SHORT REPORT: EMERGENCE OF SHIGA TOXIN 1 GENES WITHIN SHIGELLA DYSENTERIAE TYPE 4 ISOLATES FROM TRAVELERS RETURNING FROM THE ISLAND OF HISPÁNOLA

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Abstract. Shiga toxins are produced by Shigella dysenteriae type 1 and certain strains of Escherichia coli. Three cases of Shiga toxin–producing S. dysenteriae type 4 were identified among travelers to the island of Hispaniola between 2002 and 2005. Clinical and public health practitioners should be aware of this newly identified strain.

Shiga toxin (Stx, also referred to as verotoxin or verocytotoxin) is produced by the Shiga bacillus Shigella dysenteriae type 1 (Sd1), which was first described by Kiyoshi Shiga in Japan in 1898.1 In contrast, Shiga toxin 1 (Stx1), which is almost identical to Stx, and the closely related Shiga toxin 2 (Stx2) are primarily produced by Shiga toxin–producing Escherichia coli (STEC). Although these enteric pathogens all cause bloody diarrhea and life-threatening extraintestinal complications, such as hemolytic-uremic syndrome (HUS), seizures, and coma, their epidemiology and treatment are quite different.

Sd1 causes endemic bacillary dysentery in the developing world, affecting primarily children.2 It has caused large outbreaks in Central America, Africa, and Asia.3-5 Sd1 infections are associated with poverty and unsanitary, overcrowded conditions, where person-to-person or waterborne transmission is common. Humans and higher-order primates are the only hosts for Sd1. Antibiotics are the recommended primary treatment of Sd1 infections.

In contrast, STEC, notably E. coli O157:H7, has rarely been reported in developing countries in Africa or Asia where Sd1 is typically seen. However, E. coli O157:H7 has caused many outbreaks in Canada, Japan, the United Kingdom, and the United States.6 STEC colonize cows and other ruminants, and infection is commonly transmitted through meat or produce contaminated with animal feces.

The presence of Shiga toxins is known to increase the virulence of these bacteria and cause vascular damage in the colon, kidneys, and central nervous system.7 Shiga toxins are encoded in bacteriophages and thus may be transmitted horizontally.8 Production of Shiga toxins has been reported in rare instances with other bacteria, such as Citrobacter freundii, Aeromonas hydrophila, Aeromonas caviae, and Enterobacter cloacae.9 There has been one report of Stx1 production by Shigella sonnei in a patient who had traveled to Ukraine.10

We report three cases of Stx1-producing S. dysenteriae type 4 (Sd4) infection identified between 2002 and 2005 among travelers to the Caribbean island of Hispaniola, which contains two countries: Haiti and the Dominican Republic. Each case was reported to the CDC by state health departments. Retrospectively, state and local health departments obtained medical records for each patient. At the CDC, each isolate underwent polymerase chain reaction (PCR) testing for virulence marker genes, including stx1, stx2, eae, E-hly, and ipaH,11,12 antimicrobial susceptibility testing, and pulsed-field gel electrophoresis (PFGE) analysis.13

Case A. A 29-year-old male barber with a history of irritable bowel syndrome presented at a Massachusetts emergency room on November 19, 2002 and was admitted with complaints of 3 days of fever, anorexia, nausea, severe constipation, abdominal pain, and bloody diarrhea. He reported travel to Port-au-Prince, Haiti, from November 3 to 13. His vital signs were normal except for a temperature of 99.5°F, and physical exam was unremarkable except for moderate tenderness of the left lower to mid-quadrant. There was no rebound or guarding. Hematology and chemistries were unremarkable. Stool culture was negative for Giardia, Cryptosporidium, coccidia, ova, and parasites, and enteric organisms including Campylobacter, Shigella, and Salmonella. Colonoscopy revealed findings consistent with acute infectious colitis, and biopsies showed focal active colitis in the transverse colon, likely of infectious etiology. The patient received gatifloxacin and metronidazole in the hospital and was discharged on these same antibiotics on November 21. A stool specimen was forwarded to the Massachusetts Department of Public Health, where Shiga toxin testing (Meridian Premier EHEC kit; Meridian Diagnostics, Cincinnati, OH), used as a screen for STEC infections, was positive, and S. dysenteriae type 4 was subsequently isolated.

Case B. A 17-year-old male resident of Florida presented to an outpatient pediatric clinic on August 6, 2004, complaining of 5 days of fever, weakness, anorexia, abdominal cramping, and non-bloody diarrhea. He had traveled to Santo Domingo, Dominican Republic, in the week before symptom onset. Giardia was suspected, and the patient was treated with metronidazole, with improvement within 2 days. Stool cultures yielded S. dysenteriae. Results of Giardi testing were not available.

Case C. A 3-year-old boy presented to a pediatric clinic in Wisconsin on January 22, 2005 with 4 days of anorexia, 2-lb. weight loss, abdominal cramps, and bloody diarrhea. The child traveled to an all-inclusive resort in Punta Cana, Dominican Republic, from January 14 to 21, 2005; both parents, two grandparents, and other members of the traveling party reported a similar illness. The physical exam was unremarkable. On January 25, the patient had not improved with supportive care, and amoxicillin was prescribed after stool cultures revealed S. dysenteriae resistant to trimethoprim-sulfamethoxazole. By January 27, the patient was asymptomatic.

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atic. Stx1-producing Sd4 was subsequently identified by the Wisconsin State Laboratory of Hygiene.

Sd4 was isolated in each of the three cases; each isolate was positive for stx1 and ipaH genes and negative for stx2, eae, and E-hly genes by PCR testing. All three isolates had identical antimicrobial susceptibility profiles: resistant to streptomycin, tetracycline, and trimethoprim/sulfamethoxazole; the PFGE patterns with both XbaI and BlnI restriction enzymes were indistinguishable. For comparison, the four other Sd4 isolates at the CDC, sent to the CDC between 1996 and 2003, also underwent PCR testing and PFGE analysis. All were negative for stx1, and all four had PFGE patterns with the XbaI and BlnI restriction enzymes that were different from the Stx1-producing Sd4 pattern.

This is the first report to our knowledge of Stx1-producing Sd4, which may be endemic in the island of Hispanola. Because of frequent airline travel between Haiti, the Dominican Republic, and the United States and Europe, it is likely that infections caused by this organism will be seen again in the United States and other countries. Sd4, like Sd1, can cause outbreaks of bacillary dysentery, as was recently reported in Bangladesh. Because of the frequency of multi-drug resistance among Shigella, some cases may not be adequately treated, increasing the risk of transmission. Case C’s mother operated an in-home day care, and careful monitoring by the local health department may have averted an outbreak in a non-immune population.

WHO guidelines for the control of dysentery include treatment with fluoroquinolones and supplementation with zinc for all patients with shigellosis. In the United States or other areas where fluoroquinolones are not routinely recommended for children, azithromycin may be an effective alternative.

Cases can go undetected because persons with mild infections may not seek medical care, and stool culture may not detect the organism, as shown by Case A. Although stool culture is the standard clinical diagnostic method, it may fail to detect a substantial proportion of Shigella cases. These cases emphasize the importance of routine Shiga toxin testing among persons with bloody diarrhea or severe non-bloody diarrhea associated with foreign travel.

Although the increased use of Shiga toxin testing in clinical laboratories represents important progress for both diagnosis and public health surveillance, failure to follow up positive Shiga toxin tests with culture is an area of increasing concern. This can result in incorrectly diagnosing STEC infection and patients not being prescribed antibiotics when actually indicated for treatment. Also, if culture is not routinely performed, cases may escape public health detection, and outbreaks or trends in incidence may go unrecognized.

Microbiologists, clinicians, and public health authorities should be aware of this newly identified strain and further study its microbiologic, clinical, and epidemiologic characteristics, including its prevalence in the island of Hispanola. Clinical and public health laboratories should routinely perform Shiga toxin testing on specimens from patients with bloody diarrhea or severe travel-associated diarrhea, and follow up positive results with culture and reporting.

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