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## **Leflunomide as a cause of collagenous colitis: an entity to consider**

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Dear Editor,

Leflunomide belongs in the group of disease-modifying anti-rheumatic drugs (DMARDs) used in the treatment of psoriatic, rheumatoid, and reactive arthritis. Approximately 20 % of patients will experience some adverse event, mainly weight loss, abdominal pain, and diarrhea. We describe the clinical, endoscopic, and histological findings in a patient with psoriatic arthritis (PA) who developed severe chronic diarrhea after drug use.

A 64-year-old female began treatment with leflunomide for PA. Good tolerance was reported for the first 18 months, which later evolved to intermittent episodes of liquid stools up to 15 times a day, abdominal pain, significant weight loss, and hypokalemia. The enteric pathogen evaluation, including *Clostridioides difficile*, was negative. A colonoscopy with ileoscopy showed edema in the colonic mucosa. Biopsies of the colonic mucosa

demonstrated an increase in intraepithelial lymphocytes and a thickened collagen layer (Fig. 1A-B). Immunostaining for cytomegalovirus was negative. Diarrhea and hypokalemia persisted despite the use of oral budesonide and mesalazine; symptoms improved 20 days after stopping leflunomide.

The fact that symptoms only improved after withdrawing leflunomide establishes a causal relationship between this drug and the probable etiopathogenesis of collagenous colitis. Considering this experience and that of other authors, leflunomide-induced colitis should be included in the differential diagnosis of chronic diarrhea in patients treated with this drug.

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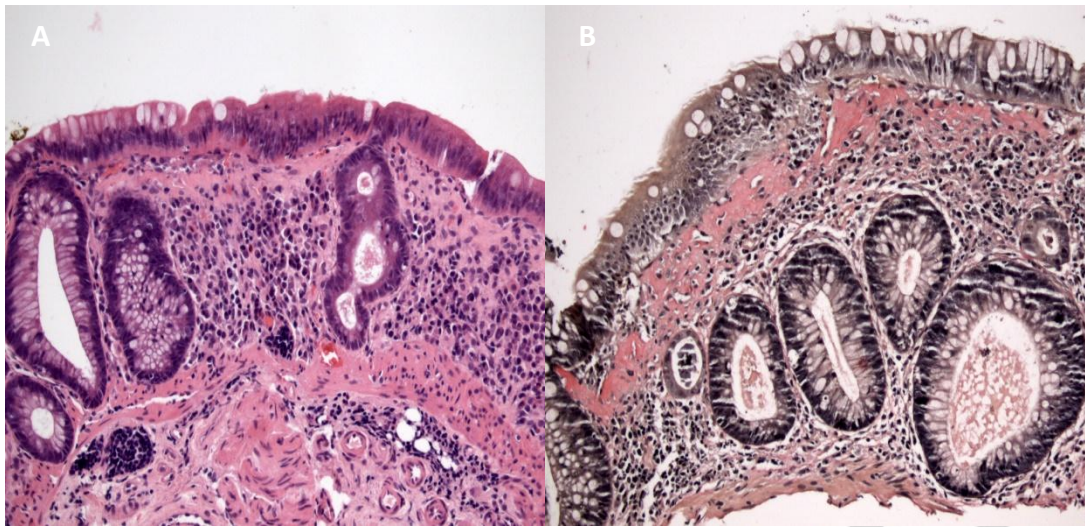


Fig. 1. A and B: colonic mucosa biopsies showing slight architectural distortion and a luminal subepithelial collagen band, which contains fragments of karyorectic cells and erythrocytes (HE x200 and Van Gieson Trichrome x200, respectively).