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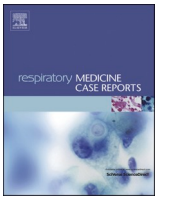

Case report

The tale of the traveling cheese: Shigella in a lung transplant patient

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ABSTRACT

Shigellae are Gram-negative, nonmotile, facultatively anaerobic, non-spore-forming rods. Shigella is a common cause of gastroenteritis in areas of overcrowding and poor sanitation, but is seen less frequently in the developed world. Infection is mainly acquired through the fecal-oral route, but consumption of unpasteurized dairy remains a high risk for transmission. In the developing world, Shigella is a childhood illness and with adequate hydration is fairly self-limiting. The use of antibiotics depends on the severity of illness, the age of the patient and immune status. In immunocompromised patients, chronic symptomatic or relapsing infection has been described. In this report, we describe a case of a lung transplant patient, one year out of his transplant, on triple immunosuppressive therapy, who presented with septic shock secondary to Shigella gastroenteritis after ingesting unpasteurized cheese brought back from Peru. This case highlights the importance of educating transplant patients on how to reduce certain harmful exposures that may be fatal in immunosuppressed individuals.

1. Introduction

Shigella is a facultative anaerobic, non-motile gram-negative rod that belongs to the family enterobacteriacae. It is a common cause of gastroenteritis worldwide and is seen more frequently in developing countries where overcrowding is rife and sanitation is poor. In developed countries, sporadic common-source outbreaks are transmitted by uncooked food or contaminated water. It is an antigenically diverse pathogen that comprises four species – *Shigella dysenteriae*, S. flexneri, S. boydii and S. sonnei. S. flexneri is the leading cause of endemic shigellosis in low and middle income countries [3]. S. sonnei is the number one cause in high income countries [4]. The number of diarrhea deaths attributable to shigella worldwide is estimated at over 200,000 [1]. Nearly 60% of deaths occur in children under the age of 5 years. Humans are the primary reservoir and transmission is most commonly via the fecal-oral route [2]. Outbreaks are usually initiated by a food or waterborne source and then spread by person-to-person contact [6]. Since the introduction of pasteurization, there has been a large reduction in the number of foodborne illnesses associated with milk and other dairy. The consumption of raw and unpasteurized cheese still remains a risk factor for shigella.

2. Case report

This is a case of a 62-year-old Peruvian man who underwent a bilateral lung transplant for end stage idiopathic pulmonary fibrosis in November 2018, a year prior to this presentation. Pre-transplant the patient status was Cytomegalovirus +/+, Ebstein Barr Virus

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+/+. His transplant was complicated by Primary Graft Dysfunction Grade 3 as well as aspiration pneumonia. Tracheostomy was required for prolonged ventilator dependent respiratory failure. He also received monthly intravenous immunoglobulin (IVIG) treatment for high donor specific antibodies, which he started in January 2019 and completed in July 2019. At the time of presentation, his immunosuppression regimen consisted of tacrolimus 0.5 mg and mycophenolate 500mg twice daily and Prednisone 10mg daily.

He had been progressing well until he presented to the emergency department with a reported fever of 103° Fahrenheit from home, around 40 episodes a day of profuse non-bloody, watery diarrhea and abdominal discomfort. He did not complain of nausea or vomiting. He revealed that he had eaten soft, white, unpasteurized cheese that was brought from Peru two days prior.

He was hypotensive with a blood pressure of 72/39, a heart rate of 107 beats per minute and SaO2 of 96% while breathing ambient air. A physical exam revealed mild diffuse abdominal tenderness, but the other systems exam was normal.

Laboratory examination revealed a white blood cell count of 18,000 cells/mcl, platelet (PLT) count of 147,000 cells/mcl, creatinine 1.30 mg/dL, lactic acid 3.2 mmol/L. Computerized tomography (CT) of his abdomen showed fluid filled loops of the colon and small bowel, reflecting enteritis and diarrhea (see Image 1). Stool studies were sent. The patient was treated with intravenous fluids, tacrolimus was held due to new acute kidney injury, mycophenolate was held due to leukopenia and Cefepime and Metronidazole were administered for empiric coverage for abdominal pathogens. On day 4 of admission, Shigella flexneri (sensitive to Levofloxacin and Ceftriaxone, resistant to Ampicillin) was isolated from the stool cultures and an infectious disease consultation obtained. The patient had clinically recovered on Cefepime and he completed the antibiotic course for a total of 5 days. He was discharged the following day on his routine triple immunosuppressive therapy. His leukopenia and acute kidney injury resolved prior to discharge.

3. Discussion

The population at risk for shigellosis are children, patients with human immunodeficiency virus (HIV), especially men having sex with men and solid organ transplant recipients, the elderly and malnourished patient population. After oral ingestion, shigella survives the acidic environment of the stomach and the competitive intestinal microbiota to travel to the small and large intestine. The organisms are highly adapted to mucosal invasion and can cause systemic illness [5]. Shigella causes macrophage cell death, invasion of and multiplication within epithelial cells, death of the host epithelium, and alteration of the host inflammatory response [7,8].

The incubation period for shigellosis is usually 1–4 days. Asymptomatic infection can occur, usually in previously infected patients. It presents with fevers, headaches and vomiting followed by diarrhea. In immunocompetent patients, the illness is usually mild and symptoms last for a few days. In some individuals, especially immunocompromised patients, there can be a progression to dysentery with blood diarrhea cramping and high fevers. It can also cause complications such as bacteremia, colonic obstruction, toxic megacolon, hemolytic uremic syndrome, seizures and reactive arthritis [[9–11,14],14]. Disease presentation varies based on the serogroup of the infecting organism, with *Shigella dysenteriae* or Shigella flexneri causing bloody diarrhea and Shigella Sonnei causing mild disease. Persistent diarrhea and malnutrition are long-term complications seen in children from low income countries infected with S dysenteriae [12].

All high risk patients with diarrhea, especially children, MSM, travelers and solid organ transplant recipients should be tested for shigella. Patients not responding to conventional treatment should undergo repeat culture and sensitivity testing. Bacterial culture is the gold standard for diagnosis of shigella infections. This helps with antibiotic susceptibility as well. Several nucleic acid-based diagnostic tests for shigella and other enteric pathogens have emerged in the recent past [13]. In the United States at present there is also concern about multidrug-resistant Shigella infections in high risk patients who are more likely to require antibiotic treatment,

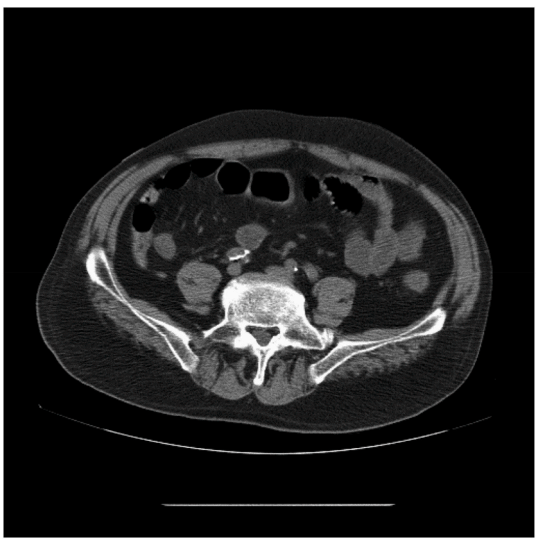

Image 1. CT abdomen showing dilated small bowel loops.

such as men who have sex with men, patients who are homeless, and immunocompromised patients such as transplant patients. These patients often have more severe disease, prolonged shedding, and recurrent infections. Infections are one of the main concerns for patient prognosis in the immediate period post-transplant as well as further down the line. The risk of infection changes over time, especially with the modification of immunosuppression. Treatment of shigella is centered on the maintenance of hydration and electrolytes. Anti-motility drugs are not recommended as these may prolong symptoms and pathogen shedding [16]. Oral ciprofloxacin and azithromycin are the first-line agents for shigellosis in adults. Parenteral ceftriaxone is reserved for immunocompromised and very sick patients. Susceptibility testing is recommended, especially in high risk patient population and multidrug resistant areas. The Center for disease control (CDC) recommends antibiotic therapy for shigella treatment in all immunocompromised patients and individuals who have severe illness and require hospitalization. The CDC also described strains with increasing resistance to fluoroquinolones [17]. In addition to antibiotic therapy, small trials have found some benefit with zinc therapy to reduce symptom duration [18]. Prophylactic strategies are based on the patient's known or likely exposures to infection according to the results of serologic testing and epidemiologic history [15]. Hand washing is a key prophylactic intervention and helps reduce shigella transmission by 70% within household members [20]. There are shigella vaccines in the developmental stages.

Organ transplant puts patients at high risk for shigellosis. Many factors affect the risk of infection such as, the patient's immunosuppressed state, exposures, and invasive procedures that they may have been subjected to Ref. [19]. Infections can be due to reactivation of endogenous organisms that reactivate in periods of severe immune suppression, donor-acquired organisms or from the environment. Epidemiological exposures can be divided into four overlapping categories: donor derived infections, recipient derived, nosocomial and community infections. Our case would fall into community infections, which although common elsewhere in the world, is far less common in the United States.

A major goal after a transplant is to reduce the risk of exposure to harmful organisms in these susceptible individuals. Transplant patients are given prophylactic antibiotics and immunizations to hopefully prevent infection. Promotion of certain lifestyle changes is a key part of this aspect of transplant are such as hand washing, avoidance of sick individuals and dietary advice. Dietary advice such as, avoidance of unsanitized water, unwashed fruit and vegetables, uncooked meat or fish and unpasteurized milk. Travel is a major risk factor for exposure to certain infections and this needs to be emphasized strongly for transplant patients, especially in the early stages of immunosuppression. Travel should be avoided, but if patients have to travel, emphasis on hand hygiene and strict dietary advice must be emphasized.

4. Conclusion

Infections in transplant patients are better avoided than treated. The immunosuppressed patients are at high risk of decompensating once infected and reducing immunosuppression may lead to catastrophic rejection. Each transplant patient must be educated on adherence to prophylactic regimens, hygiene practices and given strict dietary advice. Travel to countries where the patient is likely to be easily exposed to more infectious agents should be discouraged initially. The patients must be educated on the risks and taught how best to protect themselves.

Disclosure

The case was presented as a poster presentation at the 2021 National Chest Conference.

Declaration of competing interest

The authors have no conflict of interest to declare.

References

[1] GBD 2016 Diarrhoeal Disease Collaborators, Estimates of the global, regional, and national morbidity, mortality, and aetiologies of diarrhoea in 195 countries: a systematic analysis for the Global Burden of Disease Study 2016, Lancet Infect. Dis. 18 (11) (NOVEMBER 01, 2018) 1211–1228.
[2] K.L. Kotloff, J.P. Winickoff, B. Ivanoff, et al., Global burden of Shigella infections: implications for vaccine development and implementation of control strategies, Bull. World Health Organ. 77 (1999) 651–666.
[3] S. Livio, N.A. Strockbine, S. Panchalingam, et al., Shigella isolates from the global enteric multicenter study inform vaccine development, Clin. Infect. Dis. 59 (2014) 933–941.
[4] P.K. Ram, J.A. Crump, S.K. Gupta, M.A. Miller, E.D. Mintz, Part II.Analysis of data gaps pertaining to shigella infections in low and medium human development index countries, 1984–2005, Epidemiol. Infect. 136 (2008) 577–603.
[5] P.J. Sansonetti, Rupture, invasion, and inflammatory destruction of the intestinal barrier by Shigella: the yin and yang of innate immunity, Can. J. Infect Dis. Med. Microbiol. 17 (2006) 117–119.
[6] L.A. Lee, S.M. Ostroff, H.B. McGee, et al., An outbreak of shigellosis at an outdoor music festival, Am. J. Epidemiol. 133 (1991) 608–615.
[7] A. Phalipon, P.J. Sansonetti, Shigella's way of manipulating host intestinal innate and adaptive immune system: a tool box for survival? Immunol. Cell Biol. 85 (2007) 119–129.
[8] M.M. Levine, H.L. DuPont, S.B. Formal, et al., Pathogenesis of Shigella dysenteriae 1 (Shiga) dysentery, J. Infect. Dis. 127 (1973) 261–270.
[9] W.A. Khan, J.K. Griffiths, M.L. Bennish, Gastrointestinal and extra-intestinal manifestations of childhood shigellosis in a region where all four species of Shigella are endemic, PLoS One 8 (2013) e64097.79.
[10] M.L. Bennish, Potentially lethal complications of shigellosis, Rev. Infect. Dis. 13 (suppl 4) (1991) S319–S324.
[11] A. Avital, C. Maayan, K.J. Goitein, Incidence of convulsions and encephalopathy in childhood shigella infections. Survey of 117 hospitalized patients, Clin Pediatr (Phila) 21 (1982) 645–648.
[12] R.E. Black, K.H. Brown, S. Becker, A.R. Alim, I. Huq, Longitudinal studies of infectious diseases and physical growth of children in rural Bangladesh. II. Incidence of diarrhea and association with known pathogens, Am. J. Epidemiol. 115 (1982) 315–324.
[13] M.S. Riddle, H.L. DuPont, B.A. Connor, ACG clinical guideline: diagnosis, treatment, and prevention of acute diarrheal infections in adults, Am. J. Gastroenterol. 111 (2016) 602–622.

[14] Medical Microbiology, fourth ed., (Chapter 22), Shigella. Thomas L Hale and Gerald T Keutsch.
[15] A. Jay, M.D. Fishman, Infection in solid-organ transplant recipients, N. Engl. J. Med. 357 (2007) 2601–2614.
[16] H.L. DuPont, R.B. Hornick, Adverse effect of lomotil therapy in shigellosis, JAMA 226 (1973) 1525–1528.
[17] CDC recommendations for diagnosing and managing shigella strains with possible reduced susceptibility to ciprofloxacin.April 18, 2017.
[18] S.K. Roy, R. Raqib, W. Khatun, et al., Zinc supplementation in the management of shigellosis in malnourished children in Bangladesh, Eur. J. Clin. Nutr. 62 (2008) 849–855.
[19] M.G. Averya, Michaelsb, Strategies for Safe living after solid organ transplantation R. K, Am. J. Transplant. 13 (2013) 304–310.
[20] R.V. Tauxe, K.E. Johnson, J.C. Boase, S.D. Helgerson, P.A. Blake, Control of day care shigellosis: a trial of convalescent day care in isolation, Am. J. Publ. Health 76 (1986) 627–630.