

CASE REPORT

Treatment of Crohn's Disease Recurrence After Ileoanal Anastomosis by Azathioprine

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Ileoanal anastomosis is a surgical procedure used in the treatment of ulcerative colitis. Crohn's disease is considered a contraindication of this procedure (1). As experience in this technique has grown, it has become evident that a clinically apparent acute pouch inflammation syndrome, termed pouchitis, has become a major complication. The cause of pouchitis is unknown. However, in a small number of patients operated on for ulcerative colitis or indeterminate colitis, Crohn's disease will occur in the reservoir, mimicking pouchitis (2). The localization of Crohn's disease in the ileal reservoir may lead to pouch excision and to a permanent terminal ileostomy (3).

Immunosuppressive drugs are efficient in the treatment of inflammatory bowel diseases (4). Azathioprine and 6-mercaptopurine showed a dramatic effect in the treatment of chronic active disease in patients who were deemed unresponsive to corticosteroids or sulfasalazine (5).

In this study we report on two patients with Crohn's disease of the reservoir after ileoanal anastomosis who have been successfully treated with azathioprine.

CASE REPORT

Case 1. Mr. B, a 20-year-old man, had suffered from ulcerative colitis since 1986. In 1987, a subtotal colectomy with ileorectal anastomosis was performed for an acute severe attack of colitis (Truelove index severe). In 1988, an ileoanal anastomosis with a J reservoir was performed for acute proctitis unresponsive to treatment by corticosteroids. The histological examination of the reservoir showed a nonspecific inflammation in the resected rectum and the diagnosis of Crohn's disease was suspected. In January 1989, a bloody diarrhea with abdominal pain, fever, weight loss, and malaise appeared. Ileoscopy of the reservoir showed mucosal edema with large ulcerations in the reservoir. ESR was 60 at the first hour. Despite successive treatments by metronidazole (Flagyl 1.5 g/day for 15 days) amoxicilline, and clavulanic acid (Augmentin 2 g/day for 15 days), 5-aminocyclic acid (Mesalazine, locally), and corticosteroids (0.5 mg/kg for one month), there was no clinical or endoscopic improvement of the pouchitis. Repeated biopsies of the reservoir and of the ileum showed active inflammation with cryptic abscess but there was no granulomata. In July 1989, a fistula *in ano* was diagnosed, and new biopsies of the reservoir showed the presence of granulomata. A diagnosis of Crohn's disease was done and a treatment by azathioprine (100 mg/day, 2 mg/kg) and corticosteroids (prednisolone 60 mg/day) was started in September 1989. The follow up was characterized by a clinical improvement, a weight gain of 15 kg, and an improvement of diarrhea (stool frequency = 4-5 per day). During that time, corticosteroids were progressively decreased and stopped on May 1990. In December 1990, the endoscopy of the reservoir showed the disappearance of ulcerations and inflammation. Biopsies showed a slight chronic inflammation of the mucosa without ulcerations or granuloma. At that time ESR was normal. In March 1991, the patient stopped azathioprine. Since that time to now, his

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clinical condition has been satisfactory and the endoscopic appearance of his reservoir is normal.

Case 2. Miss M, a 16-year-old, had suffered from ulcerative colitis since December 1984. Despite corticosteroid treatment (prednisolone 1 mg/kg/day) and total parenteral nutrition, her clinical situation did not improve and an ileoanal anastomosis was performed on May 1985. Histological examination of the operated colon showed cryptic abscess, mucosal ulcerations, and no granulomata. In March 1988, diarrhea recurred. An endoscopy of the reservoir showed diffuse aphthoid ulcerations, suggesting pouchitis. A clinical improvement was observed after treatment by metronidazole (Flagyl 1.5 g/day for 15 days). In March 1989, diarrhea, fever, and abdominal pain recurred. Endoscopy showed diffuse ulcerations and inflammation of the reservoir. Granulomata was present on the biopsies of ileal reservoir and of the gastric antrum. ESR was 75 at the first hour. Prednisolone (50 mg/day) was started and her clinical situation improved. Endoscopy of the reservoir showed the presence of ulcerations. Prednisolone was decreased to 35 mg/day. In July 1989, azathioprine (50 mg/day, 1 mg/kg) was started. The evolution was characterized by an improvement in clinical symptoms and in endoscopic lesions. Prednisolone was progressively decreased and stopped in September 1989. In July 1991 the patient stopped azathioprine and since that time, her clinical and biological situation has been satisfactory.

DISCUSSION

Pouchitis is a poorly understood complication of ileoanal pouch surgery and continent ileostomy, which occurs mainly in patients operated on for ulcerative colitis. Pouchitis is characterized by a combination of watery diarrhea, cramping lower abdominal pain, and systemic upsets such as fever and arthralgia with endoscopic finding of erythema, contact bleeding, and ulcerations in the ileal reservoir. Postulated etiologies of this syndrome include bacterial overgrowth in the reservoir or recurrence of Crohn's disease in the terminal ileum. The differential diagnosis between pouchitis and recurrent Crohn's disease is difficult since the histological and endoscopic features of these two diseases are very similar (6, 7). In our two patients, the diagnosis of Crohn's disease can be affirmed since granulomata was found in the ileal reservoir and gastric antrum in one patient and since the other patient has a fistula *in ano* and granulomata in the reservoir. In one patient, the diagnosis of Crohn's disease was suspected at the histological examination of the resected rectum (patient 1). Recent data from the Mayo Clinic have shown that the occurrence of Crohn's disease in patients operated on for indeterminate colitis was higher than in patients with ulcerative colitis (International Symposium on AIA,

Versailles, France, September 1992). The diagnosis of pouchitis in such patients must be very prudent and histological examination of multiple biopsies must be done to find granulomata, which in this condition are very suggestive of Crohn's disease.

Our two patients went into a complete clinical remission after a few months of treatment by corticosteroids and azathioprine. Azathioprine induced a disappearance of the inflammatory process and allowed a reduction and discontinuation of corticosteroids. Furthermore, the ileoscopy of the reservoir showed a disappearance of ulcerations and inflammation. No side effects were observed after, respectively, 18 and 24 months of treatment by azathioprine. However, since Crohn's disease is a recurrent disease, these patients are most likely to have another bout of pouchitis in the future. A longer follow-up is necessary, to see the outcome of the reservoir in future.

The mechanisms of action of azathioprine in inflammatory bowel disease have been discussed but this drug affects almost every aspect of the inflammatory immune response. Azathioprine has been shown to decrease the production of mediators such as prostaglandins, leukotrienes, and platelet-activating factor (PAF). Since we have previously shown that stool PAF levels were increased in patients with pouchitis (8) and in patients with Crohn's disease (9), we suggest that azathioprine can decrease PAF production and promote healing of ileal ulcerations and inflammation. In one patient, stool PAF levels were monitored before and after azathioprine treatment. In this case (unpublished data), stool PAF concentration decreased and then was not detectable when a complete healing of the reservoir was observed.

These two observations suggest that immunosuppressive drugs are a good option for permanent ileostomy in cases of recurrence of Crohn's disease in the reservoir after ileoanal anastomosis. In these two patients, clinical and endoscopic long-term monitoring is necessary since recurrence of Crohn's disease in the reservoir is possible.

SUMMARY

Ileoanal anastomosis is a surgical procedure performed in patients with ulcerative colitis. In a small number of patients operated on for ulcerative colitis, Crohn's disease occurs in the reservoir, mimicking pouchitis, and may lead to pouch excision and to a permanent terminal ileostomy. Two pa-

tients with recurrent Crohn's disease in the reservoir after ileoanal anastomosis were treated with azathioprine for 18 and 24 months, respectively. Azathioprine induced a complete clinical and endoscopic remission. These two observations suggested that immunosuppressive drugs were a good option for permanent ileostomy in cases of recurrence of Crohn's disease in the reservoir after ileoanal anastomosis.

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