Drug induced colitis secondary to Leflunomide

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INTRODUCTION

- Leflunomide is a disease modifying antirheumatic drug that works by inhibition of de novo pyrimidine synthesis resulting in antiproliferative and anti-inflammatory effects.
- Though diarrhea is the most common side effect of leflunomide, it is typically self-limited.
- Overt colitis induced by leflunomide is distinctly rare, with only a few cases in literature.
- We report a case of leflunomide-induced colitis that was initially misdiagnosed as ulcerative colitis.

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This case highlights both the importance of keeping leflunomide induced colitis in the differential and the potential adverse effects of delay in diagnosis.

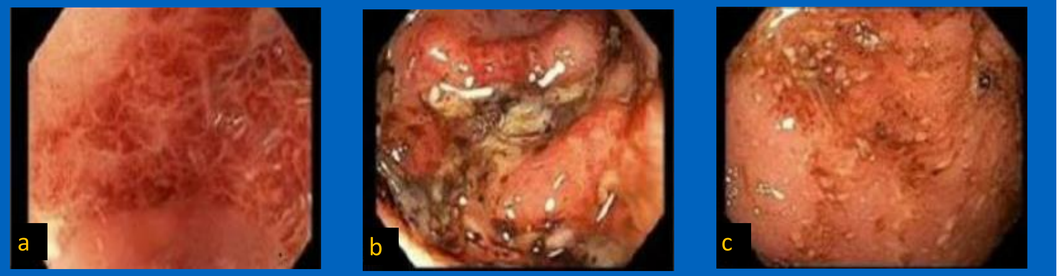

Figure 1 (a) erythema and congestion; (b) ulceration; (c) erosions with exudates

DISCUSSION

- Leflunomide can cause diarrhea in about 17% of patients. However, only a few cases of leflunomide-induced colitis are reported, with symptoms developing 10 days to 30 months after initiation.
- No characteristic endoscopic or histologic features have been found, with prior reports variably describing punctiform ulcers, hemorrhagic colitis, cryptitis, crypt abscesses, granulomas, enterocutaneous fistulas, lymphocytic colitis, and collagenous colitis.
- Diagnosis is challenging due to rarity of condition, variable interval from medication initiation to symptoms, and differing histological findings.
- Diagnostic criteria or treatment have not been proposed, but discontinuation of leflunomide can be diagnostic and therapeutic.

CASE DESCRIPTION/METHODS

- A 72-year-old woman was initiated on leflunomide for treatment of rheumatoid arthritis. A few weeks later, she developed chronic diarrhea with endoscopy yielding a diagnosis of ulcerative colitis.
- She reported lower abdominal pain, 10-12 loose stools daily with intermittent blood, fecal urgency, and thirty-pound weight loss.
- She was started on oral mesalamine and rectal hydrocortisone but continued to have symptoms, resulting in severe electrolyte abnormalities which caused ventricular tachycardia requiring hospitalization.
- Labs revealed serum C-reactive protein of 107 mg/L, fecal calprotectin of 499 µg/g, and negative Clostridium difficile toxin.
- Flexible sigmoidoscopy showed diffuse mucosal congestion and erythema, with some discrete deep ulcers.
- Histopathology revealed diffuse moderately active colitis with surface erosion, with no chronic regenerative changes to suggest inflammatory bowel disease.
- Diagnosis of leflunomide-induced colitis was made given temporal correlation and absence of evidence of alternative causes. Leflunomide was discontinued, and patient was started on course of steroids with improvement of symptoms.