Advances in the diagnosis and management of toxic megacolon

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ARTICLE

Gan SI, Beck PL. A new look at toxic megacolon: An update and review of incidence, etiology, pathogenesis, and management. *Am J Gastroenterol* 2003;98:2363-71.

ARTICLE SUMMARY

Toxic megacolon (TM) is defined as the dilation (greater than 6 cm) of the entire colon or of a segment, with signs and symptoms of systemic toxicity. While associated primarily with inflammatory bowel disease (IBD), TM is also a documented complication of infectious, ischemic and metabolic insults to the colon. The incidence of this disease varies depending on the etiology and the study population. Estimates of the lifetime incidence of TM in patients with ulcerative colitis (UC) range from 1% to 2.5%. For patients admitted to hospital with UC, the incidence of TM is between 6% and 17%. In their review, Gan and Beck also noted an alarming increase in the number of cases of TM due to pseudomembranous colitis, even though other infectious or noninfectious causes of TM are exceedingly rare. The mechanisms responsible for the toxic dilation of the colon are not well understood and likely involve local damage to colonic smooth muscle and mucosa, as well as impaired motility secondary to the release of soluble inflammatory mediators; particularly, nitric oxide (NO). Diagnosis of this condition requires radiographical documentation of colonic dilation and evidence of systemic illness, as summarized in Jalan's criteria. Computed tomography (CT) may be useful in diagnosing colitis and for the timely identification of perforations and abscesses. Distension of the small bowel and stomach, as demonstrated by plain radiographs, may be a predictor of a poor outcome in TM. Once identified, the management of TM is based on a foundation of supportive measures, bowel rest and decompression. Medical management is advocated in uncomplicated cases, but surgical intervention may be required in patients who demonstrate progressive dilation or toxicity, or signs of perforation. Overall, surgical management remains the best way to minimize the morbidity and mortality of TM.

COMMENTARY

For 50 years, researchers and clinicians have studied the causes, pathophysiology and treatment of TM, and Gan and Beck summarized these efforts in their review. Patients diagnosed with TM are faced with a possibly fatal condition that may require intensive care and a prolonged hospital stay. Certainly the varied causes of TM are now well documented, but most physicians associate TM with fulminant IBD (1,2). In addition to reviewing the incidence of TM in IBD, the authors described the changing epidemiology of this disease. Of particular relevance was their prediction of more cases of TM due to *Clostridium difficile*, as a consequence of the widespread use of broad-spectrum antibiotics. Hospital-acquired *C difficile* infections are on the rise in the United States and the United Kingdom (3). Canada has seen its own recent *C difficile* outbreaks in Montreal, Quebec and Calgary, Alberta (4). Current rates of infection are at least five times greater than those reported before 2000, and there has been a concomitant increase in the number of cases of TM. Recent data also suggest that the risk of *C difficile* infection increases with the size of the hospital and the length of stay in intensive care units (4). This highlights for the clinician the broad, and inherently unwell, patient population at risk of developing TM.

To diagnose TM, the physician must rely on a combination of clinical criteria and radiographical evidence of dilation, as described by Jalan et al in 1969 (5). Gan and Beck outline the limited data to support the use of CT or other techniques for the diagnosis of TM. We discovered an article, written since their review was published, that examined the utility of ultrasound as a primary diagnostic tool in a small number of patients with TM (6). The limited use of radiographical techniques may be due to our incomplete understanding of the pathophysiology of this disease. The relationship between clinical disease activity and radiologically visible intestinal inflammation is poorly defined, thus limiting the present utility of ultrasonography and CT in diagnosis. We agree with the authors of this review, however, that CT is the best means of identifying septic complications and perforation and, thus, should be used early in cases of TM. We also concur that direct visualization of the colon using endoscopy has no place unless the etiology of the disease is unknown (eg, IBD versus infectious). Under those

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circumstances, a limited sigmoidoscopy may be performed, with minimal insufflation. Lastly, Gan and Beck also drew our attention to the lack of clinical, radiographical or laboratory parameters that are useful in determining the prognosis. They were able to find only a single, small prospective study that identified gastric and small bowel distension as a significant predictor of a poor outcome in TM. Based on this review, we would emphasize the importance of a global assessment, including serial clinical examinations, laboratory tests and abdominal radiographs, when considering a diagnosis of TM (2). We would further recommend that all patients at risk for TM, even those with signs of only mild toxicity, should undergo a CT scan performed upon admission to identify possible complications.

Supportive measures with or without decompression, steroids, antibiotics and surgery have all been used in the treatment of TM. The authors presented evidence supporting either early surgical intervention or a trial of medical management, but the lack of any prospective data precludes concrete conclusions. The tone of the paper perhaps best reflects the current pattern of practice of most gastroenterologists, who offer medical management, including antibiotics and corticosteroids in IBD-related cases, as long as patients demonstrate improvement. Nevertheless, the reviewers were not able to determine what constitutes a satisfactory trial of medical therapy. Some physicians are comfortable managing persistent megacolon for up to seven days in patients with no overt signs of perforation or worsening toxicity. Practically, the decision to proceed with surgery is almost certainly made on a case-by-case basis with a view to the patient's present condition and comorbidities. It is important to note that, if missed, mortality from perforation is 40%, as opposed to 8% or less if surgery is performed in a more controlled setting (7). Since this article was published, there have been reports of the use of tacrolimus (8) or infliximab (9) as rescue therapy for UC patients with TM, with the avoidance of emergency surgery. Immunosuppressive therapy may become another tool for clinicians whose patients do not want surgery or who may not survive a prolonged procedure. When an operation is indicated, the optimal procedure, avoiding unnecessary risk, is a subtotal colectomy with end-ileostomy (7). Gan and Beck also cite evidence supporting decompression with a blowhole colostomy procedure for patients with either severe toxicity or known perforation (10). However, the blowhole

decompression procedure is performed only rarely and the reported experience with this procedure is, therefore, limited to a few centres.

Looking to the future, the authors noted that NO levels are increased in cases of TM, and this may represent a key pathway driving the toxic dilation. Recent work suggests that the suppression of NO production may be the reason why corticosteroids are effective in IBD-related cases of TM (11). Early use of corticosteroids may prevent the progressive cascade of inflammation and dilation. Future therapies involving suppression of inducible NO are in the experimental stages.

Gan and Beck provide physicians with an insightful and comprehensive review of TM, highlighting the strengths and weaknesses of current treatment regimes while acknowledging the paucity of good prospective data. Gastroenterologists and surgeons are reminded of the complex clinical presentation and course of this disease, and the importance of an aggressive medical treatment strategy with consideration of early surgical intervention.

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