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CASE REPORT

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Prolonged ileus as a sole manifestation of pseudomembranous enterocolitis

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Abstract *Background:* Pseudomembranous colitis usually manifests as fever and diarrhea in hospitalized patients treated with systemic antibiotics. We present a case that represents a unique variant. *Case presentation:* The 44-year-old man suffered of several weeks of abdominal pain, low-grade fever, nausea, vomiting, and lack of bowel movements. Upper gastrointestinal barium swallow and passage series revealed evidence of severe intestinal hypomotility. A thorough evaluation for the cause of the patient's ileus and abdominal pain was unrevealing, and symptomatic treatment was ineffective. Following the administration of opiates and dietary fiber supplementation the patient's abdominal pain and distention rapidly worsened, requiring an urgent subtotal colectomy. The macroscopic and microscopic appearance of the excised colon as well as results of the colonic cytotoxin essay and fecal enzyme-linked immunosorbent assay essay confirmed the diagnosis of severe *Clostridium difficile* induced pseudomembranous colitis as the cause of the patient's illness. *Conclusion:* To our knowledge, this is the first reported case of *Clostridium*-difficile induced disease consisting of prolonged ileus in the absence of diarrhea in a patient not previously taking antibiotics.

Keywords Pseudomembranous enterocolitis · *Clostridium difficile* · Ileus · Pseudo-obstruction

Introduction

Pseudomembranous colitis usually manifests as fever and diarrhea in hospitalized patients receiving systemic antibiotics. We present a case of *Clostridium difficile* induced disease in a patient not previously taking antibiotics who had suffered prolonged ileus but without diarrhea.

Case report

A 44-year-old man patient was admitted for examination following 2 weeks of diffuse abdominal pain, nausea, vomiting, and constipation. The patient noted no fever, diarrhea, or urinary symptoms. Significant past medical history included a painful, mainly sensory, nonprogressive peripheral polyneuropathy. It had been thoroughly evaluated previously, with repeated lumbar punctures, spinal magnetic resonance imaging studies, and an infectious, metabolic, autoimmune, and paraneoplastic workup, all yielding negative results. Five years earlier idiopathic recurrent deep vein thrombosis of the calves had required the implantation of an inferior vena cava filter and the administration of chronic warfarin treatment. The patient denied the use of any other prescribed, over-the-counter, natural medications and the abuse of illicit drugs and alcohol.

On admission the patient looked ill, with normal pulse rate, temperature, blood pressure, and arterial oxygen saturation. Physical examination was notable for a mildly distended abdomen with diffusely hypoactive bowel sounds and for the previously known decreased sensation of the distal calves up to the level of the middle-ankle region. Laboratory tests, including complete blood count, renal and hepatic function tests, and erythrocyte sedimentation rate were within normal values, while the international normalized ratio was 2.5 the reference levels due to chronic warfarin treatment. Abdominal computed tomography angiography at admission showed an infrarenal inferior vena caval filter, with normal-looking, nondistended small and large bowels and patent mesenteric vessels. Evaluation during admission included infectious

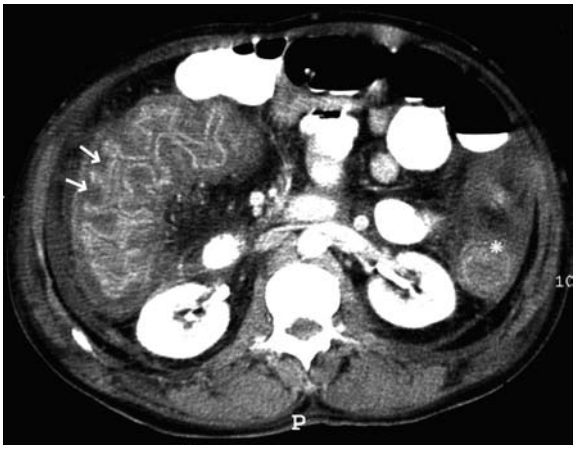

Fig. 1 Abdominal computed tomography section showing a severely thickened and edematous right (*white arrows*) and left (*asterisk*) colonic mucosa

serologies, which were positive for remote infections with Epstein-Barr virus and cytomegalovirus and were negative for human Immunodeficiency virus, syphilis, and hepatitis A, B, and C viruses. Blood, sputum, stool, and urine cultures for bacteria, *Mycobacterium*, and funguses were repeatedly sterile. Autoimmune serology was negative for anti-nuclear factor, anti-phospholipid antibodies, cytoplasmatic and perinuclear anti-neutrophilic cytoplasmatic antibodies, and cryoglobulins, with normal levels of C3 and C4. No paraprotein was found in the patient's serum or urine. Hemoglobin electrophoresis was negative for sickle cell disease and trait. There was no evidence of porphyrins in feces or blood. Vitamin B_{12} and B_1 and folic acid levels were within the normal range, and repeated studies showed no evidence of a hypercoagulable disorder. Endoscopy and duodenal biopsy were normal. Upper gastrointestinal barium swallow and passage series revealed severe intestinal hypomotility and were otherwise unremarkable. A nerve conduction study revealed a mild sensory polyneuropathy of the distal calves, unchanged from a study performed a year earlier.

During the next 18 days the patient's constipation, nausea, vomiting, and several unexplained bouts of low-grade fever slowly progressed, unresponsive to nasogastric decompression, fluid replacement, cathartics, and promotility agents. On the 19th day he was given a therapeutic trial of high-fiber diet and mistakenly a few courses of an opiate-containing antipain medication, shortly after which he developed a marked aggravation of his abdominal pain and distention, with concomitant worsening of his nausea and vomiting. Within a day his temperature increased to 39°, pulse rate to 150 bpm, blood pressure dropped to 80/40, white blood cell count increased to $15{,}000\times10^6$, and pH and HCO_3 dropping to 7.2 and 17 mmol/l, respectively. The patient was transferred to an intensive care unit, intubated, aggressively hydrated, and put on a wide-spectrum antibiotic coverage of intravenous vancomycin, ceftazidime, and metronidazole. A repeated infectious workup was negative. Plain abdominal radiography was notable for diffusely widened intestinal loops of bowel, while abdominal computed tomography revealed evidence of severe diffuse mucosal thickening of the entire colon and some of the small intestine, with patent mesenteric vessels, and no sign of colonic perforation or megacolon (Fig. 1).

Despite aggressive treatment the patient's condition continued to deteriorate rapidly, requiring an urgent exploratory laparotomy, which revealed inflammation of the entire colon and distal ileum, without evidence of perforation, abscess formation, or adhesions. Subtotal colectomy and resection of the distal ileus was performed, with ileostomy formation. Pathology results of the excised colon and ileum showed severe pancolitis and ileitis, with pseudomembrane formation, deep mucosal ulceration, and an intense, mainly neutrophilic inflammatory exudate extending to all layers of the colon and ileum. Colonic *Clostridium difficile* cytotoxin essay was positive for the presence of *C.difficile* toxin A and B. Neither crypt abscesses in the intestinal wall nor vasculopathy, vasculitis, and thrombus formation in mesenteric arteries and veins were noted. The mesenteric nervous system showed no evidence of any pathological process such as inflammation, demyelinization, or axonal degeneration. Several stool samples taken shortly before surgery returned positive for *C. difficile* toxin A and B by enzyme-linked immunosorbent assay and were negative for the presence of *Shigella*, *Salmonella*, *Campylobacter*, and intestinal parasites.

It was concluded that the patient's prolonged ileus was a result of an atypical clinical variant of *C. difficile* infection, without a prior documented use of antibiotics and without diarrhea. The slowly progressive colitis was probably aggravated by the use of opiates and high fiber diet. Following a long rehabilitation process the patient's clinical condition gradually improved, and he finally regained regular bowel movements through his fully functioning ileostomy. The abdominal pain, which has originally brought him to medical care, completely resolved. He is intended for ileocolic reimplantation in the near future.

Discussion

C. difficile infection is a common nosocomial disease, usually caused by alteration of the normal intestinal flora secondary to exposure to systemic antibiotics [1]. Clinically this infection causes a wide spectrum of illnesses, ranging from an asymptomatic carrier state [2, 3] and colitis with or without pseudomembrane formation [4] to life-threatening severe pancolitis [5, 6]. Treatment consists of cessation of systemic antibiotics, antibiotic treatment with metronidazole or vancomycin, decompressive colonoscopy, and, infrequently, emergency colectomy [7, 8].

Several rare clinical variants of *C. difficile* infection, described below, pose a great diagnostic challenge for the treating physicians. Due to their rarity their exact prevalence is currently unknown.

Some reported patients suffer of *C. difficile* infection with fever and abdominal pain but with a total absence of diarrhea. Infection in these patients usually leads to severe complications, including fulminant colitis and intestinal perforations, most probably due to a delay in diagnosis [9, 10]. *C. difficile* induced toxic megacolon is an extremely rare complication of severe pseudomembranous enterocolitis, manifesting as diffuse bowel dilatation and systemic toxicity, often leading to life-threatening bowel perforation [11, 12].

Patients suffering of inflammatory bowel disease (IBD) are more vulnerable to *C. difficile* induced disease than the general population. In this group of patients pseudomembranous colitis may present as acute diarrhea imitating IBD exacerbation or even, more rarely, as the first bout of prolonged diarrhea in patients who are only later diagnosed as suffering from IBD. In either case

C. difficile infection is at times erroneously treated with corticosteroids, aggravating the pseudomembranous colitis [13].

Other rare presentations of *C. difficile* infection include protein-losing enteropathy [14], intussusception in adults [15], colonic volvulus [16], chronic relapsing colitis in young children leading to failure to thrive [17], colitis accompanied by extracolonic manifestations [18], enteritis after proctocolectomy [19], colitis induced by cancer chemotherapy [20], and pseudomembranous colitis presenting as an acute abdomen [21]. One other reported patient has suffered of *C. difficile* infection presenting as acute intestinal pseudo-obstruction without diarrhea [22]. In contrast to our reported patient, his pseudo-obstruction followed a recent antibiotic treatment for pneumonia, while his abdominal complaints only lasted 1 week. Conservative treatment including hydration, colonic decompression and treatment with intravenous metronidazole resulted in his full recovery. Our patient is the first documented case of *C. difficile* causing a prolonged (over 3 weeks) ileus in the absence of diarrhea, signs of toxic megacolon or acute abdomen, or a previous exposure to systemic antibiotics. Although our patient has previously suffered of several chronic illnesses, including a hypercoagulation tendency and a mild sensory polyneuropathy, his repeated computed tomography angiography, intestinal pathology results, and positive *C. difficile* toxin essays are all in strong favor of *C. difficile* being the only causative agent of his prolonged ileus. We believe that if it were not for the high fiber supplementation and opiate treatment given prior to our patient's final deterioration, his unexplained ileus would have lasted even longer before the correct diagnosis reached. Earlier gastroenterological surgical consultation and intervention may be appropriate in similar future cases.

A possible mechanism for this rare variant is the well-known in vitro inhibitory effect of *C. difficile* toxin B on spontaneous and carbachol-induced intestinal smooth muscle activity [23]. In a rare susceptible patient *C. difficile* infection may cause a clinically significant toxin B mediated inhibition of colonic smooth muscle function, resulting in intestinal ileus and pseudo-obstruction. Our patient's peripheral polyneuropathy could have theoretically involved his mesenteric nervous system, making him such a susceptible person.

In conclusion, we suggest that *C. difficile* infection be considered in the differential diagnosis of any patient suffering of prolonged ileus, even in the absence of a prior exposure to systemic antibiotics. This rare variant should be added to the list of unusual manifestations of *C. difficile* infection. Until a larger, population-based trial establishes the prevalence of this and other rare variants, a high clinical index of suspicion is needed for the early recognition and treatment of this potentially life-threatening *C. difficile* infection.

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