members of the family Enterobacteriaceae and tribe Escherichieae; they are grouped into 4 species: *Shigella dysenteriae, Shigella flexneri, Shigella boydii,* and *Shigella sonnei,* also known as groups A, B, C, and D, respectively(JB Yen et al., 2003)

Shigellosis is still an important public health problem in developing and underdeveloped countries. It may lead to rare but potentially fatal various extra intestinal complications like septicemia, involvement of CNS, urinary tract and liver especially in young malnourished children. The disease is difficult to prevent as only few bacteria are required for causing infection and there is increasing infection with multi drug resistant strains. It is usually a self-limiting disease, involves only the gut, is transmitted by the fecal-oral route, and has an incubation time of from 12 hours to 1 week.The disease is mediated by enterotoxin and manifests with acute bloody diarrhoea and fever often occurring in an outbreak due to contamination of water(B. G. Marcia, 2012).Resolution of symptoms is expected within one week in most cases with *Shigella*

dysentery, and usually only supportive care is required. *Shigella* rarely invades the bloodstream and results in septic shock. Macrophages not only fail to kill *Shigella* bacteria that they phagocytize, but also are killed by them

Clinical features of this reported case indicate some important points about *Shigella* infections which should be considered when managing patients with diarrhoea and sepsis, especially in endemic areas.

Case report

A 23 year-old female presented with a persistent high-grade fever of 3 days duration associated with vomiting, loose motions and dry cough.On presentation she was febrile (103°F), tachycardic (120/bpm),her blood pressure was 90/60mmHg. She had no edema, pallor, clubbing, cyanosis and icterus. Her peripheral blood count showed pancytopenic pattern: total white blood cell count of 2400 cells/μL, hemoglobin of 8 gm/dL, and platelet of 44,000/μL. Her absolute neutrophil count was 432/μL.Her human immunodeficiency virus (HIV) serology test was negative.Urinalysis, liver enzymes, and bilirubin were all normal.There was no hemoparasite detected on blood-film examination.Blood culture was taken for this patient taking into account her presentation with systemic inflammatory response syndrome and severe neutropenia. Blood cultures were processed by automated method (BACTEC 9050).The identification and sensitivity was performed by conventional as well as by automated method (API, Biomerieux).The isolate was identified as *Shigella flexneri* based on biochemical characteristics and found sensitive to cefoperazone sulbactam, piperacillin tazobactam, cefepime, imipenem, meropenem, ciprofloxacin, except ampicillin, ceftriaxone and cotrimoxazole The stool sample showed plenty of yeast cells with pseudohyphae on saline wet mount and *Candida albicans* was isolated from stool culture. Patient was treated initially with injection ciprofloxacin, metronidazole for 4 days, and then Injection cefoperazone sulbactam was added. However, patient did not respond to the treatment. Then these antimicrobials were discontinued by physicians and injection meropenem was started. Patient started responding and became afebrile. The blood count started to improve starting from the first week of treatment and normalized at the end of the month. Her vital signs stabilized after 7 days.

Discussion

Infection with *Shigella* is generally considered to be confined to the gastrointestinal tract. Invasion of the bloodstream occurs in only 0.4% to 7.3% of patients and has been thought to be a rare event if there are no coexisting risk factors such as malnutrition or young age (Keusch GT, 1998). *Shigella* bacteremia is mostly caused by *S. flexneri*,which has been reported to be more virulent than other *Shigella* species, and it is the most commonly isolated species in the developing world(Duncan B, 1981).Though an invasive disease, it usually do not reach the tissue beyond the lamina propria and hence very rarely cause bacteremia except under very special circumstances like immunocompromised status.Since the mechanism of bacteremia remains unclear, invasiveness may be associated with a mixture of soluble bacterial proteins encoded by a 140-MD plasmid and may lead to a net exudative loss of immunoglobulins, complement and other plasma proteins required for lysis and opsonization of

invading bacilli, and this may pave the way for overwhelming sepsis to occur (Bello CS et al., 2003).

Shigella bacteremia is often associated with a high mortality with a case fatality rate of 46% (Martin T et al.,1983).The condition needs to be treated aggressively with institution of appropriate parenteral antimicrobial agents,IV fluids or blood administration for maintenance of intravascular volume. Appropriate and timely antimicrobial therapy not only shortens the duration of fever and shedding of organisms from stools but also results in fewer complications.

In the present case, the antimicrobial sensitivity of the *Shigella flexneri* isolate is consistent with the reports of similar previous studies. A case report from Mumbai described four cases of *Shigella* septicemia, three caused by *Shigella* dysentery serotype 1 and one by *Shigella flexneri* with a mortality rate of 75% (K Saraswathi et al.,2002).All these isolates were sensitive to gentamicin, amikacin, norfloxacin and nalidixic acid while resistant to amoxicillin, chloramphanicol, tetracycline and cotrimoxazole. Vassil St. Georgiev reported septicemia caused by *Shigella sonnei* in a newborn (VS Georgiev et al,1997). Sharma and Arora reported an uncommon case of *Shigella flexneri* bacteremia in an adult from New Delhi(S Sharma, A Arora.,2012) as also reported by a few other authors. An antimicrobial resistance of 40%,33%,70% and 64% has been reported by Mache for chloramphanicol, cotrimoxazole, ampicillin and tetracycline, respectively among pediatric outpatient *Shigella* isolates in Southwest Ethiopia(A Mache, 2001).To prevent the emergence of multidrug resistant *Shigella*, it is important to evaluate the choice of antimicrobial therapy and optimal duration of treatment (S Gupta et al.,2010).

Scragg and Rubidge reported *Shigella bacteremia* cases who were stool culture negative(Scragg JN et al.,1978).In our case also, the blood but not the stool culture was positive for *S.flexneri* while *Candida albicans* was isolated from stool culture after the antibiotic treatment was started.It has recently been demonstrated that elevated *Candida* counts in stool are a result of antibiotic treatment of diarrhoea per se rather than a cause of Antibiotic associated diarrhoea (AAD).In studies where the effect of broad-spectrum antibiotics on the composition of the intestinal microflora of humans was investigated, an increase in yeasts and a decrease in anaerobes were observed.

On pubmed literature search, there were limited reports of *S. bacteremia* in adults from India. Majority of the *Shigella* bacteremia cases occurred in children and adults with an underlying disease, such as diabetes, leukemia, sickle cell disease, malignancy, cirrhosis, immunosuppressive therapy, and HIV infection. In our case, the young age appeared to be the only risk factor predisposing her to sepsis. As this patient was having fever, vomiting, loose motions, dry cough, pancytopenia and *C.albicans* superinfection, it is very difficult to know whether the *Shigella flexneri* bacteremia had unique clinical manifestations or not.

Conclusion

The present case illustrates that *Shigella* infection should be considered in the differential diagnosis of sepsis associated with a diarrheal disease in adults who have travelled to or lived in an endemic area. Blood as well as stool cultures should be taken. An early and precise diagnosis is of prime importance because appropriate antibiotics in addition to supportive care can be life saving for such patients.

Acknowledgment

The author acknowledges the immense help received from the scholars whose articles are cited and included in references of this manuscript.

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