Breakthrough Cutaneous Crohn's Disease Healed With Risankizumab

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ABSTRACT

Introduction: Extraintestinal manifestations of Crohn's disease are associated with substantial morbidity and commonly present as arthropathies or painful lesions involving the skin, eyes, and mouth. However, they can involve nearly any organ system and do not correlate directly with intestinal inflammation, complicating diagnosis and treatment. As treatment options expand, this article explores the potential role of risankizumab in the treatment of cutaneous Crohn's disease.

Case Presentation: A 75-year-old man developed a gluteal fissure consistent with cutaneous Crohn's disease despite longstanding maintenance with adalimumab, an anti-tumor necrosis factor-α (TNF-α) monoclonal antibody. He transitioned to risankizumab, an interleukin-23 (IL-23) inhibitor, with resolution of cutaneous disease involving the gluteal cleft and continued luminal remission.

Discussion: This case report is the first to demonstrate successful treatment of anti-TNF-resistant cutaneous Crohn's disease with an IL-23 inhibitor. No other published cases were found.

Conclusions: While TNF-α inhibitors remain the standard of care for extraintestinal manifestations of Crohn's, IL-23 inhibitors are a promising therapy option.

INTRODUCTION

Extraintestinal manifestations (EIM) are known to affect up to 50% of individuals diagnosed with inflammatory bowel disease (IBD) and burden patients with Crohn's disease more than those with ulcerative colitis.[1-3] These symptoms increase the morbidity associated with IBD and often have a greater negative impact on quality of life than the underlying intestinal disease itself.[4] Metastatic Crohn's disease is a rare EIM in which inflammatory skin lesions occur at sites that are not contiguous with active luminal disease and often develop independently of intestinal disease activity. The limited nature of these lesions and poor understanding of their etiology have contributed to a lack of consensus regarding management.[5,6] Classic cutaneous Crohn's disease findings include linear gluteal cleft ulcers and fissures with sharply demarcated borders resembling knife cuts, perianal and peristomal skin tags, fistulae, and abscesses. Patients with ileocolonic Crohn's disease and EIMs are more challenging to manage, statistically requiring a greater number of biologic therapies over time than those with ileal Crohn's disease and associated EIMs.[7] Anti-tumor necrosis factor α (TNF-α) monoclonal antibodies are often first-line therapies for patients with IBD and EIMs, as they have demonstrated substantial efficacy in treating both luminal disease and many identified EIMs.[4,8] This case demonstrates successful resolution of cutaneous Crohn's disease with continued luminal remission upon transitioning from adalimumab to riskanizumab.

CASE PRESENTATION

A 75-year-old man with a history of severe ileocolonic Crohn's disease, maintained on adalimumab, presented for gastroenterology follow-up with complaints of new intergluteal irritation and gluteal cleft fissuring over the past few months. His symptoms began with discomfort in the perianal region and progressed to scant intermittent blood streaking with wiping and the development of gluteal cleft splitting. He reported variable consistency and frequency of bowel movements unchanged from baseline, typically ranging from 3 to 6 episodes per day. He denied purulence or fecal discharge from the area. On examination, he was

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found to have pathognomonic knife-like fissuring along the gluteal cleft overlying an erythematous base, separate from the anal mucosa.

In 1975, the patient was diagnosed with stricturing and fistulizing ileocolonic Crohn's disease with perianal involvement and abscess formation requiring incision and drainage. He underwent 2 small bowel resections in 1986 and 1996. Biologic therapy with infliximab was initiated in 2006 and discontinued after 18 months because of an infusion reaction. He subsequently transitioned to maintenance therapy with adalimumab in 2008. A 2020 restaging colonoscopy was complicated by a transverse colon perforation requiring emergent laparotomy and intensive care unit admission. Because of infectious complications during recovery, his immunosuppression was held for approximately 18 months. Adalimumab was reinitiated in November 2021 with induction dosing.

Given his lapse in biologic therapy, quantitative drug levels and antibody testing were ordered following induction and demonstrated therapeutic adalimumab levels of 9.8 ug/mL without antibodies. Posterior gluteal cleft fissuring was noted during an office visit on April 19, 2023. He was evaluated by dermatology, which affirmed the diagnosis of cutaneous Crohn's disease and jointly monitored his disease. Biopsy was not obtained because of his clinical history and pathognomonic fissuring on examination.

Despite adequate adalimumab levels and stable intestinal symptoms, the patient was counseled regarding breakthrough cutaneous Crohn's disease and was transitioned to riskanizumab. His intergluteal fissure demonstrated marked improvement at a routine 6-month follow-up. Restaging colonoscopy performed 1 year later demonstrated complete resolution of the fissure and continued luminal remission on riskanizumab. The patient reported substantial improvement in quality of life due to pain relief, fissure healing, and peace of mind associated with disease control.

DISCUSSION

The proinflammatory cytokine TNF-α has been identified as a major contributor in the recruitment and perpetuation of the inflammatory cascade responsible for a variety of EIMs in Crohn's disease, especially cutaneous eruptions.[9,10] Given this mechanism, anti-TNF-α therapies (infliximab and adalimumab) have been well studied and demonstrate significant efficacy in treating both luminal and extraintestinal disease.[11,12] TNF- α inhibitors may be considered preventive, as patients with Crohn's disease maintained on this class have demonstrated an overall reduction in the development of EIMs.[12] However, their efficacy is not absolute, as clinical data continue to demonstrate substantial variability in individual responsiveness, dosing requirements, and adverse effects. Despite this patient's therapeutic adalimumab level of 9.8 ug/mL and absence of anti-drug antibodies, he developed breakthrough intergluteal Crohn's development.

This case raises questions regarding optimal management, as dose escalation, trialing another anti-TNF agent, introduction of concomitant immunomodulators, or a change in therapeutic class are all reasonable options. The incidence of breakthrough EIMs despite quantitatively adequate drug levels is not well documented.

The US Food and Drug Administration has approved risankizumab, an interleukin-23 (IL-23) inhibitor, for the treatment of moderate-to-severe Crohn's disease. The drug is traditionally used in patients with plaque psoriasis and psoriatic arthritis. The pathophysiology of psoriasis and spondyloarthritis has highlighted the role of IL-23 signaling in the maturation and stabilization of the inflammatory cascade.[13,14] Specifically, IL-23 is a fundamental component of barrier tissue defense and is secreted by respiratory, gastrointestinal, epithelial, and secretory cells to maintain mucosal integrity and homeostasis.[14] When dysregulated, IL-23 promotes heightened local inflammation, making it an ideal target for cutaneous autoimmune sequelae such as the cutaneous Crohn's disease observed in this patient. A multicenter European case series identified 10 patients with anti-TNF-refractory cutaneous Crohn's disease, among whom ustekinumab, an IL-12/IL-23 inhibitor, induced remission in 5 cases and partial remission in 4 cases.[15] Risankizumab was chosen in this case instead of ustekinumab because of evidence demonstrating the superiority of risankizumab over ustekinumab for moderate-to-severe Crohn's disease in patients with previous failure of anti-TNF treatment.[16]

CONCLUSIONS

To our knowledge, this is the first case report documenting resolution of cutaneous Crohn's disease with risankizumab. IL-23 inhibitors represent a promising therapeutic option for patients with cutaneous Crohn's disease. Future large-scale clinical studies comparing EIM responsiveness to different biologic and systemic therapies, along with continued phenotypic correlation, are needed to further optimize treatment strategies.

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