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Review article

Current Status of the Treatment of Fulminant Colitis☆

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ABSTRACT

Fulminant colitis is not a well-defined entity that constitutes a severe complication. It usually occurs in the course of ulcerative colitis and *Clostridium difficile* colitis. A multidisciplinary management combining a gastroenterologist and surgeons is crucial with intensive medical treatment and early surgery in non-responders. It is important to distinguish if we are facing a flare of IBD or, on the contrary, it is an infectious colitis, due to the fact that although general therapeutic measures to adopt will be the same, they will demand opposed specific measures.

Estado actual del tratamiento de la colitis fulminante

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RESUMEN

La colitis fulminante es una entidad cuya definición no está bien establecida y que supone una complicación grave. Sus principales causas son la colitis ulcerosa y la infección por *Clostridium difficile*. El manejo multidisciplinar integrado por gastroenterólogos y cirujanos es fundamental, con un tratamiento médico intensivo de inicio y cirugía precoz en los pacientes que no responden. Es importante dilucidar si nos encontramos ante un brote de EII o por el contrario, se trata de una colitis infecciosa, ya que aunque las medidas terapéuticas generales a adoptar serán las mismas, exigirán medidas específicas opuestas.

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Introduction

The exact definition of fulminant colitis (FC) has not been well established. The first definition from 1950 described an acute severe colitis that was rapidly progressive, resulting in death within the first year.[1] It is generally accepted that this term refers to acute severe inflammation of the colon, associated with systemic toxicity either with or without colic dilatation.[2] Nonetheless, it is an imprecise definition, and it is often difficult to determine what is considered severe colitis and what is FC, with the currently preferred term of acute severe colitis.[3,4] In ulcerative colitis (UC), according to the diagnostic criteria of Truelove and Witts,[5] acute colitis is defined when patients present more than 6 bloody stools per day, tachycardia, hypotension, high fever, changes in mental state, anemia requiring transfusion, pain and abdominal distension, and water-electrolyte imbalance. In the context of colitis due to *Clostridium difficile* (CD), Dallal[6] defined FC according to the existence of tachycardia, need for mechanical ventilation, oliguria, and hypotension requiring vasopressor treatment.

When associated with total colic dilatation or segmental dilatation of more than 6 cm in the absence of obstruction, the condition is considered a toxic megacolon. This entity, unlike FC, is perfectly defined and requires surgical treatment within 24–72 h.[7] Both are serious situations that require specialized hospital care with intensive monitoring by gastroenterologists and surgeons.

This manuscript is a review of the relevant articles obtained from a search of the literature on the MEDLINE database between 1990 and 2014, using the search terms: ''fulminant colitis'', ''toxic megacolon'', ''severe colitis'', ''ulcerative colitis'', ''severe ulcerative colitis'', and ''*Clostridium difficile* colitis''.

Etiology

The most frequent causes of fulminant colitis are UC and infectious colitis, although there are reports of cases caused by Crohn's disease, ischemic colitis, radiation colitis, and colitis induced by drugs or vasculitis[2] (Fig. 1).

Historically, it had been almost exclusively associated with inflammatory bowel disease (IBD) and specifically UC. In recent decades, however, the incidence of infectious FC has increased[8–10] along with the higher incidence of colitis due to CD, which is more aggressive and refractory.[11,12] Nonetheless, in our setting, infection due to CD is a much less frequent cause of infectious colitis and severe colitis than in the United States. While their incidence has not been properly evaluated, existing data show that we are still far from the problem seen in American hospitals, although we have also witnessed a progressive increase.[13] *Clostridium difficile* is a spore-forming, Gram-positive anaerobic bacillus that grows by forming colonies and can cause anywhere from diarrhea without colitis to FC. Approximately 3%–8% of CD disease develops FC and many of these patients require urgent colectomy.[14] The main risk factor for developing CD disease is prior antibiotic use. Clindamycin, cephalosporins, and fluoroquinolones present the highest risk. Other risk factors have been reported, such as advanced age, prolonged hospitalization, immunosuppression, IBD and the use of protein pump inhibitors.[11,14] Other infectious agents have also been less frequently implicated in the cause of FC, including bacteria (*Salmonella*,[15] *Shigella*,[16] and *Campylobacter*[17]), as well as viruses (*Citomegalovirus*[10] [CMV] and *Herpes simplex*[18]), and parasites (*Entamoeba hystolytica*[19]).

The possible role of some infections as triggering factors for episodes in patients with IBD has not been clearly proven,[8,9] although it is recommended to rule out a possible overinfection in patients with active IBD.[20] The most frequently involved agents are CD and CMV.[21] The increased incidence of CD infection among patients with IBD is well known, and IBD is an independent risk factor for infection.[11,14] Patients with UC in treatment with corticosteroids or immunosuppressants present elevated risk for CMV infection.[10,21]

Inflammatory causes:

- Ulcerative colitis
- Crohn's disease

Infectious causes:

- Bacterial: pseudomembranous colitis due to Clostridium difficile, Salmonella, Shigella, Yersinia, Campylobacter, etc.
- Viral: Cytomegalovirus
- Parasites: Entamoeba histolytica, Cryptosporidium

Other causes:

- Ischemia
- Drugs
- Radiotherapy

Fig. 1 – Causes of fulminant colitis.

Diagnosis

Patients with FC present a series of dilemmas for the specialists who treat them. The first is to determine whether it is an IBD exacerbation, in which case the immunosuppressant treatment should be intensified, or, on the contrary, an infectious colitis, in which case this strategy can worsen the patient's condition. This doubt can arise at the onset or in a patient who has been previously diagnosed with IBD.

The first step should be a thorough, detailed patient medical history to acquire information about any known personal or family history of IBD, epidemiologic data that raise the suspicion of an infectious origin (contact with other people with diarrhea, trips or previous antibiotic use), use of medications or drugs that could cause colitis (non-steroid anti-inflammatories or cocaine), or vascular diseases or vasculitis that could be related with an ischemic origin.

Lab work usually detects anemia and leukocytosis with neutrophilia (occasionally leucopenia due to the septic state). Electrolytic alterations are common due to dehydration, as is hypokalemia due to the increased excretion of potassium or colon mucous inflammation. Hypoalbuminemia is also