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Brief Clinical Observation

Collagenous pouchitis

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Abstract

Collagenous colitis is characterised by watery diarrhoea, normal colonic mucosa on endoscopy, diffuse colitis with surface epithelial injury, and a distinctive thickening of the subepithelial collagen table on histology. Some patients can develop medically refractory collagenous colitis, in which case they may require surgical intervention. This is the first report of collagenous pouchitis in a collagenous colitis patient with proctocolectomy and ileal pouch-anal anastomosis. A patient with medically refractory collagenous colitis who underwent a total proctocolectomy and ileal pouch-anal anastomosis was sequentially evaluated with an endoscopy and histology of the colon, distal small intestine, and ileal pouch. A 58-year-old female had a 10-year history of collagenous colitis before having a total proctocolectomy and ileal pouch-anal anastomosis for medically refractory disease. The histologic features of collagenous colitis were present in all colon and rectum biopsy or resection specimens, but were absent in the distal ileum specimen. The post-operative course was complicated by persistent increase of stool frequency, abdominal cramps, and incontinence. A pouch endoscopy was performed 3 years after ileal pouch-anal anastomosis which showed the histologic features of collagenous colitis in the ileal pouch, collagenous pouchitis, while the pre-pouch neo-terminal ileum had no pathologic changes. After antibiotic therapy, the histologic changes of collagenous pouchitis resolved. This is the first reported case of collagenous pouchitis. Since the abnormal collagen table and its associated features were only present in the pouch and absent in the neo-terminal ileum, and the patient had histologic improvement after antibiotic therapy, it would suggest that faecal stasis and bacterial load may play a role in the pathogenesis.

Keywords: Collagenous colitis; Pouchitis; Restorative proctocolectomy

1. Introduction

Collagenous colitis (CC) is a condition characterised by watery diarrhoea, endoscopically normal colonic mucosa, diffuse histologic colitis with surface epithelial injury, and a distinctive thickening of the subepithelial collagen table at histologic examination. In the normal intestine, collagen type IV, laminin, and fibronectin produced by epithelial cells constitute the normal components of the basal lamina propria [1]. Thickening of basal lamina in CC may be caused by the deposition of type I and III collagens which is produced by fibroblasts [2].

Microscopic colitis, including CC, accounts for 4–13% of patients investigated for chronic diarrhoea [3]. In Europe, CC has an incidence of 0.6–2.3 cases per 100,000 person-years and a prevalence of 10–15.7 cases per 100,000 persons [4,5]. In the US, the incidence of CC was 6.2 cases per 100,000 person-years as reported in a population-based study in Olmsted County, MN, from 1998 to 2001. In contrast, the incidence of lymphocytic colitis and CC were 6.4 cases per 100,000 person-years and 3.9 cases per 100,000 person-years, respectively, from the same population from 1994 to 1997 [6]. The findings suggest that CC, as well as lymphocytic colitis, has become increasingly recognised.

The aetiology and pathogenesis of CC and the deposition of a subepithelial collagen table are unknown but are thought to be due to a response to chronic injury. Several categories of medicines have been reported to be associated with CC, including non-steroidal anti-inflammatory drugs (NSAIDS) [7–9], antibiotics [8], lansoprazole [10], ticlopidine [11], and cimetidine [12]. There are several lines of evidence which

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suggest that CC may be associated with infections or inflammation and an abnormal immune response to luminal antigens [13,14]. An infectious aetiology was speculated based on findings that acute onset of disease occurred in up to 40% of patients with CC [15]; some of the patients responded to antibiotic therapy [16]; diversion of faecal stream after ileostomy or colostomy placement alleviated symptoms and reduced the thickness of the subepithelial collagen table [14]; the presence of faecal cytotoxins in patients with CC was neutralised by cholestyramine [16]; and there was chronic mucosal inflammation in CC as evidenced by mucosal histology and the presence of faecal leucocytosis [17]. The presence of pseudomembrane in colon biopsy specimens in some patients with CC would also support infection or toxin-related aetiology [14]. The subepithelial collagen deposition along the GI tract was reported in patients with infection from *Helicobacter pylori* [19], HIV [20], *Yersinia enterocolitica* [21,22], and *Clostridium difficile* infection [23]. Besides the faecal diversion models [14], there is no human model which could duplicate the clinical and histopathologic pattern of CC.

While the majority of patients with CC respond to medical therapy, some may develop a clinically refractory course, which then requires surgical intervention. Reported surgical treatment modalities include subtotal colectomy [24], hemicolectomy [25], and ileostomy or colostomy [14]. There have been case reports of ileal pouch-anal anastomosis (IPAA) following total proctocolectomy [14,26,27]. The role of IPAA in the treatment of refractory CC has not been established. However, faecal stasis, bacterial overload, and colonic metaplasia in IPAA would render such a surgery a unique model by which one could study the aetiology and pathogenesis of CC.

2. Case report

A 58-year-old Caucasian female presented with IPAA dysfunction and diarrhoea. She had suffered from chronic diarrhoea for years and was diagnosed with irritable bowel syndrome at age 20. At age 44, she was diagnosed as having CC with histologic features diffusely involving the colon and rectum. Upper endoscopies and small bowel biopsies showed no evidence of coeliac disease or collagenous enteritis. She was treated with a variety of medicines, including bismuth subsalicylate, 5-aminosalicylates, corticosteroids, subcutaneous somatostatin, 6-mercaptopurine, and infliximab. Her symptoms of diarrhoea and incontinence, as well as histologic features of CC, persisted. At age 54, she underwent a total proctocolectomy with an end ileostomy. Histologic evaluation of the colon and rectum specimen again showed mucosal changes of CC (Fig. 1). However, the terminal ileum of the proctocolectomy specimen showed no pathologic changes (Fig. 2). The post-operative course was complicated by increased ileostomy output, which resulted in several hospitalisations for dehydration. At age 55, a J-type IPAA was performed at a local hospital. Immediately after the ileostomy take-down, she experienced persistent diarrhoea and incontinence. Two years later, a pouch endoscopy showed mild inflammation of pouch mucosa on endoscopy and histology. She was treated for 'pouchitis' with ciprofloxacin, metronidazole, cholestyramine, oral and topical 5-aminosalicylates, bismuth subsalicylate, selective serotonin reuptake inhibitor antidepressants, or oral budesonide. However, her diarrhoea and incontinence symptoms failed to respond to regimens.

One year later, she was seen in our Pouchitis Clinic for chronic refractory, debilitating diarrhoea (stool frequency of 20–25 times per day), incontinence, bloating, and abdominal cramps. Her physical examination was unremarkable with no signs of malabsorption or malnutrition. There were multiple skin tags and erythema at the perianal area. She was diagnosed with depression due to the persistent bowel symptoms after the IPAA surgery. She also had osteoporosis and gingivitis. She never smoked or excessively used alcohol and she did not use NSAIDs or proton pump inhibitors. CBC, liver function tests, electrolytes, coeliac serology, antinuclear antigen, serum gastrin, and 5-HIAA were all normal. The diagnostic evaluation included CT scan of the abdomen and pelvis, small bowel series, serum trypsinogen, stool *C. difficile* toxin A and B, stool ova and parasites, stool cultures, stool

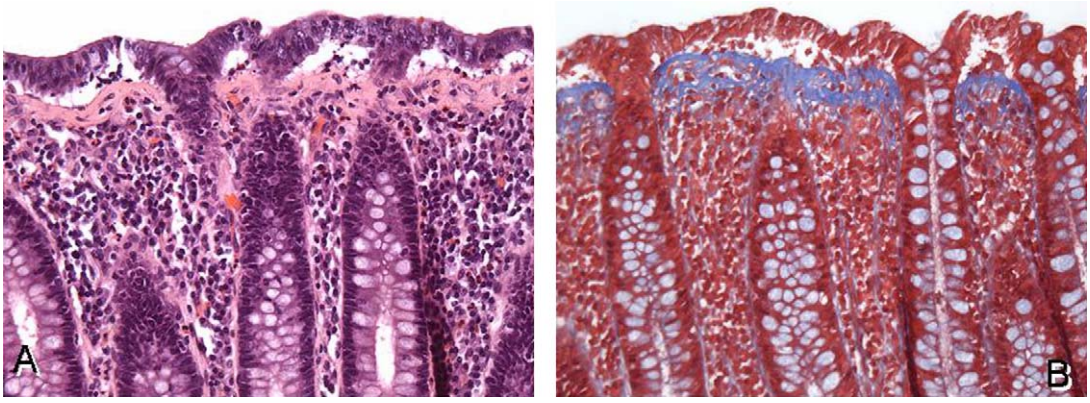

Fig. 1. Photomicrographs of CC from the total proctocolectomy with H & E (A) and trichrome (B) stains (20×). Histologic features include a thickened subepithelial collagen table with entrapped capillary vessels, intraepithelial lymphocytosis, and surface epithelial separation.