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MANAGEMENT OF TOXIC MEGACOLON

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Abstract:

Introduction: *Toxic megacolon is differentiated from different types of colonic expansion, for example, Ogilvie syndrome and Hirschsprung disease by the extra presence of systemic toxicity and the incendiary or irresistible etiology of the hidden disease. Albeit toxic megacolon might be viewed as uncommon, frequency is expected to increase due to the quickly expanding prevalence of pseudomembranous colitis. Because early discovery and intervention profoundly affect survival, it is important that physicians know about this possibly lethal complication to attenuate morbidity and mortality*

Aim of work: *In this review, we will discuss study of disease transmission, etiology, pathophysiology, clinical signs and symptoms, emergency management, and prognosis of toxic megacolon in adults.*

Methodology: *We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1985, through February 2017. The following search terms were used: toxic megacolon, presentation and management of toxic megacolon, gastrointestinal pathology, ulcerative colitis, inflammatory bowel disease*

Conclusions: *In summary, surgical intervention remains a pillar in the management of TM. Albeit short trials of therapeutic treatment are surely warranted, any indication of complication (either clinically or on CT scan), worsening, or inability to improve must be sign for colectomy. surgeons ought to be consulted early over the span of the disease, and frequent surgical reconsideration is critical. excessive delays will probably prompt pointless morbidity and mortality.*

Key words: *Toxic Megacolon, Inflammatory Bowel Disease, Ulcerative Colitis.*

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INTRODUCTION:

An infrequent occurring yet severe and potentially fatal complication of colitis is toxic megacolon. Toxic megacolon is characterized as segmental or complete colonic widening of greater than 6 cm in the presence of acute colitis and indications of systemic toxicity. Toxic megacolon is differentiated from different types of colonic expansion, for example, Ogilvie syndrome and Hirschsprung disease by the extra presence of systemic toxicity and the incendiary or infectious etiology of the hidden disease. Albeit toxic megacolon might be viewed as uncommon, frequency is expected to increase due to the quickly expanding prevalence of pseudomembranous colitis. Because early diagnosis and intervention profoundly affect survival, it is important that physicians know about this possibly lethal complication to attenuate morbidity and mortality. This review will discuss epidemiology, etiology, pathophysiology, clinical signs and symptoms, emergency management, and prognosis of toxic megacolon in adults [1; 2].

METHODOLOGY:

• Data Sources and Search terms

We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1985, through February 2017. The following search terms were used: toxic megacolon, presentation and management of toxic megacolon, gastrointestinal pathology, ulcerative colitis, inflammatory bowel disease

• Data Extraction

Two reviewers have independently reviewed the studies, abstracted data, and disagreements were resolved by consensus. Studies were evaluated for quality and a review protocol was followed throughout.

The study was approved by the ethical board of King Abdulaziz University Hospital

ETIOLOGY:

In the past, toxic megacolon was believed to be a complication exclusively of ulcerative colitis. Crohn disease was then perceived as a reason, and continuedly ended up obvious that any inflammatory state of the colon can incline patients to toxic dilation. Recent research has attracted attention to a demographic shift from chronic inflammatory causes to infectious causes related with the development of toxic megacolon. Current information propose that toxic megacolon is more often was a cause by pseudomembranous colitis than by ulcerative colitis. As the prevalence of CDI increments and medications turn out to be increasingly refractory, physicians are expected to encounter more patients with CDI-related toxic megacolon in the future [3].

Toxic megacolon additionally assumes a vital role in immunocompromised patients. Cytomegalovirus and CDI are the prevalent causes for toxic megacolon in patients with human immunodeficiency virus (HIV). In the setting of underlying inflammation of infectious colitis, extra risk factors for the event of toxic megacolon incorporate discontinuation of steroids, utilization of barium enemas, and drugs that slow colonic motility, for example, opiates and antidiarrheal or anticholinergic drugs [4].

PATHOPHYSIOLOGY:

The actual pathologic mechanism of toxic megacolon is not yet clearly comprehended, albeit most investigators concur that few pathologic components likely add to the development of this phenomenon. The progress of complication from uncomplicated ulcerative colitis to toxic megacolon is best reviewed to date. While in ulcerative colitis typically response to inflammation by being presented in the superficial mucosa, in the other hand, the description of toxic megacolon is by the severe inflammation that expands into the layer of smooth muscles. One critical risk factor that develops toxic megacolon is the complication of inflammation that expands beyond the submucosa layer and into the muscularis and serosa layers. As inflammation advances, neutrophils damage the muscle layer and bring on additional damage by stimulating proteolytic proteins, cytokines, and leukotriene B4, bringing about dysmotility, which prompts dilation [2]. The severity of inflammation gives off an impression of being connected with the degree of colonic dilation. In infectious causes, for example, pseudomembranous colitis, C. difficile toxins A and B disturb the epithelial barrier and cause epithelial cell necrosis and electrophysiologic changes in the colonic mucosa, prompting marked colonic inflammation [5].

The regular absorptive function of the bowel is altered by inflammation which causes water, sodium and potassium to be trapped in lumen of colon. The ability of the bowel therefore is decreased due to the resultant hypokalemia and other electrolyte abnormalities. The barrier mechanism of the colon becomes dysfunctional, which allows the ingestion of poisons, organisms, and toxic wastes, prompting systemic toxicity. The systemic symptoms related with toxic megacolon are not straightforwardly identified with bacteremia, colonic perforation, or

ischemia yet to oxide-induced inflammatory mediators, for example, interleukin-8, macrophage inflammatory protein-2, substance P, and tumor necrosis factor-α, discharged in the colon. The gross pathologic features of toxic megacolon are like both ulcerative colitis and Crohn disease with pronounced widening of the colon, thinning of the bowel wall, and deep ulcers [5].

Nitric oxide, a powerful inhibitor of smooth muscle tone, has been hypothesized to assume a major role in the pathogenesis of toxic megacolon. Nitric oxide is produced in the macrophages and smooth muscle cells of the inflamed colon and is a non-adrenergic, noncholinergic neurotransmitter. Nitric oxide, discharged by invading neutrophils, may paralyze muscle cells and lead to colonic dilation. In a review of colon sections removed amid a surgical procedure from patients with toxic megacolon, extreme nontoxic ulcerative colitis, and nonobstructive colon malignancy, specialists reported greater amounts of inducible nitric oxide synthase in the muscle samples of people with toxic megacolon than in the other 2 groups. Due to nitric oxide is also a marker of inflammation, its actual association in the pathogenesis of toxic megacolon stays unclear [6].

CLINICAL MANIFESTATIONS:

Majority of individuals appear during a relapse of established IBD however, a substantial number appear amid their initial flare or within 2 to 3 months of diagnosis. The development of toxic megacolon early in the disease is a at the highest risk with patients suffering IBD. Around 60% of cases present within the first 3 years, while up to 30% of patients present within 3 months of being diagnosed with IBD. The usual presentation of patients to the emergency room is during an ongoing bout of severe colitis, and signs and symptoms are commonly present for around a week or further before the onset of acute dilation [7]. These manifestations consist of diarrhea (dysentery), fevers, chills, and abdominal pain. The initial manifestations of toxic megacolon are inconsistent however, may be heralded by abdominal distention, improvement in diarrhea, constipation, obstipation, decreased bowel sounds, and constitutional symptoms such as fever, tachycardia, and hypotension. Abdomen can be extremely painful either locally or diffusely, however, these manifestations may be masked by high-dose corticosteroids or a diminished level of consciousness [5].

DIAGNOSIS:

The combination of radiographic evidence of colonic dilation greater than 6 cm and Clinical signs of systemic toxicity are the basis in diagnosing toxic megacolon. Patients that are presented in emergency room with abdominal distention and acute or chronic diarrhea should immediately be considered toxic megacolon [7]. The initial description by Jalan et al [8] in 1969 of clinical criteria for toxic megacolon diagnosis, remains the most widely accessed criteria and consist of any of the following: (1) fever > 38.6°C (101.5°F); (2) heart rate > 120 beats/min; (3) white blood cell count > 10.5/μL; or (4) anemia. One of the following criteria should also be present in patients: dehydration, hypotension, electrolyte disturbances, or mental status changes.

Plain abdominal films are used as well in the radiologic diagnosis. Although dilation of as much as 15 cm are not uncommon, colonic dilation of more than 6 CM is suggestive of diagnosis. The two parts of colon which are most prone to dilation are the transverse and ascending. The loss of colonic haustra and colonic air-fluid levels are the features in radiograph imaging. Similar features which are found on plain abdominal radiographs are thin colonic walls, loss of colonic haustra, and dilation >6 cm with gaseous content in US findings among patients with toxic megacolon [9]. Though it is hard to differentiate between other causes of colonic dilation using US, due to its wide availability, it may be a valuable diagnostic tool in early detection or suspicion of toxic megacolon. When features of toxic megacolon are present it is an indication for abdominal computed tomography (CT). complications such as perforation or ascending pyelophlebitis can be diagnosed using CT scan which is useful in determining the cause of these complications [2].

Laboratory studies in individuals with toxic megacolon can represent several nonspecific abnormalities and reflect systemic toxicity and the severity of the colitis. Anemia and leukocytosis with left shift are a known feature, and the leukocyte count can reach as high as 40,000/μL [10].

Neutropenia, not leukocytosis, can be seen among patients with HIV or individuals treated by chemotherapy. Metabolic acidosis and electrolyte imbalances such as low potassium, calcium, chloride, phosphate, and magnesium may occurs from chronic diarrhea. Electrolyte imbalances, particularly hypokalemia, have been reported in over half of patients. Hypokalemia and hypoalbuminemia are related with extreme diarrhea, volume loss, and a poor prognosis in general. Elevated inflammatory markers, for example, erythrocyte sedimentation rate and C-reactive protein are often observed and are

helpful while observing the progression of the disease [2]. Blood cultures should be acquired to preclude bacteremia since sepsis happens in up to 25% of patients with toxic megacolon. Stool samples ought to be sent for culture, sensitivity, and C difficile toxin A and B measure in patients with a background marked by anti-biotic use or chemotherapy. Ova and parasite disease ought to be considered in patients with HIV [10].

MANAGEMENT:

Emergency Management

Toxic megacolon is a life-threatening emergency. The ED physician's first need is the diagnosis and management of life-threatening complications, for example, septic shock, hypovolemic shock, severe anemia, and dehydration. Central components of emergency management incorporate fluid resuscitation, electrolyte correction, decompression, administration of anti-microbials, and surgical consultation [1].

Anemia, dehydration, and electrolyte deficits, especially hypokalemia, disturb colonic dysmotility and ought to be forcefully treated. Intravenous crystalloids ought to be utilized for fluid resuscitation except if the patient is in a serious condition of shock or hypoalbuminemia, in which case colloids should be used. Blood products might be required to address severe anemia. All type of drugs that decrease gastric motility must be ceased promptly, including anticholinergic drugs, antidiarrheal drugs, and narcotics [2].

Nasogastric or long tube suction must be utilized for decompression. Long tubes can be very effective for colonic decompression than are nasogastric tubes; nevertheless, they should be set in the ileum under fluoroscopic guidance. Administration of broad-spectrum anti-biotics agents is suggested, not as the main treatment for IBD or for toxic dilation, but rather to decrease septic complications and mortality if perforation ever occurred. Broad-spectrum intravenous anti-biotics agents with coverage equivalent to ampicillin or cephalosporin, in addition to gentamicin and metronidazole, is a proper regimen [10].

The pillar of therapeutic treatment for individuals who suffer toxic megacolon caused by ulcerative colitis is high-dose intravenous steroids. Treatment with steroid should be started swiftly and should not be delayed by pending microbiological results. Most authors suggest a daily dose of either 400 mg hydrocortisone (100 every 6 hours) or 60 mg methylprednisolone given intravenously for 5 days [11]. If steroid treatment does not prompt remission, rescue treatment with cyclosporine must be considered. In patients with toxic megacolon caused by pseudomembranous colitis, offending anti-biotic agents should be pulled back. The most widely recognized anti-biotics associated with CDI are clindamycin, cephalosporins, and fluoroquinolones. Vancomycin must be administered as first-line treatment as indicated by current guidelines issued by the Society for Healthcare Epidemiology of America and the Infectious Disease Society of America [12].

Managing pain is difficult in patients with toxic megacolon since nonsteroidal anti-inflammatory medications may exacerbate bleeding and narcotics adversely influence gut peristalsis, causing an increased risk of colonic perforation. Narcotics should be utilized with absolute caution, in spite of the fact that tramadol may have less effect on motility when utilized on a short-term basis. One study has shown that low-dose ketamine is a safe and effective analgesic in kids with toxic megacolon, in spite of the fact that reports of effectiveness among adults were missing from the literature [13].

A surgical consultation should be acquired as quickly as possible. Great results from therapeutic treatment decreases the need for surgery in half of patients who encounter toxic megacolon; but surgical intervention might be vital in up to 80% of patients with toxic megacolon whose outcome is due to of C. difficile colitis. Absolute need for surgery consists signs of organ failure, shock, uncontrollable hemorrhage, perforation, and progressive dilation following 24 to 72 hours of therapeutic therapy. In urgent circumstances, most surgeons support a subtotal colectomy, mucous fistula, and ileostomy since this method is related with a lower morbidity and mortality compared to a total proctocolectomy. An early consultation for surgery is vital to enhancing results, since surgery in patients without proof of perforation results in much lower mortality (2% to 8%) than does a colectomy after perforation has happened (40% or more). The fear in delaying surgery is that the surgeon will at that point be managing an acutely sick patient with a friable colon that will tend to tear at the splenic flexure [10].

Intensive care unit admission. Any indication of complication, worsening, or inability to improve should be viewed as a sign for a colectomy. Excessive delays will probably prompt pointless morbidity and mortality.

SURGICAL MANAGEMENT:

The issue of timing of surgery in patients with TM has powered a significant measure of discussion in the literature. Absolute signs for colectomy incorporate perforation, uncontrollable bleeding, and

progressive dilation. In view of a high death rate in patients with perforation and on the outcomes in a few patients treated medically early in their course, a few investigators have recommended that operative management be executed when the diagnosis is made. In view of high death rates in patients with perforation and a lower short-term death rate among patients with early surgery, Jalan et al. prescribed surgery shortly after diagnosis however did not preclude a short trial of therapeutic treatment with corticosteroids. Goligher's often cited proclamation to " save the patient, not the colon" depended on a study that diminished the rate of perforation from 32.5% to 11.6% and mortality from 20% to 7% by methods for early surgery. The investigators concluded that surgery should be performed soon after diagnosis [14].

Not all proof would agree with such an aggressive methodology, and most specialists would concur that a trial of therapeutic treatment is the best beginning routine. This depends on studies appearing low mortality with therapeutic management. **Katzka et al. [15]** for example, reported 19 patients who were medically managed with anti-infection agents and corticosteroids for up to 7 days and noticed a more prominent than half salvage of colons. There was no mortality and the majority of patients were well up to 11 years in follow-up. Current had comparative outcomes with 68% of 19 patients being effectively managed with a mean follow-up of 6.5 yr. These studies recommend that medical treatment can be proceeded for at least 7 days insofar as long as there is proof of clinical enhancement. If there is no enhancement, elective surgery is far desirable over emergent surgery for complications, given the great difference in result. **Greenstein et al. [16]** found a significantly diminished mortality in those experiencing elective surgery (5%) versus emergent (30%). Moreover, prolonged periods of delay (over 1 month) brought about a considerably higher mortality (40%).

Whenever demonstrated, the surgical method of decision in progressively elective circumstances is a total colectomy and ileostomy. In critical circumstances, however, most surgeons support a subtotal colectomy, mucous fistula, and ileostomy, as this methodology is related with a lower morbidity and mortality than is total proctocolectomy. Moreover, this allows for the potential making of a pouch at a later date. Tragically, there remains a high perioperative perforation rate related with this methodology that is accepted to result from iatrogenic disturbance of the gut at destinations of recently walled-off perforation. The fecal soilage and sepsis that follow are often the reason for postoperative mortality. Hence, **Turnbull et al. [17]** have recommended that in cases in which these fixed holes are found, colectomy ought to be relinquished for a decompression technique alluded to as a "less than colectomy" or "blowhole" operation. In essence, this is a temporary ileostomy and transverse colostomy performed to diffuse the toxicity of the circumstance and to allow the best possible bowel cleansing important for a safe definitive procedure. The consequences of Turnbull et al. were great, with just a single death in a progression of 42 patients. All patients subsequently experienced elective colectomies or were anticipating such an operation at the time of publication. Not all patients were totally stabilized by the procedure, as may have been expected given the proceeded with presence of a fulminant sigmoid colitis. In spite of decompression, four patients kept appearing signs of toxicity and required progressively expedient colectomy after 12–18 days. **Khoo et al. [18]** described an alternative type of decompression by methods for a chest tube embedded into cecum through the terminal ileum. This obviated quick surgery and allowed opportunity for arrangement of the colon. In spite of the fact that this methodology was expressed to be successful in TM, real outcomes were not presented.

CONCLUSION:

In summary, surgical intervention remains a pillar in the management of TM. Albeit short trials of therapeutic treatment are surely warranted, any indication of complication (either clinically or on CT scan), worsening, or inability to improve must be sign for colectomy. surgeons ought to be consulted early over the span of the disease, and frequent surgical reconsideration is critical. excessive delays will probably prompt pointless morbidity and mortality.

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