

**Title:**

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DOI: 10.17235/reed.2021.8015/2021

Link: [PubMed \(Epub ahead of print\)](#)

**Please cite this article as:**

Nuñez Paulina, Quera Rodrigo , Flores Lilian , Contreras Luis . Leflunomide as a cause of collagenous colitis: an entity to consider . Rev Esp Enferm Dig 2021. doi: 10.17235/reed.2021.8015/2021.

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

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*Keywords: Leflunomide. Collagenous colitis. Chronic diarrhea.*

*Dear Editor,*

Leflunomide belongs to 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, highlighting 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.

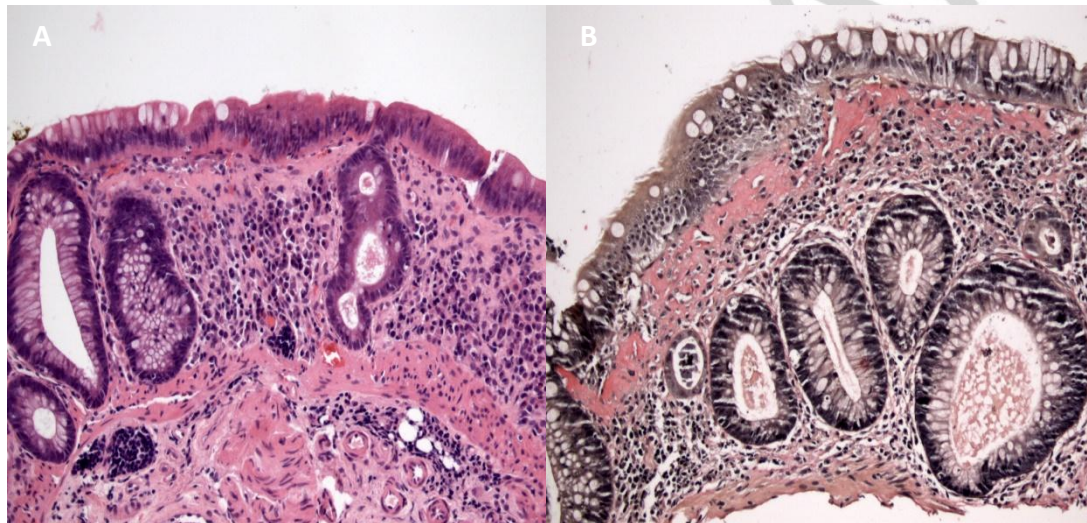
A 64-year-old woman who began treatment with leflunomide for PA. Good tolerance was reported for the first 18 months, but later evolved with intermittent episodes of liquid stools, up to 15 times a day, abdominal pain, significant weight loss and hypokalemia. The enteric pathogen evaluation including *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 thickened collagen layer (Figure 1 A-B). Immunostaining for cytomegalovirus was negative. Despite the use of oral budesonide and mesalazine, diarrhea and hypokalemia persisted. 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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**Figure 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 200X and Van Gieson Trichrome 200X respectively).