

Refractory pouchitis

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The introduction of reconstructive surgery following proctocolectomy for ulcerative colitis has made a substantial improvement in the quality of life for the majority of patients. Although a temporary stoma is usually required, the fashioning of an ileal-anal pouch avoids a permanent stoma. In most series, 80% or so of patients are satisfied with the operation even if they have to empty their pouch frequently and may need to take anti-diarrhoeal agents. The major difference from when they had an intact, but inflamed, colon is that they no longer suffer from urgency and the fear of incontinence. Less than 10% have any seepage, mostly at night, and this usually improves with time. Nevertheless, the operation is not without its problems and pouch dysfunction is frequently seen.

Pouch dysfunction

Table 1 lists some of the commonest causes of pouch dysfunction. If pouchitis is excluded by "pouchoscopy" and biopsy, each of these causes needs to be considered. However, a more detailed discussion of these factors is beyond the remit of this chapter.

Table 1. — Causes of pouch dysfunction

Pouchitis, prepouch ileitis, cuffitis
Pelvic infection, pouch-vaginal fistula
Small volume, non-compliant pouch
Partial ileal obstruction
Small-bowel motility disorder
Dietary intolerance
Crohn's disease

Pouchitis

Pouchitis is the term used to describe pouch mucosal inflammation and presents with increasing diarrhoea, often with blood, pelvic discomfort, malaise and occasionally fever. Some patients may have acute extra-intestinal symptoms (e.g. erythema nodosum or an acute arthropathy), especially if they had these manifestations prior to colectomy. Inspection of the pouch mucosa shows it to be actively inflamed, often with a patchy distribution. There may be discrete ulceration. Thus the diagnosis of pouchitis has to be made by visualising the pouch mucosa and by taking biopsies.

Since the inflammation is frequently patchy, it is recommended that biopsy specimens are taken from the

anterior and posterior walls both low down and from the upper part of the pouch. Pouchitis has to be differentiated from pre-pouch ileitis and cuffitis. The former condition consists of ileal inflammation proximal to the pouch and can produce symptoms similar to pouchitis. It is uncommon, its pathogenesis is not understood and it usually responds to antibiotics or corticosteroids — it is not necessarily Crohn's disease. Cuffitis refers to inflammation in the cuff between the dentate line and the ileo-anal anastomosis. It causes extreme urgency, pain, frequency and often bleeding. The cause is unknown but may reflect residual colitis — treatment can be difficult but many cases seem to respond to local anaesthetic (e.g. lignocaine gel) or suppositories of either mesalazine or corticosteroid.

Epidemiology of pouchitis

The frequency of pouchitis has varied considerably between series. This has been due to differences in definition — some large American centres initially adopted a symptomatic definition and thus were able to make a diagnosis on the telephone. Other centres have required endoscopic inflammation and evidence of acute inflammation on biopsy for the diagnosis, in conjunction with a negative stool culture. Nevertheless, at least 45% of patients will have at least one attack of acute pouchitis, and two thirds of these will have more than one attack. Acute pouchitis usually occurs within one year of the pouch being formed but some patients may go several years before their first attack. In the major centres, there is a general impression that the incidence and frequency of pouchitis has diminished but this is not well documented. In 10-15% of patients, the pouchitis appears refractory to treatment or symptoms recur soon after stopping antibiotics.

Pathogenesis of pouchitis

The most obvious risk factor for pouchitis is a previous diagnosis of ulcerative colitis. Thus, it is exceptionally rare for pouchitis to occur in patients who have had

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a restorative proctocolectomy for familial polyposis. Pouchitis has also been associated with a particular HLA type (DRB1*0103), the presence of pANCA, and non-smoking – all features that may be associated with ulcerative colitis itself. Most investigators regard “idiopathic” pouchitis as ulcerative colitis occurring in ileal mucosa which has undergone colonic metaplasia. This occurs to a variable extent in any pouch regardless of the initial diagnosis. Thus it would appear that those with previous ulcerative colitis may be genetically prone to develop inflammation in colonic epithelium in response to luminal contents. The effectiveness of antibiotics for acute pouchitis and of pro-biotics for refractory pouchitis (see later) would support this concept.

Assessment of pouchitis

As implied above, there has been confusion regarding the diagnosis, classification, and measurement of activity of pouchitis. Most clinicians require histological evidence of acute inflammation to make the definitive diagnosis. A histological scoring system has been developed which scores acute and chronic changes separately and an aggregate score of 6/12 denotes pouchitis. This scoring system works well in practice but occasionally patients will have a high score but no symptoms. Thus, the Mayo Clinic have devised a Pouchitis Disease Activity Index (PDAI) which is primarily based on symptoms and endoscopic appearances. This has proved useful for clinical trials but can be falsely elevated by symptoms which might arise from any of the other causes of pouch dysfunction as well as pouch inflammation. In clinical practice, the histological index is probably the most useful but, for clinical studies, both forms of assessment should be used.

Treatment

The majority of isolated attacks of acute pouchitis can be treated with antibiotics (e.g. metronidazole, ciprofloxacin) which are usually given for 7-14 days. One randomised controlled trial of metronidazole has provided good evidence for this practice although the numbers included were quite small.

Treatment becomes much more difficult for those few patients who have chronic-active pouchitis which is not responding to antibiotics or which relapses rapidly on stopping antibiotics. For these few patients, it is useful to go through the following check-list :

1. Check that pouchitis is present histologically.
2. Check for pre-pouch ileitis or cuffitis even if pouchitis is confirmed. In particular, check the length of the cuff.
3. Check for stenosis at the pouch-anal anastomosis.
4. Check for completeness of pouch emptying. Many patients with refractory pouchitis will have incomplete emptying i.e. greater than 15% counts in an iso-

tope study remaining after evacuation even in the absence of anastomotic stenosis.

5. Check for pathogens, bacterial overgrowth in the ileum proximal to the pouch (e.g. secondary to partial obstruction from adhesions) and particularly for dietary intolerance all of which can make symptoms of pouchitis much more severe. A pelvic CT or magnetic resonance scan should be done to exclude pelvic sepsis. Crohn's disease must always be considered but neither the presence of pre-pouch ileitis nor the presence of granulomata in pouch biopsies should automatically lead clinicians to change the diagnosis to Crohn's disease.

Treatment of refractory pouchitis is unsatisfactory but the following steps are useful and are listed in the order of preference :

1. Consider prolonged courses of antibiotics — this is most appropriate for ciprofloxacin in view of the risk of peripheral neuropathy if long-term metronidazole is used.
2. If anastomotic stenosis is present, dilatation under anaesthetic followed by twice daily insertion of a plastic dilator can be helpful.
3. If incomplete emptying is documented or suspected, in the absence of stenosis, draining the pouch with a large-bore catheter (e.g. a Medena catheter) every 1-2 hours can be highly beneficial.
4. Determine whether cuffitis is present. This can lead to incomplete evacuation of the pouch with subsequent stasis. Biopsies just above the dentate line (in the anal transitional zone) are often painful and local anaesthetic should be used.
5. If pouch evacuation is good and prolonged antibiotic is ineffective, then treatment with mesalazine or corticosteroids can be instituted. Suppositories or foams can be used but oral therapy may be necessary. If patients are still symptomatic, immunosuppressants such as azathioprine or 6-mercaptopurine will help some.
6. 5% or less of pouch patients will not be helped by any of these measures. Some will opt for pouch removal and a permanent ileostomy. If the cuff is long (> 2.5 cms), is inflamed, or is thought to be a factor in delayed emptying, then it is possible to take down the anastomosis, remove some of the cuff and re-anastomose the pouch within 2 cms of the dentate line. Alternatively, a mucosectomy is performed and the pouch is then hand-sewn directly onto the dentate line. If surgery is contemplated, it is probably better to de-function the pouch first for a period before revision is undertaken.

Novel therapies

Bismuth-carbomer foam enemas have been beneficial on an anecdotal basis but a small double-blind trial failed to show an advantage over placebo. Butyrate ene-

mas have not been successful and a comparative trial versus glutamate suppositories showed no difference in response rates — no placebo group was included.

The most promising approach for new therapies has been the use of probiotics. Gionchetti *et al.* have reported a placebo-controlled trial of a novel probiotic. Each capsule contained three species of Lactobacilli, two of Bifidobacteria and Streptococcus salivarius, the total number of organisms being 10^{11} per capsule. Patients who were said to have refractory pouchitis were finally brought into remission with antibiotics and then randomised to the probiotic or placebo for a period of one year. Further pouchitis occurred in only 3 of 20 patients compared with all patients receiving placebo. Unfortunately, as soon as the probiotic is stopped, the orally administered bacteria rapidly disappear from the stool and pouchitis returns. Nevertheless, this is an exciting development which clearly warrants further studies especially as probiotics are also being promulgated for the treatment of ulcerative colitis itself.

Conclusions

Overall, a restorative proctocolectomy provides a satisfactory operation for the majority of patients requiring surgery for ulcerative colitis. For the 5% or so who suffer a chronic pouchitis, there is now a clear algorithm for assessing the precise cause of symptoms and subsequent treatment. Defunctioning, refashioning or eventually pouch removal may be required in a few patients. The use of probiotics offers the most interesting new development.

Further reading

1. JEWELL D.P. Pathogenesis and treatment of pouchitis. *In* : RUTGEERTS P., COLOMBEL J.-F., HANAUER S.B., SCHOLMERICH J., TYTGAT G.N.J., VAN GOSSUM A. (eds.). *Advances in Inflammatory Bowel Diseases - Falk Symposium 106*. Dordrecht/Boston/London, Kluwer Academic Publishers ; 1999. pg. 301-309.
2. GIONCHETTI P., RIZZELLO F., VENTURI A. *et al.* Oral bacteriotherapy as maintenance treatment in patients with chronic pouchitis : a double-blind, placebo-controlled trial. *Gastroenterology*, 2000 ; **119** (2) : 305-309.