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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Rapid Resolution of Vulvar Crohn's Disease With Ustekinumab

Gianna Stoleru, MD[1], Gordon Robbins, MD[2], John C. Papadimitriou, MD, PhD[3], and Uni Wong, MD[2]

[1]*Department of Medicine, University of Maryland Medical Center, Baltimore, MD*
[2]*Department of Medicine, Division of Gastroenterology and Hepatology, University of Maryland Medical Center, Baltimore, MD*
[3]*Department of Pathology, University of Maryland Medical Center, Baltimore, MD*

ABSTRACT

In the evaluation of patients with inflammatory bowel disease, assessment of extraintestinal manifestations of disease is integral to clinical management. The patient described in this case is a 24-year-old woman with a history of inflammatory colonic Crohn's disease (CD) who presented to the hospital with one week of vaginal pain and swelling. Initial assessment focused on infectious etiologies, though final diagnosis of vulvar CD was made on biopsy. Clinical course and treatment of vulvar CD are poorly defined in existing literature. This case highlights the multidisciplinary management of inflammatory bowel disease patients and successful treatment of a rare extraintestinal manifestation with anti-interleukin 12/23 therapy.

INTRODUCTION

Crohn's disease (CD) is a complex condition that burdens patients with a constellation of extraintestinal manifestations (EIMs) of disease. In this case, we describe a woman with inflammatory colonic CD who presented to the hospital with a chief complaint of vaginal pain and swelling. She was ultimately found to have CD involvement of her vulva and was successfully treated with anti-interleukin (IL) 12/23 therapy. This case highlights the importance of multidisciplinary management of inflammatory bowel disease (IBD) patients and successful treatment of a rare EIMs of CD with anti-IL 12/23 therapy.

CASE REPORT

A 24-year-old woman, G1P1001, with a history of inflammatory colonic CD and complex perianal involvement presented with one week of vaginal pain and swelling. Her CD was refractory to thiopurine, infliximab, and adalimumab, requiring proctocolectomy 3 years prior to this presentation. Her surgery was complicated by partial perineal wound dehiscence requiring multiple debridement and perineal flap. Due to her medically refractory complex perianal CD, she was not a candidate for ileal pouch-anal anastomosis. Ileoscopy one year prior to presentation showed no evidence of small bowel CD, which can develop after proctocolectomy in patients with colonic CD. She was not on any therapy for CD since proctocolectomy, and was taking chronic suppressive valacyclovir for recurrent genital herpes simplex virus.

Pelvic exam revealed diffuse labial edema and erythema with friable tissue and purulent discharge coating her labia majora (Figure 1). No vesicular lesions were visualized. Wet prep from her vaginal exam was positive for bacterial vaginosis, and she tested negative for gonorrhea, chlamydia, and syphilis. Pelvic computed tomography scan demonstrated cellulitis without evidence of abscess, and she was started on piperacillin/tazobactam and linezolid as broad-spectrum treatment of cellulitis while continuing valacyclovir. Given no symptomatic improvement after 4 days of treatment, she underwent pelvic magnetic resonance imaging which showed a 1 cm labial abscess. The abscess was not identified during exam under anesthesia. However, biopsies of her vulva revealed granulomatoid and plasma cell-rich inflammation consistent with vulvar CD (Figure 2). Herpes simplex virus staining was not performed. Antibiotics were discontinued, and the patient was started on prednisone 40 mg daily with taper. She was transitioned to ustekinumab 390 mg intravenous infusion once and then 90 mg subcutaneously every 8 weeks as an outpatient. Ustekinumab was chosen

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Correspondence: Gianna Stoleru, MD (Gianna.Stoleru@som.umaryland.edu).

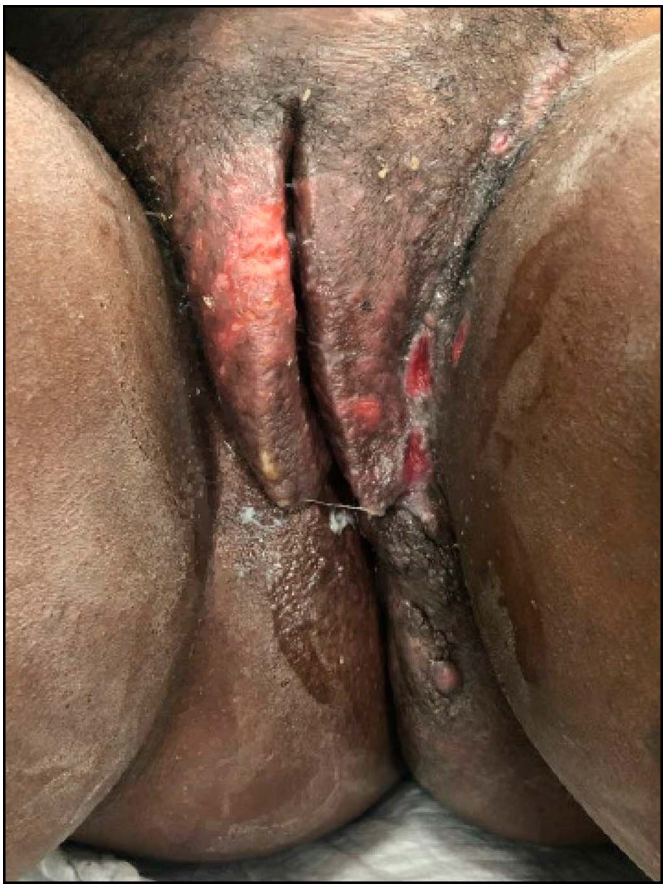

Figure 1. Pelvic examination findings at presentation, including diffuse labial edema, erythema with friable tissue, and purulent discharge.

given her prior failure to 2 anti-tumor necrosis factor α therapies and a long drug holiday with risk of antibody formation. The patient had near complete resolution of her symptoms 4 months after initiation on anti-IL 12/23 therapy (Figure 3).

DISCUSSION

While patients with IBD often have primary gastrointestinal (GI) symptomology, EIM of disease are common. The most commonly affected sites outside of the GI tract include joints, eyes, skin, and the hepatobiliary system.[1] Existing literature suggests that EIMs are also more likely to occur in patients with CD than ulcerative colitis. Interestingly, studies suggest that cutaneous symptomology of CD is present in 18%–44% of patients. While the pathophysiology is not completely understood, it is thought that antibodies sensitized to gut antigens may develop cross-reactivity with skin antigens and present cutaneously.[2]

Vulvar symptoms of CD are a rare EIM. Vulvar CD is typically categorized as either metastatic disease with granulomatoid histopathology or as direct extension of bowel involvement to the vulva possibly secondary to fistulas.[3] As seen with other EIM, vulvar CD can present as the primary manifestation of undiagnosed CD or as a manifestation of known disease. Stereotypically, vulvar lesions are described as linear and "knife like" ulcerations, though further review would suggest significant variability in presentation.[3] Quite possibly, the most common presentation is vulvar edema.[2] As with our patient, vulvar pain and pruritus are identified approximately 34% and 9% of the time, respectively.[4]

While vulvar CD should be considered in patients with known underlying IBD, it can be a challenging diagnosis to make in patients without diagnosed CD or in patients in remission, as in the case of our patient after proctocolectomy. The differential diagnoses for this clinical presentation includes vulvar cellulitis, tuberculosis, lymphogranuloma venereum, syphilitic or herpetic lesions, sarcoidosis, or pyoderma gangrenosum. Ultimately, lack of response to antibiotic therapy, basic laboratory testing, and tissue biopsy can help establish the final diagnosis.

Given the rarity of vulvar CD as an EIM, there are no randomized trials or strict guidelines dictating first line therapy.[5] While there is literature suggesting improvement in vulvar CD with anti-tumor necrosis factor α therapy such as infliximab, adalimumab, and certolizumab,[4,6,7] this case is one of the first to show that anti-IL12/23 therapy can be effective.[8] This case specifically highlights the use of ustekinumab for treatment of a rare cutaneous EIM, vulvar CD, and the importance of multidisciplinary management of patients with CD. Recurrence rates

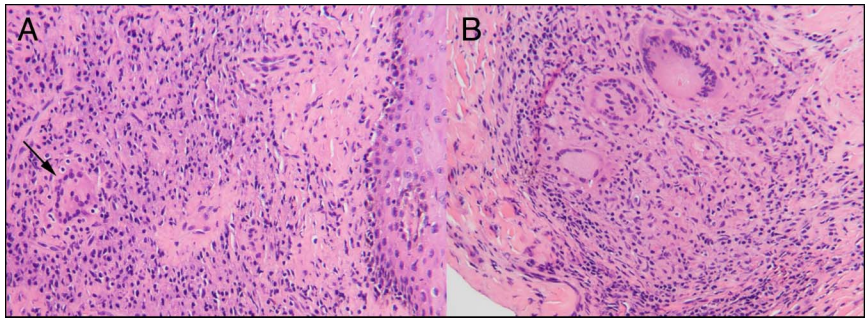

Figure 2. Light microscopy of vulva labia majora showing (A) Crohn's type granuloma with giant cells (arrow), involving labial mucosa with vulvar squamous epithelium seen on the right and (B) Crohn's type granuloma with giant cells, involving deeper vulvar tissue (hematoxylin and eosin stain, 20× magnification).

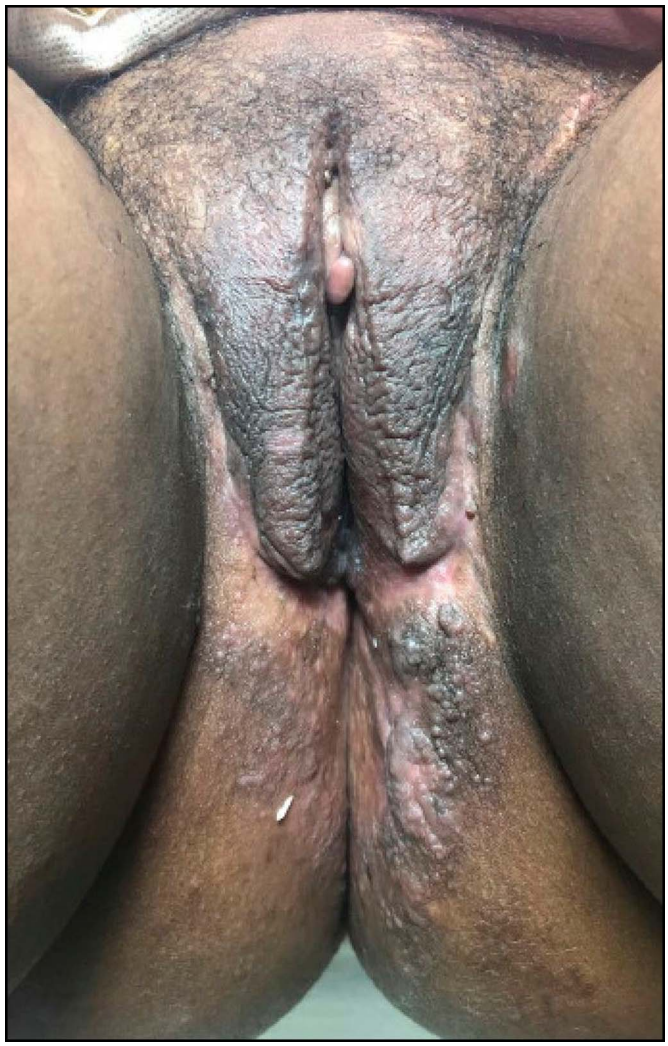

Figure 3. Pelvic examination findings after ustekinumab therapy exemplifying gross near complete resolution of disease.

of vulvar CD after treatment are not well described, and further follow up of cases is needed to guide management.

DISCLOSURES

Author contributions: G. Stoleru, G. Robbins, and U. Wong wrote the manuscript, revised the masnucript for intellectual content, and approved the final manuscript. JC Papadimitriou proved the images and approved the final manuscript. U. Wong is the article guarantor.

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REFERENCES

1. Isene R, Bernklev T, Høie O, et al. Extraintestinal manifestations in Crohn's disease and ulcerative colitis: Results from a prospective, population-based European inception cohort. *Scand J Gastroenterol.* 2015;50:300–5.
2. Bender-Heine A, Grantham JT, Zaslau S, Jansen R. Metastatic Crohn disease: A review of dermatologic manifestations and treatment. *Cutis.* 2017;99(6):E33–40.
3. Foo WC, Papalas JA, Robboy SJ, Selim MA. Vulvar manifestations of Crohn's disease. *Am J Dermatopathol.* 2011;33(6):588–93..
4. Barret M, de Parades V, Battistella M, Sokol H, Lemarchand N, Marteau P. Crohn's disease of the vulva. *J Crohn's Colitis.* 2014;8(7):563–70.
5. Kurtzman DJB, Jones T, Lian F, Peng LS. Metastatic Crohn's disease: A review and approach to therapy. *J Am Acad Dermatol.* 2014;71(4): 804–13.
6. Kiuru M, Camp B, Adhami K, Jacob V, Magro C, Wildman H. Treatment of metastatic cutaneous Crohn disease with certolizumab. *Dermatol Online J.* 2015;21(11):13030/qt17z6j2hv.
7. Miller FA, Jones CR, Clarke LE, Lin Z, Adams DR, Koltun WA. Successful use of adalimumab in treating cutaneous metastatic Crohn's disease: Report of a case. *Inflamm Bowel Dis.* 2009;15(11):1611–2.
8. Adbat R, Markova A, Farraye FA. Ustekinumab for treatment of cutaneous Crohn's disease. *UC Davis Dermatol Online J.* 2016;22(10):13030/qt6v402170.