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Case report

When scars tell a story: cases of scar sarcoidosis preceding or following diagnosis of systemic disease

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Summary
Sarcoidosis is a systemic granulomatous disease of unknown etiology, characterized by the formation of non-necrotizing granulomas in various organs, with the lungs and mediastinal lymph nodes being the most commonly affected sites. "Scar sarcoidosis" refers to the rare phenomenon in which sarcoid granulomas develop in pre-existing scars, such as surgical scars, tattoos, or sites of previous skin trauma. We report two cases of patients who presented with sarcoid granulomas developing in previous scar sites. The first case involved a 37-year-old man with a prior diagnosis of stage II pulmonary sarcoidosis who later developed erythematous plaques over scarred areas. A skin biopsy confirmed non-necrotizing granulomas. The second case describes a 45-year-old woman who presented with erythematous-violaceous plaques over previous traumatic scars, with subsequent tests revealing systemic sarcoidosis. Scar sarcoidosis highlights the diverse clinical presentations of sarcoidosis, emphasizing the need for clinicians to be vigilant of new or unusual manifestations. Recognizing this form of sarcoidosis can facilitate early systemic diagnosis and impact patient management. These cases underscore the importance of a multidisciplinary approach in diagnosing and managing sarcoidosis, given its dynamic and unpredictable nature.

Key words: sarcoidosis, scar, skin biopsy

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Introduction

Sarcoidosis is a systemic granulomatous disease of unknown etiology, characterized by the formation of non-necrotizing granulomas in various organs, with lungs and mediastinal lymph nodes being the most commonly affected sites [1]. While the pathogenesis of sarcoidosis remains unclear, it is believed to result from an exaggerated immune response to environmental triggers in genetically susceptible individuals [2]. "Scar sarcoidosis" refers to the rare phenomenon in which sarcoid granulomas develop in pre-existing scars, including surgical scars, tattoos, or sites of prior skin trauma such as venipuncture or burns [3]. This localized form of sarcoidosis may represent either a manifestation of systemic disease or an isolated cutaneous involvement. Recognizing scar sarcoidosis is important for early diagnosis, as it can be a precursor to or occur alongside more widespread organ involvement. We herein describe two patients who presented with sarcoid granulomas developing in previous cutaneous scars, underscoring the need for awareness of this unique clinical presentation.

Case presentation

Case 1

An otherwise healthy 37-year-old man presented with skin-colored subcutaneous nodules on the lower extremities, associated with left-sided inguinal lymphadenopathy. His family history was notable for tuberculosis, with a brother diagnosed 15 years earlier, although the patient had no personal history of TBC and had undergone routine screenings without indication for prophylaxis. The patient subsequently underwent excisional biopsy of the inguinal lymph node: histopathological analysis revealed granulomatous giant cell inflammation consistent with sarcoidosis, characterized by non-necrotizing granulomas, rare plasma cells, and small, mature lymphocytes. Following the lymph node biopsy, a pulmonary evaluation including CT scan, BAL, and TBNA was performed. CT showed bilateral lymphadenopathy and reticulonodular opacities with a perilymphatic distribution. BAL revealed lymphocytosis with CD4+ T-cell predominance and was negative for infections. TBNA of station 7 lymph nodes showed non-necrotizing granulomas. Based on these findings, stage II sarcoidosis was diagnosed, and systemic corticosteroids were started, which led to clinical improvement. Regular follow-ups were scheduled to monitor disease progression. Several months into the treatment, the patient developed new skin lesions, characterized by erythematous-violaceous patches and plaques located on areas of previous traumatic scars, including the right wrist (Fig. 1a), left palm, left elbow, and right knee. Dermatoscopically, these areas were characterized by a well-defined erythematous plaque surrounding a central scar, which appears as a linear, slightly hypopigmented area with super-

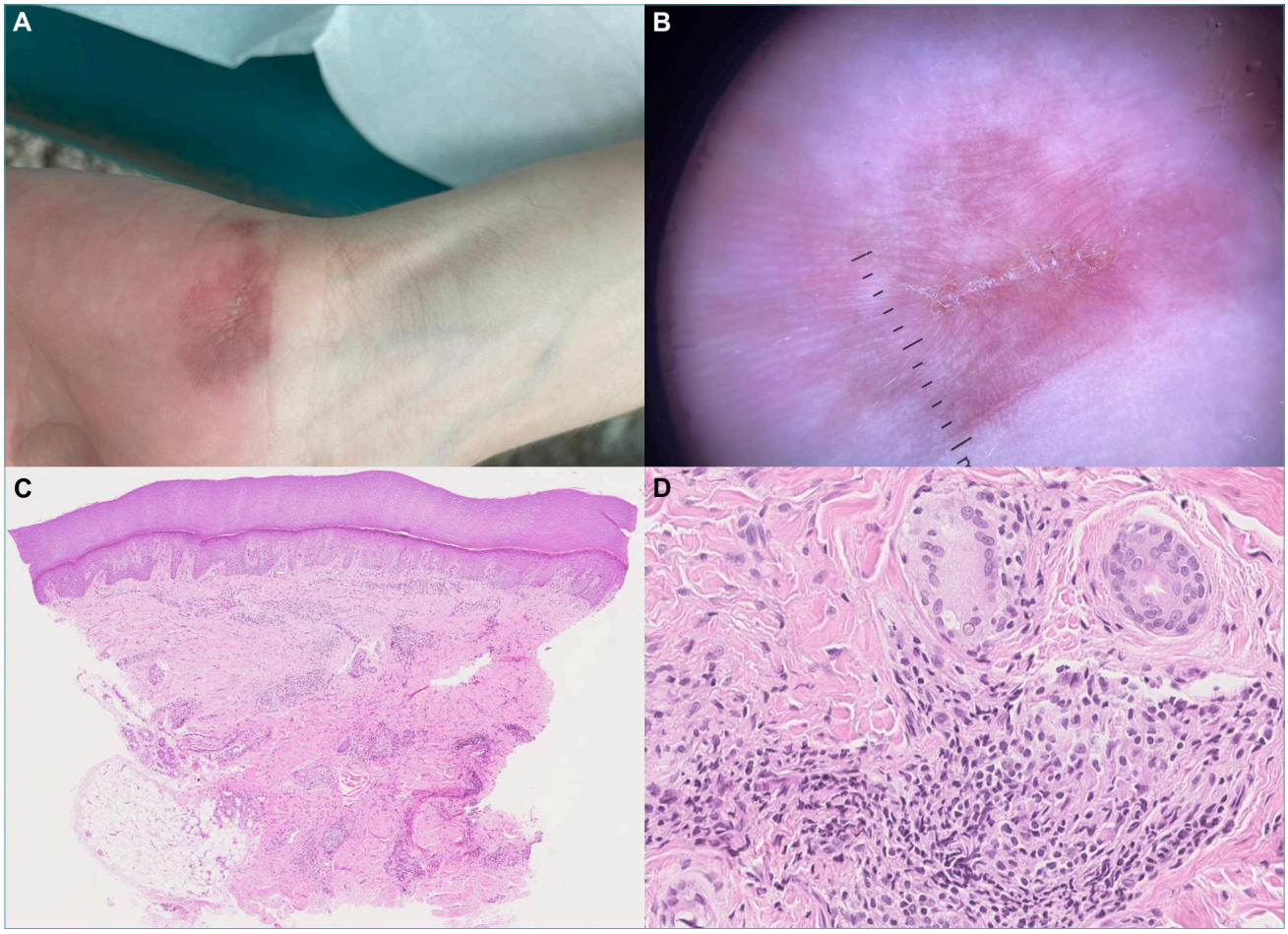

Figure 1. Clinical photograph of an erythematous-violaceous plaque overlying a pre-existing scar on the patient's wrist (A). Dermoscopic image showing an erythematous, yellowish background surrounding a linear central scar, with crusty scales along the scar line, consistent with granulomatous involvement of the scar tissue (B). Low-power histological view showing a granulomatous inflammatory infiltrate in the dermis, with no necrosis, distributed around fibrotic scar tissue (C, hematoxylin and eosin stain, original magnification x10). (D) Higher magnification of the dermal infiltrate, highlighting non-necrotizing granulomas composed of epithelioid histiocytes and multinucleated giant cells (D, hematoxylin and eosin stain, original magnification x10).

ficial scaling (Fig. 1b). Given the history of systemic sarcoidosis and the appearance of these cutaneous manifestations in scarred areas, a decision was made to proceed with a skin biopsy to further investigate the etiology of the lesions. Histologically, a non-necrotizing granulomatous process associated with scar-like dermal fibrosis was evident. At low magnification, a granuloma annulare-like pattern associated with scar-like fibrotic areas was observed (Fig. 1c). This pattern was also confirmed at higher magnification, where giant cell granulomatous aggregates accompanied by numerous lymphocytes were evident (Fig. 1d). No necrosis was observed, the observation under polarized light was negative, and special stains for the identification of microorganisms, including mycobacteria, were negative. Following pathological-clinical correlations and multidisciplinary case discussion, final diagnosis of scar sarcoidosis was made. After corticosteroid therapy, the cutaneous lesions improved.

Case 2

A 45-year-old woman with no significant past medical history presented with erythematous-violaceous plaques over previous traumatic scar sites located on the forearm, flank, and retroscapular area. A skin biopsy was performed (Fig. 2a), revealing a non-necrotizing granulomatous giant cell inflammation with ill-defined collections of histiocytes in the dermis, accompanied by scar-like fibrosis (Fig. 2b). A mitotic figure was observed within the histiocytic aggregates (Fig. 2c); however, no cytological atypia or necrosis was present. Therefore, an immunoreaction for cytokeratins and EMA was performed to exclude epithelioid sarcoma, both of which resulted negative. The observation under polarized light and special stains for microorganisms, including mycobacteria, were negative, leading to a diagnosis of granulomatous dermatitis. To further evaluate potential systemic involvement, blood tests were ordered, which revealed an elevated level of angiotensin-converting enzyme (ACE), a common marker associated with sarcoidosis. Based on these findings, a chest CT scan was performed, which showed bilateral hilar lymphadenopathy. A TBNA biopsy of the hilar lymph nodes was conducted. Histopathological analysis of the lymph node samples revealed non-necrotizing granulomas organized in lymphohistiocytic aggregates, consistent with a granulomatous process. The final diagnosis was established as systemic sarcoidosis, with cutaneous manifestations localized to previous scar sites, referred to as scar sarcoidosis. Following the diagnosis, the patient was initiated on systemic corticosteroid therapy to address both pulmonary and cutaneous manifestations of sarcoidosis.

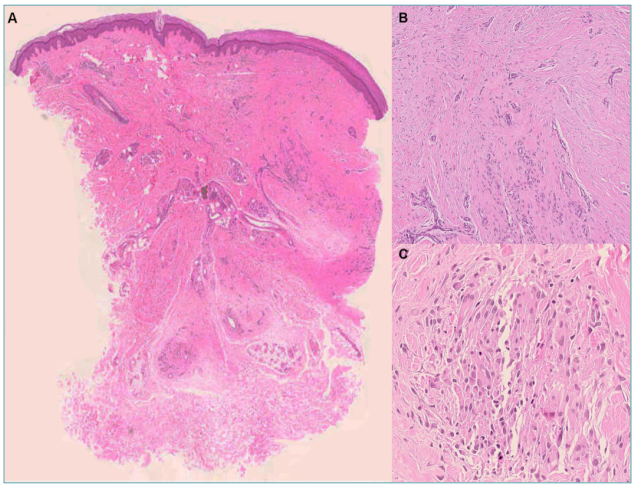

Figure 2. Low-power view showing a scar with granulomatous inflammatory infiltrate within the dermis, with preserved epidermis (A, hematoxylin and eosin stain, original magnification x10). Intermediate magnification displaying dense collagenous fibrosis interspersed with scattered inflammatory cells (B, hematoxylin and eosin stain, original magnification x100) (C) High-power view highlighting non-necrotizing granulomas composed of epithelioid histiocytes and multinucleated giant cells (C, hematoxylin and eosin stain, original magnification x200).

Discussion

Cutaneous manifestations of sarcoidosis are protean, ranging from subtle papules to more extensive plaques and nodules [4]. The skin lesions are often erythematous or violaceous and may develop on the face, neck, upper back, and extremities. Common presentations include maculopapular lesions, which are small, red-brown papules frequently seen on the face and around the eyes; plaque sarcoidosis, which consists of larger, indurated, scaly lesions that can become chronic and disfiguring; and lupus pernio, a distinctive form of sarcoidosis that appears as purplish, swollen plaques on the nose, cheeks, and ears, is often associated with more severe systemic disease. Another manifestation is erythema nodosum, an acute, self-limited presentation characterized by tender, red nodules, usually on the legs [5]. The clinical heterogeneity of sarcoidosis is also reflected in the multiple histological patterns that this disease can present, and the cases described are a clear example of this. Although the classic morphology of non-necrotizing giant cell granulomas lacking lymphocytes (so-called “naked granulomas”) best represents the typical inflammatory infiltrate of sarcoidosis, Case 1 exhibited a granuloma annulare-like pat-

tern, while Case 2 showed poorly formed aggregates of histiocytic elements. These morphological features can lead to a wide range of differential diagnostic considerations, including infectious processes, immune disorders, and even neoplastic conditions, such as histiocytosis or epithelioid sarcoma. It is the clinicopathological correlation that ultimately guides the diagnosis, and in the two presented cases, it allowed for the correct identification of scar sarcoidosis.

Scar sarcoidosis, while rare, presents a unique insight into the clinical manifestations and pathophysiology of sarcoidosis. This phenomenon involves the formation of sarcoid granulomas within pre-existing scar tissue, which could include sites of previous surgical incisions, traumatic scars, or tattoos. The cases presented here, in which patients developed erythematous plaques over scarred areas, underscore the diagnostic importance of this unusual presentation. Recognizing scar sarcoidosis is critical, as it can provide clues toward systemic involvement or even signal disease recurrence.

The pathogenesis of scar sarcoidosis remains poorly understood, although several hypotheses exist. One prevailing theory suggests that scar sarcoidosis arises from an exaggerated immune response to antigens sequestered within scar tissue, possibly as a result of localized inflammation or the presence of foreign materials, infections, or minor injuries introduced during the healing process. This immune response leads to the formation of non-necrotizing granulomas, which histologically resemble those found in systemic sarcoidosis, reinforcing the concept that scar sarcoidosis is likely a localized expression of an underlying systemic disease rather than an independent condition [3].

In Case 1, a patient with a pre-existing diagnosis of pulmonary sarcoidosis developed erythematous plaques over scars, months after his initial diagnosis. Histopathological examination confirmed the presence of non-necrotizing granulomas. The development of scar sarcoidosis in this patient illustrates how cutaneous lesions can emerge long after initial disease onset and may represent either disease recurrence or a localized immune phenomenon.

Case 2, by contrast, presents a different clinical pathway. Here, a patient with no prior sarcoidosis diagnosis developed erythematous plaques over scars, which initially presented as isolated cutaneous symptoms. Histological analysis revealed non-necrotizing granulomas, similar to Case 1. However, in this case, subsequent investigations, including elevated ACE levels and CT imaging revealing bilateral hilar lymphadenopathy, pointed towards systemic sarcoidosis. This case underscores the diagnostic value of recognizing scar sarcoidosis in patients without known sarcoidosis, as these cutaneous manifestations may precede or predict systemic involvement [6]. Thus, skin biopsies can play an essential role in the early detection of systemic sarcoidosis, guiding further investigations and enabling prompt diagnosis.

The literature on scar sarcoidosis is limited, though it consistently describes cases of patients with established systemic sarcoidosis developing granulomas at sites of prior skin injuries 7. The rarity of this phenomenon and the absence of a definitive mechanism suggest that scar sarcoidosis could be related to genetic predisposition, environmental factors, or specific immune responses. These cases underscore the necessity of vigilant, long-term monitoring in sarcoidosis patients, even after apparent disease stabilization or treatment, as new cutaneous or systemic manifestations may indicate changes in disease activity or recurrence.

Treatment for cutaneous sarcoidosis, including scar sarcoidosis, is generally guided by the severity and extent of the lesions [8]. Therapeutic options range from topical corticosteroids, intralesional steroid injections, to systemic corticosteroid therapy, depending on the degree of cutaneous involvement and associated systemic symptoms. In Case 1, systemic corticosteroid therapy was already in place to manage pulmonary sarcoidosis, which likely contributed to the control of cutaneous lesions. For patients whose skin lesions are resistant to corticosteroids or are symptomatic, additional immunomodulatory agents, such as hydroxychloroquine or methotrexate, may be considered. These agents provide alternative options for managing persistent sarcoid lesions, particularly in cases where systemic corticosteroid use may be undesirable due to side effects or potential complications.

Conclusions

In summary, scar sarcoidosis highlights the complex and unpredictable nature of sarcoidosis, emphasizing the need for clinicians to remain alert to new or unusual manifestations of the disease. Although skin biopsy plays a fundamental role in the diagnosis of this entity, it is only through extensive clinicopathological correlations that a diagnosis of scar sarcoidosis can be established. Recognizing scar sarcoidosis can significantly impact patient management, as it may signal disease progression, recurrence, or the need for therapeutic escalation. Consequently, these cases contribute to a better understanding of sarcoidosis' clinical spectrum and underscore the importance of a multidisciplinary approach in diagnosing and managing this dynamic condition.

Conflicts of interest statement

The authors declare no conflicts of interest.

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Authors contribution

Conception and design of the study: FF. Data collection: FF, GC, CC, JT, AP,. Manuscript writing: FF, GC, CC. Critical revision and editing: FF, MA, APDT. Approval of the final version: APDT.

Ethical consideration

This manuscript meets the ethical standards. Specific informed consent is routinely obtained.

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