Cutaneous ulcers in sarcoidosis

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Abstract

Sarcoidosis is a disease characterized by immunological granuloma formation in various organs. Cutaneous manifestations occur in about 25% of patients with rare cases showing ulcerative sarcoidosis, that can be debilitating if not treated promptly. This article presents a patient with isolated ulcerative sarcoidosis and reviews existing literature. A 44-year-old woman presented with a non-healing ulcer on her right gluteal area. A skin biopsy confirmed sarcoidosis with non-necrotizing granulomas. Systemic involvement of sarcoidosis was ruled out. Treatment involved topical corticosteroids and intralesional corticosteroid injections, resulting in complete healing. This case emphasizes the importance of considering ulcerative sarcoidosis in non-healing wounds and the efficacy of corticosteroid treatment.

Keywords: cutaneous, Lofgren syndrome, sarcoidosis, ulcers

Introduction

Sarcoidosis is a multi-system disease of unknown etiology [1]. The characteristic feature of sarcoidosis is the formation of immunological granulomas in the involved sites [1]. The incidence of sarcoidosis varies according to age, sex, race, and geographic origin. It is estimated at around 16.5/100,000 in men and 19/100,000 in women [1]. Sarcoidosis predominantly affects the lungs and lymphatic system. Other organs may be involved such as the skin, bones, liver, muscles, spleen, and nervous system [1,2]. Skin manifestations arise in one-fourth of patients with sarcoidosis [3]. The cutaneous lesions are classified as nonspecific and specific, with the latter exhibiting noncaseating granuloma formation [2]. Specific lesions present in a variety of morphologies including papules, plaques, nodules, scar sarcoidosis, and lupus pernio [4]. The specific cutaneous lesions commonly present as an infiltrated plaque with a reddish-brown discoloration, but may appear in some instances as yellowish-brown or as maculopapular lesions that are violaceous in color [2]. Nonspecific lesions lack a granulomatous inflammation and primarily include calcinosis cutis and erythema nodosum [5]. Less frequent clinical presentations include scarring and non-scarring alopecia, erythroderma, nail dystrophy, and verrucous, ichthyosiform, psoriasiform, hypopigmented, or ulcerative skin lesions [2,4]. Among these many potential clinical manifestations, ulcerative sarcoidosis is a rare disease variant [3-5]. There is a paucity of information on ulcerative sarcoidosis [1,2], despite being a multisystemic condition that can be debilitating if left untreated. In this article we present a case of isolated ulcerative sarcoidosis and review the available data on the topic. The review covered research literature sources based on MEDLINE, PubMed, and Google Scholar databases with 'ulcerative sarcoidosis' as the key search word.

Case Synopsis

A 44-year-old woman presented with a non-healing ulcer for 8 weeks on the right gluteal area. The lesion first appeared as red painful erythematous papules

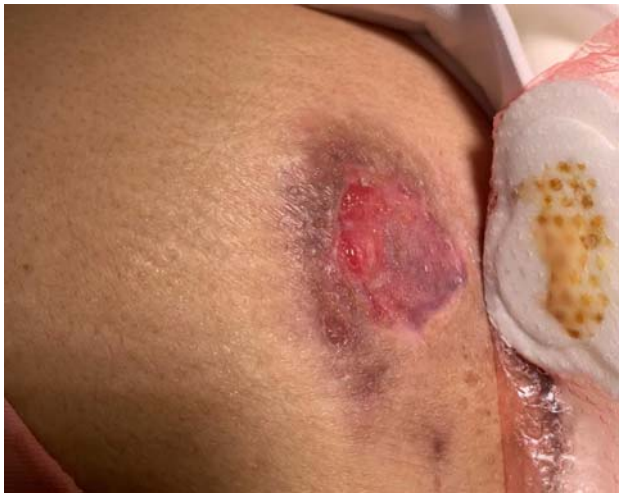

Figure 1. *The right upper gluteal area exhibits a well-demarcated erythematous, eroded, and ulcerated nodule measuring 3×3 centimeters, encircled by a hyperpigmented rim.*

that later formed an ulcer. The patient took oral amoxicillin/clavulanic acid for 7 days, but there was no improvement. The history was negative for pruritus, oral or genital ulcers, or other skin manifestations. The patient solely had bilateral knee pain. Otherwise, review of systems was negative. The patient's medical history was notable for Lofgren syndrome diagnosed two months prior to presentation, with complete remission. The patient previously suffered from erythema nodosum over both legs anteriorly that was healed at the time of presentation. On physical examination, a 3x3 cm ulcer with red elevated edges was observed over the right upper gluteal area (**Figure 1**). A punch biopsy of the lesion showed a non-necrotizing granuloma with granulation tissue fibrosis consistent with sarcoidosis (**Figure 2**). Various tests, including gram stains were negative and wound swab culture only showed the presence of normal flora.

The patient was assessed for systemic involvement, which was ruled out. Initially, the patient received treatment with clobetasol ointment twice daily for one month, resulting in ulcer's size reduction from 3×3 to 0.7×0.5 centimeters (**Figure 3**). After one month of clobetasol ointment use, the patient underwent two sessions of 5mg/ml intralesional triamcinolone acetonide steroid injections two weeks apart and utilized pimecrolimus 1% twice daily. This combined treatment led to nearly complete healing after three months.

Case Discussion

Skin manifestations arise in one-fourth of patients with sarcoidosis [3]. Ulcers are a rare variant of the cutaneous manifestations of sarcoidosis [3-5]. The rates of occurrence of sarcoidal ulcers have been approximated to be 1% among White patients, whereas the rate stands at 5% in worldwide populations [6]. Powell reported a prevalence of 3.25-to-one whereas Bukiej's literature review described a female-to-male ratio of 1.8:1 [6,7].

Ulcerative sarcoidosis lesions typically exhibit diameters of less than one-cm and manifest a spectrum of colors, including shades of red-brown to purple, with occasional presentations in yellow-brown, hypopigmented, or skin-toned variations [3]. In a literature review reported that lower extremities are the most commonly affected sites and a recent comprehensive review comprising 34 cases, demonstrated that 85% (29 out of 34) of these cases exhibited involvement of the legs along with other locations including face, arms, trunk, and genital area

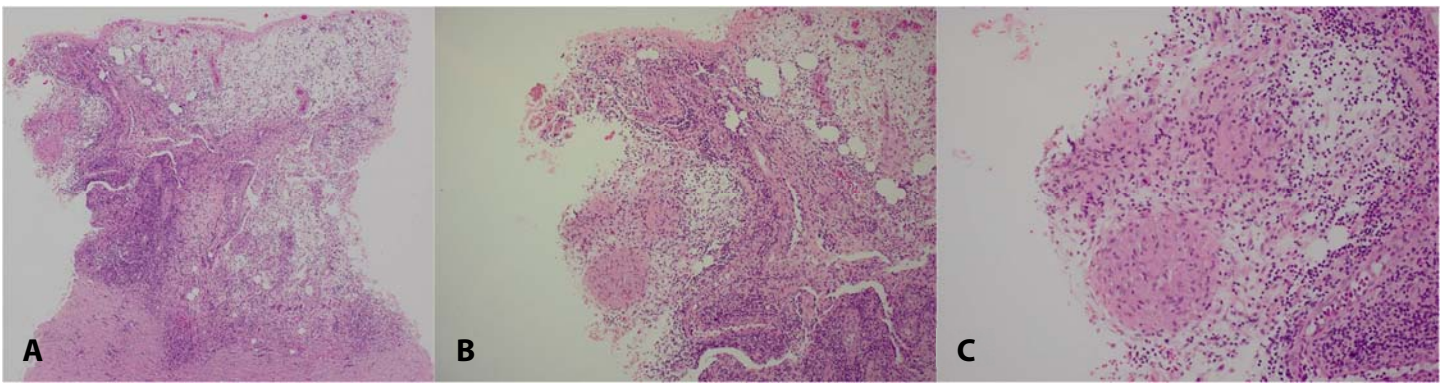

Figure 2. ***A)*** *(H&E histopathology showing ulcerated skin with diffuse and nodular mixed inflammatory infiltrate, 40×.* ***B)*** *Well-formed non-necrotizing granuloma, 100×.* ***C)*** *Well-formed non-necrotizing granuloma, 200×.*

[7]. Our patient presented with a lesion on the right buttock. The literature classifies the condition into two categories: specific sarcoidal lesions with non-caseating granulomas and non-specific eruptions that do not exhibit granulomatous inflammation [2]. The two categories of sarcoidal lesions tend to occur at trauma sites, in scars, or around tattoos. However, this was not the case with our patient [8].

The exact mechanism of ulceration in sarcoidosis remains unclear [9,10]. Although ulcers most commonly arise in preexisting skin lesions or scars, they may also appear de novo [7]. Ulcerative sarcoidosis, acknowledged as one of the great imitators, underscores the importance of evaluating clinical, epidemiological, radiographic, laboratory, and histopathological criteria for an accurate diagnosis. Recognizing the differential diagnosis is crucial. Hence, skin biopsy is indicated for all patients

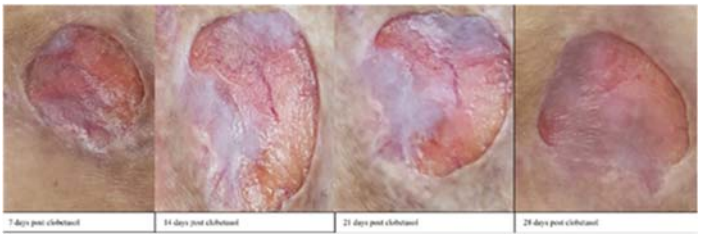

Figure 3. *Progressive stages of ulcer healing observed following the twice-daily application of clobetasol ointment.*

with wounds suspected to be ulcerative sarcoidosis [2]. It frequently mimics necrobiosis lipoidica (NLD), a rare, chronic, granulomatous skin disorder affecting approximately 0.3% of individuals with diabetes, primarily observed on the legs [11,12], (**Table 1**). Other differential diagnoses of cutaneous sarcoidosis include sporotrichosis, tuberculosis, stasis dermatitis with venous ulceration, and metastatic breast cancer (7). Our patient's biopsy showed non-necrotizing granuloma with

Table 1. *Illustrates a comprehensive comparison of clinical features, pathology, associations, and treatment modalities between necrobiosis lipoidica (NLD) and ulcerative sarcoidosis.*

	Ulcerative sarcoidosis	Necrobiosis lipoidica (NLD)
Clinical features	Red-brown to purple, with occasional variations in yellow-brown, hypopigmented, or skin-toned shades. Less than 1 cm in diameter. Lower extremities commonly affected [3,7]. The ulcer presents as violaceous or annular red to red–brown papule with central atrophy and hypopigmentation that develops within a scar [15]	Firm, reddish papules evolving into atrophic plaques on both shins. Plaques with violaceous to erythematous borders, central yellow-brown discoloration, and telangiectasia [15]. The ulcer presents as pink-to brown plaques with violaceous to erythematous rim, elevated boarders, central yellow-brown discoloration, central atrophy, and telangiectasia [15]
Pathology	Noncaseating granulomas. Atypical features: necrotizing granulomas and granulomatous vasculitis [7].	Palisaded granulomatous inflammation with degenerated collagen fibers. Diffuse involvement of entire dermis and subcutaneous fat septae. Absence of mucin, abundant plasma cells, multinucleated giant cells. Variable epidermal atrophy and vascular hyalinization [15].
Association	Cutaneous sarcoidosis occurs in up to one third of patients with systemic sarcoidosis [14].	Rare in diabetics (0.03%), but 22% of NLD patients develop diabetes or glucose intolerance [15].
Treatment	Topical/intralesional/systemic corticosteroids. Ineffective or intolerable due to adverse effects: Antimalarials like chloroquine or hydroxychloroquine and methotrexate [7].	Early lesion: Topical/intralesional steroids Topical calcineurin inhibitors Chronic cases: Systemic steroids, colchicine, cyclosporine, TNF alpha inhibitors, CO_2 laser, stanozolol, and pentoxyfylline [15].

granulation tissue fibrosis, most consistent with sarcoidosis.

The primary goals of treatment are to alleviate the patient's symptoms, decrease the psychological impact on the patient, and prevent disfigurement [13]. The choice of the appropriate treatment modality depends on the severity and extent of the disease [6]. The established standard treatment for cutaneous sarcoidosis typically encompasses the use of topical, intralesional, and systemic corticosteroids. In cases in which corticosteroid therapy is ineffective or intolerable due to adverse effects, supplementary treatments, such as antimalarials like chloroquine or hydroxychloroquine, as well as methotrexate are considered [7].

Our patient received initial therapy with a topical corticosteroid ointment which produced significant clinical improvement in her ulcer after one month. Intralesional corticosteroid therapy was then administered twice, two weeks apart. Within three months of the initiation of therapy, the lesion resolved completely.

Conclusion

This case highlights the significance of early recognition and proper management of ulcerative sarcoidosis. Comprehensive research and documentation of such cases will contribute to improved diagnostic and treatment strategies. Further investigations are warranted to uncover the underlying mechanisms of ulceration in sarcoidosis and explore therapeutic interventions to better manage this multisystemic disease, ultimately enhancing patient outcomes.

Potential conflicts of interest

The authors declare no conflicts of interest

References

1. Shatnawi NJ, Al-Zoubi NA, Al-Bakkar LA, Gharaibeh LM, Hamouri S. Nonhealing leg ulcer as the presentation of sarcoidosis: a case report. *Int J Low Extrem Wounds.* 2023;22:742-747. [PMID: 34374584**.]**
2. Paparone, Pamela, Paparone, Paige and Paparone, Philip. Sarcoid Ulcer of the Leg: A Challenging Chronic Wound. 2010. https://www.hmpgloballearningnetwork.com/site/wounds/case-report-and-brief-review/sarcoid-ulcer-leg-challenging-chronic-wound. Accessed on March 1, 2024.
3. Das S. Clinical manifestations of sarcoidosis and granulomatous disorders. sarcoidosis granulomatosis diagnosis and management. *IntechOpen*. 2020;29;37:67. [DOI: 10.5772/intechopen.92236].
4. Samuel B, Barret J, Sidky K, Gosney J. Rare presentation of sarcoidosis. *Lab Med.* 2011;42:516-522. [DOI: 10.1309/LMU1FTKI76IMJZIQ].
5. Woolley, A., Lynn, M. and Singh, N. Case study: Sarcoidosis, *South Sudan Med J.* 2014;7:62-65. https://www.ajol.info/index.php/ssmj/article/view/132629. Accessed on August 1, 2024.
6. Bukiej A, Wu J, Sequeira W. Ulcerative cutaneous sarcoidosis successfully treated with infliximab. *Clin Rheumatol.* 2021;40:3063-3068. [PMID: 33728543].
7. Powell E, Rosen T. Ulcerative sarcoidosis: a prototypical presentation and review. *Cutis.* 2017;100:312-316. [PMID: 29232421].
8. Momah N, Otesile A, Pawa R, Shedlofsky S. Sarcoidosis presenting as necrotizing sarcoid granulomatosis of the liver, sclerosing cholangitis, and gastric ulcer. *ACG Case Rep J.* 2014;1:164-166. [PMID: 26157862].
9. Kato Y, Okabe H, Hoshi M, Yamamoto T. Ulcerative sarcoidosis on the leg and scalp. *Our Dermatol Online.* 2020;11:331-332. [DOI: 10.7241/ourd.20203.30].
10. Fujii H, Torii H. Case of sarcoidosis with seasonal cutaneous ulceration. *J Dermatol.* 2017;44:1331-1332. [PMID: 27859639].
11. Fernandez-Faith E, McDonnell J. Cutaneous sarcoidosis: differential diagnosis. *Clin Dermatol.* 2007;25:276-87. [PMID: 17560305].
12. Kota SK, Jammula S, Kota SK, Meher LK, Modi KD. Necrobiosis lipoidica diabeticorum: s case-based review of literature. *Indian J Endocrinol Metab.* 2012;16614-20. [PMID: 22837927].
13. Fram G, Kohli S, Jiang A, Kaatz S. Sarcoidosis presenting as facial and scalp ulceration with secondary bacterial infection of the skin. *BMJ Case Rep.* 2019;12:e231769. [PMID: 31748362].
14. Katta R. Cutaneous sarcoidosis: a dermatologic masquerader. *Am Fam Physician.* 2002;15;65:1581-4. [PMID: 11989634].
15. Alikhan A, General Dermatology. In: Review of dermatology, Alikhan A, Hocker, T.L.H. 2nd ed. Elsevier limited; 2022. P. 153-154.