Case Reports

Infliximab in the treatment of ulcerative colitis with toxic megacolon

Parupudi V J Sriram, K S Pavan Reddy, Guduru V Rao,*
Darisetty Santosh, Duvvuru Nageshwar Reddy

Departments of Gastroenterology and *Gastrointestinal Surgery,
Asian Institute of Gastroenterology, Hyderabad 500 082

Toxic megacolon is a gastrointestinal emergency requiring prompt management to avoid fatal outcome. Although a majority of patients respond to conservative treatment, those not responding have been treated with intravenous cyclosporine or emergency surgery. Infliximab has been tried in patients with severe steroid-refractory ulcerative colitis. We report the successful use of this drug in the management of toxic megacolon in a 48-year-old woman not responding to the routine measures and who refused surgery. [Indian J Gastroenterol 2004;23:22-23]

Key words: Inflammatory bowel disease, ulcerative colitis

Toxic megacolon is a rare but potentially lethal complication of idiopathic inflammatory bowel disease or infectious colitis, characterized by total or segmental non-obstructive colonic dilatation to at least 6 cm, associated with systemic toxicity.1 The initial mode of treatment is conservative, in the form of parenteral hydration, nasogastric aspiration, intravenous antibiotics and parenteral hydrocortisone. Absence of response even after 48-72 hours usually necessitates emergency colectomy. Some of these cases have been reported to respond to intravenous methyl prednisolone, cyclosporine and, more recently, biological agents such as monoclonal antibodies against TNF-alpha.2 We report a lady with severe ulcerative colitis with toxic megacolon not responding to conventional medical management, treated successfully with intravenous infliximab.

A 48-year-old woman, on treatment for ulcerative pancolitis, developed exacerbation of symptoms in the form of pain in abdomen, bloody diarrhoea and fever. She was initially treated elsewhere with nil oral, parenteral antibiotics, hydrocortisone and rehydration, but deteriorated. On examination, she was dehydrated, severely pale and febrile. She had distension of abdomen and decreased intestinal peristalsis. Serum biochemistry revealed anaemia (haemoglobin 8 g/dL) and hypokalaemia (serum potassium 1.9 mEq/L). E. histolytica and giardia infection were excluded by stool examination and the C. difficile toxin assay was negative. Abdominal X-ray showed diffuse colonic dilatation, predominantly in the transverse colon, measuring 7 cm (Fig).

She was treated in the intensive care unit with bowel rest, rehydration with potassium correction, blood transfusions, parenteral hydrocortisone (100 mg IV 6 hourly), and antibiotics (cefotaxime 2 g 8 hourly, amikacin 375 mg 8 hourly, metronidazole 500 mg 8 hourly). There was no response over the next 72 hours and she developed features of impending perforation in the form of diffuse abdominal tenderness and hypoperistalsis. An immediate colectomy was planned, but the patient refused surgery. Intravenous cyclosporine was contemplated but it was not readily available.

She was started on infliximab infusion (5 mg/kg). The abdominal distension and pain started decreasing by the 3rd day (Fig). She was continued on bowel rest and antibiotics while the parenteral corticosteroids were tapered. Over the next two weeks she gradually recovered and became completely asymptomatic, passing 4-5 formed stools daily without blood. She was started on oral feeding and could be discharged from the hospital on day 15 on oral mesalazine, prednisolone and azathioprine. On her last follow-up 6 months later, she continued to be asymptomatic on oral mesalazine and azathioprine.

Management of toxic megacolon requires aggressive medical therapy. Emergency surgery is considered in case of deterioration. The mortality associated with surgery prior to the onset of perforation is much less (2%-8%) than that with perforation (>40%).

In the absence of response to medical management, non-surgical alternatives such as colonoscopic decompression,3 knee-elbow position,4 intravenous cyclosporine and, more recently, the anti-TNF alpha monoclonal antibody, infliximab,5 have been tried.

Infliximab is a genetically engineered IgG1 murine-human chimeric antibody that neutralizes both the soluble
and transmembrane TNF, as well as blocks the TNF-producing cells via complement fixation, antibody-dependent cytotoxicity, and apoptosis of T lymphocytes. Although the role of infliximab in the management of Crohn’s disease is well accepted, there are only few studies on its utility in ulcerative colitis. In the study by Evans et al., five of 8 patients responded to infliximab while all three placebo-treated patients needed colectomy. Sands et al. reported 50% response rate with the use of infliximab in a double-blind placebo-controlled study of steroid-refractory ulcerative colitis, while none responded in the placebo group. Chey et al. successfully treated with infliximab 16 of 17 patients with severe refractory ulcerative colitis admitted for elective colectomy. So far, there are no reports of infliximab use in the management of toxic megacolon.

To conclude, early detection and prompt institution of medical therapy are crucial in the management of toxic megacolon. Early surgery may be necessary in patients who do not respond to medical therapy. When surgery is not possible, infliximab appears to be promising.

References

Correspondence to: Dr Nageshwar Reddy, Director and Chief Gastroenterologist. Fax: (40) 2332 4265. E-mail: nage@satyam.net.in, dnr1988@yahoo.com
Received June 2, 2003. Accepted July 24, 2003

Acknowledgement
The Editorial Board of the Journal expresses sincere gratitude to Dr K R Palaniswamy and the Organizing Committee of the 44th Annual Conference of the Indian Society of Gastroenterology, Chennai for the generous contribution of Rs 300,000 to the Journal