Megacolon toxic of idiophatic origin: case report

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Received: 08-08-17
Accepted: 13-04-18

Abstract

Toxic megacolon is a pathology whose mortality rate is over 80%. A progressive inflammatory process compromises the colon wall, and secondary dilation of the intestinal lumen occurs due to inflammatory or infectious processes. Its clinical presentation is bizarre. but the basic pillars for management are opportune diagnosis and adequate medical management with antibiotics, water resuscitation, and metabolic correction. If necessary, effective surgical management can prevent the development of complications that worsen the disease and the prognosis of a patient. In this article we present the case of a patient who died after developing septic shock secondary to toxic megacolon. Cholangitis grade III was suspected, but discarded after ultrasonography, and this resulted in generated distortions in approach and initial management. Due to clinical deterioration and abdominal distension, the patient underwent diagnostic laparoscopy which revealed severe ischemic compromise of the entire colon but without involvement of the small intestine. For this reason, a total colectomy was performed. The pathology report and clinical history ruled out ulcerative colitis or Crohn's disease which confirmed the diagnosis of toxic megacolon. The patient had no risk factors for the development of pseudomembranous colitis. We conclude that this was a case of idiopathic toxic megacolon.

Keywords

Toxic megacolon, infectious colitis, acute abdomen, colitis, cholangitis, sepsis.

INTRODUCTION

Toxic megacolon (TM) was first described in 1950 as a complication due to Clostridium difficile infection characterized by progressive inflammation that compromises all four layers of the colon and is associated with dilation of more than six cm of a segment or the entire circumference of the opening. (1, 2) Mortality rates range from 19% to 80%, and incidence varies depending on cause. For ulcerative colitis, the incidence ranges from 2.5% to 17% while for pseudomembranous colitis it ranges from 0.4% to 3%. Incidence has increased value due to indiscriminate use of antibiotics. (3-5)

The classic etiology of TM is ulcerative colitis, but Crohn's disease has gradually taken its place since 1950 when it was discovered to predispose patients to TM. (6) Other etiologies have also been identified. They include Shigella, salmonella, entamoeba, campylobacter, ischemic colitis, cytomegalovirus (CMV) and Kaposi's sarcoma in immunosuppressed patients (2, 6).

Risk factors for development of TM in patients with infectious colitis include discontinuation of steroid treatment, use of barium enemas and drugs that reduce colon motility such as narcotics, antidiarrheal agents and anticholinergic agents. Since clinical presentation occurs very infrequently, the clinical criteria elaborated in 1969 continue to be accepted. The key indicators are a fever over 38.6 ° C (101.5 ° F), heart rate over 120 beats per minute, leukocytes over 10.5/ μL, and anemia indicated by hemoglobin less than 7 g/dL.

TM can also be associated with any of the following: dehydration, hypotension, electrolyte disturbances and changes in mental state. (7)

The pillars of TM management are rehydration, correction of electrolytes, administration of blood products, management of immunosuppressive therapy and timely antibiotic treatment. (3, 8, 9). The absolute indications for surgery include signs of organ failure, shock, uncontrollable low gastrointestinal bleeding, evidence of perforation, acute abdomen and progressive colonic dilation after 24 to 72 hours of medical treatment. (10-12)

We present the case of a patient with sepsis of abdominal origin. The initial focus was typical cholangitis, so diagnostic laparoscopy was performed due to clinical deterioration. Macroscopic evidence of TM led to total colectomy plus ileostomy. This diagnosis was subsequently confirmed by the pathology report. On this occasion, no clear etiology was found, so this episode of TM was classified as of possible idiopathic origin.

CLINICAL CASE

The patient was a 54-year-old woman with a history of hypertension, hypothyroidism and morbid obesity (body mass index [BMI]: 50.2). Her conditions were being managed with verapamil, levothyroxine, acetylsalicylic acid and atorvastatin. She was admitted to a level one emergency department after four days of fever, right hemisphere abdominal pain radiating to the ipsilateral lumbar region, asthenia, adynamia and tremors. The first level paraclinical tests found thrombocytopenia, so they remitted her to a more advanced level hospital due to their suspicion of arbovirus.

She was admitted to the emergency department in poor condition with rapid respiration, dehydration, fever and somnolence. She subsequently developed respiratory insufficiency and was rapidly intubated without complications. She was transferred to the intensive care unit (ICU), and additional paraclinical tests found thrombocytopenia (70,000), metabolic acidosis with hyperlactatemia and kidney injury Acute Kidney Injury Network (AKIN) level III kidney damage. It was considered that the patient was suffering from septic shock and possible pyelonephritis, so treatment with antibiotics using piperacillin tazobactam was combined with resuscitation by goals, inotropic support, management of comorbidities and microbiological tracking.

Her evolution during her hospital stay was torpid. She presented oligoanuria, distal hypoperfusion, borderline blood pressure and jaundice in the sclera. Follow up tests showed that her leukocytosis had increased and also indicated neutrophilia, thrombocytopenia, moderate metabolic acidosis with an elevated anion gap, normal transaminases and amylase, renal function deterioration, and direct hyper-

bilirubinemia with an obstructive pattern. Her chest X-rays were normal. Hepatobiliary ultrasound was requested due to a suspicion of type III cholangitis secondary to obstruction of the biliary tract, and antibiotic management was staggered with ertapenem. Due to deterioration of renal function, she was evaluated in the nephrology service which initiated renal replacement therapy with hemodialysis. The results of requested blood cultures reported findings of multi-resistant Escherichia coli. A urine culture was negative (Table 1).

Since the ultrasound report did not show a vesicular lithiasis or dilation of the bile duct, a septic process of biliary origin was ruled out. Subsequently, abdominal distension became evident in the patient. The general surgery service performed diagnostic laparoscopy and found evident amounts of free fluid in the abdominal cavity, predominantly from a right parietal colic leak associated with marked distention of the entire colon but with no evidence of mechanical obstruction. The procedure was converted into exploratory laparotomy due to findings of TM (Figure 1) and a total colectomy plus ileostomy was performed. In addition, patient was treated with ceftriaxone, oral vancomycin and metronidazole for c. difficile, salmonella, Shigella and campylobacter.

Figure 1. Total colectomy, suspicion of toxic megacolon.

PATHOLOGY REPORT

The pathology report for the colon and a segment of the terminal ileum showed TM with severe luminal dilation

Table 1. Principal paraclinical test results during hospital stay

Paraclinical test	1	2	3	4	5
Leukocytes	7000	9300	16 400	28 300	39 400
Neutrophils (%)	77	89	82,2	91,1	91
Hgb	12	12	10,3	9,4	8,6
Platelets	69 000	79 000	49 800	53 000	41 000
CRP	Negative			48	
AST		64	89		72
ALT		40	28		44,6
PT/PTT/INR		Normal		Normal	Normal
Sodium		134	135	137	
Potassium		3,7	4,31	4,6	
Chlorine		102	104	107	
Calcium		1,01	1,04	1	
Cr/BUN	1,85/31	1,55/36	3,68/45,3	4,32/55,8	4,07/56,8
Total bilirubin		2,43	3,25	1,8	1,53
Direct bilirubin		1,47	2,2	1,3	0,99
Alkaline phosphatase		671			885
Amylase		35			21
Arterial gases					
pH		7,16	7,22	7,20	
PCO$_2$		46	37	35	
HCO$_3$		16	15,4	13	
PO$_2$		145	145	153	
Lactate		4,1	1,7	1,6	
Excess base		-11	-11	-13,3	
HBsAg					Negative
VDRL					Negative
HIV					Negative

BUN: blood urea nitrogen; Cr: creatinine; HBsAg: hepatitis B surface antigen; HCO3: bicarbonate; INR: international normalized index; PCO$_2$: partial carbon dioxide pressure; CRP: C-reactive protein; PO2: partial oxygen pressure; PT: prothrombin time; PTT: partial thromboplastin time; AST: Aspartate transaminase; ALT: alanine transaminase; VDRL: Venereal Disease Research Laboratory test; HIV: human immunodeficiency virus.

of the cecum to the sigmoid measuring 22 cm in circumference and 107 cm in length. It also showed flattening of the mucosa and peripheral layers of the wall without inflammation of the mucosa or wall, suggestive of ulcerative colitis or Crohn's disease.

During the postoperative period, the patient improved clinically in terms of leukocytosis, increased urinary output, decreased Cr and a better pattern of arterial blood gases. Vasopressor support was decreased. On the other hand, no signs of infection were observed in the surgical wound. On the eighth day following surgery the patient had no need for respiratory support and was hemodynamically stable. Sudden onset of dyspnea was observed with evidence of cardiorespiratory arrest. The blue code for advanced resuscitation maneuvers was activated. After 20 minutes without success, the patient succumbed with pulmonary thromboembolism as a possible cause of death.

DISCUSSION

TM is a lethal disease whose general incidence is difficult to determine given current available literature. Nevertheless, it has been determined that its incidence is closely related to its cause. According to some studies, ulcerative colitis is six times as likely to lead to the development of TM than is Crohn's disease. (3) One study that included 1,236 hospitalized patients has shown an incidence of 10% for these two pathologies. (4)

At present, the incidence of TM secondary to pseudomembranous colitis is considered to be approximately 0.4% to 3% of cases. This rate has been increasing in the last decade due to the deliberate use of antibiotics which has caused adaptive genetic changes microorganisms resulting in higher levels of virulence and the consequent emergence of strains resistant to conventional treatments. These strains include BI/NAP1/027. (13-15)

Although the pathophysiological mechanism of this disease has not yet been fully elucidated, some studies show severe and progressive infiltration of the neutrophil-mediated inflammatory response that manages to compromise the mucosa through the smooth muscle layer to the serosa. As inflammation progresses, neutrophils invade the muscle layer and cause additional damage by releasing proteolytic enzymes, cytokines, and leukotriene B4 (LTB4) resulting in dysmotility and consequent secondary dilation of the colon (Figure 2). (1) In addition, infectious agents such as pseudomembranous colitis and toxins A and B of C. difficile can interrupt the epithelial barrier and cause epithelial cell necrosis and electrophysiological changes in the colonic mucosa resulting in marked inflammation of the colon (8).

Commonly, these patients come to emergency services after suffering bloody diarrhea for more than a week. This is often associated with chills, fevers, abdominal pain, and intermittent colic. The onset of TM is inconsistent and can manifest as abdominal distension, diarrhea, constipation, decreased bowel sounds and systemic symptoms such as fever, tachycardia and hypotension. Symptoms may be masked by high doses of corticosteroids or an altered level of consciousness. (1, 3, 7) Diagnosis of TM is based on identification of the clinical picture and clinical criteria described by Jalan in 1969. (16) These criteria are associated with systemic toxicity and radiological and/or ultrasound evidence of dilation of the colon of more than six cm. (7, 17)

A simple abdominal x-ray can identify dilation of the colon up to 15 cm while ultrasound can identify dilation greater than six cm. (17) On the other hand, computerized axial tomography (CT) is useful for determining the causes of abdominal complications. (7) Laboratory results indicating possible TM include leukocytosis or leukopenia associated with neutrophilia and anemia, electrolyte alterations, and alterations of renal, hepatic and/or pulmonary functioning. Patients with leukocytosis of over 40,000 have been described as having poor prognoses. (9) It is necessary to take blood cultures to rule out bacteremia since septicemia occurs in up to 25% of patients with TM. (3) Stool samples should be sent for culturing, and assayed for
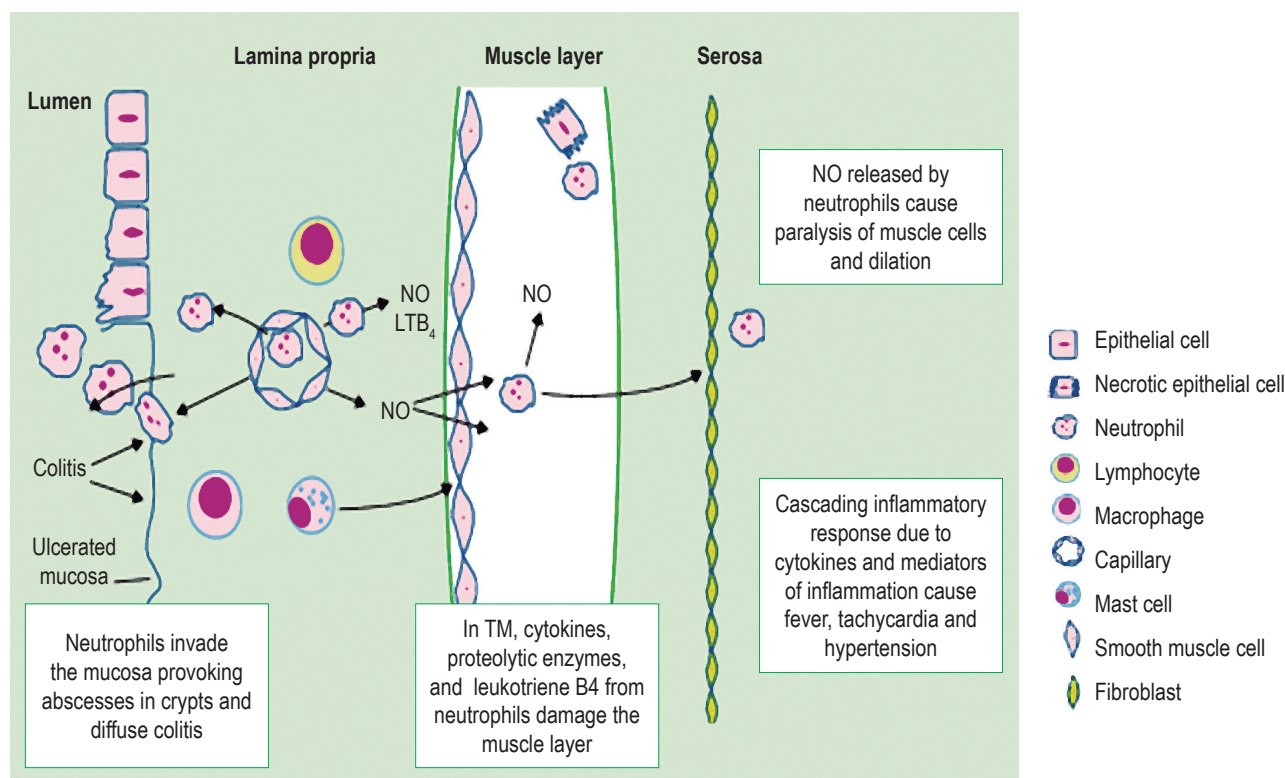

Figure 2. Neutrophil invasion through colon walls. LTB4: leukotriene B4; NO: nitric oxide. Taken from: Sheth SG et al. Lancet. 1998; 351 (9101): 509-13.

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C. difficile toxins A and B for patients with histories of antibiotic use or chemotherapy. Parasite infections should be considered in patients with HIV. (1, 8)

The central components of management include rehydration, correction of hydroelectrolytic disorder, colonic decompression (if possible), administration of antibiotics and pertinent consultation with the general surgery service. Anemia, dehydration and electrolyte deficits, particularly hypokalemia, aggravate dysmotility of the colon and must be treated aggressively. (18) The literature recommends administration of broad spectrum antibiotics such as ampicillin, sulbactam or third-generation cephalosporin together with an aminoglycoside or metronidazole. (9, 19)

The mainstay of medical management of patients with TM caused by ulcerative colitis is high doses of intravenous (IV) steroids. Most authors recommend a daily dose of 400 mg of hydrocortisone (100 mg every 6 hours) or 60 mg of IV methylprednisolone (1 mg/kg) for 5 days. If this management is not effective, rescue therapy with cyclosporine may be considered. (8, 19)

For cases of TM caused by pseudomembranous colitis, predisposing antibiotics should be identified and removed. The most common antibiotics associated with C. difficile are clindamycin, cephalosporins, and fluoroquinolones. (20) Vancomycin associated with metronidazole should be administered as first-line therapy in accordance with current guidelines issued by the Society for Healthcare Epidemiology of America and the Infectious Disease Society of America. In cases in which resistant C. difficile strains NAP1/ BI/027 are suspected or confirmed in cases of TM, Fidaxomicin or a macrolide are the antibiotics of choice. (18, 21)

Timely medical treatment reduces the need for surgery by 50%, (1) but surgical intervention may be necessary in up to 80% of patients, mainly in patients with TM secondary to C. difficile. The surgical treatment of choice for a large number of surgeons is subtotal colectomy plus a mucosal fistula and ileostomy because the rate of morbidity and mortality is less than those of total proctocolectomies. It is very important to have a priority assessment done by the general surgery service since complications and intestinal perforations cause very high percentages of mortality (from 8% to approximately 40%). (1)

Morbidity and mortality rates for TM patients are high, and patients who survive an episode of TM after responding to medical treatment also have poor prognoses of six to twelve months survival. Recurrence rates are over 18%, and recurrence may require colectomy. Among patients with ulcerative colitis who initially respond to medical therapy, 60% will require a colectomy in the following 12 months and 80% will require a colectomy within 5 years of the first event. (8)

In relation to the case presented here, there is very little literature regarding TM cases masked by suspected acute cholangitis. (22). It is important to emphasize that the patient had poor prognostic factors including age over forty, hypoalbuminemia, renal failure and hyperlactatemia. These factors increased her risk of mortality exponentially. In addition, no risk factors for pseudomembranous colitis were identified. After the surgical intervention, the patient presented clear clinical improvement, but a secondary entity, possibly pulmonary thromboembolism, caused death.

CONCLUSIONS

TM is a well-recognized and highly lethal complication of acute colitis. Physicians should expect an increase in the incidence of TM due to the increasing number of acute colitis cases associated with the use of broad spectrum antibiotics and co-infections of strains of hypervirulent C. difficile resistant to conventional therapies.

It is essential that patients with TM be diagnosed quickly and correctly, and managed comprehensively to reduce morbidity and mortality. Emergency physicians can minimize excessive delays in diagnosis by suspecting and ruling out this entity in all patients with abdominal distension, acute or chronic diarrhea, and signs of systemic inflammatory response and, thus, improve the prognoses of these patients.

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