Toxic Shock–Like Syndrome Associated with Staphylococcal Enterocolitis in an HIV-Infected Man

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A human immunodeficiency virus–infected individual developed severe secretory diarrhea due to infection with Staphylococcus aureus. When octreotide therapy was initiated, a toxic shock–like syndrome developed that was associated with fever, multisystem organ damage, and ultimately, desquamation of the palms and soles. The isolate was methicillin susceptible and produced enterotoxins B and C. This is, to our knowledge, the first reported case of toxic shock syndrome to develop secondary to staphylococcal enterocolitis in an adult.

Diarrhea in HIV infection is multifactorial in etiology; may be caused by unusual, novel, or multiple pathogens; and is often long term [1]. Although food poisoning from ingestion of preformed Staphylococcus aureus toxin is a well-recognized gastrointestinal syndrome, and although both antibiotic-associated and nosocomial cases of staphylococcal enterocolitis have been reported [2, 3], S. aureus infection is not commonly considered to be a cause of diarrhea in HIV-infected individuals. We describe an HIV-infected man with secretory diarrhea caused by S. aureus enterocolitis who developed a toxic shock–like syndrome (TSS) when the diarrhea was controlled pharmacologically.

Case report. A 54-year-old diabetic, homosexual man presented to a health care facility with diarrhea and dehydration.

His HIV serostatus was unknown. Multiple stool evaluations for enteric bacterial pathogens, parasites, and Clostridium difficile toxins A and B had negative results. The patient responded to rehydration and was discharged, but he was readmitted 1 week later because of continued diarrhea and recurrent azotemia (blood urea nitrogen level, 83 mg/dl; serum creatinine level, 7.1 mg/dl). Stool evaluations again had negative results. Colonoscopy was performed, revealing few cytomegalovirus inclusions but no inflammation. Treatment with oral valganciclovir (450 mg twice per day) was initiated, and the patient was discharged. During the second hospital visit, the patient was found to be HIV seropositive, with a CD4+ lymphocyte count of 117 cells/mm3 and a plasma HIV RNA level of 15,000 copies/mL. Trimethoprim-sulfamethoxazole therapy was administered for Pneumocystis pneumonia prophylaxis, but treatment was switched to atovaquone after 3 days because the patient developed a rash.

The patient’s diarrhea worsened, despite anti–cytomegalovirus infection therapy, and he was readmitted to the hospital 2 weeks later. He was hypotensive on physical examination. A mild, diffuse, erythematous, maculopapular eruption was noted on the patient’s trunk and back that was attributed to the prior exposure to trimethoprim-sulfamethoxazole. Severe azotemia with acidosis and an elevated anion gap, progressive anemia, thrombocytosis, leukopenia, neutropenia, elevations of liver function, and a further decrease in CD4+ lymphocytes to 50 cells/mm3 were found. Treatment with intravenous fluids and abacavir-lamivudine plus efavirenz was initiated.

Upper gastrointestinal endoscopy demonstrated grossly normal mucosa; examination of tissue biopsy samples also had normal findings. Colonoscopy revealed grossly abnormal ileal mucosa with villus flattening, and there was marked colonic edema. Biopsies of tissue samples obtained from the ileum and colon demonstrated superficial acute inflammation, mild chronic inflammation in the lamina propria, and evidence of epithelial cell injury and focal architectural disarray. Many cocci adherent to the superficial epithelium were observed under light microscopy (figure 1A), and electron microscopy revealed clusters of organisms in close apposition to injured epithelial cells (figure 1B). Rare cytomegalovirus inclusions, but no acid-fast or protozoal organisms, were observed. The same day, stool culture findings reported moderate S. aureus that was susceptible to methicillin and most other antistaphylococcal antibiotics but was resistant to penicillin.
The patient required ~9 L/day of intravenous fluids, plus ≥2 L/day administered orally, to maintain hydration status. Loperamide and tincture of opium were added, but copious diarrhea persisted and severe azotemia recurred. Pharmacologic control of diarrhea was sought using octreotide in ascending doses to 250 μg subcutaneously every 8 h, after which the volume of diarrhea decreased substantially.

The patient then became febrile (temperature, 41°C) and developed a left brachial vein thrombosis. Despite administration of anticoagulation therapy with low molecular weight heparin, and tincture of opium were added, but copious diarrhea persisted and severe azotemia recurred. Pharmacologic control of diarrhea was sought using octreotide in ascending doses to 250 μg subcutaneously every 8 h, after which the volume of diarrhea decreased substantially.

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Reports of the first cases of hospital-associated staphylococcal enteritis were published in 1942, and the first case of antibiotic-associated staphylococcal enteritis was published in 1948 [13]. Many reports followed in the ensuing 2 decades, after which this entity virtually disappeared from the literature for more than a decade, before reemerging [2, 3]. As suggested by Rhee et al. [14], this might be explained in part by changes in antibiotic use patterns. Early antibiotics inhibited neither S. aureus nor Clostridium difficile, allowing either species to overgrow, whereas clindamycin, used during the 1970s and early 1980s, inhibited S. aureus but not C. difficile. The more recent increased use of metronidazole, which has activity against C. difficile but not against S. aureus, may be associated with re-emergence of this organism. Previous use of vancomycin for antibiotic-associated colitis, generally presumed to be due to C. difficile toxins, also may have masked disease caused by S. aureus.

Observations in this case and from older clinical descriptions suggest that staphylococcal enterocolitis and C. difficile colitis might be differentiated on clinical grounds. The diarrheal syndrome in patients with C. difficile colitis is typical for patients with colitis—that is, frequent, small-volume bowel movements, but infrequent dehydration. In contrast, staphylococcal enteritis affects both the small and large intestines and fluid losses may be great, as suggested by Bartlett [13]. A 1953 editorial in the New England Journal of Medicine on the topic of antibiotics and staphylococcal enteritis [15] specifically mentioned that the diarrheal syndrome often resembled cholera. In our case, the ileum was severely affected, resulting in copious diarrhea and necessitating fluid replacement with $>10$ L of fluid per day by combined oral and parenteral routes.

To our knowledge, no studies have specifically compared the histopathology of S. aureus- and C. difficile-related colitis. C. difficile is well known to produce a pseudomembranous colitis, although not all cases demonstrate pseudomembranes, with ischemic features that are most prominent histologically. In contrast, the colonic and ileal mucosae in this case and in some published reports were edematous diffusely, without pseudomembranes, ulcerations, or other mucosal lesions.

This case also illustrates the potential dangers of administration of antidiarrheal therapy in cases of infectious enteritis. Although guidelines usually proscribe antidiarrheal agents for patients with bloody diarrhea or proven infections with Shiga toxin-producing Escherichia coli, our patient had nonbloody diarrhea, and antidiarrheal use was prompted by volume of hydration required. Octreotide, an octapeptide of somatostatin well known for its ability to inhibit intestinal and pancreatic fluid secretion, is effective in the treatment of some patients with AIDS who have severe diarrhea [16]. However, its use appears in this case to have promoted full expression of TSS, because clinical progression was temporally related to treatment-associated reduction in stool volume. The possible mechanism is a decrease in fecal clearance of luminally produced toxin, allowing for greater transmembrane uptake.

In summary, this case demonstrates that TSS may develop as a consequence of staphylococcal enterocolitis. As such, these observations suggest that the gastrointestinal tract may be an important reservoir of S. aureus.

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**References**