

## MEDICAL TREATMENT OF FULMINANT ULCERATIVE COLITIS

### Severe disease

- Patients with a severe or fulminant presentation usually have extensive colonic involvement, often extending to the cecum (pancolitis).
- These patients typically have frequent loose stools (greater than 10 per day) with severe cramps, fever, and bleeding often necessitating blood transfusion.
- They may suffer rapid weight loss.
- In severely ill patients, the inflammatory process may extend beyond the mucosa to involve the muscle layers of the colon.
- In this setting, colonic motility is impaired, the colon dilates, bowel movements may become less frequent, and a pattern termed **toxic megacolon** ensues.
- 1/3 of patients present with pancolitis.
- Less than 10 percent present with fulminant disease.

### TREATMENT

- **Pancolitis**
  - Mild to moderate symptoms are treated with the combination of oral 5-ASA or sulfasalazine and topical therapy with either 5-ASA or steroid enemas.
  - The addition of oral prednisone (40 to 60 mg/day) should be considered in two settings:
    - those with more severe symptoms
    - those who fail to respond to oral 5-ASA and topical therapy.
  - Once a patient has achieved remission, long-term maintenance therapy should be considered with a standard maintenance dose of an oral 5-ASA agent.
  - At times, the addition of maintenance topical 5-ASA may further decrease the risk of disease exacerbation.
- **Severe ulcerative colitis** –
  - the mainstays of therapy are bowel rest, and parenteral steroids.
  - In some cases, flare-up coincides with a recent increase in dose or addition of a 5-ASA agent. The medication should be withheld in this setting.
  - Parenteral steroids - Hydrocortisone (100 mg IV q8h), Prednisolone (30 mg IV q12h), or Methylprednisolone (16 to 20 IV q8h).
  - For patients with persistent symptoms after 48 to 72 hours of such therapy, the addition of 5-ASA or hydrocortisone enemas once or twice a day may be helpful, particularly if lower colonic symptoms of tenesmus and urgency predominate.
  - The role of antibiotics in the patient with severe colitis who is not toxic is not clear.
    - Controlled trials assessing the addition of intravenous metronidazole to parenteral steroids in severe colitis did not show benefit compared to steroids alone.
    - there may be a subgroup of patients who do not fully respond to steroids and continue to run low grade fevers with elevated WBC; they may respond to a course of broad-spectrum antibiotics.
  - In contrast, broad-spectrum antibiotics should be given to all patients who present with fulminant disease with high fever, leukocytosis and peritoneal signs or megacolon.
  - Supine abdominal films should be obtained at the time of admission.

- Patients with intestinal dilation should receive decompression with a NGT and may benefit from insertion of a rectal tube.
- **Indications for colectomy or cyclosporine**
  - Patients with toxic megacolon who do not respond to therapy within 72 hours should be considered candidates for colectomy.
  - Less severely ill patients usually respond to parenteral corticosteroids within 7 to 10 days.
  - Those who do not respond become candidates for colectomy or intravenous cyclosporine.
  - Surgery is recommended if a response to cyclosporine is not seen in 7 to 10 days.
  - In a controlled trial, 20 steroid-resistant patients with severe colitis were randomly assigned to placebo or cyclosporine given at a dose of 4 mg/kg per day as a continuous infusion.
    - Response within a mean of seven days occurred in 9 of 11 patients given cyclosporine versus none of those given placebo.
    - Furthermore, all placebo-treated patients who were then given cyclosporine had a response.
  - A separate controlled trial of 30 patients suggested that cyclosporine monotherapy (i.e. in patients who had not received corticosteroids) was associated with a similar rate of remission as patients treated initially with corticosteroid (64 versus 53%).
  - Cyclosporine may be particularly suitable in steroid-resistant patients with new onset ulcerative colitis presenting as severe or fulminant disease, especially those who are not psychologically prepared for colectomy.
  - However, only a few reports have described the long-term outcome of patients who have had their colon salvaged with cyclosporine.
  - In one report, cyclosporine permitted the avoidance of colectomy for up to 5.5 years in 62% of 42 patients who initially had severe steroid-refractory ulcerative colitis;
  - patients who also received treatment with 6-MP or Azathioprine were more likely to retain their colons (80 versus 55%).
  - A second study included 86 patients of whom 72 (84%) had responded to initial intravenous cyclosporine.
    - Sixty-nine patients were discharged on oral cyclosporine.
    - Azathioprine was added in 64 patients.
    - A second course of cyclosporine was needed in 11 patients while one received a total of three courses.
    - During average follow-up of 773 days, 18 (25%) of responders underwent colectomy.
    - Serious complications were observed in four patients including three who died of opportunistic infections and one who developed anaphylactic shock.
  - Many of the studies described above administered cyclosporine at a dose of 4 mg/kg per 24 hours with the goal of achieving a stable trough level of 300 to 400 nanograms/mL.
    - However, a lower dose of cyclosporine (2 mg/kg adjusted to a stable trough level of 150 to 250 nanograms/mL) appears to have similar efficacy and may have less toxicity.

- A controlled trial involving 73 subjects found that a clinical response occurred in a similar proportion of patients by eight days (84 versus 86% in the 4 versus 2 mg/kg groups, respectively)
- Short term colectomy rates were also similar (13 versus 9%).
- Although the overall rate of adverse effects was similar, there was a trend toward a higher incidence of hypertension in the higher-dose group.
- For responding patients who have not previously been on AZA or 6-MP, oral CSA (8 mg/kg per day) should be continued for three to four months while 6-MP or azathioprine is introduced.
- Blood trough levels should be maintained in the range of 150 to 300 nanograms/mL.

#### References:

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