Not all pseudomembranous colitis is caused by *Clostridium difficile*

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A 43-year-old woman presented to hospital with a two-day history of acute left lower quadrant pain, nonbloody diarrhea and one episode of bilious emesis. She had a history of complicated systemic lupus erythematosus including end-stage renal disease requiring chronic hemodialysis. She had a remote history of pulmonary tuberculosis that had been appropriately treated. Four months earlier, she was admitted with community-acquired pneumonia and treated with 10 days of levofloxacin. There was no recent travel history, infectious contacts or suspicious food consumed, and no family history of inflammatory bowel disease. She immigrated to Canada from Cambodia in 1988, but had never returned to visit. Her medications included long-standing prednisone (15 mg daily), azathioprine, levothyroxine, carvedilol, pantoprazole, acetylsalicylic acid and pravastatin.

Her examination revealed a fever of 39°C, pulse rate of 103 beats/min, a left sternal heave, a grade 2/6 systolic murmur at the left lower sternal border radiating to the apex with an S4, and a tender abdomen in the left lower quadrant without rebound or guarding. Laboratory results revealed a total leukocyte count of 12.4×10^9/L with a normal differential, and normal liver enzymes and serum lipase. Her blood cultures were negative. Abdominal x-rays showed mural thickening in the splenic flexure and descending colon, but no evidence of obstruction. An abdominal computed tomography scan revealed evidence of pancolitis. She underwent sigmoidoscopy which demonstrated only pseudomembranes on rectal biopsy. However, stool enzyme immunoassays for *Clostridium difficile* toxins A and B (C *difficile* ToxA-BII, Techlab, USA) were repeatedly negative; she did not respond clinically to oral metronidazole, and a repeat sigmoidoscopy one week later was unchanged. A diagnostic test was performed. What is the diagnosis?

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DIAGNOSIS

Although no parasites had been seen on the rectal biopsy, stool analysis revealed moderate amounts of larvae of *Strongyloides stercoralis* supporting the diagnosis of *Strongyloides* hyperinfection. Interestingly, the patient's peripheral eosinophil cell count was 0×10^9/L.

DISCUSSION

Manifestations of *S stercoralis* can include coughing and wheezing due to larval migration, or a wide array of gastrointestinal symptoms including abdominal pain, diarrhea, constipation, weight loss, bowel obstruction or gastrointestinal bleeding. In retrospect, our patient had a two-month history of perianal and generalized pruritis, as well as intermittent abdominal cramps and loose stools. The severity of her presentation is in keeping with *Strongyloides* hyperinfection, a syndrome of accelerated autoinfection with a large burden of organisms confined to organs usually involved in the autoinfective cycle (1); it is distinct from disseminated disease (see below).

Pseudomembranous colitis is an unusual manifestation of hyperinfection; however, endoscopic changes are known to extend from stomach to colon, including friable and edematous mucosa, ulcerations and polyps, as well as exudates or xanthoma-like lesions in the colon. (2). To our knowledge, pseudomembranous colitis has only been reported as a manifestation of *S stercoralis* infection in one other publication (3).

S stercoralis is a potentially life-threatening condition that should always be considered in immunocompromised individuals who originate from endemic areas and have unexplained gastrointestinal or respiratory symptoms. In these hosts, eosinopenia is typical (1). Although eosinophilia is more likely in healthy hosts (4), it is not universal (5,6). Unfortunately, stool examination for parasites and ova using conventional techniques has a low sensitivity and may fail to detect the organism in up to 70% of uncomplicated cases. Various other techniques have been developed to increase detection rates when the helminth is suspected (4). Serology is not rapidly available in many centres and does not differentiate recent from remote infection and, therefore, a high degree of suspicion is required to request special stool detection methods and/or colonoscopy in high-risk individuals.

The *Strongyloides* species is found in Africa, Asia, Southeast Asia, Central and South America, and certain areas of southeastern USA, but is increasingly imported to North America through migration and travel. Our patient had lived in labour camps in Cambodia for five years during the 1970s, followed by another four years in a refugee camp in Thailand. Given the chronicity of this infection, it can cause potentially severe disease in immunocompromised hosts with a remote history of exposure. Severe manifestations range from hyperinfection (which may occasionally be seen in immunocompetent individuals) to the more severe dissemination. The latter is an overwhelming infection with involvement of organ systems outside those of the autoinfective cycle, often associated with sepsis or meningitis with Gram-negative or mixed organisms originating from the gastrointestinal tract. However, the distinction between these entities is artificial and blurred. Risk factors include a broad array of immunosuppressive conditions and medications, among which corticosteroids are particularly common (1).

Although ivermectin monotherapy is usually adequate for immunocompetent hosts, combination treatment with albendazole (400 mg twice a day for seven days) and ivermectin (200 µg/kg once daily for one to two days) has been recommended for immunosuppressed individuals due to the high risk of treatment failures (7). These may need to be continued until there is evidence of clearance in some hosts. Veterinary parenteral formulations of ivermectin have also been used in life-threatening cases (8-10). Ivermectin and albendazole combination therapy resulted in clinical response in our case within two days. The dose of prednisone was tapered to 7.5 mg daily by the time of discharge, and azathioprine was discontinued. However, our patient had a clinical relapse five weeks later, but responded rapidly to retreatment with one week of albendazole and ivermectin combination therapy. She remained symptom-free with negative stool samples after one year of follow-up. *Strongyloides* serology performed at the time of diagnosis and 12 months later showed a decrease in titre from an optical density of 46% to less than 8% (negative), suggesting a satisfactory response (5).

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