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CASE REPORT | COLON

A Small Blemish: Isotretinoin-Induced Microscopic Colitis

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ABSTRACT

Microscopic colitis is a form of colonic inflammation that presents with chronic nonbloody diarrhea that can only be diagnosed histologically with biopsies obtained during colonoscopy. We report a rare case of isotretinoin-induced microscopic colitis in a patient who was prescribed this medication for nodular acne with a 1-year history of nonbloody diarrhea, bloating, cramping, and foul-smelling gas. Cessation of this medication in addition to initiating treatment with budesonide resulted in remission of the patient's symptoms. The presence of chronic diarrhea in patients who are taking isotretinoin should raise suspicion for this condition and warrant further investigation.

INTRODUCTION

Microscopic colitis (MC) usually manifests as a chronic, watery, and nonbloody diarrhea seen typically in older patient populations with a propensity for women.[1,2] MC is distinguished from other forms of colitis by normal-appearing colonic mucosa on colonoscopy, although sometimes erythema or edema can be observed.[2] The 2 subtypes of this disease are collagenous colitis and lymphocytic colitis (LC).[1,2] Collagenous colitis is characterized by thickening of the subepithelial collagen layer, whereas LC is characterized by an increased number of intraepithelial lymphocytes with normal crypt architecture.[3,4] Multiple pathophysiologic mechanisms for MC have been proposed.[2] These include an intestinal reaction to luminal antigen from diet, genetic factors, hormonal influence, abnormalities in fluid homeostasis, autoimmunity, bile acid malabsorption, infection, or medication induced.[2] Although MC is associated with certain conditions, such as diabetes, thyroid dysfunction, psoriasis, and celiac disease, it is believed to develop from exposure to a stimulus, such as medications. Medications well known to cause MC include nonsteroidal anti-inflammatory drugs, proton pump inhibitors, and selective serotonin reuptake inhibitors.[1,2,4] Once the diagnosis has been established, treatment strategies include stopping any known inciting medications and treating with budesonide for both the induction and the maintenance of remission if needed.[4,5] Clinical remission can be defined as a mean of <3 stools per day and a mean of <1 watery stool per day per the Hjortswang criteria.[6] Realistically, clinical remission can be gauged by patient satisfaction from his/her response to therapy.[4] Proof of histological remission is not routinely assessed.[4] We present a case of a patient who was only taking isotretinoin for nodular acne who was found to have MC.

CASE REPORT

A 28-year-old active-duty man with a history of nodular acne on isotretinoin presented with a 1-year history of chronic, watery, and nonbloody diarrhea as well as abdominal bloating, cramping, and foul-smelling gas. He tried dairy-free and gluten-free diets without improvement. He denied any constitutional symptoms, nausea or vomiting, and weight loss. He reported having similar symptoms 2 years ago, which began after initially starting isotretinoin for nodular acne. Owing to these persistent symptoms, he had been scheduled for endoscopic evaluation at that time; however, his symptoms resolved after self-discontinuing isotretinoin on going to field training for a military exercise. After his field training exercises, he did not follow up because of the SARS-CoV-2

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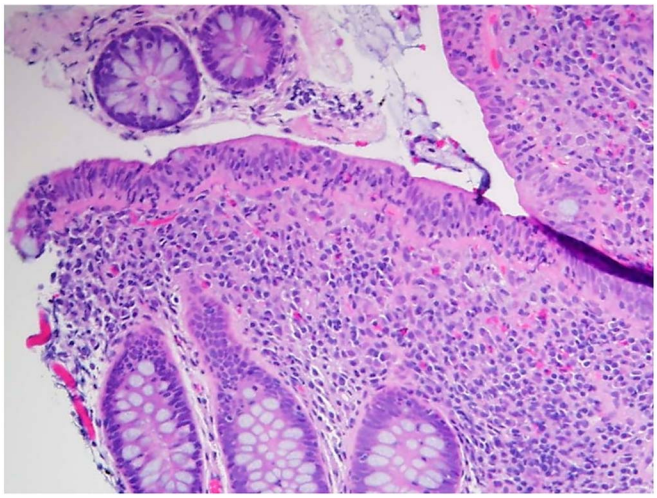

Figure 1. (20×) Random colon: Expansion of the lamina propria by chronic inflammatory infiltrate and superficial injury with loss of surface mucin.

pandemic. He had resumed taking isotretinoin again approximately 1 year ago after which his gastrointestinal symptoms started again. The patient was taking no other medications. Physical examination and laboratory testing were all normal, including an infectious and inflammatory workup. Celiac serologies were negative. Abdominopelvic computed tomography was unremarkable. He had an unremarkable esophagogastroduodenoscopy. Colonoscopy revealed mild erythema and edema that extended from the anal verge to 20 cm. Biopsies of this area and random biopsies throughout the colon were obtained. Biopsies obtained during the procedure revealed LC throughout the colon and rectum (Figures 1 and 2). The history and time line suggest that his LC may be related to his isotretinoin use. He was counseled to avoid using isotretinoin and was treated with a 3-month course of budesonide. He had immediate response; however, his symptoms returned after completion of therapy. The recurrence prompted initiating another course of steroid therapy with symptom control after the second course was completed.

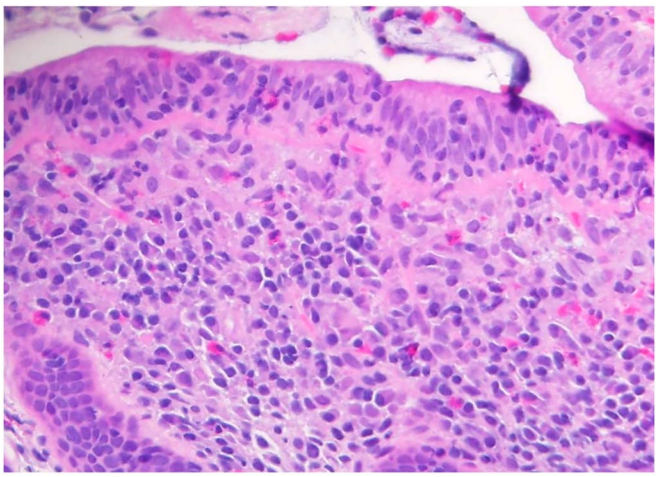

Figure 2. (40×) Random colon: Higher magnification showing a marked increase in intraepithelial lymphocytes and prominent eosinophils.

DISCUSSION

Isotretinoin is a vitamin A derivative that is used to treat severe, recalcitrant nodular acne.[7] In addition to teratogenicity, isotretinoin can cause hyperlipidemia and elevations in liver-associated enzymes.[8] There have been previous concerns about an association between isotretinoin and inflammatory bowel disease, but this association is less clear, and more recent data suggest that isotretinoin use is not associated with an increased risk of developing ulcerative colitis and Crohn's disease.[9] To the best of our knowledge, there has only been 1 other report of isotretinoin being associated with MC.[10] Although further study in this area is required to establish a stronger correlation, isotretinoin should be considered as a potential trigger for MC in the absence of other causes. Our patient was not taking any other medications at the time of his presentation. Endoscopic and histologic findings were not consistent with potential competing etiologies, such as inflammatory bowel disease or celiac disease. In addition, his symptoms correlated well with the timing of isotretinoin use. When he had self-discontinued isotretinoin during his military training, his symptoms had resolved. When he started isotretinoin, he was rechallenging himself, which resulted in a return of his symptoms, thus confirming a reasonable suspicion that his symptoms were associated with this medication. Of the medications known to cause MC, isotretinoin is not enumerated among them. In patients who are taking isotretinoin who are found to have MC without any other medications commonly associated with MC, isotretinoin should be considered as a possible instigator and discontinued. Its cessation could improve the quality of life for many patients, including the younger patient population who are more likely taking this medication. Moving forward, it is reasonable to counsel patients on this potential adverse effect of isotretinoin when starting this medication.

DISCLOSURES

Author contributions: L. Dukate and K. Pak wrote, edited, and found supportive resources for the case report. W. O'Connell reviewed the case report and assisted with biopsy pathology. Z. Junga initially evaluated the patient, performed colonoscopy, and reviewed the case report. Loren R. Dukate is the article guarantor.

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