The unusual presentation of genital Crohn's disease in a patient with breast cancer: A case report

Fatemeh Mokhtari, MD
Maryam Gholami, MD
Samaneh Mozafarpoor, MD

Skin Diseases and Leishmaniasis Research Center, Department of Dermatology, Medical School, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding Author:
Maryam Gholami, MD
Center for Research in Skin Diseases and Leishmaniasis, Alzahra Hospital, Soffe Blvd., Isfahan, Iran
Email: Maryam.gholami712@gmail.com

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Cutaneous Crohn's disease (CCD) is a relatively rare disease. Two-thirds of the affected patients are female with a mean age of onset of 35 years. CCD is divided into a genital type and an extra-genital type, each with their own unique different clinical manifestations. The usual presentation of genital Crohn's disease (CD) is in the form of erythema and edema of the labia and scrotum. Here, we have reported the rare case of a patient with late-onset genital CCD. The patient was a 61-year-old woman with a history of chemotherapy for breast cancer. She presented with genital, intergluteal, and perianal ulcers without any fistula, sinus or scars, which was treated as an unusual presentation of CD. The patient has not had any intestinal manifestation during three years of follow-up.

Keywords: genital, cutaneous, Crohn's disease, breast cancer

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INTRODUCTION

Cutaneous Crohn's disease (CCD) is a rare inflammatory disease with fewer than 100 cases reported in the literature. It usually occurs in the second to fourth decades of life. Two-thirds of patients with CCD are female and there is a mean age of onset of 35 years. Nearly 20% of Crohn's disease (CD) patients with cutaneous manifestations have no previous diagnosis of intestinal CD and are diagnosed anywhere from 3 months to 8 years after the first manifestation of the disease [1]. The pathogenesis of CD is due to a genetic abnormality, but symptoms only manifest after a break in the mucosal barrier or changes in the intestinal flora balance, which lead to an exaggerated T-cell response to the intestinal bacteria [2].

Along with the gastrointestinal (GI) manifestations of CD, extra-GI involvement occurs in 20%–45% of patients. In the genital type, common presenting signs are labial erythema and edema. The extra-genital type exhibits dusky erythematous plaques with ulcers and undermined margins, draining sinuses, fistulas, and scars. Perianal lesions consist of ulcers, fissures, sinus tracts, and vegetative plaques that may extend to the buttocks and abdomen [3,4]. Less common reactive cutaneous lesions in CCD include cutaneous polyarteritis nodosa (PAN), erythema multiforme (EM), nail clubbing, leukocytoclastic vasculitis (LCV), Epidermolysis bullosa acquisita (EBA(, palmar erythema, a pustular response to trauma (pathergy), and pyoderma gangrenosum (PG), that frequently occur as ulcers on the lower legs and erythema nodosum (EN) on the shins [5].

This study is a case report of a 61-year-old female with genital CD who initially presented with genital ulcers and a history of chemotherapy for breast cancer. She was successfully managed by oral metronidazole (250 mg TDS), an effective treatment for CD, after its definite diagnosis, despite the late age of onset for cutaneous CD and her unusual clinical manifestations.

CASE REPORT

This 61-year-old female visited our hospital 3 years ago with complaints of the appearance

of genital ulcers with non-pruritic burning pain. The primary evidence of these lesions was discovered about 9 years ago following surgery and chemotherapy for cancer in the left breast. After remission of the breast cancer, erosions and ulcers continued in her genital and perianal area with courses of exacerbation and remission.

Examination of the perineum, perianal, and groin areas showed erythematous patches and plaques with defined borders and irregular shapes along with erosions and ulcers of various sizes that discharged into the perineum (pubis and labia major), perianal area, and inguinal area (Figure 1). No abnormality was detected in any other parts of the skin, with the exception of follicular pustular lesions and furuncles on the trunk without a history of trauma, which partially resolved after the application of dalacin solution. There were no abnormalities detected in the nails or oral mucosa, and there were no signs of fever or lymphadenopathy. There was no observed GI, genitourinary or other organ involvement.

Over this long period prior to referral to our clinic, the patient underwent several additional biopsies to rule out differential diagnoses of metastasis due to breast cancer, inverse psoriasis, seborrheic dermatitis, infections (deep mycosis, fungal infections), extramammary Paget's disease, and histiocytosis. Unfortunately, the biopsies did not provide a diagnosis.

She underwent further assessments that included smear, bacterial and fungal cultures, PCR, IHC, a PPD test, chest X-ray, endoscopy, and colonoscopy, all of which showed normal results without any pathological changes. During this period, the patient was under conservative topical and systemic antibiotic therapy but the lesions did not heal and her quality of life continued to decline.

At the time of her referral to our clinic, CCD with an unusual manifestation was considered. A skin biopsy showed the following: acanthosis, spongiosis, and lymphocytic exocytosis in the epidermis and perivascular infiltration of inflammatory cells with formation of non-caseating granuloma that consisted of giant cells in the dermis (Figure 2). Ultimately, the patient was diagnosed with CCD and treated initially with topical steroids and metronidazole (250 mg TDS), which led to apparent healing and increased quality of life (Figure 3). Gradually, the dose of metronidazole was decreased, and then stopped, and the patient underwent monthly follow-up visits.

After the disease had subsided for a few months, the patient relapsed and developed lesions following exposure to a severe life stress. The lesions were not responsive to metronidazole alone; hence, she was prescribed short-term prednisolone (1 mg/kg) and azathioprine (2 mg/kg). After controlling the course of the disease, metronidazole was started again, then subsequently she received a decreased dosage, which was gradually stopped after achieving a complete remission.

Of note, after definite diagnosis of CCD, a colonoscopy was performed and the results indicated no signs of GI CD. In addition, the patient was examined for internal organ involvement, autoimmune diseases, and HIV, which were negative.

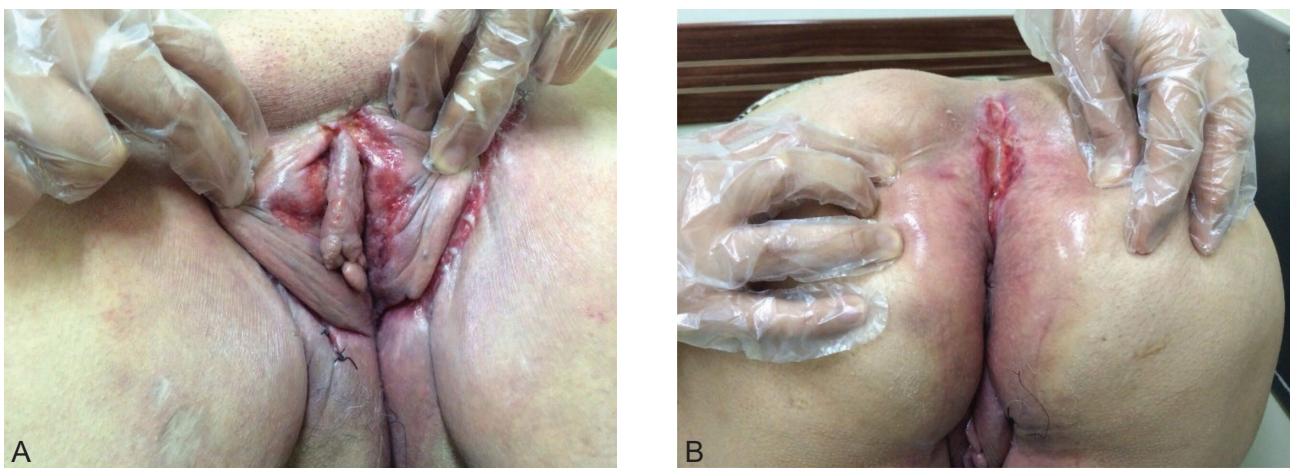

Figure 1. Genital Crohn's disease (CD) before treatment. Multiple ulcers on the genitalia in the folds, (A) interlabial creases and (B) gluteal cleft.

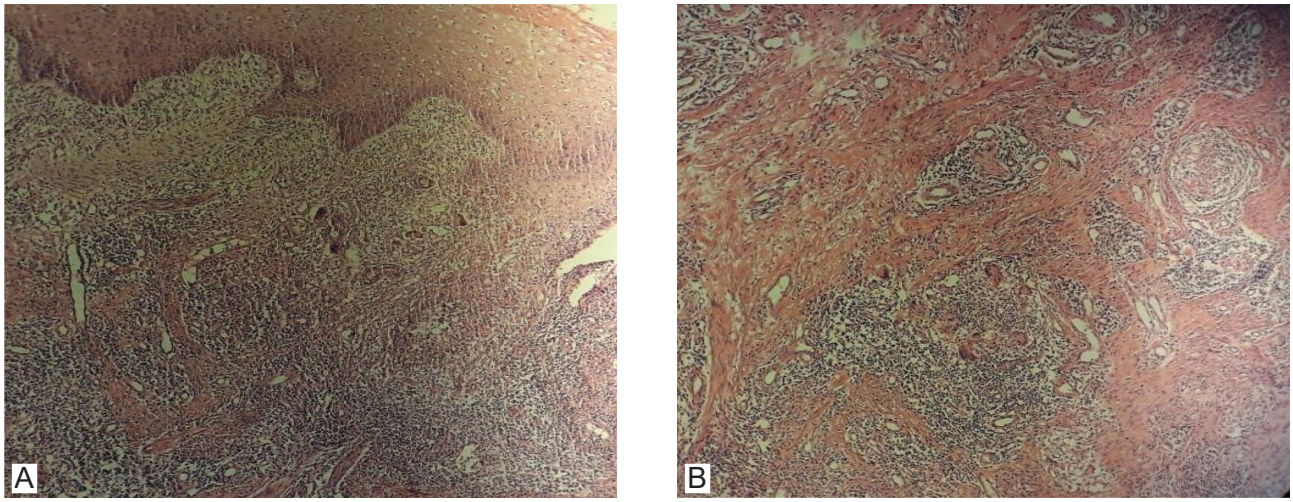

Figure 2. Histopathology of genital Crohn's disease (CD). (A) acanthosis, spongiosis, and lymphocytic exocytosis in the epidermis and perivascular infiltration of inflammatory cells with formation of non-caseating granuloma that consisted of giant cells in the dermis. (H&E, 10×). (B) Formation of non-caseating granuloma that consisted of giant cells in the dermis (H&E, 40×).

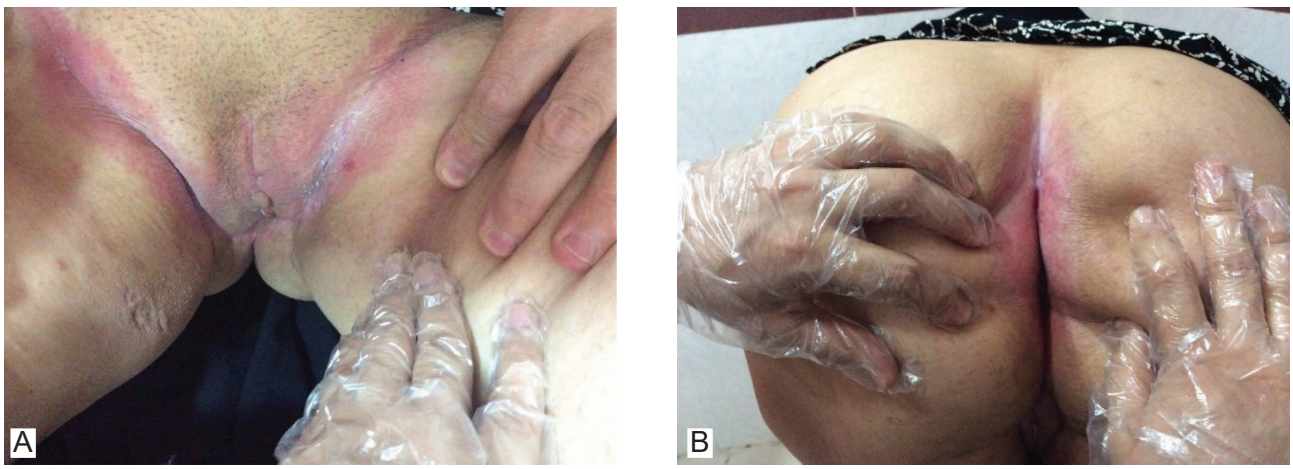

Figure 3. Genital Crohn's disease (CD) after treatment. Healing of ulcers on the genitalia in the folds, (A) inguinal folds, and (B) gluteal cleft.

During the three-year follow-up, the general condition of the patient has been good with improved quality of life. At the present time, the disease is under control and small erosive lesions appear in response to mild to moderate stress, which are responsive to metronidazole and topical steroids. No evidence of recurrence of breast cancer or a metastasis has been observed.

DISCUSSION

The usual presentation of genital CD is in the form of erythema and edema of the labia and scrotum but manifestations of non-genital CD are mostly in the form of erythematous plaques, which frequently ulcerate, and lead to sinus formation, fistulas, and scars [6]. Our patient did not have the usual manifestations of genital CD, and did not completely present with the usual non-genital signs. For this reason, she was not diagnosed as a case of CCD for a long period of time, which resulted in decreased quality of life for the patient.

Hence, because of the possibility of unusual presentations of genital CD, it is necessary for this disease to always be included in the differential diagnosis of erosive lesions of the genital area. The case we have reported showed no evidence of GI manifestations of CD.

The genital lesions quickly began to disappear after administration of a routine anti-CD regimen. Interesting observations in this study were that the trigger for the lesions appeared to be associated

with previous chemotherapy for breast cancer or its related autoimmune responses. With regard to the pathogenesis of the disease, intestinal flora changes and T-cell activation might have occurred after chemotherapy in this patient. Anti-cancer drugs might have also led to T-cell activation and caused the cutaneous manifestations.

In genital CD, labial erythema and inflammation are common presenting signs. The reported case in this study did not have these manifestations and presented with apparent non-pruritic painful genital ulcers. There was no sign of fistulas, draining sinuses, or scars, even in the perianal area, where such lesions are more commonly seen. After complete remission, no scars were evident on the skin. There were no reactive cutaneous lesions, but we observed follicular pustular lesions and furuncles without a history of trauma that partially resolved after the application of dalacin solution. Whether these lesions were part of the cutaneous manifestations of CD or the result of staphylococcal and streptococcal colonization of the genital ulcers and subsequent seeding to other areas remains unanswered. The mean age of onset of CCD is 35 years [1], while our patient had a much older age of onset.

A review of the literature showed similar findings in the reported cases. In a case presented by Panackel et al., a young girl was described with ulceration of the external genitalia initially diagnosed as intestinal tuberculosis; however, she did not respond to anti-tuberculosis treatments. One year later, she developed a perianal abscess and genital EN. In her biopsy non-caseating epithelioid granulomas, multinucleated giant cells, and perinuclear cuffing with lymphocytes were detected. The patient underwent treatment with prednisolone and topical steroids plus azathioprine, which effectively improved the lesions [7]. In a study conducted in Denmark, 67 of 71148 patients with breast cancer who received chemotherapy instead of radiotherapy were diagnosed with CD and showed a lower rate of survival compared with those without CD [8]. A number of retrospective studies have shown extra-intestinal lesions of CD in about 11% of the patients with rare involvement of the genital tract [9]. Thus, along with the common manifestations of CD, genital involvement, especially non-caseating granulomas, should be seriously considered as a rare extra-intestinal consequence of CD.

CONCLUSION

Skin lesions of CD, especially genital CD, may be observed in patients with a history of breast cancer as a nonspecific and unusual manifestation of CCD. For timely diagnosis and proper treatment, CCD should be considered in the differential diagnosis of patients with breast cancer who present with cutaneous lesions, especially in the genital area.

Conflict of Interest: None declared.

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