Letter

Foreign body granuloma following leech therapy in hidradenitis suppurativa: A case complicated by lymphedema

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To the Editor

Hidradenitis suppurativa (HS) is a chronic inflammatory dermatosis characterized by a variable clinical course that significantly impairs quality of life. Despite recent therapeutic advances, its management remains challenging, potentially leading patients to pursue alternative therapies.[1] We report a novel case of leech therapy–associated foreign-body granuloma with concurrent lymphedema that developed during anti–tumor necrosis factor (TNF) therapy in a patient with HS.

A 58-year-old woman presented with a well-demarcated, inverted triangular lesion in the pubic region measuring 10 × 15 cm. Physical examination revealed cutaneous thickening with a characteristic *peau d'orange* appearance, indicative of underlying lymphedema (**Figure 1**). Firm nodular lesions were observed within the affected area (**Figure 2**). The patient reported a long-standing history of HS involving the genital region (**Figure 3**).

The patient's treatment history revealed multiple therapeutic interventions for HS with variable responses (**Table 1**). Initial management with systemic doxycycline (200 mg/day) and topical clindamycin resulted in inadequate clinical improvement. Between 2017 and 2019, the patient independently performed weekly leech therapy sessions around the genital lesions. Although lesions in the pubic area initially regressed, new lesions developed in the genital region. The patient initiated adalimumab at the standard HS dose in 2019 and has achieved Hidradenitis Suppurativa Clinical Response (HiSCR50) to date.[2] In 2022, a triangular lesion with associated lymphedema and nodular lesions in the pubic region was first detected, prompting a comprehensive diagnostic evaluation.

Diagnostic imaging studies, including ultrasonography and positron emission tomography–computed tomography (PET/CT), demonstrated increased skin thickness in the affected area without additional significant findings.

Figure 1. *Clinical appearance of a well-demarcated, inverted triangular lesion in the pubic region demonstrating cutaneous thickening with a characteristic* peau d'orange *appearance, indicative of underlying lymphedema and fibrosis.*

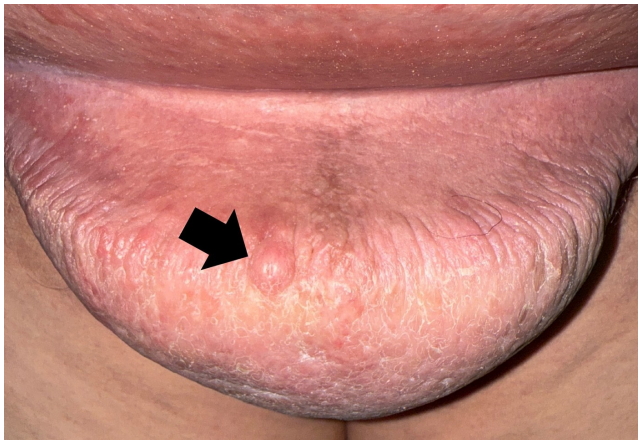

Figure 2. *Firm nodular lesions within the affected area (arrow).*

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Figure 3. *Hidradenitis suppurativa lesions in the genital region demonstrating a knife-cut sign with linear ulcerations, hyperpigmentation, and scarring.*

A 4-mm punch biopsy of the nodular lesions was performed for histopathological assessment. Microscopic examination at low magnification revealed mild epidermal acanthosis, papillomatosis, and prominent dermal fibrosis, with well-circumscribed granulomatous infiltrates in the deep dermis (Figure 4). Higher magnification demonstrated infiltrates composed of epithelioid histiocytes and multinucleated giant cells within the fibrotic dermis, consistent with foreign-body granulomas (Figure 5).

Cutaneous Crohn disease was considered in the differential diagnosis because of both the knife-cut appearance of some lesions and the granulomatous infiltrates observed on histopathology. The knife-cut sign has been described in several cutaneous conditions (Table 2), including HS.[3] However, further histopathological assessment did not reveal features typical of Crohn disease. In addition, comprehensive imaging studies, including diffusion-weighted magnetic resonance imaging (MRI), contrast-enhanced MRI, and PET scans, showed no evidence of intestinal involvement or fistula formation, further supporting the diagnosis of foreign-body granuloma.

Figure 4. *Histopathological examination showing mild epidermal acanthosis, papillomatosis, and prominent dermal fibrosis with well-circumscribed granulomatous infiltrates (black arrow) in the deep dermis (hematoxylin-eosin, ×40).*

The clinical and histopathological findings in this case presented a diagnostic challenge with several potential etiologies. The characteristic features of granulomatous inflammation with multinucleated giant cells in the deep dermis strongly suggested a foreign-body reaction. The chronological association between leech therapy applied to the genital region and the subsequent emergence of lesions in the same anatomical area provides compelling evidence that leech therapy may have acted as a precipitating factor.

Foreign-body granulomas form as a result of the immune response to exogenous materials perceived as for-

Table 1. *Timeline of the Patient's Clinical History and Treatments.*

Time Period	Clinical Findings	Treatment	Clinical Response
Pre–2017	HS involving the genital region	Systemic doxycycline (200 mg/day) and topical clindamycin	Inadequate response
2017–2019	Active HS lesions	Weekly leech therapy sessions targeting the periphery of genital lesions	Initial perceived improvement, followed by progressive worsening
2019–2022	HS lesions	Adalimumab at the standard HS dosage	HiSCR50 achieved
2022–present	Newly detected inverted triangular lesion with lymphedema and nodular lesions in the pubic region	Adalimumab at the standard HS dosage; diagnostic workup initiated	HiSCR50 achieved

Abbreviations: HS, hidradenitis suppurativa; HiSCR, Hidradenitis Suppurativa Clinical Response.

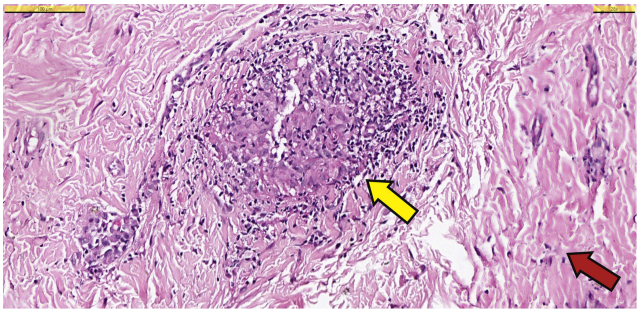

Figure 5. *Histopathological view demonstrating granulomatous infiltrates composed of epithelioid histiocytes (yellow arrow) and multinucleated giant cells (red arrow) within the fibrotic dermis, consistent with a foreign-body granulomatous reaction (hematoxylin-eosin, ×200).*

eign. The saliva of medicinal leeches contains numerous bioactive compounds, including hirudin, hyaluronidase, and various proteases.[4] These proteins, particularly high–molecular weight components, may act as antigenic stimuli that trigger granulomatous inflammation after prolonged or repeated exposure.

Lymphedema is a pathological condition characterized by tissue fluid accumulation resulting from compromised lymphatic transport capacity.[5] Impaired lymphatic circulation leads to vessel dilatation and subsequent structural alterations, including connective tissue proliferation and persistent inflammatory responses.[5] In the present case, the characteristic *peau d'orange* appearance and increased skin thickness on imaging supported the diagnosis of lymphedema.

Chronic lymphedema may instigate inflammatory reactions, including granuloma formation, through sustained protein-rich exudate accumulation and resultant tissue remodeling. While intralymphatic granulomatous lesions causing lymphatic obstruction have been documented, the development of granulomas in the setting of preexisting lymphedema is exceptional.[6] Elastolytic granulomas arising within chronic lower-extremity lymphedema have been reported in visceral lymphangiodysplasia.[7] However, in most cases, patients initially present with lymphedematous changes before the underlying granulomatous pathology is identified, making causality difficult to establish.

Based on the histopathological findings of epithelioid histiocytes and multinucleated giant cells in the deep dermis, along with the clinical history and examination, a diagnosis of foreign-body granuloma secondary to leech therapy complicated by lymphedema was established. To our knowledge, this is the first documented case of foreign-body granuloma following leech therapy for HS. Although hirudotherapy has recognized anticoagulant and anti-inflammatory effects mediated by bioactive salivary compounds,[4] prolonged exposure may trigger granulomatous inflammation, likely owing to a combination of mechanical trauma from leech bites and immune responses to foreign antigens in leech saliva.

The extended interval of 5 years between initiation of leech therapy and detection of granulomas is unusual, as foreign-body reactions typically manifest within 6 months.[8] We hypothesize that this delayed presentation may be attributable to 3 interrelated factors. First, the immunomodulatory effects of adalimumab may have masked the early inflammatory response to leech antigens.[9] TNF–α is critical for granuloma formation and maintenance, and its inhibition may suppress early granulomatous responses while paradoxically allowing later granuloma development through altered immune pathways. Second, preexisting chronic inflammation from HS may have created an immunologically primed environment. HS involves dysregulation of innate and adaptive immune responses, potentially lowering the threshold for foreign-body reactions.[10] Third, the relationship between lymphatic dysfunction and granuloma formation appears bidirectional. Chronic HS-associated lymphatic impairment may be exacerbated by granulomatous inflammation, which can further obstruct lymphatic vessels and promote perilymphatic fibrosis, creating a self-perpetuating inflammatory cycle.

HS itself is associated with lymphatic dysfunction and lymphedema, particularly in advanced disease. Although lymphedema most commonly affects the scrotal region, it may occur in other anatomical areas involved by HS.[5] In the present case, preexisting subclinical lymphatic dysfunction may have been exacerbated by prolonged leech therapy and subsequent foreign-body granulomas, contributing to the pronounced lymphedema observed.

Table 2. *Cutaneous Conditions Associated With Knife-Cut Sign.*

Condition	Clinical Features	Pathophysiology
Crohn disease	Perianal fissures, cutaneous fistulas	Granulomatous inflammation
Herpes simplex virus infection	Linear erosions, particularly in immunosuppressed patients	Viral cytopathic effect
Hermansky-Pudlak syndrome	Bleeding tendency and oculocutaneous albinism	Platelet dysfunction
Hidradenitis suppurativa	Linear fissures in intertriginous areas	Chronic follicular inflammation

Following diagnosis, the patient was maintained on adalimumab, and colchicine was added, resulting in slight improvement over 6 months. Management of foreign-body granulomas remains challenging, with most reported treatment strategies derived from cosmetic procedure–related cases and consisting primarily of intralesional or systemic corticosteroids.[11] The combination of adalimumab and colchicine provided modest benefit, mainly in reducing inflammation. Colchicine, which has anti-inflammatory and antifibrotic properties,[12] may have contributed to this partial response, although persistent lymphedema suggests the need for additional therapeutic approaches.

The present case highlights how limited treatment options for HS may drive patients toward alternative therapies with potential risks, underscoring the need for more effective management strategies. Additionally, recognition of the knife-cut sign in HS broadens our understanding of the clinical spectrum of this complex disease.

Potential conflicts of interest

The authors declare no conflicts of interest.

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