

Title:

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Authors:

Sandra Borrego Rivas, Alia Martín Izquierdo, Patricia Suárez Álvarez, Irene Latras Cortés, Mónica Sierra Ausín

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Small bowel ulcers and hypoproteinemia, differential diagnosis beyond inflammatory bowel disease

Sandra Borrego Rivas (sandra.borrego.r@gmail.com), Alia Martín Izquierdo, Patricia Suárez Álvarez, Irene Latras Cortés, Mónica Sierra Ausín.

Complejo Asistencial Universitario de León.

ABSTRACT

Protein-losing enteropathy is a relatively uncommon syndrome characterized by excessive loss of proteins into the intestinal lumen. It can be caused by various etiologies.

Inflammatory bowel disease (IBD) is the first condition we think of when we meet a patient with intestinal ulcers and hypoproteinemia. However, there are many other complicated and relatively novel etiologies, which we must be aware of in order to perform an appropriate differential diagnosis, such as the one we present.

Keywords: Ulcerative jejunitis. Protein-losing enteropathy.

Dear Editor,

Protein-losing enteropathy is a relatively uncommon syndrome characterized by excessive loss of proteins into the intestinal lumen. It can be caused by various etiologies. It may be the result of intestinal mucosal damage or obstruction of gastrointestinal lymphatics.

We present a 66-year-old male with chronic diarrhea, a calprotectin level of 2189 mg/kg, and severe hypoproteinemia with ulceration and stenosis of the terminal ileum observed during colonoscopy, with inconclusive biopsies. Given suspected inflammatory bowel disease (not previously treated with NSAIDs) with lack of response to oral corticosteroids, he was hospital admitted for further studies.

Abdominal CT showed mucosal hypercaptation of the terminal ileum, submucosal thickening, and vasa recta ingurgitation, all suggesting chronic inflammation with activity. Gastroscopy reveals atrophy of duodenal villi and the enteroscopy finds extensively ulcerated ileum mucosa, colon not affected. Histology found cytomegalovirus overinfection, with no definitive diagnosis of IBD.

There was no response to intravenous corticosteroids or ganciclovir. Infliximab was started, and discontinued due to infusional reaction after the second dose and lack of clinical response (suspected immunogenicity).

Despite supplemental enteral and parenteral nutrition, there was persistent worsening and development of strictures in the ileum, so 70 cm ileum resection with ileocecal anastomosis was performed. Histological examination revealed architectural distortion, villous atrophy, superficial ulcers and reactive pseudopolyps, with no granulomas.

After surgery, diarrhea and panhypoproteinemia persisted. Endoscopic capsule showed atrophy and small ulcers in jejunum, so ustekinumab was started despite the low suspicion of IBD, although there was no response either.

The investigation of ulcerative protein-losing enteropathy (EPP) was resumed. Normal stool clearance of alpha-1 antitrypsin was observed. Renal and cardiac etiologies were excluded.

Histology was never compatible with IBD and the patient did not recover despite treatment for the infections (with confirmed negativisation). Lupus, sarcoidosis, and amyloidosis were ruled out, as well as solid neoplasms and intestinal lymphoma. Despite duodenal atrophy, celiac disease was excluded (negative serology, non-compatible intraepithelial gamma-delta lymphocytes and non-response to a gluten-free diet). Biopsies also excluded eosinophilic gastroenteritis, Menetrier's disease, or Whipple's disease.

A rare entity called chronic non-specific ulcers of small intestine (CNSU), which causes patchy small bowel mucosa ulceration without systemic inflammation, remains to be ruled out.

Another condition to be considered in case of previous compatible history is graft-versus-host disease, as reported in an article in this same journal. Since the patient had no hematological history, this condition was excluded.

Due to the unknown specific etiology of the ulcerations, we carried out a treatment based on the immunomodulatory effect of azathioprine, combined with octreotide to reduce intestinal debit, finally leading to a clinical remission with normalization of all nutritional deficiencies and inflammatory biomarkers.

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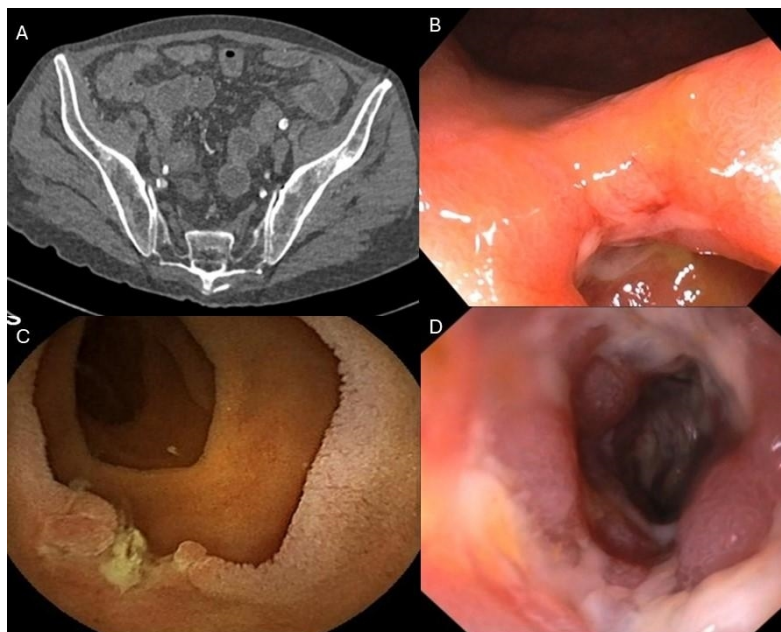


Fig 1. A. CT scan showing hypercaptation of the ileum, submucosal thickening and vasa recta ingurgitation.

B. Colonoscopy showing ulcerated ileum.

C. Endoscopic capsule with small ulcer in jejunum.

D. Enteroscopy with extensive ulceration of the ileum.