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Case Report

Genital Ulceration due to Erythema Nodosum Leprosum in a Young Male: A Case Report

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Genital ulceration is a rare and underrecognized manifestation of Erythema Nodosum Leprosum (ENL) that may closely mimic sexually transmitted infections and other non-venereal genital dermatoses, resulting in diagnostic delay and inappropriate management. We report a 25-year-old man with recurrent ENL episodes who developed a painful ulcerative lesion over the glans penis along with systemic and cutaneous features of multibacillary leprosy. Histopathological examination revealed foamy macrophages with neutrophilic infiltrates. The patient responded well to multidrug therapy and systemic corticosteroids. This case highlights genital ulceration as a rare manifestation of ENL, emphasizes the importance of histopathology with Fite staining in establishing the diagnosis, and underscores the need for a high index of suspicion to avoid misdiagnosis especially in endemic regions.

Keywords: Erythema Nodosum Leprosum, Genital Ulcer, Lepromatous Leprosy, Hansen's Disease, Type 2 Lepra Reaction, Fite Stain

Introduction

Leprosy, caused by *Mycobacterium leprae*, is a chronic granulomatous disease with a wide spectrum of cutaneous and neurological manifestations. Among its immunological complications, Type 2 lepra reaction or Erythema Nodosum Leprosum (ENL) is a systemic inflammatory reaction seen in multibacillary leprosy, particularly the lepromatous (LL) and borderline lepromatous (BL) leprosy. ENL is mediated by immune complexes and typically presents with crops of painful erythematous nodules, systemic symptoms, and, occasionally, internal organ involvement (Bhat & Vaidya 2020). Genital involvement in ENL is rare and often misdiagnosed as a sexually transmitted infection (STI), and other non venereal causes of genital ulcers. We report an unusual case of ENL manifesting with genital ulceration, confirmed via histopathology and Fite staining, underscoring the importance of considering Hansen's disease in non-venereal genital ulcers, especially in endemic regions.

Case Report

A 25-year-old man presented with a one-year history of recurrent episodes of painful

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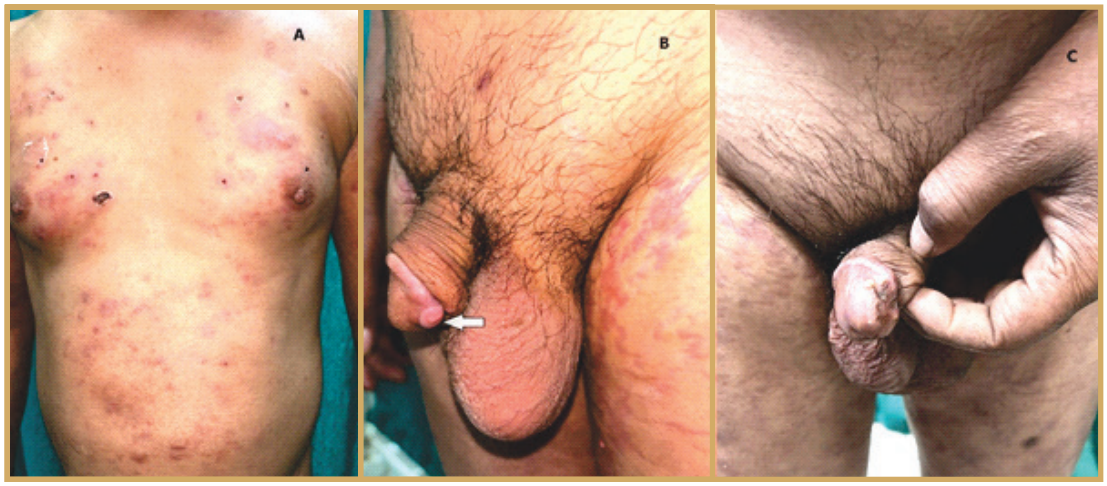

Fig. 1 : Clinical inspection of the patient showing various manifestations of ENL in a case of Lepromatous Leprosy. (A) Erythematous and painful lesions with necrosis in few on abdomen, (B) Distinct fluid-filled lesion on the glans penis (marked with arrow), (C) Ulceration of the genital lesion post few days.

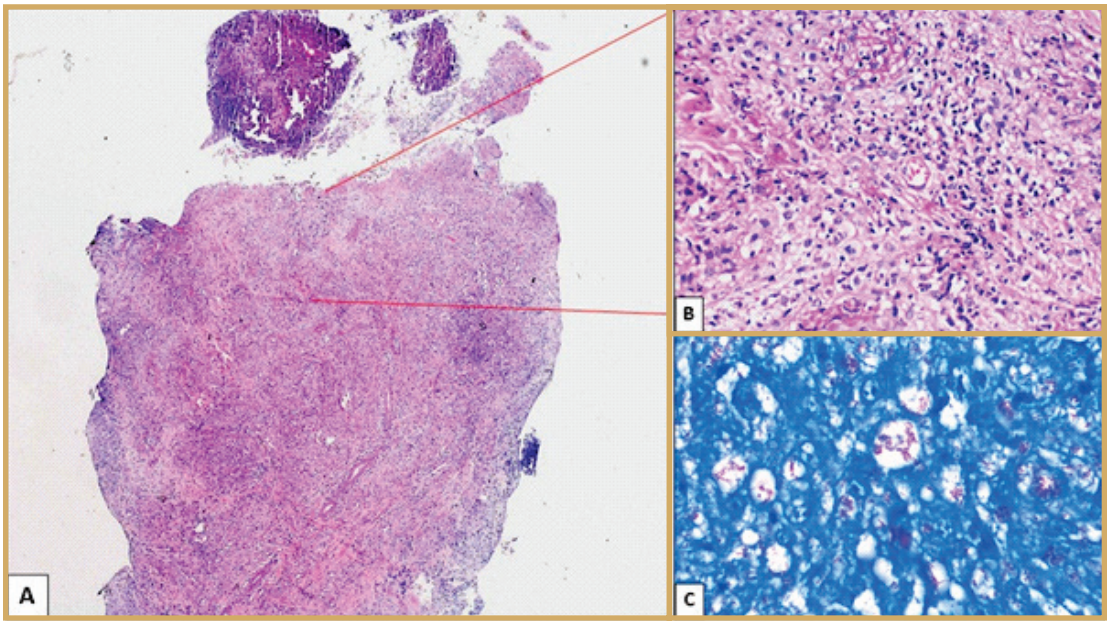

Fig. 2 : Histopathological examination of the genital ulcer. (A) Haematoxylin and eosin (H&E, 40X) stained section shows a skin biopsy with ulcerated and denuded epidermis. Upper mid and deep dermis shows dense lympho-histiocytic infiltrate, (B) Higher magnification demonstrates sheets or clusters of macrophages with neutrophilic invasion ((H&E, 200X), (C) Fite stain shows presence of numerous lepra bacilli (red arrow) (Fite stain; x1000).

erythematous skin lesions occurring every 2-4 months, associated with fever and arthralgia, with the current episode ongoing for 14 days (Fig. 1A). Each episode was characterised by tender erythematous lesions, some of which progressed to vesicles that ruptured within 1–2 days, resulting in necrotic erosions with overlying blackish crusts. These lesions typically healed over 10–14 days, leaving post-inflammatory hyperpigmentation. Episodes were accompanied by fever and joint pain involving the knees, ankles, and elbows.

During the current episode, the patient developed painful necrotic skin lesions for 14 days initially on the left elbow, followed by bilateral upper limbs, chest, abdomen, back, lower limbs, face, along with a blister on penis that progressed to a painful ulcer, not associated with dysuria or fowl smelling urethral discharge. He denied any prior sexual exposure. On examination multiple well defined erythematous tender nodules present predominantly on back, chest and abdomen with central erosions and haemorrhagic crust present in few lesions. Neurological examination revealed glove and stocking hypoesthesia with intact power in upper and lower limbs and no motor deficit. There was grade 2 thickening of bilateral ulnar nerve and bilateral common peroneal nerves. On genital examination single well defined erythematous tender nodule with overlying vesiculation present on glans penis (Figs 1B, 1C). There was no cervical, axillary or inguinal lymphadenopathy.

Slit skin smear was done from earlobes and genital lesion with bacteriological index (BI)-3+ and zero respectively. Morphological index (MI) from ear lobe was 12%. Skin punch biopsy was done from lesion on glans which revealed ulcerated, denuded epithelium with sheets of foamy macrophages present pan dermally. Pan dermal aggregate of lymphohistiocytic infiltrate predominantly present around vessels and adnexa along with neutrophilic infiltrate showing nuclear dust. Fite stain shows presence of numerous lepra bacilli (Fig. 2). Tzanck smear, VDRL (Venereal Disease Research Laboratory Test), TPHA (Treponema Pallidum Hemagglutination Assay) of patient were negative. Gram stain didn't reveal any bacteria and pus culture was negative. Patient was diagnosed as a case of lepromatous Leprosy in type 2 reaction and was started on multibacillary-MDT (MB-MDT) with tablet prednisolone 1mg/kg/day along with wound care which included ointment mupirocin 2% local application twice daily and normal saline compresses. Within one week, patient's genital lesion started to heal with hyperpigmentation and no residual scarring along with his systemic complaints. He came for follow-up monthly post resolution this episode of ENL.

Discussion

Erythema Nodosum Leprosum (ENL) is a type 2 lepra reaction, classically occurring in patients with lepromatous (LL) or borderline lepromatous (BL) leprosy. It is an immune complex-mediated (Type III hypersensitivity) reaction, characterized by crops of tender erythematous nodules and plaques, often accompanied by fever, malaise, arthralgia, lymphadenopathy, and, in severe cases, internal organ involvement (Bhat & Vaidya 2020). Histologically, ENL lesions show neutrophilic infiltration superimposed on a background of chronic granulomatous inflammation, with nuclear dust, vasculitis, and abundant bacilli in macrophages (Adhe et al 2012).

While cutaneous involvement is the hallmark, genital lesions in ENL are rare. Kumar et al (2001) have reported external genital lesions occurring in 6.6% of leprosy patients, more commonly in BL group. Genital lesions are often mistaken for sexually transmitted infections like herpes,

chancroid, or other nonvenereal causes including local manifestations of systemic diseases (Behçet's disease, Crohn's disease, pyoderma gangrenosum), phagedenic ulcer, autoimmune blistering diseases (pemphigus, pemphigoid), and drug reactions.

ENL is a complex immunological reaction involving innate and adaptive immune mechanisms. Neutrophils are a characteristic but time-dependent histological feature, with endothelial activation mediated by E-selectin facilitating their migration. Upregulation of Fcγ receptors (CD64) on neutrophils, triggered by release of Mycobacterium leprae antigens following MDT initiation, contributes to enhanced pro-inflammatory cytokine release (Schmitz et al 2016). Although immune complex deposition and vasculitis support a type III hypersensitivity component, immune complexes may represent an epiphenomenon rather than the primary driver. Increasing evidence supports a predominantly T-cell–mediated response, with elevated CD4+ T cells, reduced CD8+ T cells, diminished regulatory T cells, and a Th1-skewed cytokine profile. Key cytokines implicated include TNF-α, IFN-γ, IL-1β, and IL-6, with therapeutic responses to TNF-α inhibitors reinforcing their pathogenic role. Genetic polymorphisms involving TLRs, NOD2, NRAMP1, and HLA-DRB1 further influence susceptibility, highlighting the multifactorial immunopathogenesis of ENL. CCL-5 (chemokine [C-C motif] ligand 5) and IFN-γ, has been identified as key upstream regulator of ENL. In addition, CCL-2, CCL-3, and superoxide dismutase-2 (SOD-2) have been proposed as potential biomarkers for disease activity (Mehta et al 2025).

The pathophysiology behind genital involvement is not fully understood, but may be related to the high vascularity and susceptibility of penile skin to immune-complex deposition and vasculitic injury during reactional episodes (Rupan et al 2022, Kumar et al 2001).

In our patient, the genital lesion was a tender erythematous nodule with vesiculation on the glans penis, which ulcerated within days. The ulcer's non-venereal nature was supported by lack of sexual contact history, absence of dysuria, urethral discharge, foul odour, or regional lymphadenopathy, negative VDRL, TPHA, gram stain, Tzanck smear and by the histopathological findings of foamy macrophages packed with acid-fast bacilli on Fite staining—a hallmark of multibacillary leprosy. The histology also demonstrated dense lymphohistiocytic infiltrates with neutrophils and nuclear dust, consistent with ENL pathology.

Management of ENL with genital involvement does not differ from conventional ENL therapy, but prompt recognition is essential to prevent secondary infection, scarring, and functional impairment. Systemic corticosteroids remain the mainstay for acute control, with alternatives such as thalidomide, clofazimine in higher doses, or immunosuppressants for recurrent or steroid-dependent cases (Bhat & Vaidya 2020). Our patient responded well to prednisolone 1 mg/kg/day, with marked improvement in genital and cutaneous lesions within two weeks. In sexually active men presenting with genital ulcers, clinicians should maintain a broad differential diagnosis beyond sexually transmitted infections, particularly in endemic regions. A comprehensive history, full dermatological examination, and appropriate investigations including STI screening, slit-skin smear, and biopsy are essential for appropriate diagnosis and management.

Conclusion

This case adds several important points to our knowledge regarding unusual presentation of ENL in leprosy. Few take home points are:-

1. Genital ulceration can be a manifestation of ENL and should be considered in endemic areas.
2. Histopathology with Fite staining remains crucial for confirming the diagnosis and excluding other etiologies.
3. A high index of suspicion is necessary to avoid misdiagnosis.

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