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Review Article

Incidence, prevalence, pathogenesis, and manifestations of toxic megacolon

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ABSTRACT

Toxic megacolon is an inflammatory condition that affects the colon, leading to nonobstructive dilatation and serious morbidity. It can be found as total and segmental. In the present literature review, we have discussed the epidemiology, pathogenesis, and manifestations of toxic megacolon based on relevant data from studies in the literature. Unfortunately, reports regarding the prevalence and incidence of toxic megacolon are scarce. Therefore, it is difficult to draw a suitable conclusion in this context, and further studies are encouraged. Nevertheless, infection with *Clostridium difficile* might be the commonest etiology, and estimates indicate that this is a significant risk factor for developing the condition. In addition, colonic motility is usually inhibited by the significant presence of certain inflammatory mediators. Furthermore, the clinical manifestations of toxic megacolon are not very specific, and the diagnosis can be made through adequate history taking, together with clinical and radiological manifestations. Finally, prompt management of the condition is essential to intervene against the development of serious complications.

Keywords: Toxic megacolon, Colon dilatation, Epidemiology, Prevalence, Incidence, Pathogenesis, Clinical manifestations, Diagnosis

INTRODUCTION

Toxic megacolon is an inflammatory condition that affects the colon, leading to nonobstructive dilatation and serious morbidity. It can be found as total and segmental. Although estimates indicate that the condition is not a very common one, it can lead to various complications and even death. In addition, previous studies have reported that the condition can be associated with toxicity.[1,2] Many risk factors were reported for the

condition. For instance, it has been shown that the commonest risk factor is having a history of inflammatory bowel diseases, particularly ulcerative colitis. However, investigations also reported that different inflammatory conditions related to the colon might also predispose to the development of toxic megacolon.[3]

It should be noted that the diagnosis of toxic megacolon might be difficult because these symptoms can be misdiagnosed with other underlying gastrointestinal conditions, especially among patients with inflammatory bowel conditions.[4] Moreover, the prolonged administration of steroids and analgesics might also impair the manifestations in these patients. Therefore, it is critical to comprehend the pathogenesis and different presentations of toxic megacolon to presume a better diagnostic ability.[5] In the present literature review, we will discuss the prevalence and incidence, pathogenesis, and manifestations of toxic megacolon based on studies from relevant studies in the literature.

LITERATURE REVIEW

This literature review is based on an extensive literature search in Medline, Cochrane, and EMBASE databases which was performed on 27th December 2021 using the medical subject headings (MeSH) or a combination of all possible related terms, according to the database. To avoid missing potential studies, a further manual search for papers was done through Google Scholar while the reference lists of the initially included papers. Papers discussing incidence, prevalence, pathogenesis, and manifestations of toxic megacolon were screened for useful information. No limitations were posed on date, language, age of participants, or publication type.

DISCUSSION

Prevalence and incidence

Not many investigations, especially the epidemiological ones, are currently available in the literature, and the ones reporting prevalence and incidence are scarce with not many recent updates. In the present section, we have collected the available data in the literature and will discuss them based on the currently available information. However, further future studies are encouraged to update the current evidence. Accordingly, in the general population, it can be concluded that the exact overall incidence and epidemiological characteristics of toxic megacolon are not adequately comprehended.[1] Furthermore, the condition has impacted different age groups, which has also been recorded among patients of both genders. Furthermore, it has been demonstrated that being affected with inflammatory bowel diseases, especially within the early stages of these diseases. It has been furtherly shown that colon dilatation cannot occur once fibrosis affects it.[6,7] In this context, many investigations aimed to assess the prevalence and incidence of toxic megacolon among patients with inflammatory bowel diseases. However, the results of these studies are not consistent. For instance, some previous studies showed that the incidence of toxic megacolon among patients with Crohn's disease is remarkably higher than patients with ulcerative colitis (4.4-6.3% versus 1-2.5%). On the other hand, other studies indicate that the incidence is much higher among patients with ulcerative colitis 8-10% versus 2.3%).[2,3,7] Furthermore, many risk factors have been reported for toxic megacolon. For instance, it has been shown that different conditions, including toxic megacolon, can develop secondary to *Clostridium difficile* infection.[8-10] However, it has been reported that many patients usually have asymptomatic disorders. Moreover, much data regarding the prevalence of toxic megacolon secondary to *Clostridium difficile* shows that the prevalence has increased over the past years, indicating a strong association between the infection and toxic megacolon. Previous studies amid 1990 show that the prevalence increased from 0.4 to 3% to be increased up to 4.3% after 1990.[2,3,6,11-13] It should also be noted that toxic megacolon might develop secondary to systemic disorders usually associated with impaired immunity and increased inflammatory reactions. For instance, a case report from Saudi Arabia reported that toxic megacolon developed secondary to diabetic ketoacidosis and colonic ischemia.[14]

Pathogenesis

Current studies also indicate that the exact pathogenesis and development of toxic megacolon are not adequately comprehended. However, some studies indicate that there is a strong association between reduced smooth muscle contraction and the presence of inflammatory conditions affecting the colon. Most of the currently available data support the association between the pathogenesis of toxic megacolon and ulcerative colitis.[15,16] In patients with toxic megacolon, it has been reported that the underlying inflammation observed among patients with ulcerative colitis (which only affects mucosa and superficial layers of submucosa) usually extends to involve the underlying muscle layer, inducing toxic megacolon as a complication and extension of ulcerative colitis. The severity of the condition and extent of colon dilatation has also been reported to be potentially correlated to the depth of inflammation.[17] Besides, some studies also reported that colonic motility is usually inhibited by the significant presence of certain inflammatory mediators. In this context, it has been shown that colonic smooth muscle relaxation is mediated by nitric oxide release, which is a noncholinergic, nonadrenergic neuromuscular transmitter.[18] This was further shown in a previous animal study, which indicated the significant expression of inducible nitric oxide synthase (iNOS).[19] Furthermore, previous studies that recruited patients with ulcerative colitis also reported similar conclusions.[20,21] In patients with toxic megacolon, Mourelle et al. [20] reported that elevated levels of iNOS were observed in the muscular propria of the affected colonic segments in the included

patients. Another animal investigation also reported that selective inhibition of NOS could significantly relieve intracolonic pressure, motility, and colonic diameter in rat models with colitis.[22] An in vitro study was also conducted by Cao et al. [23] and found that the mucosal cells of patients with ulcerative colitis are observed with increased levels of NO, interleukin (IL)-1β, H_2O_2 into the mucosa of the affected segments, which was also found to be more significant than what observed in the control group. Applying adequate treatment modalities to these pathological events was also associated with reduced contractility of the colon and enhanced prognostic outcomes. Accordingly, it has been reported that the pathological sequelae of toxic megacolon and complicated ulcerative colitis can be inhibited by pretreatment of these patients with the hemoglobin scavenger hemoglobin, IL-1β, and H_2O_2 scavenger catalase. This indicates the significant impact and involvement of these mediators in the pathogenesis of the condition.

Colonic motility might also be impacted by the potential presence of abnormal neuromuscular segment events secondary to the underlying inflammatory process. This has been furtherly indicated in a previous study by Strong et al which reported that in a guinea pig with colitis, it has been shown that impeded motility developed secondary to the development of inflammation-induced inhibitory purinergic neuromuscular transmission.[24] However, it should be noted that the authors of this study also demonstrated that such pathology was not associated with permanent defects in neuronal fibers or losing neurons within the myenteric ganglia. Accordingly, these findings might represent significant remarkable features of the disease and that the underlying pathogenesis is unique to the condition, unlike the pathology of congenital Hirschsprung's disease, where the main histological sequelae are attributed to agangliogenesis affecting a colon segment.[25]

Manifestations

It has been shown that the complications of toxic megacolon are usually encountered earlier in patients with a history of inflammatory bowel diseases. Estimates also show that around 5% of patients suffering from a severe attack of Crohn's disease usually develop toxic megacolon. Within the 1st three months after being diagnosed with toxic megacolon, it has been reported that around 50% of these patients usually suffer from this complication during this period.[26] Patients with pancolitis also suffer from an increased risk of developing toxic megacolon. However, it has been shown that the disease can also affect patients with left-sided colitis only. Evidence indicates that severe bloody diarrhea is the commonest clinical presentation of patients with toxic megacolon. In the same context, other manifestations were also reported in the literature. For instance, it has been shown that sluggish bowel sounds, diffuse abdominal distension and tenderness, fever, tachycardia, and hypotension are other clinical presentations that were observed among patients with toxic megacolon. A previous study also aimed to study the clinical presentations of patients with *Clostridium difficile* colitis-related toxic megacolon. It has been shown that diarrhea was the main presentation in these patients, being prevalent in all of them. Moreover, other manifestations were also commonly reported among these patients. These include malaise (91%), and abdominal pain and distension (82%).[12] It has been furtherly shown that many systemic manifestations were also reported for patients with toxic megacolon. For instance, some studies reported that electrolyte derangement, metabolic alkalosis, and leukocytosis are some laboratory findings observed among these patients.

Although many presentations have been reported for patients with toxic megacolon, It should be noted that these manifestations are not specific to the disease. Besides, evidence indicates that the administration of strong analgesics can significantly mask these manifestations by patients, making it difficult to diagnose the condition. On the other hand, it has also been demonstrated that free colonic perforation might be a potential complication, regardless of dilatation. However, in such studies, where these complications were reported, the incidence is rare and occurs only among patients with ulcerative colitis, usually with no toxic megacolon diagnosis.[27,28] In addition, the frequent administration of steroid therapy in these patients might also impair the clinical manifestations and potential complications occurring secondary to peritonitis. Accordingly, an adequate medical history should be obtained from the patient, including steroid administration frequency and duration. Furthermore, a physical examination is also important in these events to detect cases with atypical presentations of perforation and peritonitis presenting with atypical manifestations. For instance, physicians should also evaluate hepatic dullness in these patients daily. This is critical in these events, especially for patients with severe colitis. In this context, radiographic studies are encouraged to identify the underlying pathology and help establish a proper diagnosis.[29]

Radiological studies might also help detect these manifestations in the affected patients and establish a proper diagnosis. Evidence shows that dilatation of the colon to an extent >6 cm is the main radiological finding that can be observed in these patients. Moreover, evidence indicates that the extension might be up to 15 cm.[30,31] A previous study by Fazio et al reported that the colon diameter of a patient with toxic megacolon extended to 9.2 cm.[32] The most dilated parts of the colon are the ascending and transverse ones. Moreover, it has been reported that loss of disturbance of colonic haustrations and colonic air-to-fluid levels are other features that can be radiologically detected in patients with toxic megacolon. Moreover, the diagnosis of toxic megacolon can also be established in the pediatric population. In this context, a previous study reported that

children with a history of inflammatory bowel diseases together with clinical manifestations suggestive of toxic megacolon and a colonic diameter of 56 mm are suggestive of toxic megacolon in these children.[33] However, a previous study indicated that the diameter of the affected colonic segments does not usually exceed 40 mm.[34] Maconi et al also conducted a case series to investigate the ultrasound radiological findings of toxic megacolon in patients with inflammatory bowel diseases.[35] The authors reported that the radiological findings were similar to those observed with plain abdominal radiographs, including loss of colonic mucosal haustrations, increased colonic diameter (>6 cm), thin colonic walls, and increased gaseous contents. However, it should be noted that all of the reported findings are not specific to the presence of toxic megacolon. Accordingly, it is difficult to differentiate between the condition and other etiologies of colonic dilatation. However, it should be noted that these radiological findings can add to the diagnosis of toxic megacolon when the presence of the condition is suspected and should be conducted as an adjuvant diagnostic approach. A previous retrospective investigation also demonstrated the efficacy of computed tomography in detecting pathological events suggestive of the pathology of toxic megacolon.[36] These manifestations include pericolic stranding, hyperemic mucosa, multilayered appearance attributed to various densities of edematous submucosa, thickened haustra with alternating low and high-density bands, and diffuse thickness of the colonic wall. Moreover, it has been reported that conducting CT studies might be more reliable in detecting the underlying pathology and manifestations of toxic megacolon than abdominal radiographic studies.

CONCLUSION

Unfortunately, reports regarding the prevalence and incidence of toxic megacolon are scarce. Therefore, it is difficult to draw a suitable conclusion in this context, and further studies are encouraged. Nevertheless, infection with *Clostridium difficile* might be the commonest etiology, and estimates indicate that this is a significant risk factor for developing the condition. Furthermore, the clinical manifestations of toxic megacolon are not very specific, and the diagnosis can be made through adequate history taking, together with clinical and radiological manifestations.

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REFERENCES

1. Jalan KN, Sircus W, Card WI. An experience of ulcerative colitis. I. Toxic dilation in 55 cases. Gastroenterology. 1969;57(1):68-82.
2. Autenrieth DM, Baumgart DC. Toxic megacolon. Inflammatory Bowel Dis. 2012;18(3):584-91.
3. Ausch C, Madoff RD, Gnant M. Aetiology and surgical management of toxic megacolon. Colorectal Dis. 2006;8(3):195-201.
4. Andreyev HJ, Davidson SE, Gillespie C, Allum WH, Swarbrick E. Practice guidance on the management of acute and chronic gastrointestinal problems arising as a result of treatment for cancer. Gut. 2012;61(2):179-92.
5. Pascu M, Müller AR, Wiedenmann B, Dignass AU. Rescue therapy with tacrolimus in a patient with toxic megacolon. Int J Colorectal Dis. 2003;18(3):271-5.
6. Norland CC, Kirsner JB. Toxic dilatation of colon (toxic megacolon): etiology, treatment and prognosis in 42 patients. Medicine (Baltimore). 1969;48(3):229-50.
7. Grieco MB, Bordan DL, Geiss AC, Beil AR, Jr. Toxic megacolon complicating Crohn's colitis. Ann Surg. 1980;191(1):75-80.
8. Kelly CP, LaMont JT. Clostridium difficile--more difficult than ever. The New England journal of medicine. 2008;359(18):1932-40.
9. Bagdasarian N, Rao K, Malani PN. Diagnosis and treatment of Clostridium difficile in adults: a systematic review. JAMA. 2015;313(4):398-408.
10. McDonald LC, Gerding DN, Johnson S. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clinical Infect Dis. 2018;66(7):e1-48.
11. Berman L, Carling T, Fitzgerald TN. Defining surgical therapy for pseudomembranous colitis with toxic megacolon. J Clin Gastroenterol. 2008;42(5):476-80.
12. Trudel JL, Deschênes M, Mayrand S, Barkun AN. Toxic megacolon complicating pseudomembranous enterocolitis. Diseases Colon Rectum. 1995;38(10):1033-8.
13. Hokama A, Ohira T, Kishimoto K, Kinjo F, Fujita J. Impending megacolon: small bowel distension as a predictor of toxic megacolon in ulcerative colitis. Internal Emergency Med. 2012;7(5):487-8.
14. Mansouri F. Toxic Megacolon with Colonic Ischemia Masquerading as Diabetic Ketoacidosis: A Case Report. Saudi J Med Pharmaceutical Sci. 2020;06:58-63.
15. Reddy SN, Bazzocchi G, Chan S. Colonic motility and transit in health and ulcerative colitis. Gastroenterology. 1991;101(5):1289-97.
16. Snape WJ Jr, Kao HW. Role of inflammatory mediators in colonic smooth muscle function in ulcerative colitis. Dig Dis Sci. 1988;33(3):65s-70.
17. Buckell NA, Williams GT, Bartram CI, Lennard-Jones JE. Depth of ulceration in acute colitis: correlation with outcome and clinical and radiologic features. Gastroenterology. 1980;79(1):19-25.
18. Boeckxstaens GE, Pelckmans PA, Herman AG, Van Maercke YM. Involvement of nitric oxide in the

inhibitory innervation of the human isolated colon. Gastroenterology. 1993;104(3):690-7.
19. Lundberg S, Holst M, Hellström P. Expression of iNOS mRNA associated with suppression of colonic contraction in rat colitis. Acta Physiologica. 2006;187(4):489-94.
20. Mourelle M, Casellas F, Guarner F. Induction of nitric oxide synthase in colonic smooth muscle from patients with toxic megacolon. Gastroenterology. 1995;109(5):1497-502.
21. Palatka K, Serfozo Z, Veréb Z. Changes in the expression and distribution of the inducible and endothelial nitric oxide synthase in mucosal biopsy specimens of inflammatory bowel disease. Scand J Gastroenterol. 2005;40(6):670-80.
22. Mourelle M, Vilaseca J, Guarner F, Salas A, Malagelada JR. Toxic dilatation of colon in a rat model of colitis is linked to an inducible form of nitric oxide synthase. Am J Physiol. 1996;270(3 Pt 1):G425-430.
23. Cao W, Fiocchi C, Pricolo VE. Production of IL-1beta, hydrogen peroxide, and nitric oxide by colonic mucosa decreases sigmoid smooth muscle contractility in ulcerative colitis. Am J Physiol Cell Physiol. 2005;289(6):C1408-16.
24. Strong DS, Cornbrooks CF, Roberts JA, Hoffman JM, Sharkey KA, Mawe GM. Purinergic neuromuscular transmission is selectively attenuated in ulcerated regions of inflamed guinea pig distal colon. J Physiol. 2010;588(Pt 5):847-59.
25. Candiotto A, Pascoli I, Gritti A, Busato E, Dal Pozzo G. Toxic megacolon complicating a Clostridium difficile infection in a pregnant woman. J Med Microbiol. 2010;59(Pt 1):124-6.
26. Roys G, Kaplan MS, Juler GL. Surgical management of toxic megacolon. Am J Gastroenterol. 1977;68(2):161-6.
27. Greenstein AJ, Barth JA, Sachar DB, Aufses AH, Jr. Free colonic perforation without dilatation in ulcerative colitis. Am J Surg. 1986;152(3):272-5.
28. Greenstein AJ, Aufses AH, Jr. Differences in pathogenesis, incidence and outcome of perforation in inflammatory bowel disease. Surg Gynecol Obstetr. 1985;160(1):63-9.
29. Desai J, Elnaggar M, Hanfy AA, Doshi R. Toxic Megacolon: Background, Pathophysiology, Management Challenges and Solutions. Clin Experimental Eastroenterol. 2020;13:203-10.
30. Present DH. Toxic megacolon. Med Clin N Am. 1993;77(5):1129-48.
31. LaMont JT, Kandel GP. Toxic megacolon in ulcerative colitis. Early diagnosis and management. Hospital practice (Office ed). 1986;21(9):102A-102D, 102H, 102K-102M passim.
32. Fazio VW. 11 - Toxic Megacolon in Ulcerative Colitis and Crohn's Colitis. Clin Gastroenterol. 1980;9(2):389-407.
33. Benchimol EI, Turner D, Mann EH. Toxic megacolon in children with inflammatory bowel disease: clinical and radiographic characteristics. Am J Gastroenterol. 2008;103(6):1524-31.
34. Turner D, Walsh CM, Benchimol EI. Severe paediatric ulcerative colitis: incidence, outcomes and optimal timing for second-line therapy. Gut. 2008;57(3):331-8.
35. Maconi G, Sampietro GM, Ardizzone S. Ultrasonographic detection of toxic megacolon in inflammatory bowel diseases. Dig Dis Sci. 2004;49(1):138-42.
36. Imbriaco M, Balthazar EJ. Toxic megacolon: role of CT in evaluation and detection of complications. Clin Imaging. 2001;25(5):349-54.

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