

CASE REPORT

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Protein losing enteropathy: A rare complication of ulcerative colitis

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Abstract

Protein-losing enteropathy (PLE) is a rare gastrointestinal condition that has been related to inflammatory bowel disease (IBD), namely ulcerative colitis (UC) and Crohn's disease (CD). These pathologies damage the mucosal integrity, thereby leading to an increased transfer of plasma proteins into the bowel lumen. Because of its rarity, incidence and prevalence of this condition are not well known. Depending upon the underlying cause, the clinical course of PLE is highly variable, but mainly consists of edema, ascites, pericardial and pleural effusions. Here, we report a case of PLE caused by UC, in which total colectomy lead to complete improvement of hypoalbuminemia.

Keywords: Protein-losing enteropathy, alpha-1 antitrypsin, ulcerative colitis, inflammatory bowel disease

Introduction

UC, a chronic relapsing IBD, is characterized by colonic inflammation that starts in the rectum and can extend proximally to the entire colon. The inflammation in UC is continuous and limited to the mucosal layer of the bowel wall. The etiopathogenesis of UC is incompletely understood, but immune-mediated mechanisms are responsible for dysregulated immune responses against intraluminal antigens in genetically predisposed individuals [1,2].

The diagnosis is based on the history, as well as clinical, radiological, endoscopic and histological features. Tests for perinuclear antineutrophil cytoplasmic antibodies and anti-*Saccharomyces cerevisiae* antibodies are often positive in these patients, and can help distinguish the condition from CD. UC typically presents clinically as bloody diarrhea with associated abdominal pain, tenesmus, and urgency. The differential diagnosis for UC includes CD and infectious colitis caused by bacterial, viral, or parasitic pathogens. UC must also be distinguished from microscopic colitis, a common cause of non-bloody diarrhea, abdominal pain, and weight loss in adults. Patients in whom UC is suspected should have bacterial stool cultures performed. Those with a history of

recent antibiotic use should be tested for *Clostridium difficile* toxin. Additional testing to exclude infectious etiologies may be performed depending on the patient's history. Approximately one-third of patients with UC have extraintestinal manifestations including pyoderma gangrenosum, uveitis, migratory arthritis and primary sclerosing cholangitis [1,2].

PLE is a rare gastrointestinal condition that has been related to IBD, namely UC and CD [3-5]. These pathologies damage the mucosal integrity, thereby leading to an increased transfer of plasma proteins into the bowel lumen. Because of its rarity, incidence and prevalence of this condition are not well known. Depending upon the underlying cause, the clinical course of PLE is highly variable, but mainly consists of edema, ascites, pericardial and pleural effusions. Here, we report a case of PLE caused by UC, in which total colectomy lead to complete improvement of hypoalbuminemia.

Case Report

A 33-year-old female patient was diagnosed with UC in 2011 after presenting with 6 months of abdominal pain and bloody diarrhea. Clinical remission was achieved with medical treatment (combination of oral and rectal topical 5-aminosalicylic acid) in 1 month. She was in complete remission for 4 years with this treatment regimen.

In March 2015, the patient admitted to an outside hospital with

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an acute flare of colitis. She was treated with oral steroid therapy (40 mg of prednisone daily) that was tapered off over the course of 3 months and disease remission was achieved. Her condition deteriorated again in March 2016 with bleeding from the rectum and diarrhea. When she admitted to our hospital, combination therapy with oral prednisolone 40 mg/day and azathioprine 100 mg/day were added to therapy. On follow up, however, there was no response to treatment and her symptoms did not improve. For this reason, after induction regimen, adalimumab 40 mg subcutaneous injection every two weeks was added to therapy. Unfortunately, no significant clinical or laboratory improvement was observed in the following weeks. Laboratory analysis were as follows; hemoglobin: 11.6 g/dL, ferritin: 314.8 ng/mL, albumin: 2.9 g/dL, sodium: 130 mEq/L, erythrocyte sedimentation rate: 83 mm/h and INR: 1.31. Adalimumab dose was increased to one administration per week. Flexible sigmoidoscopy at that time showed active inflammation from the rectum to the distal descending colon, with development of diffuse inflammatory pseudopolyps (Figure1). Cytomegalovirus inclusions were not found in rectal biopsy specimens.

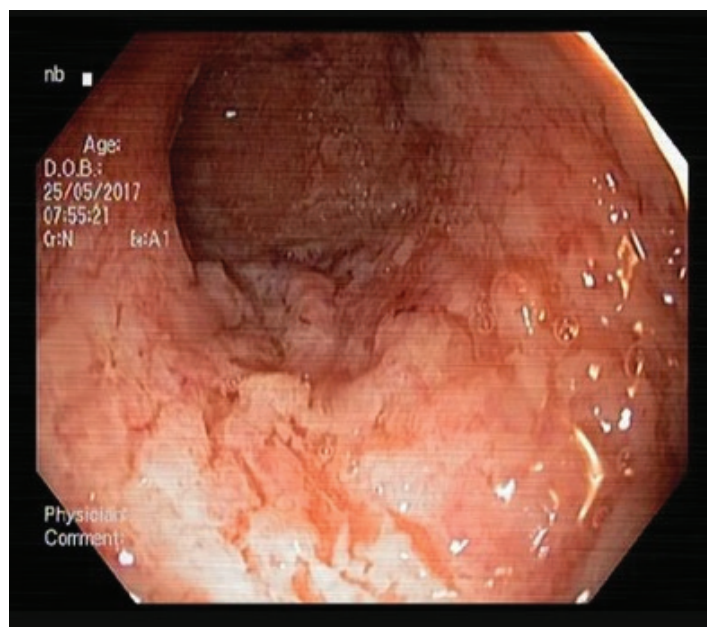


Figure 1: Friable, diffusely edematous and erythematous mucosa in a diffuse circumferential distribution from the anal verge to the sigmoid colon

Although intensive anti tumor necrosis factor (TNF) therapy alleviated the clinical condition of the patient, serum albumin levels continued to be below 2.5 g/dL. After possible etiologies which can lead to hypoalbuminemia (renal or liver failure, malabsorption syndrome, and severe malnutrition) were excluded by appropriate biochemical and radiological analysis, the condition was diagnosed as PLE. Due to the failure of medical treatment of UC and also PLE, the patient underwent a total abdominal proctocolectomy, rectal mucosectomy and “J” pouch ileoanal pull through without a temporary diverting ileostomy. After surgical intervention, the patient quickly regained weight in 3 months and returned to her normal life with a normal albumin level and 3-4 non-bloody bowel movements daily.

Discussion

PLE is an infrequent but severe complication of IBD and hypoalbuminemia may be the presenting symptom of this

condition [4,5]. The diagnosis of PLE in IBD can be made by the presence of persistent hypoalbuminemia and lack of the other etiologies which can lead to significant protein loss (renal or liver failure, malabsorption syndrome, and severe malnutrition) [6,7]. In addition, the diagnosis can be improved by the demonstration of elevated $\alpha 1$ -antitrypsin (AAT) concentration in stool. AAT is a circulating glycoprotein, which represents the majority of serine protease inhibitors and mainly synthesized in the liver. It is relatively resistant against enzymatic digestion and its amount in stool reflects the internal concentration of the protein. For this reason, an elevated fecal AAT concentration is a sensitive marker for intestinal protein loss and for an increased mucosal permeability [8,9]. In the present case, other possible etiologies, which can lead to hypoalbuminemia, were excluded by appropriate biochemical and radiological analysis. However, because of the insufficiency of laboratory equipment, we couldn't evaluate the fecal clearance of AAT. On the other hand, we think that, the improvement of hypoalbuminemia after surgery is another confirmation of the PLE diagnosis in our patient.

PLE occurs in various etiologies through different pathophysiologic processes, therefore, no single treatment reliably improves the condition and therapeutic approaches depend on the underlying etiology. Nutritional support focusing on protein deficiency is important, but it provides only limited health benefits. In the acute setting, albumin solutions may be used but it doesn't have long term efficacy. As mentioned above, the main goal in the treatment of PLE due to UC is the control of the underlying inflammatory process [10-12]. In general, medical treatment including anti-inflammatory agents, immunomodulators and immunosuppressives is the first step in the management of patients with UC. However, surgical therapy may be required in patients who become refractory to medical therapy. As shown in the present case, even when clinically improved, persistence of inflammation can still lead to massive loss of protein into the gastrointestinal lumen. Hence, hypoalbuminemia in our case did not show any improvement despite long term and intensive anti-TNF therapy. On the other hand, total colectomy lead to complete improvement of hypoalbuminemia along with the eradication of the bowel inflammation.

In conclusion, PLE is an uncommon but devastating complication of UC. It should be considered in any patient with hypoalbuminemia in whom other causes have been excluded. The presence of PLE may be a sufficient indication for surgical intervention in this clinically relevant condition

Conclusions

In conclusion, PLE is an uncommon but devastating complication of UC. It should be considered in any patient with hypoalbuminemia in whom other causes have been excluded. The presence of PLE may be a sufficient indication for surgical intervention in this clinically relevant condition

Competing interests

The authors declare that they have no competing interests.

Financial Disclosure

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Ethical approval

A consent for publication of this case report was obtained from the patient.

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