A Rare Case of Leflunomide-Induced Colitis: Clinical, Endoscopic & Microscopic Findings

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Introduction

- Leflunomide-induced colitis is a rare entity. A wide range of endoscopic findings and late-onset of symptoms makes this a challenging diagnosis to make.
- This is a case of an elderly woman with rheumatoid arthritis (RA) who complained of subacute diarrhea. Colonoscopy with biopsy was performed. Cessation of leflunomide resolved diarrhea. Investigation of other inflammatory or infectious etiologies were negative.
- Our hope is to aid in the recognition of this drug-induced colitis to reduce hospitalization length and improve treatment.

Case Presentation

- 79-year-old woman with a past medical history of RA on Leflunomide, COPD, and gout, presented to the hospital with 7 days of watery diarrhea. She reported more than 6 bowel movements daily. She denied recent sick contacts, travel, or changes in diet. She had started taking Leflunomide 2 months ago. She denied family history of inflammatory bowel disease or colorectal cancer.
- Vitals on admission: RR 14, HR 109 bpm, BP 96/67, Temperature 36.4C°
- Pertinent initial labs included serum creatinine 1.76, CRP 40.7, ESR 58.
- CT abdomen/pelvis demonstrated loss of haustral folds from the the splenic flexure to the rectum, with wall thickening, suggestive of colitis.
- She was empirically treated for infectious colitis with ceftriaxone and metronidazole. There was a positive fecal lactoferrin. *Clostridoides difficile* toxin and stool testing for *Salmonella*, *Shigella*, *Campylobacter*, *E. coli* 0157:H and ova and parasites returned negative.

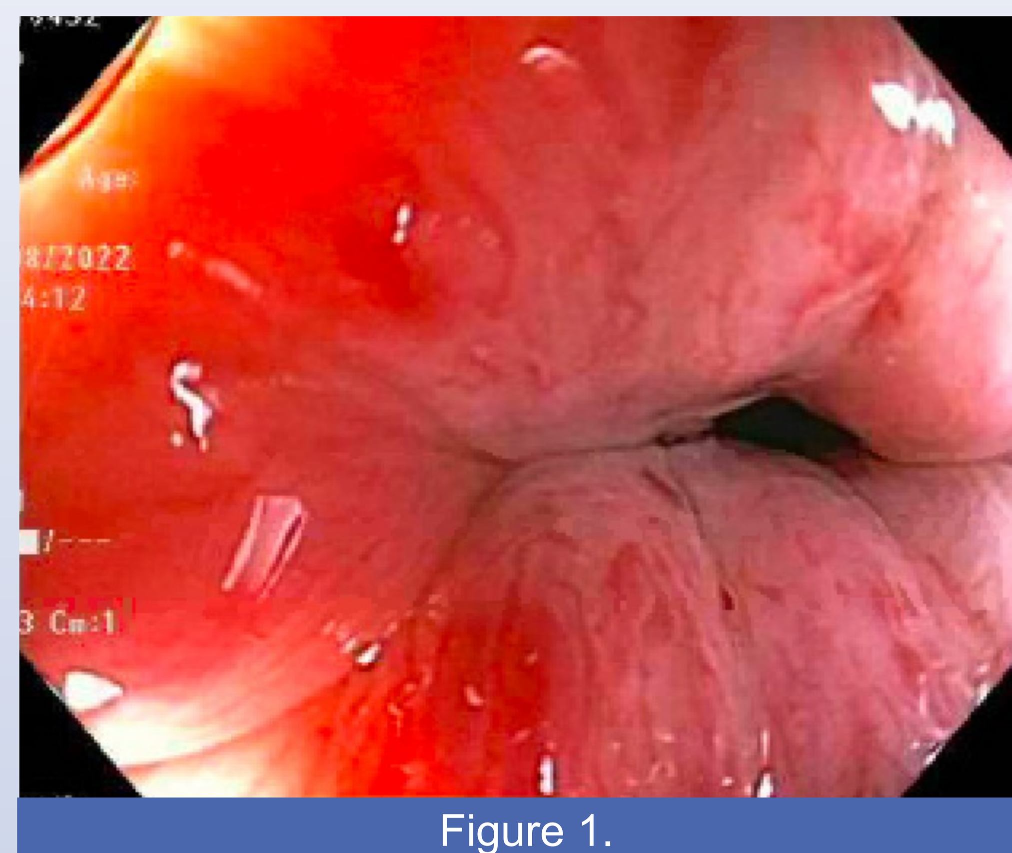

Figure 1.

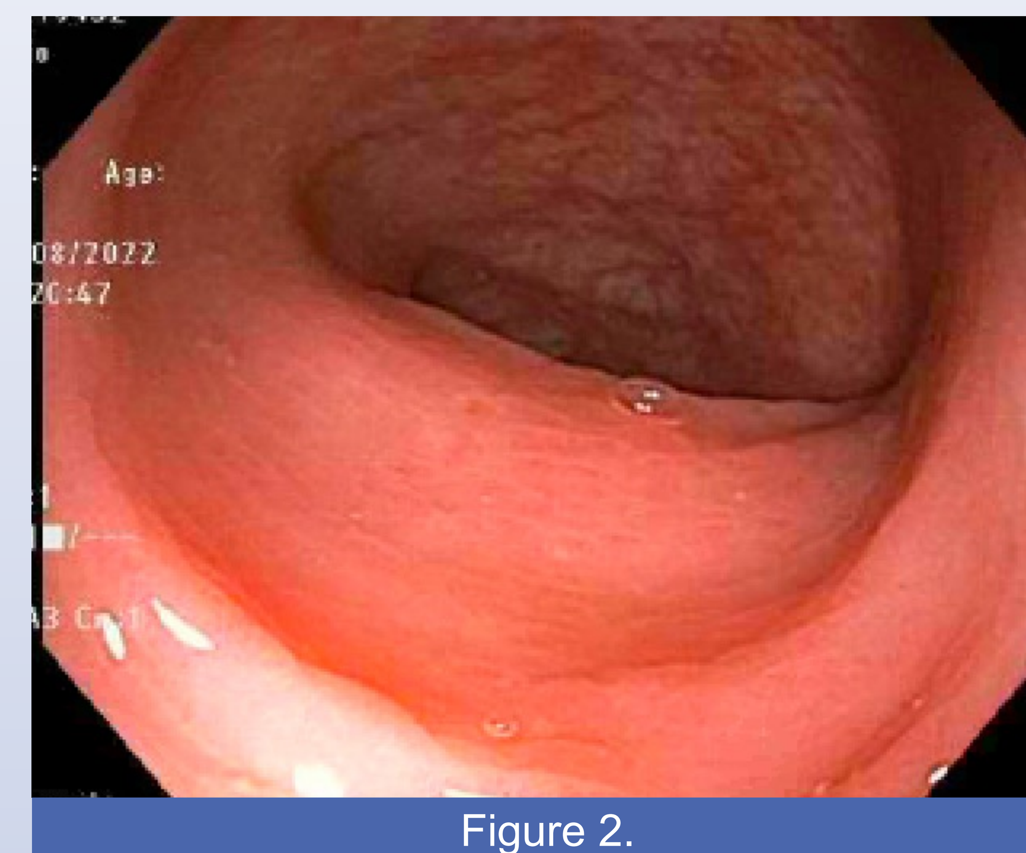

Figure 2.

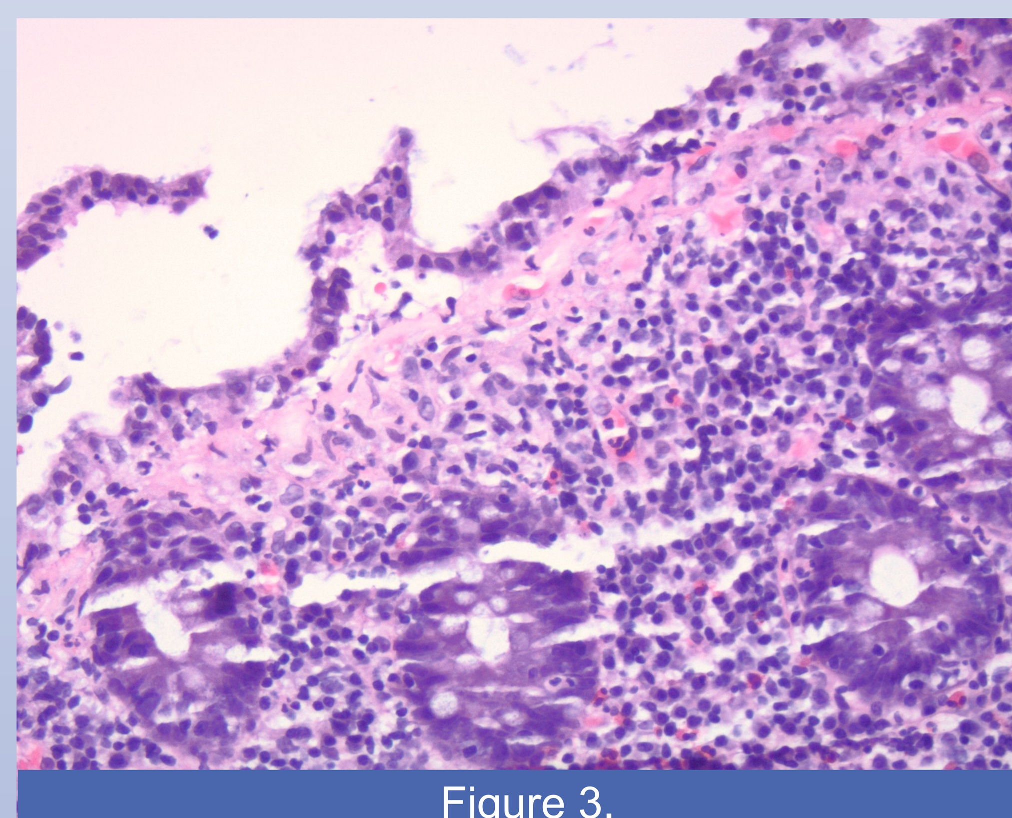

Figure 3.

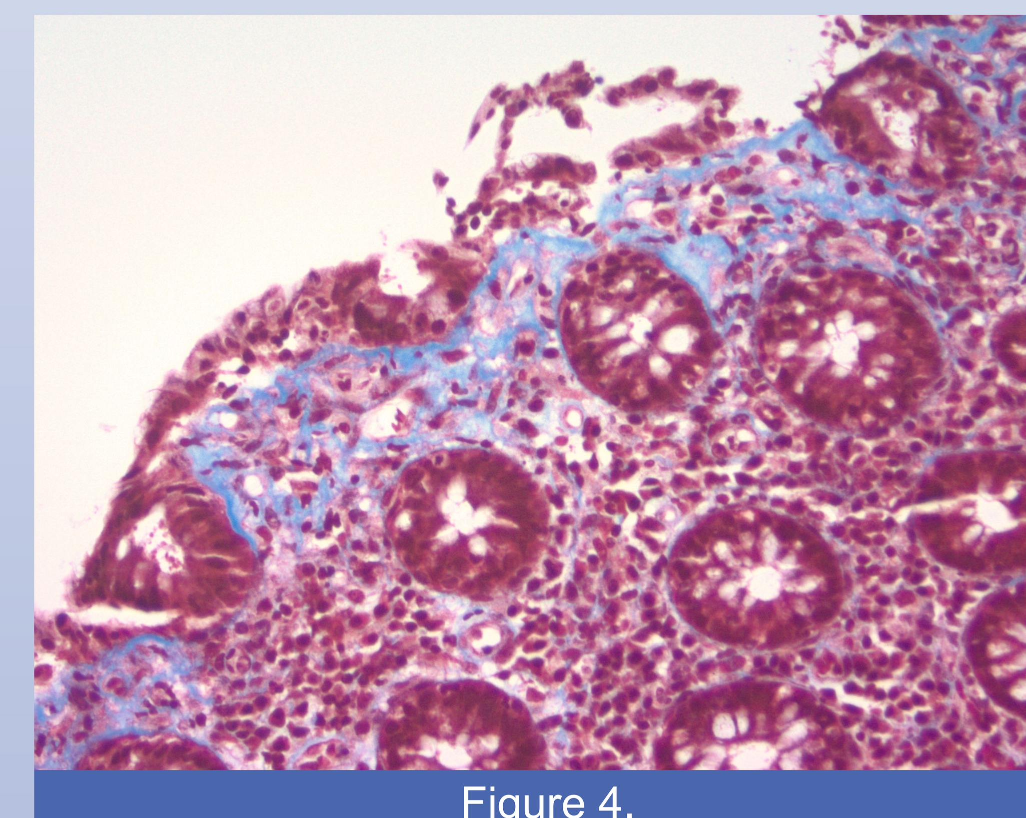

Figure 4.

Colonoscopy & Biopsy Findings

- In-patient colonoscopy demonstrated areas of congested and erythematous mucosa from the rectum, sigmoid and transverse colon (Figure 1, 2).
- Biopsies demonstrated increased lymphocytic infiltration of the lamina propria and thickened epithelial layer and crypts with increased intraepithelial lymphocytes (Figure 3, 4).

Treatment

- Patient was asked to trial cessation of leflunomide before discharge and upon a two week follow up, diarrhea had resolved. She was prescribed hydroxychloroquine for RA by her rheumatologist.

Discussion

- Leflunomide is a disease modifying drug used to treat RA among other types of inflammatory arthritis. In approximately 20% of patients, adverse gastrointestinal side effects of abdominal pain, diarrhea and nausea are well recognized.
- Drug-induced colitis has only been described in a few case reports, and even fewer endoscopic descriptions exist. Paucity of this diagnosis may be attributed to its nebulous presentation.
- Symptoms improved with 1-2 formed bowel movements daily after 2 weeks. Biopsy findings can reveal luminal subepithelial collagenous bands and colonic crypt formation including crypt abscesses. There remains a range of endoscopic findings associated with leflunomide colitis, including mucosal hyperemia, ulceration and vasculature effacement.
- Unlike most typical drug reactions, symptom onset can range from 18-24 months. As our case exemplifies, this delay in presentation can lead to unnecessary testing and prolonged hospitalization. Due to this patient's symptom improvement with supportive care, drug cessation was enough. But, for severe colitis, steroids, cholestyramine washout, and biologics may be considered.

References

1. Chis R, Gladman D, Vajpeyi R, Cino M. Leflunomide-Induced Colitis in Immunosuppressed Patient with Systemic Lupus Erythematosus and Rheumatoid Arthritis. *Journal of the Canadian Association of Gastroenterology*. 2021;4(Supplement 1):222-223. doi:10.1093/jcag/gwz016
2. Lui J, de la Fuente J, Halland M. Colitis in a Rheumatologic Patient. *Gastroenterology*. 2020;159(6):2034-2035. doi:10.1016/s0016-5085(19)35972-4
3. Verschueren P, Vandooren AK, Westhovens R. Debilitating diarrhoea and weight loss due to colitis in two RA patients treated with leflunomide. *Clin Rheumatol*. 2005 Feb;24(1):87-90. doi: 10.1007/s10067-004-1033-1.
4. You D, Yen T. Leflunomide-Induced Colitis. *The American Journal of Gastroenterology*. 2012;107. doi:10.1016/s0002-9270(03)01892-6

Acknowledgements

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