Toxic megacolon due to fulminant *Clostridium Difficile* colitis

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To the editor

A 92 year-old male patient was submitted for an elective right nephrectomy for kidney adenocarcinoma. Postoperatively, a three-day hospitalization in the ICU was required during which ampicillin/sulbactam was prophylactically administrated. From the 7th to the 9th postoperative day, he developed extensive abdominal distention, diffuse abdominal pain, diminished bowel sounds, fever (> 38.9°C), elevated leukocytosis (WBC 46,200 cells/μL), signs and symptoms compatible with systemic toxicity (hypotension and tachycardia), but no diarrhea. Plain Abdominal X-ray disclosed a toxic megacolon (transverse colon diameter > 10 cm) and absence of air in the rectal lumen, without radiological signs of obstructive ileus or volvulus. Colonoscopy with minimal gas insufflation, showed an inflamed and edematous mucosa with numerous discrete raised nodular lesions covered with yellow exudates up to the splenic flexure in a dilated and non-peristaltic bowel (Fig. 1). Stool cultures were positive for *clostridium difficile*.

Based on the above, the diagnosis of fulminant colitis was made. Since intracolonic administration of vancomycin was considered risky, the patient was started on intravenous administration of 500 mg metronidazole three times daily and oral administration of 500 mg vancomycin four times daily. A subtotal colectomy with ileostomy on an emergency basis was recommended to the patient's relatives, but they declined. Although the patient's general condition improved over two days, haemodialysis sessions were required and he finally died on the 16th postoperative day.

Clostridium difficile-associated disease, results in a broad spectrum of clinical manifestations ranging from mild gastrointestinal complaints or mild diarrhea to life-threatening pseudomembranous colitis, fulminant colitis, toxic megacolon with septic shock and death (1). Exposure to antibiotics (in order of frequency : clindamycin, ampicillin and/or amoxicillin and cephalosporins) (2), exposure to *Clostridium difficile* (which typically occurs in hospitals) and host factors (the ability of the host's immune system to produce protective antibodies against the toxins of *Clostridium difficile*) play an important role in reducing the severity of disease further preventing recurrences (3) and represent the three main factors which are involved in the pathogenesis of *Clostridium difficile*-associated disease. Fulminant

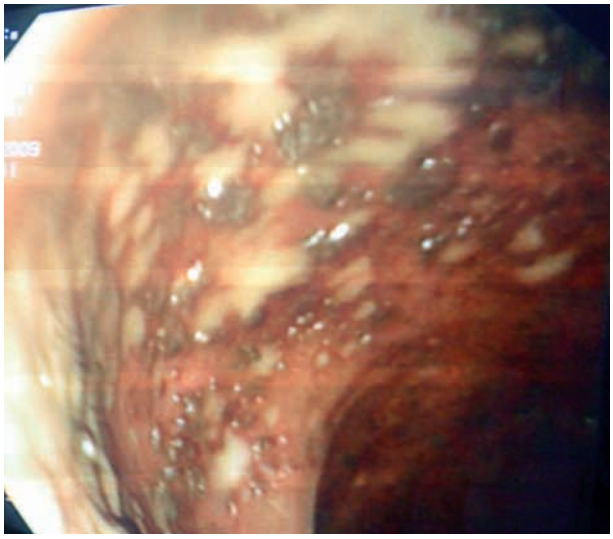

Fig. 1. — Colonoscopic view : Inflamed and edematous mucosa with numerous discrete raised nodular lesions covered with yellow exudates are seen.

Clostridium difficile colitis (FCDC) occurs in 3% of patients with *Clostridium difficile* infection (4). Although there is no specific definition for FCDC, in the majority of the patients the disease presents with severe abdominal pain, distention, dehydration, hypotension, oliguria, azotemia, high fever and marked leukocytosis (up to 40,000 white blood cells/mm3) (5). FCDC is more common in patients with malignant disease, renal failure, immunosuppression or on antiperistaltic agents. Patients with FCDC have a 57% 30-day mortality rate, a 49% in-hospital mortality rate and a 38% 5-year survival rate if they survive longer than 30 days after hospital discharge (6). However, the diagnosis of FCDC remains difficult, while diarrhea is absent in 20% of the patients and these patients are at greatest risk for toxic megacolon development (7). Clinical criteria for diagnosing toxic megacolon are any 3 of the 4 following : (i) temperature greater than 38,6°C, (ii) heart rate greater than

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120 beats/min, (iii) white blood cell count greater than 10.5×10^9/L, or (iv) anemia. Patients should also have one of the following : dehydration, mental changes, electrolyte disturbances or hypotension (8). A radiological diagnosis is established when the transverse or ascending colon are dilated over 6 cm (9).

Metronidazole given intravenously can be used to treat patients who cannot tolerate an oral agent. Intravenous administration of vancomycin is not efficacious, while good results have been reported with intracolonic administration of vancomycin (10). When a patient does not respond to medical therapy within 48-72 hours or when perforation, uncontrolled bleeding, or progressive dilation occurs, subtotal colectomy with ileostomy should be offered as the procedure of choice (8).

The patient we describe, developed FCDC without diarrhea (as it happens in 20% of the cases), because he was elder (92 years-old), immunosuppressed (suffering from renal adenocarcinoma), had been exposed to antibiotics (ampicillin/sulbactam represents the second commonest factor for *Clostridium difficile* infection) and had been exposed to the hospital environment (hospitalization in the ICU) where *Clostridium difficile* is present. Postoperative ileus further predisposed to toxic megacolon development.

In conclusion, patients who are immunosuppressed are more likely to develop FCDC and to have atypical presentations such as absence of diarrhea or toxic megacolon. Thus, any elderly or immunosuppressed patient should be presumed to have *Clostridium difficile* colitis until proven otherwise.

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