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Lecture

Treatment of Inflammatory Bowel Disease complications

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The most frequent intestinal complications of Ulcerative colitis (UC) are: i) toxic colitis, ii) toxic megacolon, iii) perforation, iv) hemorrhage and v) development of colorectal cancer, whereas complications of Crohn's disease are: i) small bowel obstruction, ii) perianal disease and fistulas, and iii) intra-abdominal abscesses. This section is going to summarize the treatment of these intestinal inflammatory bowel disease (IBD) complications. The IBD extraintestinal complications and their management will be analyzed in a different session of the same IBD Congress.

ULCERATIVE COLITIS

Toxic colitis

Toxic colitis is initially treated with fluid resuscitation, nasogastric decompression, high-dose of steroids intravenously, broad-spectrum antibiotics and intravenous hyperalimentation to prevent nutritional deterioration or to correct any deficiencies.[1] It is worthwhile to mention that narcotics, anticholinergic drugs and antidiarrheal agents should be avoided due to toxic megacolon precipitation. Surgery is indicated for toxic colitis that does not improve quickly with medical treatment (within 48 to 72h) or in patients in whom peritonitis or perforation is developing.

Toxic Megacolon

Toxic megacolon is a life-threatening variant of toxic colitis. When toxic megacolon is promptly treated, subsequent surgery is not inevitable. Even among patients in whom prompt resolution has occurred, about half require surgery within a year and most eventually require colectomy. Firstly, medical therapy may lead to improvement, obviating the need for surgery. Nasogastric suction, broad-spectrum antibiotics and fluid & electrolyte replacement should be administered aggressively. If there is no improvement within 48 hours, colectomy and ileostomy should be performed because of the high risk of perforation. In this unusual situation, the patient is served best with a skin-level transverse colostomy and loop ileostomy that decompress the colon and diverts intestinal contents.[1] Subsequent colectomy can be performed securely after recovery. If perforation occurs before or during surgery, subtotal colectomy seems to be the best choice of treatment.[2]

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Perforation

Acute perforation occurs infrequently, with the incidence directly related to both the severity of the initial attack and the extent of damaged bowel. It is the most lethal complication of acute colitis (associated mortality 40-50%). It occurs most frequently in the presence of toxic megacolon but the latter is not a prerequisite for the development of perforation. Abdominal colectomy with ileostomy and Hartmann closure of the rectum is the procedure of choice.

Hemorrhage

Massive hemorrhage accounts for 10% of all emergency colectomies for ulcerative colitis.[3] It is a rare complication occurring in less than 1% of patients. Surgical intervention is indicated after hemodynamic stabilization. Uncontrollable hemorrhage from the entire mucosa of the colon may be the one clear indication for emergency colectomy. It seems that the best management of these patients is subtotal colectomy and end ileostomy with mucous fistula or Hartman pouch.[1]

Colorectal cancer development[4,5]

The risk of colorectal cancer (CRC) in UC depends upon the duration and extent of disease. In addition pa-

tients with UC complicating primary sclerosing cholangitis (PSC) may be at increased risk for CRC compared to those without PSC.[6,7] The American Gastroenterological Association (AGA) recommends that colonoscopic surveillance should begin after 8 years in patients with pancolitis and after 15 years in patients with left colon colitis, whereas colonoscopy should be repeated every one to two years.[8] The American Society for Gastrointestinal Endoscopy (ASGE)[9] recommends that patients with UC who have pancolitis should begin surveillance colonoscopy after 8 years of disease with 4 biopsies to be obtained every 10cm from the cecum to the rectum and any other suspicious lesions or masses. Moreover, ASGE recommends colonoscopy to be repeated every 1 – 3 years. The British Society of Gastroenterology guidelines recommends[10] that regular surveillance should begin after 8 to 10 years (from onset of symptoms) for pancolitis and after 15 to 20 years for left-sided colitis. For patients with pancolitis, a colonoscopy should be conducted every three years in the second decade of disease, every two years in the third decade and yearly by the fourth decade of disease. Two to four random biopsy specimens every 10cm from the entire colon should be taken with additional samples of suspicious areas.

The finding of carcinoma or high-grade dysplasia is an indication for colectomy.[5] Colectomy is also indicated for any degree of dysplasia associated with a lesion or mass whereas expert pathologists should confirm the finding of dysplasia. For patients with low-grade dysplasia confirmed by an expert pathologist, the ASGE acknowledges that most experts recommend colectomy. However, in patients in whom colectomy is an feasible or unacceptable, frequent surveillance (e.g. every three to six months) is considered an acceptable alternative. Moreover, the ASGE recommends that prophylactic colectomy should be considered in patients with longstanding colitis.[9] The definition of longstanding was not specified.

CROHN'S DISEASE

Small intestinal or ileocolonic obstruction

The most common cause of *small bowel* obstruction in Crohn's disease is the formation of a *stricture*. Obstructive episodes often are precipitated by inflammatory edema that causes further narrowing in a stenotic segment of the small bowel. Treatment with nasogastric suction, fluids intravenously (IV) as well as steroids IV may result in resolution of the obstruction. Surgery is necessary in patients failing to improve with conservative therapy or who present with recurrent obstructive episodes.[11] The European evidence based Consensus on the diagnosis and management of Crohn's disease states that localized ileocaecal Crohn's disease with obstructive symptoms can be treated by primary surgery (evidence level 2b, grade C).[12] Albeit this consensus statement was agreed, many disagreed strongly with this; some would accept this only in very selected cases, while a minority thought that it could well be discussed with the patient as primary treatment of choice. The argument could be summarized that while corticosteroids would probably bring such a patient into remission, they would almost always have an operation sooner or later. In the same Consensus, conventional stricturoplasty is advised when the length of the stricture is < 10cm. However, in extensive disease with long strictured bowel segments, where resection would compromise the effective small bowel length, non-conventional stricturoplasties may be attempted (evidence level 2a, grade C).[12] A phlegmon in the bowel wall, carcinoma or active bleeding mucosal disease are contraindications to stricturoplasty. According to the Consensus, in cases with multiple strictures in a short segment and when bowel length is sufficient to avoid short bowel syndrome, resection may be preferable.

In cases of colon strictures, the Consensus states that stricturoplasty is not recommended (evidence level 4, grade D) perhaps due to concern of an increased chance of cancer in a colonic stricture when compared with the small bowel.[12]

In an attempt to avoid surgery in patients with symptomatic Crohn's strictures, various nonnsurgical techniques have been successfully utilized,[13] including:

- Balloon dilation (± corticosteroid injections)
- Savary dilation
- Endoscopic needle knife incisions
- Self-expandable metal stents
- Finger dilation

Some clinical situations to consider nonsurgical management of strictures are:

- Endoscopically accessible
- Multiple prior intestinal resections
- Shorter strictures (less than 8cm)
- Consider intralesional steroid injection if significant inflammation present

According to the European Consensus, hydrostatic balloon dilation is an accepted technique for the man-

agement of mild to moderate stenosing disease with a short to mid-term benefit.[12] Moreover, it is stated that in Crohn's disease stenoses, dilatation should only be attempted in institutions with 24 hour surgical service (as perforation or other complications may occur requiring surgical intervention).[14,15]

Inspired by the success of using intralesional corticosteroids in caustic strictures of the esophagus,[16] case report studies investigated local steroids injections with stricture dilation achieving a prolonged symptom-free period.[17] Experience with self-expanding metal stents in Crohn's disease has been limited but studies have provided satisfying results.[18]

Perianal disease and fistulas

Perianal disease is a frequent and recurrent manifestation of Crohn's disease with high morbidity and mortality and it includes such lesions as anal fissure, ulcerated hemorrhoidal tissues, intrarectal ulcers, subcutaneous fistulas, anal stricture and deep perianal abscesses and fistulas. For *simple perianal fistulas*, according to the European evidence based consensus on the diagnosis and management of Crohn's disease,[19] it is important to know if they are symptomatic. If they are not, nothing has to be done but if they are symptomatic the options of non-cutting Seton or fistulotomy are recommended (evidence level 3, grade D). Combination with medical treatment, such as metronidazole (750-1500 mg/day) or ciprofloxacin (1000 mg/day) is favoured (evidence level 3, grade D). Other options are azathioprine / 6- mercaptopurine and infliximab. Neither cyclosporin nor tacrolimus were favoured as a fourth option. For *complexed perianal* disease, antibiotics (metronidazole and / or ciprofloxacin) and / or azathioprine / 6-mercaptopurine should be used as the first choice of therapy in combination with surgical therapy despite a lack of clinical trials (evidence level 4, grade D).

Infliximab should be used as a second line treatment (evidence level 1b, grade B). Infliximab (Remicade, Centocor, Malvern, PA), is a chimeric monoclonal antibody (75% human, 25% mouse) that targets tumor necrosis factor (TNF), a potent proinflammatory cytokine pivotal in the initiation and promotion of intestinal inflammation.[20] Infliximab has been approved by the FDA for maintenance of remission as well, in both refractory and fistulizing Crohn's disease. Clinically accepted indications for maintenance therapy include maintenance of fistula improvement (reduction in the number of draining perianal or enterocutaneous fistulas) and complete fistula response (no draining fistulas) in patients with fistulizing Crohn's disease who responded to initial induction therapy with infliximab.[21] For treatment of simple or complex perianal fistulas, 5mg/kg infusions at weeks 0,2 and 6 induced complete closure (cessation of all drainage on two visits one month apart) in 17 to 31 (55%) of cases.[22] The ACCENT II trial confirmed this initial response and randomized responders to receive 5mg/kg every eight weeks or placebo.[23,24] At week 54, 33 of 91 (36%) on infliximab had complete closure compared with 19 of 98 (19%) receiving placebo ($p = 0.009$). There are no data on the effect of infliximab on simple Crohn's perianal fistulas. It has to be mentioned that surgical treatment is sometimes necessary for simple fistulas but is always necessary for complex perianal disease. In cases of infliximab failure, the use of AZA / 6-MP or methotrexate with antibiotics as adjunctive therapy is the first therapeutic choice (evidence level 5, grade D). Depending on the severity of the disease surgical intervention (e.g. diverting ostomy or proctectomy as the last resort) can be performed later.[19]

According to the European Consensus of Crohn's disease, Seton placement should be recommended in relation to the symptoms caused by the location and complexity of the fistulas (evidence level 4, grade D).[19] A diverting ostomy can rapidly restore the quality of life in highly symptomatic patients with severe disease refractory to medical therapy (evidence level 4, grade D). Fistulectomy and fistulotomy should not be performed because of the risk of incontinence and later need of proctectomy.

For *enterogynaecological fistulas* and especially low anal-introital fistula no need for surgical intervention exists, as these fistulas may be almost asymptomatic (evidence level 5, grade D). If the patient has a symptomatic fistula, surgery is usually necessary (including diverting ostomy) (evidence level 5, grade D). Rectovaginal fistulas failing conservative treatment should have surgery with an advancement flap and / or divertingostomy as they are associated with unacceptable symptoms (evidence level 5, grade D). Intestinal small bowel or sigmoid-gynaecological fistulas can usually be treated with resection of the diseased bowel segment (evidence level 5, grade D).[19]

For *enterovesical fistulas* surgery is the preferred approach (evidence level 5, grade D). Only in high risk patients (and after multiple operations and/or severely shortened bowel) should medical therapy be the first option (evidence level 5, grade D).[19]

For primary *enterocutaneous fistulas* either surgically (by resecting the diseased bowel segment) or medical therapy could be the treatment of choice. On the oth-

er hand, post-surgical enterocutaneous fistulas should initially be treated conservatively with nutritional support and anatomical definition (evidence level 5, grade D).[19]

Concomitant abdominal abscess

Intra-abdominal abscesses in Crohn's disease patients present with classical features such as abdominal pain and fever or with atypical manifestations such as malaise, back pain or cough (due to diaphragmatic irritation). Abscesses may be identified by CT or MRI of the abdomen and pelvis (especially for patients with iodine contrast allergy or significant renal insufficiency). According to the European Consensus on Crohn's disease, active small bowel Crohn's disease with concomitant abdominal drainage should preferably be managed with antibiotics, surgical or percutaneous drainage followed by delayed resection if necessary (evidence level 3, grade C).[12]

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