

**Title:**

**Mesalazine-induced esophageal ulcers. a rare adverse effect**

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## MESALAZINE-INDUCED ESOPHAGEAL ULCERS. A RARE ADVERSE EFFECT.

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Dear Editor,

31-year-old woman. Diagnosis of ulcerative proctitis in February/2022. Calprotectin 1832 µg/g. Colonoscopy: erythematous, friable and erosive mucosa up to 10 cm from the anal margin. Pathology: compatible with ulcerative colitis with moderate activity. Start of oral mesalazine (3 gr/24 h granules) and topical (1 gr/24 h suppository). After three months, she achieved clinical remission. Calprotectin 57 µg/g. Two months later, she consulted for solid dysphagia, loss of 10 kg, and low-grade fever for a month. Fifteen days before, she went to an emergency room where Prednisone 50 mg/24 h was started. On the day of the assessment, she was receiving 30 mg with no improvement. The next day, gastroscopy showed 6-12 mm esophageal ulcers with non-confluent shallow geographic borders (Figure 1a-b), biopsies were taken. Viral serologies and HLA B51 were requested. Given the severity of the symptoms, empirical treatment was started with Valaciclovir 1 g/12 h.

Serologies: IgG for Epstein Barr virus, cytomegalovirus and herpes virus with negative IgM. Cytomegalovirus viral load: <30 IU/ml. Pathology: acute extensively ulcerated

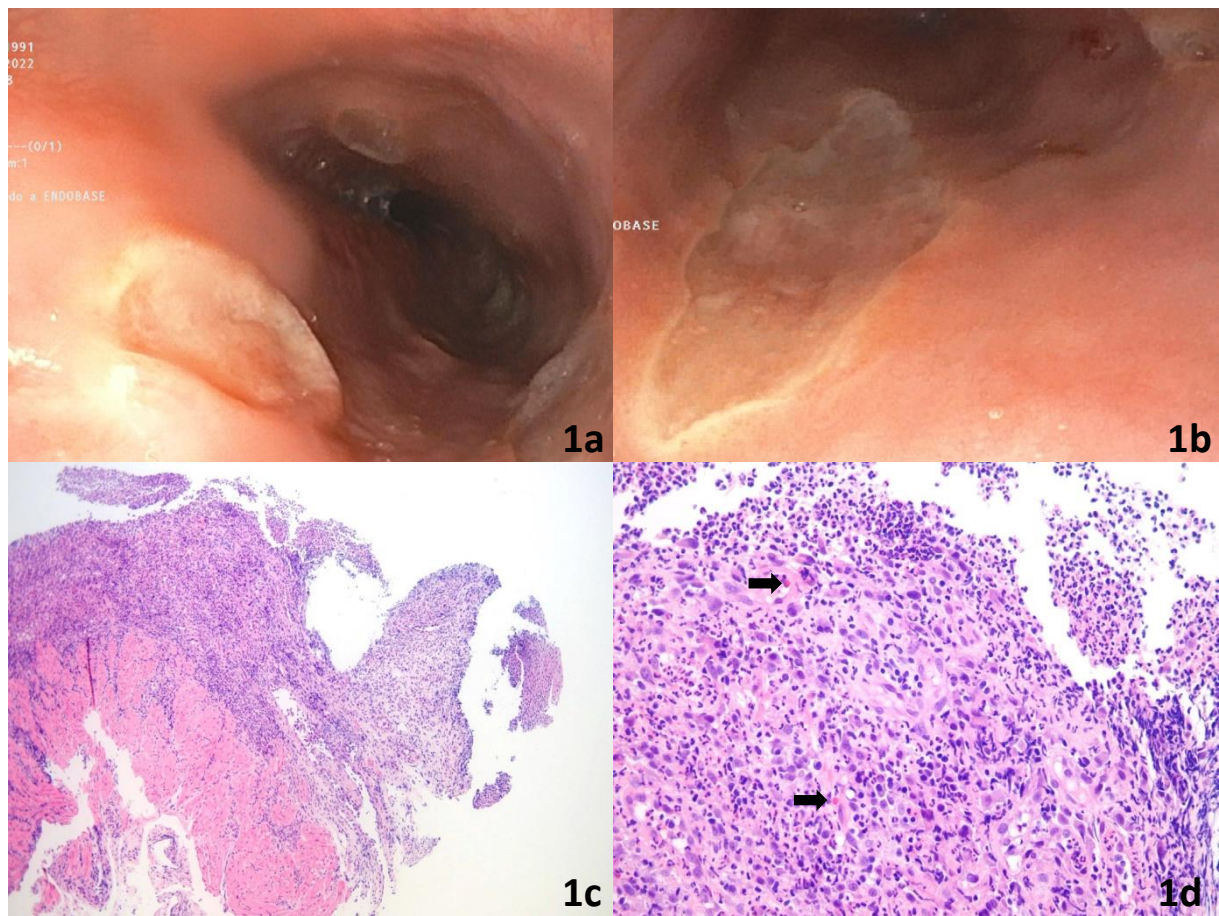
esophagitis (Figure 1c), inflammatory infiltrate and some eosinophils (Figure 1d) with negative histochemical staining for fungi, cytomegalovirus and herpes virus I and II. HLA B51 was negative.

Valaciclovir and mesalazine are discontinued after seven days given the known relationship of the latter with low-grade fever and, exceptionally, with esophageal pathology. Three days later, the patient reported clear improvement in dysphagia from the day the mesalazine was discontinued. After eight months, she was still asymptomatic. Upon resolution of the symptoms, control gastroscopy was not performed, and mesalazine has not been reintroduced due to its probable causal association.

Mesalazine has an excellent safety profile. Adverse effects include fever, headache, diarrhea and hypersensitivity symptoms. Mesalazine esophagitis is an extremely rare adverse event that, to our knowledge, has only been reported once in the literature. The AEMPS does not include it in the technical sheet. No other reviews on the drug describe it. Our patient started with dysphagia and esophageal ulcers four months after starting mesalazine. The etiological study was normal and the condition was resolved the day the drug was discontinued. Therefore, according to the traditional causality criteria, we propose mesalazine as the cause of the case described.

## REFERENCES

- 1- López-Cepero Andrada JM, López Silva M, Salado Fuentes M, et al. Ulcera esofágica por mesalazina [Esophageal ulcer due to mesalazine]. *Gastroenterol Hepatol*. 2000 Aug-Sep;23(7):362.
- 2- Park J, Cheon JH. Updates on conventional therapies for inflammatory bowel diseases: 5-aminosalicylates, corticosteroids, immunomodulators, and anti-TNF- $\alpha$ . *Korean J Intern Med*. 2022 Sep;37(5):895-905.
- 3- Tsujii Y, Nishida T, Osugi N, et al. Classification and clinical features of adverse drug reactions in patients with ulcerative colitis treated with 5-aminosalicylate acid: a single-center, observational study. *Scand J Gastroenterol*. 2022 Feb;57(2):190-196.



**Figure 1:** Mesalazine-induced esophageal ulcers. 1a-b: 6-12mm esophageal ulcers with non-confluent shallow geographic borders. 1c-d: acute extensively ulcerated esophagitis, intense inflammatory infiltrate and some eosinophils (black lines).