A case report of genital Crohn's disease with a brief review of Indian cases reported

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Abstract

Crohn's disease (CD) is a type of inflammatory bowel disease, which presents with extraintestinal manifestations in some cases, skin being one of the organs involved. Vulvar and perianal involvement leads to significant morbidity and has an adverse effect on the quality of life. We report a case of genital CD affecting the vulva, perianal region, and oral cavity, due to its rarity and diagnostic difficulty.

Key words: Crohn's disease, herpetiform ulcers, knife-like fissuring, perianal tags, vulvar swelling

Introduction

Crohn's disease (CD) is a type of inflammatory bowel disease with chronic and relapsing course, manifesting as transmural granulomatous inflammation of the gastrointestinal tract, commonly affecting the ileum and the colon.[1] Skin is one of the common organs affected with extraintestinal manifestations (EIMs) of CD. Skin involvement can be classified into specific (characterized by granulomatous inflammation) and nonspecific manifestations (characterized by nongranulomatous inflammatory process). As an EIM, skin manifestations often present with genital and perianal involvement with a female preponderance. Genital CD cases are rare to be diagnosed and reported by virtue of not having a fixed diagnostic criteria and mainly being a diagnosis by exclusion. There have been very few reports of specific cutaneous manifestations of CD in Indian literature. Hence, we report this case due to its diagnostic difficulty, with a brief review of literature and comparison with previously reported cases.

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Case Report

A 14-year-old female presented with history of vulvar and perianal raw areas since 20 days, with pain and bleeding while defecation. She had experienced similar episodes several times over the past 2 years, along with a burning sensation in the oral cavity. There was no other significant past, personal, family, or sexual history. On cutaneous examination, there was symmetrical tender vulvar swelling with multiple superficial tender herpetiform ulcers with an indurated base and jagged borders, along with perianal ulcers and tags [Figures 1a-c and 2]. There was bilateral inguinal nontender solitary lymphadenopathy. The oral cavity showed slightly erythematous, edematous upper, and lower gingivae without ulcers [Figure 3a and b]. General and systemic examinations were unremarkable. Based on these findings, clinical differentials of herpes genitalis, Behcet's disease, and periorificial tuberculosis were considered, and patient was investigated accordingly.

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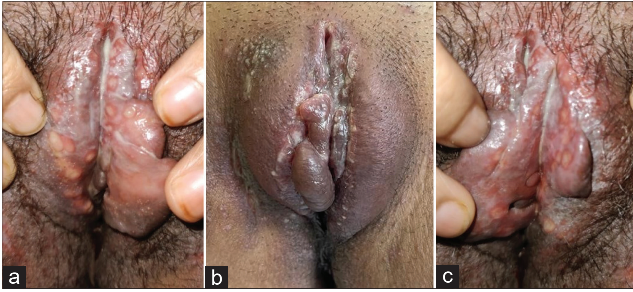

Figure 1: (a-c) Vulvar edema, erythema with multiple herpetiform erosions

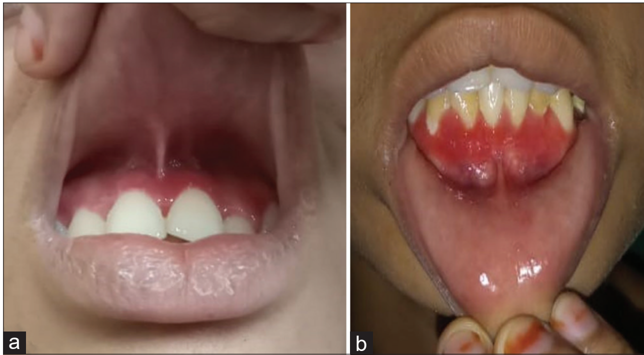

Figure 3: (a and b) Edematous and erythematous gingivae

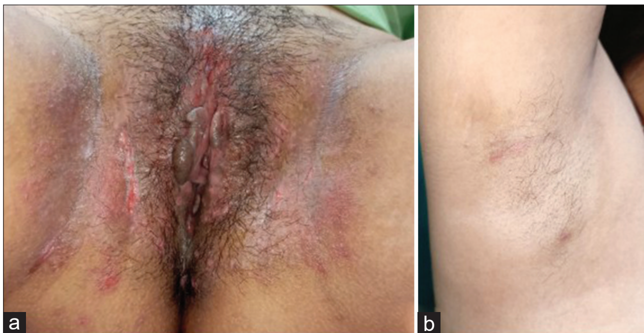

Figure 5: (a and b) Fissuring and maceration over groins and axillae seen as the disease progressed

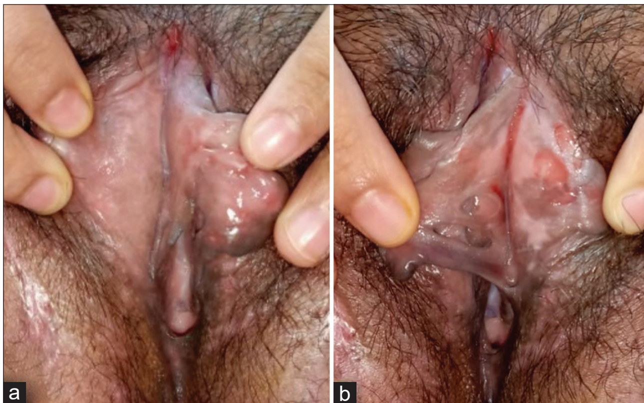

Figure 7: (a and b) Resolution of erosions after treatment with residual window-like defect in labia minora

HIV enzyme-linked immunosorbent assay, hepatitis B surface antigen, and hepatitis C virus antibody tests were negative. Tzanck smear did not reveal multinucleated giant cells, and serology for HSV1 and HSV2 for both immunoglobulin (Ig) M and IgG was negative. Pathergy test was negative, and

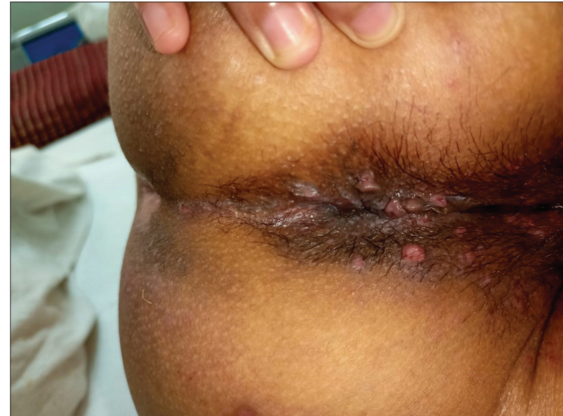

Figure 2: Perianal erosions and skin tags

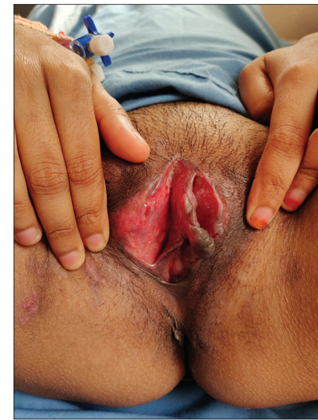

Figure 4: Knife like fissures over vulva seen as the disease progressed

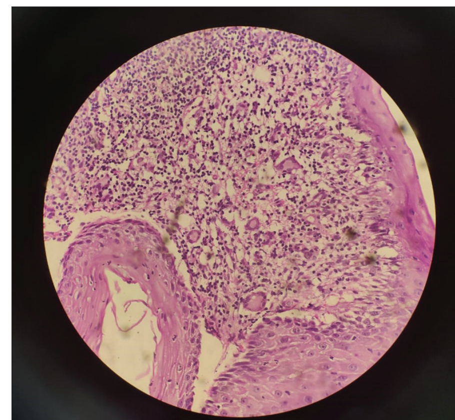

Figure 6: Histopathological examination showing granulomatous inflammation with multinucleated giant cells of foreign body type

ophthalmic examination was unremarkable. Mantoux test showed an induration of <5 mm, while Ziehl–Neelsen staining and cartridge-based nucleic acid amplification test from discharge of the ulcer base was also negative for tuberculous mycobacteria. Chest X-ray and ultrasound of abdomen and pelvis were normal. Histopathology from vulvar ulcer edge showed noncaseating epithelioid granulomas. For the above differentials, she was empirically treated with acyclovir and antitubercular drug therapy for 2 weeks and 2 months, respectively, without significant success. However, there was significant response to oral prednisolone. Based on these findings, we reviewed our diagnosis, and a differential

of cutaneous CD was considered, and prednisolone was continued with resolution of lesions.

However, she presented to us within a year with tender indurated vulvar swelling, deep knife-like fissuring and linear ulcers over bilateral labia minora, ranging from 1 to 2 cm in length, which have been described as typically seen in cases of vulvar CD [Figure 4]; along with perianal fissuring, maceration and fissuring over groins, and axillae [Figure 5]. She also developed intermittent abdominal pain, for which she was investigated. Computed tomography enterography revealed mild fat stranding in perineum. Colonoscopy showed internal hemorrhoids, and colonoscopic biopsy showed moderate inflammation with lymphoid aggregates, however, no granulomas.

Local ultrasonography and magnetic resonance imaging did not reveal any colonic connections. A repeat skin biopsy from the vulvar ulcers showed granulomatous inflammation with multinucleated giant cells, histiocytes, lymphocytes, and plasma cells [Figure 6]. Based on this clinical and investigational profile, we reached the final diagnosis of cutaneous CD. She was treated with monthly methylprednisolone pulse along with oral prednisolone, sulfasalazine, and colchicine, with adequate remission and residual window-like defect in labia minora, [Figure 7a and b] however, with relapsed episodes.

Discussion

The EIMs of CD are seen in 6%-40% of cases, of which skin is one of the commonly affected organs.[2] Skin manifestations of CD have been divided as follows:[2,3]

A. Specific: Contiguous form (orofacial, perianal), metastatic (genital and nongenital form)
B. Reactive: Erythema nodosum, pyoderma gangrenosum, bowel-associated dermatitis–arthritis syndrome, pyodermatitis vegetans, pyostomatitis vegetans, and leukocytoclastic vasculitis
C. Associated dermatoses: Psoriasis, secondary amyloidosis, vitiligo, and acquired epidermolysis bullosa
D. Secondary to complications of CD and adverse effects of treatment: Zinc deficiency, iron deficiency, essential fatty acid deficiency, steroid, and tumor necrosis factor-alpha therapy side effects.

Genital form accounts for 56% of specific cutaneous alterations.[3] The presentations of vulvar noncontiguous disease have been described by Barret *et al*.,[4] and include:

1. Tender vulvar swelling
2. Ulceration
3. Knife-like fissuring
4. Lymphedema
5. Hypertrophy, and
6. Chronic suppuration.

As in our patient, 25% of patients do not have gastrointestinal involvement at the time of presentation.[5] Feller *et al*., have classified gynecological complications of CD and their mechanisms as mentioned in Table 1.[6]

Perianal involvement in CD has been classified by Hughes' Cardiff[7] as:

1. Primary, as part of CD (including fissures and ulcerations), and
2. Secondary, as part of complications (strictures, abscesses, fistulae, and skin tags).

The elaborate clinical features under each heading along with a subsidiary classification are elaborated in Table 2.[7,8] A severity grading is given, as follows:

- Grade 0 - Not present
- Grade 1 - Lesions of little impact associated with good prognosis
- Grade 2 - Lesions associated with greater morbidity and poor prognosis.

Oral involvement in CD has a wide range of prevalence, 0.5%-80%, probably due to differences in study inclusion criteria.[9] Oral manifestations include persistent mucosal swelling and mucogingivitis, as seen in our patient. Cobblestoning of mucosa, linear ulcerations, mucosal tags, and polyps are other common findings.[10]

Table 3 compares the findings of our case with nine other such cases reported in Indian literature.[11-18] Analysis shows a preponderance in young females (Male: Female ratio of 1:9). The prevalence of genital, perianal, and oral involvement was 90%, 70%, and 20%, respectively. All

Table 1: Gynecological complications of Crohn' s disease and their mechanisms

Complications	Mechanism
Enteric fistulas from rectum, ileum, and proximal colon	Direct extension of diseased bowel
Vaginal, perineal, vulvar, ovarian, and uterine involvement	Transmural involvement and fistulization may affect all pelvic organs with fistulas, abscesses, edema, and ulceration
Granulomatous salpingitis and oophoritis	Metastatic deposit
Vulvar inflammation, abscesses, and ulceration	Granulomas or abscesses involving perineum, vulva, and vagina may form separately from diseased intestine or in the absence of active bowel disease
Destructive perineal disease	
Vaginal granulomas	

Table 2: Hughes' Cardiff classification for severity of Crohn' s disease

Ulceration (U)	Fistula or abscesses (F)	Stricture (S)
0 Not present	0 Not present	0 Not present
1 Superficial fissures • Posterior and/or anterior • Lateral • With gross skin tags	1 Low or superficial • Perianal • Anovulvar/anoscrotal • Intersphincteric • Anovaginal	1 Reversible stricture • Anal canal - spasm • Low rectum - membranous • Spasm with severe pain (no sepsis)
2 Cavitating ulcers • Anal canal • Lower rectum • With extension to perineal skin (aggressive ulceration)	2 High • Blind supralevator • High supralevator • High complex • Rectovaginal • Ileoperineal	2 Irreversible stricture • Anal stenosis • Extrarectal stricture
Subsidiary classification		
A Associated anal conditions 0 None 1 Hemorrhoids 2 Malignancy 3 Other specify	P Proximal intestinal disease 0 No proximal disease 1 Contiguous rectal disease 2 Colon (rectum spared) 3 Small intestine 4 Investigation incomplete	D disease activity (in anal lesions) 1 Active 2 Inactive 3 Inconclusive

Table 3: Comparison of case reports from Indian literature

Report	Age	Sex	Duration of skin disease	Genital involvement	Perianal involvement	Oral	Eye	Other sites	Histopathology	GI involvement
Batra *et al.*[11]	23	Female	3 years	Multiple sinuses discharging pus, linear knifecut erosions on inguinal folds, irregular exophytic hypertrophic outgrowths over vulva	Pus discharging sinuses, scars	No	No	Axillary scarring	Multiple epithelioid cell granulomas, dense chronic inflammatory infiltrate in dermis, without any caseation necrosis	Sacrococcygeal sinuses and fistulous tracts, rectal biopsy showed foci of ulceration with adjacent mucosa having few epithelioid cell granulomas with Langhans giant cells without caseation necrosis
Lanka *et al.*[12]	20	Female	6 months	Polypoidal growth over labia minora, multiple typical knifecut ulcers on the external genitalia, in the inguinocrural fold, interlabial creases	Knife-cut ulcers in natal cleft	No	No	No	Multiple noncaseating granulomas, edema, and dense lymphocytic infiltration in the dermis	No
Criton *et al.*[13]	23	Female	6 months	Vesiculation and ulcers over labia majora, multiple tender nodules with ulceration over perineum, medial aspect of thighs	No	No	No	No	Ulcerated epidermis, epithelioid cell granuloma, giant cells and lymphocytes	Diarrhea, arthritis
Criton *et al.*[13]	24	Female	1 year	Well-defined oval ulcers over labia majora	No	No	No	No	Stratified squamous epithelium with ulceration and mild dysplastic changes, subepithelium showed granulation tissue and few noncaseating granulomas with giant cells	Yes
Madnani *et al.*[14]	37	Female	4 years	Multiple, tender, indurated ulcers with beefy red granulation tissue distributed in a horseshoe pattern around the clitoris. A single knife-cut linear, deep ulcer with sharp vertical margins over labia majora, minora, clitoris	No	No	No	No	Ulcerated epidermis, diffuse lymphoplasmacytic infiltrate throughout the dermis with several scattered noncaseating epitheloid cell granulomas	No
Panackel *et al.*[15]	14	Female	3 weeks	Pain, itching, swelling papular eruptions and ulceration of external genitalia	No	No	No	No	Noncaseating epitheloid granulomas, multinucleated giant cells, and perinuclear cuffing with lymphocytes	Colonoscopy showed apthoid ulcers, cobble stone appearance, fissuring ulcers and pseudopolyps in ascending, transverse, descending, and sigmoid colon (treatment resistant CD)
Math *et al.*[16]	Elderly	Female	1 year	Edema of both labia majora with a mousy odor, multiple confluent erythematous and hyperpigmented papules and vegetating fissured plaques with oozing, erosions, and adherent crusting over the lower abdomen, mons pubis, labia majora, both groins , and thighs	No	No	No	No	Mild-to-moderate epidermal hyperplasia, predominant chronic inflammation, and foci of nonsuppurative granulomas in dermis with occasional multinucleated giant cells, moderate-to-dense mixed inflammation with ill-defined granulomas in deeper dermis	Yes (in remission)

Contd...

Table 3: Contd...

Report	Age	Sex	Duration of skin disease	Genital involvement	Perianal involvement	Oral	Eye	Other sites	Histopathology	GI involvement
Amarapurkar *et al.*[17]	28	Male	15 days	No	No	No	No	Ulcers with necrotic base over right shin and abdomen	Chronic inflammation of the dermis mixed with epithelioid and giant cells with evidence of chronic non-caseating granulomas	Ulcerative colitis (in remission)
Maheshwari *et al.*[18]	23	Female	9 months	Erythema and edema of the vulva with whitish foul-smelling discharge	Multiple, painful, nonhealing erosions	Multiple, painful, nonhealing erosions	No	No	NA	Biopsy from anal wall showed acute as well as chronic inflammation with noncaseating granulomas suggestive of CD
Our case	19	Female	4.5 years	Diffuse tender edema with multiple discrete ulcers with purulent discharge, hyperpigmented to erythematous papules over groin folds	Erosions, skin tags	Transient gingival edema and redness	Recurrent redness and watering	Fissuring and maceration over axillae	Epidermis lined by keratinized stratified squamous epithelium and shows multinucleated giant cell foreign body type at DEJ. Superficial dermis showed chronic inflammatory infiltrate in form of histiocytes, lymphocytes, and plasma cells; sparse chronic inflammatory infiltrates in perivascular and periadnexal structures	Periodic abdominal pain, colonoscopy showing internal hemorrhoids, colonic biopsy showing lymphoid aggregates with moderate inflammation

GI=Gastrointestinal; CD=Crohn s disease; DEJ=Dermo-epidermal junction

three sites were involved only in one other case apart from ours. Seven (70%) out of 10 patients had gastrointestinal involvement either at the time of presentation or in the past. No correlation was seen between severity of cutaneous disease and activity of intestinal disease. This write-up is aimed at highlighting the various manifestations of genital CD, which might help in early diagnosis and treatment, thus reducing sequelae such as fibrosis and scarring.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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