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Toxic megacolon

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ABSTRACT

Toxic Megacolon (TM) is a rare life-threatening clinical entity characterized by total or segmental colonic distension in the setting of acute colitis and signs of systemic toxicity. It arises in a setting of almost any colitis, however ulcerative colitis (UC) and clostridium difficile-associated disease (CDAD) are the most common causes. The mainstays of diagnosis are clinical and laboratory assessment of systemic toxicity and underlying colitis as well as abdominal imaging demonstrating colonic distension. Medical therapy including resuscitation, electrolyte repletion, antibiotics, discontinuation of antimotility agents, and treatment of the underlying colitis is warranted in the absence of severe toxicity, perforation, or severe hemorrhage. However, 25–50% of patients with TM ultimately require colectomy, typically in the form of total abdominal colectomy with end ileostomy.

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Toxic megacolon is a rare life-threatening clinical entity that was first described in 1950 by Marschak. It is characterized by segmental or total colonic distention of 6 cm or greater in the presence of acute colitis and systemic toxicity. It is associated with a mortality of 19%. It is a secondary complication of inflammatory and infectious colitides of multiple causes, most commonly ulcerative colitis (UC) and clostridium difficile-associated disease (CDAD) and is seen as a progression from fulminant colitis. It is differentiated from other conditions causing colonic distention such as colonic pseudo-obstruction and Hirschsprung's disease by its manifestations of systemic toxicity and an underlying inflammatory, infectious, or ischemic process.[1]

Systemic toxicity can be defined by Systemic Inflammatory Response criteria (Table 1), or, if the underlying cause of toxic megacolon is known, more specific criteria (Tables 3 and 4).[2]

Prompt recognition of toxic megacolon, initiation of medical therapy according to cause, and timely surgical intervention are the keys to management and can be life-saving.

Cause, incidence, and pathogenesis

Toxic megacolon was originally recognized as a complication of UC, however it has since become evident that almost any inflammatory condition of the colon could predispose a patient toxic dilation. Other causes include bacterial, parasitic, and viral infections, and ischemic colitis.

The incidence of toxic megacolon varies by cause. In patients with UC, it has been shown to be present in 6% of hospital admissions, with a lifetime incidence of 1–2.5%. The reported incidence of toxic megacolon in CDAD ranges between 0.4% and 3%, however this may be increasing due to increasing incidence of CDAD and the emergence of new strains.

The pathogenesis of toxic megacolon is incompletely understood. It is thought to result from severe colonic inflammation and release of inflammatory mediators that induce smooth muscle relaxation. Toxic megacolon specimens have been found to have a greater depth of inflammatory involvement than patients with fulminant colitis (Fig. 1), with greater inflammation of the circular and smooth muscle layers and higher levels of nitric oxide (NO) synthase. The resulting damage to the muscle and neuronal plexi leads to colonic dysmotility and dilation, and NO-mediated colonic smooth muscle relaxation may further contribute to dilatation. Severe dysmotility and compromised mucosal integrity allow bacterial translocation, leading to the toxic systemic response associated with toxic megacolon.[3,4]

Diagnosis

Toxic megacolon is diagnosed based on the combination of symptoms and signs of systemic toxicity in combination with radiologic evidence of colonic distension. It should be suspected in any patient who presents with diarrhea, abdominal distension, and toxicity. A preceding diagnosis of severe or fulminant colitis can often be elicited.

Clinical presentation and laboratory investigations

In a patient with known UC the underlying fulminant colitis can be diagnosed based on the criteria of modified Truelove and Witts scale[5] (Table 3) Importantly in patients with IBD, toxic megacolon

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Table 1
Systemic inflammatory response syndrome (SIRS) criteria

>=2 of the following
Temperature >38 °C or less than 36 °C Heart rate >90 beats per minute (bpm) Hyperventilation demonstrated by respiratory rate > 20 breaths/min or partial pressure carbon dioxide (PaCO2) < 32 mmHg White blood cell count>12,000 cells/mm^3 or <4000 cells/mm^3 or >10% bands

Table 2
Causes of toxic megacolon

Common
Ulcerative colitis (UC) Clostridium difficile-associated disease (CDAD)
Less common
Crohn's Disease Bacterial – Salmonella, Shigella, Campylobacter, Yersinia Viral – Cytomegalovirus Parasitic – Entamoeba histolytica, Cryptosporidium Ischemic colitis Medications – opioids, anticholinergics, chemotherapy Interventions – colonoscopy, barium enema

Adapted from The Management of Toxic Megacolon, Current Surgical Therapy, 12th ed.

has a propensity to develop in the early stages of disease, with 30% developing in the first 3 months of diagnosis. Therefore the diagnosis should be kept in mind even in patients without an established diagnosis of UC or CD.[4]

In a patient with CDAD, according to the Dallal classification of CDAD severity, fulminant clostridium difficile – associated colitis is diagnosed by the presence of heart rate > 120 beats/min, leukocytosis with more than 30% bands, oliguria, respiratory failure, and pressor requirement. Recent use of antibiotics, conditions predisposing to colonic ischemia, and recent use of medications such as antibiotics, steroids, antimotility, and chemotherapeutic agents are helpful in determining the underlying cause.

Physical exam will reveal abdominal distension, general or localized tenderness, and reduced bowel sounds accompanied with signs of systemic toxicity including fever, tachycardia, and hypotension. Rebound and guarding on abdominal exam are grave signs indicating peritonitis secondary to colonic perforation. Importantly steroid treatment can mask the abdominal exam and signs of systemic toxicity.

Jalan et al. established clinical criteria for the diagnosis of toxic megacolon in 1969[3] (Table 4) Laboratory tests are not specific and in general values associated with systemic inflammatory response are present such as leukocytosis, anemia, elevated erythrocyte sedimentation rate or serum C-reactive protein, and electrolyte abnormalities such as hypokalemia, hypomagnesemia, and hypoalbuminemia. Stool culture and *clostridium difficile* toxin assay should be sent. Blood culture should be sent as bacteremia occurs in 25% of patients with toxic megacolon.

Table 4
Jalan criteria for diagnosis of toxic megacolon

>=3 of the following
Radiographic evidence of colonic dilatation Temperature > 101.5 ° F (38.6 ° C) Heart Rate > 120 beats/min White Blood Cell Count > 10.5 ($\times 10^9$/L) Anemia
And >=One of the following
Dehydration Altered mental status Electrolyte abnormalities Hypotension

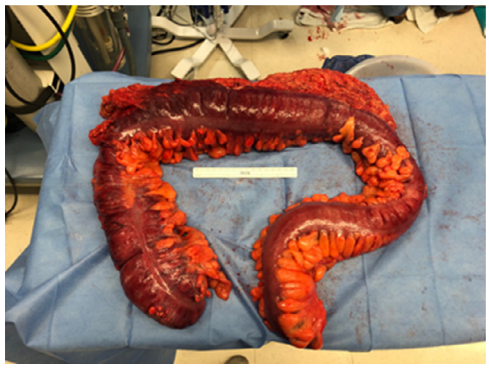

Fig. 1. Colon specimen for toxic megacolon caused by ulcerative colitis demonstrating full thickness abnormalities.

Imaging and endoscopy

Plain abdominal x-rays and computed tomography are imaging mainstays in diagnosis of toxic megacolon (Fig. 2). Plain film typically shows dilation of the ascending and transverse colon, with a transverse colon diameter of greater than 6 cm meeting diagnostic criteria. Serial plain films can be used to follow disease progression. A transverse colon diameter of greater than 8 cm heralds greater risk of perforation. Other findings include colonic air-fluid levels and loss of haustral markings. Gastric and small bowel dilation can be seen as well and are a marker of disease progression to toxic megacolon and multiorgan dysfunction in UC patients. Computed tomography (CT) scan of the abdomen and pelvis can confirm the diagnosis and exclude a distal obstruction as the cause of proximal colon dilatation due to malignancy or diverticulitis (Fig. 3). CT findings such as submucosal edema, colonic wall thickening and pericolic stranding are indicative of severe colitis while free air is indicative of perforation.[3]

Flexible sigmoidoscopy may be considered to determine the underlying cause of toxic megacolon. However generally these patients need immediate surgical intervention. The finding of

Table 3
Modified Truelove & Witts criteria

Variable	Mild disease	Severe disease	Fulminant disease
Number stools/day	<4	4–10	>=10
Blood in stool	Intermittent	Frequent	Continuous
Temperature	Normal	>37.5	>37.5
Pulse	<=90	>90	>90
Hemoglobin (Hgb)	Normal	<75% of normal	Transfusion requirement
Erythrocyte sedimentation rate (ESR)	Normal (=<30)	>30	>30
Abdominal X-Ray	Normal	Edema/thumbprinting	Dilation
Abdominal Pain	None	Mild diffuse tenderness	Distension and tenderness

Adapted from the ASCRS Textbook of Colon and Rectal Surgery, 3rd Ed.

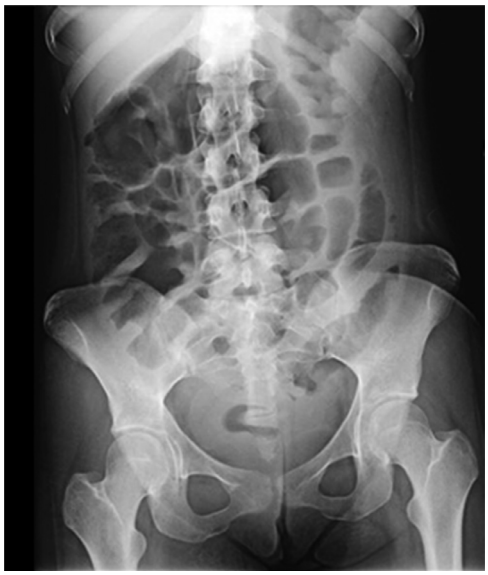

Fig. 2. Abdominal X-ray demonstrating toxic megacolon.

pseudomembranes is indicative of CDAD, whereas ulcerations and bleeding are indicative of UC. Biopsy can determine the presence of cytomegalovirus (CMV) by the presence of inclusion bodies. It should be performed very cautiously, without bowel preparation, and with minimal air insufflation. Complete colonoscopy is contraindicated due to high risk of perforation.[3]

Management

Management of toxic megacolon should involve coordinated medical and surgical modalities and close cooperation between the medical and surgical services. Aggressive attempts of medical therapy should be initiated with early surgical intervention in the absence of improvement or if secondary complication or deterioration occurs.

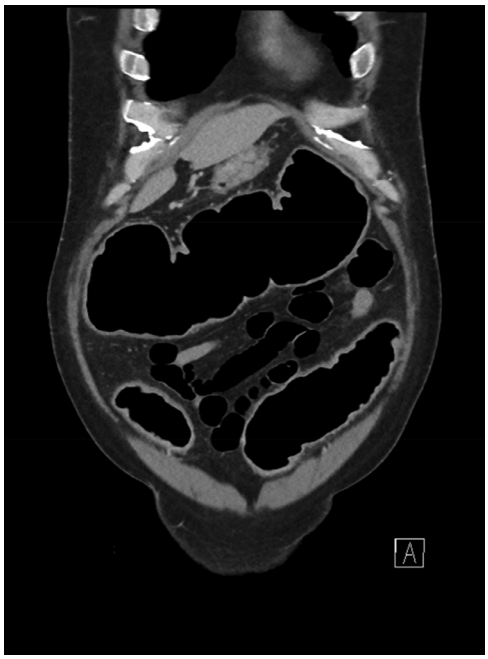

Fig. 3. Coronal computed tomography section demonstrating toxic megacolon. The transverse colon is dilated to 7 centimeters.

Medical therapy

If the patient with megacolon is truly is toxic, surgical intervention is required. However, medical management is important as well. Complete bowel rest and intravenous fluid replacement should be initiated immediately. Early correction of electrolyte abnormalities, particularly hypokalemia should occur as these abnormalities can worsen colonic dysmotility. Opioids, anticholinergics, and any other medications that affect motility should be discontinued. Prophylaxis for deep venous thrombosis should be initiated. Broad spectrum antibiotics have been found to reduce the mortality from septic complications and should be initiated early, while antibiotics that can cause *clostridium difficile* overgrowth should be discontinued.

Several techniques could be considered for decompression. Nasogastric tube suction has not been shown to improve outcomes although it may be considered, especially in cases where gastric and small bowel distension are present. Frequent patient repositioning, or "log rolling" has been shown to lead to colonic decompression in a small series and can be attempted. Patients can be instructed to roll into the prone position for 10–15 minutes every 2–3 hours and attempt to pass gas. This technique had never been validated in a controlled fashion and would be difficult in an obtunded patient.[3]

Frequent clinical reassessment, abdominal exam, electrolyte monitoring, and abdominal x-rays should be performed to assess disease progression and response to medical therapy.

Medical management in inflammatory bowel disease-associated toxic megacolon

High-dose intravenous steroids (hydrocortisone 100 milligrams every 6 hours) should be administered to patients with known IBD who have fulminant colitis. Although there is no evidence that steroid therapy increases perforation risk it may mask the signs of colonic perforation.

Aminosalicylates, anti-tumor necrosis factor alpha medications, and immunosuppressants such as cyclosporine have no role in the treatment of toxic megacolon.[3]

Medical management in clostridium difficile-associated toxic megacolon

If CDAD is suspected as a causal agent of toxic megacolon, immediate withdrawal of offending antibiotics is indicated. Treatment with oral vancomycin (500 milligrams four times daily) and/or oral or intravenous metronidazole is indicated. If a patient cannot tolerate oral vancomycin it may be administered by enema or nasogastric tube.[6]

Surgical management

Timely surgical intervention is crucial to decreasing the morbidity and mortality of toxic megacolon. Strauss et al. reported a slightly higher mortality in medically managed patients than those managed with early surgery (27% vs 19.5%) however medical management has been shown to be successful in 50–70% of patients. Importantly, secondary complications such as colonic perforation and abdominal compartment syndrome substantially increase the mortality rate to 40% and these must be avoided by close surveillance and low threshold to operate in the face of disease progression or signs of deterioration.

Lack of improvement with 48 hours of medical therapy is a relative indication for surgical intervention, while progressive colonic dilation, uncontrolled hemorrhage, clinical deterioration with progressive sepsis and pressor requirements, or complications such as perforation are absolute indices.

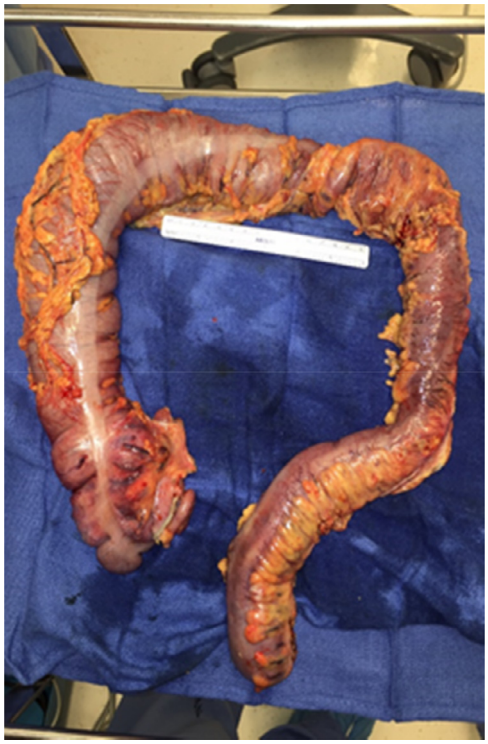

Fig. 4. Colectomy specimen for toxic megacolon demonstrating colonic dilation and transmural changes.

Early discussions regarding need for surgery should be held with the patient and family. An enterostomal therapist should be consulted early to mark the optimal site for ileostomy creation.

Mechanical bowel preparation is contraindicated. An open operation is preferred as significant colonic dilation and friability preclude the laparoscopic and robotic approaches. Furthermore hemodynamic instability necessitates the shortest operating time possible, and hypotension may be worsened by carbon dioxide pneumoperitoneum.[1]

Total abdominal colectomy and end ileostomy

The standard operation for toxic megacolon is total abdominal colectomy with end ileostomy, which removes the diseased colon and allows for restoration of intestinal continuity after patient recovery. The colon should be handled with extra care in order to prevent intraoperative perforation given the dilation and poor tissue quality (Fig. 4). Proctectomy should not be attempted regardless of the severity of proctitis as severe pelvic inflammation will make a safe and expedient operation impossible.[1]

If the rectosigmoid junction appears too inflamed to hold staples or sutures, a long stump including a portion of sigmoid can be used to create a mucous fistula which will allow for rectal decompression and will mitigate the consequences of a stump leak. The rectal stump can be brought through the inferior portion of the midline fascia and buried in the subcutaneous space. If the buried stump leaks it will manifest as a wound infection which can be managed locally rather than causing a pelvic abscess. Alternatively a drain can be placed along the rectal stump and a rectal tube can be placed.

All but very stable patients should be admitted to the surgical intensive care unit after colectomy. Intravenous steroids should be tapered to a maintenance dose and preoperative antibiotics should be discontinued within 24 hours. Early enteral feeding and adherence to enhanced recovery protocols are encouraged. If in place, the drain rectal tube is removed prior to discharge or between postoperative day 3 and 7.[1]

Rectal stump leaks typically occur between postoperative day 5 and 10. If pelvic sepsis develops, percutaneous drainage should be attempted if possible, with consideration of emergent open washout for abscesses which are not percutaneously drainable or severe/refractory sepsis.[1]

Summary

Toxic megacolon is a secondary complication of inflammatory and infectious colitis and is a life-threatening entity characterized by severe colonic distension and systemic toxicity. Immediate recognition, early initiation of resuscitation and treatment of the underlying colitis, and timely surgical intervention.

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