Protein-losing enteropathy secondary to graft-versus-host disease

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Dear Editor,

We report the case of a 23-year-old man who came to evaluation due to anasarca. Ten months prior, he underwent allogeneic hematopoietic stem cell transplantation (HSCT) for acute lymphocytic leukemia. Six months after HSCT, he developed chronic bloody diarrhea, abdominal pain, and skin plaques. Infections were discarded, leading to a suspicion of graft-
versus-host disease (GVHD). Oral prednisone and budesonide were started, with no improvement; One month before admission, he continued with bloody diarrhea and developed lower limb edema that progressed to anasarca.

At the examination, he showed generalized edema. Initial workup was relevant for hypoalbuminemia (1.1 g/dL), abnormal liver function tests (ALT 59 U/L, AST 84 U/L, ALP 329 U/L), and elevated fecal calprotectin (7051 µg/g; NRR <50 µg/g). Renal and cardiac tests were normal. Stool culture, multiplex-qualitative PCR for enteropathogens, and testing for Clostridioides difficile were negative. An abdominal CT scan showed diffuse mural thickening of the ileum (Fig. 1A-B). A retrograde double-balloon enteroscopy (DBE) showed friable mucosa, erythema, erosions, linear and circumferential target ulcers in the ileocecal region, and edema, erythema, and erosions in the colonic mucosa (Fig. 1C-D) and biopsies were performed from ileal and colonic mucosa. Ileal biopsies showed chronic and acute ulcerated ileitis, with morphological changes consistent with GVHD (Fig. 1E-F), and Ziehl Neelsen, Grocott, and periodic acid–Schiff (PAS) stains were negative.

The patient was diagnosed with protein-losing enteropathy (PLE) due to gastrointestinal GVHD. Methylprednisolone IV pulses for three days improved symptoms and liver function. He was discharged on sirolimus and prednisone (1 mg/kg), and later started ruxolitinib due to hypertransaminasemia. After two years he continues on sirolimus and ruxolitinib, asymptomatic, with normal albumin and transaminase levels.

Discussion
PLE is associated with GVHD, wherein inflammation induced by T-cells harms the intestinal barrier (1), resulting in protein losses through feces. PLE is a diagnosis of exclusion, and non-gastrointestinal causes (nutritional, renal, cardiac, or hepatic) of hypoproteinemia should be excluded (2). Histopathology supports the diagnosis of gastrointestinal GVHD. The main histological changes in acute GVHD presentations are apoptotic bodies and marked damage and inflammation of the crypts (3). Even though the clinical manifestations are chronic, acute histological findings might still be present (4).

Due to gastrointestinal, hepatic, and dermatological involvement, we decided to manage with intravenous steroids and continued with maintenance immunosuppressive therapy...
according to guidelines (5), with subsequent resolution of symptoms and liver function tests.

References


Fig. 1 A (axial) and B (coronal). Abdominal CT scan with intravenous contrast. The ileum shows diffuse mural thickening. Fig 1 C-D. Retrograde double-balloon enteroscopy (White light imaging, Fujifilm EN-450, processor EPX-4400). The mucosa shows multiple erosions and short circumferential ulcers, conditioning segmental bowel sub-stenosis. C. Circumferential ulcer with longitudinal involvement that narrows the bowel lumen. D. Underwater picture showing loss of the villous surface pattern and a deep ulcer. Fig. 1 E-F. Small bowel endoscopic biopsies (hematoxylin & eosin; E 40x; F 100x). Adjacent to the most damaged area, the remaining epithelial component showed distortion of contiguous crypts and paucity of the inflammatory component in the lamina propria (E). Apoptotic bodies are the main characteristic of the lesion (F).