

Cutaneous granulomas after cosmetic eyebrow micropigmentation as a potential marker of systemic sarcoidosis: a case report

Granulomas cutâneos após micropigmentação cosmética de sobrancelhas como potencial marcador de sarcoidose sistêmica: um relato de caso

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Abstract

Sarcoidosis is a systemic granulomatous disease of unknown etiology, characterized by the presence of non-caseating granulomas affecting multiple organs, particularly the lungs and skin. Cutaneous manifestations occur in up to 30% of cases and may represent the initial presentation. The appearance of lesions over tattoos or micropigmentation sites has been reported as a possible trigger in predisposed individuals. We report the case of a 54-year-old female patient who developed bilateral eyebrow edema and papules 1½ years after cosmetic micropigmentation. Histopathology revealed sarcoid-type granulomatous dermatitis. Further investigation identified pulmonary involvement and elevated angiotensin-converting enzyme levels, confirming systemic sarcoidosis. The patient showed partial response to corticosteroids and various topical and systemic treatments, with improvement after methotrexate and later azathioprine introduction. This case highlights the importance of considering systemic sarcoidosis in patients presenting with granulomatous reactions in cosmetic tattoos and reinforces the need for systemic screening in such presentations.

Keywords: Sarcoidosis. Pulmonary. Sarcoidosis. Cutaneous. Granuloma. Micropigmentation. Tattoos adverse effects.

Resumo

A sarcoidose é uma doença granulomatosa sistêmica de etiologia desconhecida, caracterizada por granulomas não caseosos que afetam múltiplos órgãos, particularmente pulmões e pele. As manifestações cutâneas ocorrem em até 30% dos casos e podem representar a apresentação inicial. O surgimento de lesões sobre áreas tatuadas ou de micropigmentação é relatado como possível fator desencadeante em indivíduos predispostos. Relatamos o caso de uma paciente de 54 anos que desenvolveu edema e pápulas em sobrancelhas um ano e meio após a micropigmentação cosmética. Exame histopatológico revelou dermatite granulomatosa sarcoídica. Investigação complementar identificou envolvimento pulmonar e enzima conversora da angiotensina elevada, confirmando sarcoidose sistêmica. A paciente apresentou resposta parcial a corticosteroides e a tratamentos tópicos e sistêmicos, com melhora após introdução de metotrexato e,

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posteriormente, azatioprina. Este caso destaca a importância de se considerar sarcoidose sistêmica em pacientes com reações granulomatosas em tatuagens cosméticas e reforça a necessidade de investigação sistêmica nessas apresentações.

Palavras-chave: Sarcoidose pulmonar. Sarcoidose cutânea. Granuloma. Micropigmentação. Tatuagens/efeitos adversos.

Introduction

Sarcoidosis is a multisystemic granulomatous disease of unknown etiology, characterized by the formation of non-caseating granulomas in affected tissues. The lungs and lymph nodes are most frequently involved, followed by the skin, eyes, and other organs.¹ Cutaneous manifestations occur in approximately 20-30% of patients and may represent the first clinical evidence of the disease.² These lesions are diverse, including papules, plaques, nodules, and scar infiltrations.

A well-recognized phenomenon in sarcoidosis is the appearance of granulomatous lesions in areas of previous trauma, such as surgical scars, tattoos, and cosmetic procedures.³ Micropigmentation, widely used for cosmetic eyebrow enhancement, involves dermal deposition of pigments similar to tattoos and may trigger granuloma formation in predisposed individuals.⁴

The pathogenesis involves an exaggerated immune response to exogenous pigments, which are phagocytosed by macrophages and dendritic cells in the dermis. These antigens are presented to CD4⁺ T lymphocytes, activating a Th1/Th17-predominant response with secretion of pro-inflammatory cytokines such as interferon-gamma (IFN- γ), interleukin (IL)-2, and tumor necrosis factor-alpha (TNF- α).⁵ This proinflammatory environment drives macrophage activation and transformation into epithelioid histiocytes and multinucleated giant cells, forming non-caseating granulomas. A concurrent failure in regulatory mechanisms, including impaired T regulatory cells and deficient IL-10, contributes to chronic granulomatous inflammation.^{5,6}

While granulomatous reactions in tattoos are increasingly reported, cases linking cosmetic eyebrow micropigmentation to the onset of systemic sarcoidosis remain rare. This case contributes to the growing recognition of exogenous pigment-induced sarcoidosis and underscores the need for systemic evaluation in such patients.

Case report

A 54-year-old woman with systemic arterial hypertension and depression, treated with losartan 50 mg/day,

fluoxetine 20 mg/day, and omeprazole 20 mg/day, presented with bilateral eyebrow pruritus, erythema, and edema. The lesions developed progressively over 3 months, 1½ years after cosmetic eyebrow micropigmentation. There was no prior history of similar skin lesions, autoimmune conditions, or systemic granulomatous disease.

Physical examination revealed erythematous, edematous, and slightly infiltrated plaques limited to the micropigmented eyebrow areas (Fig. 1). Dermoscopy showed a characteristic orange-yellow background with linear and dotted vessels, suggesting granulomatous inflammation (Fig. 2). No other skin lesions were present initially.

During follow-up, the patient developed progressive exertional dyspnea and decreased visual acuity, raising suspicion for systemic involvement. Ophthalmologic evaluation was pending.

A skin biopsy revealed dermal non-caseating granulomas composed of epithelioid histiocytes and multinucleated giant cells with sparse lymphocytic infiltration. Polarization microscopy did not identify birefringent foreign material; however, fine black pigment deposits consistent with tattoo ink were present within granulomas. The histopathological findings were compatible with sarcoid-type granulomatous dermatitis (Fig. 3).

Laboratory tests showed normal blood counts, renal and liver function, serum calcium, and inflammatory markers. Serologies for HIV, Hepatitis B and C, and syphilis were negative. Angiotensin-converting enzyme was elevated (190.6 U/L; reference: 13.3-63.9 U/L). Tuberculin skin test and contact allergen patch tests were negative. Electrocardiogram was normal.

High-resolution computed tomography of the chest revealed bilateral peripheral reticular opacities, predominantly in the lower lobes and middle lobe, mosaic attenuation, and mediastinal lymphadenopathy. Spirometry showed normal lung function.

Initial treatment with topical corticosteroids (fludrocortide under occlusion, fluticasone), calcineurin inhibitors (tacrolimus 0.1%), and desonide was ineffective. Systemic agents including colchicine 1 mg/day and allopurinol 100 mg/day were also unsuccessful. Systemic prednisone (40-50 mg/day) provided only



Figure 1. Infiltrated and erythematous plaques located in the area of eyebrow micropigmentation.

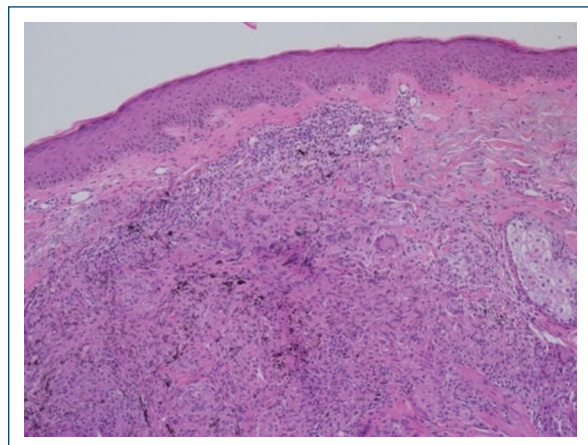


Figure 3. Granulomatous dermatitis with sarcoid features associated with dermal pigment deposition. H&E stain, original magnification $\times 100$.



Figure 2. Dermoscopy showing an orange-yellow background, linear vessels of variable caliber, and white scar-like areas.

transient relief, with symptoms recurring upon tapering. Intralesional triamcinolone hexacetonide (2.5 mg/mL) and Q-switched laser therapy targeting pigment reduction showed no clinical benefit.

Doxycycline 200 mg/day for 30 days yielded partial improvement. Subsequently, methotrexate 20 mg/week combined with prednisone 50 mg/day was initiated, resulting in significant improvement of cutaneous and respiratory symptoms. Prednisone was tapered to 10 mg/day without relapse. After 7 months of stable disease on methotrexate, the patient was transitioned to azathioprine 150 mg/day with prednisone 10 mg on

alternate days, achieving sustained control of both cutaneous and systemic manifestations (Figs. 4 and 5).

Discussion

Cutaneous sarcoidosis represents a key clinical clue to systemic disease and may precede internal organ involvement in up to 30% of patients.² The development of sarcoid lesions over tattoos or micropigmented areas is an increasingly recognized phenomenon, likely representing a Koebner-like response in genetically susceptible individuals.^{3,4}

The pathophysiological mechanism involves chronic exposure of the immune system to exogenous pigments, leading to persistent antigenic stimulation. This triggers a Th1/Th17-mediated immune response with overproduction of IFN- γ , IL-2, and TNF- α , promoting granuloma formation.⁵ Simultaneously, defective regulatory mechanisms, particularly reduced IL-10 production and impaired Treg function, contribute to the persistence of inflammation.^{5,6}

Although localized granulomatous reactions in tattoos are relatively common, progression to systemic sarcoidosis is less frequently reported. A retrospective study found that 29% of papulonodular tattoo reactions to black pigment were associated with cutaneous or systemic sarcoidosis.³ However, the literature on sarcoidosis triggered by cosmetic micropigmentation remains scarce, reinforcing the importance of this report.

Management of cutaneous sarcoidosis is often challenging, particularly in refractory cases. Topical



Figure 4. Regression of infiltration and erythema at the site of previous lesions after systemic treatment with azathioprine and prednisone.



Figure 5. Dermoscopy after treatment showing reduction of orange areas and linear vessels.

therapies may suffice in mild disease but are frequently ineffective when lesions are infiltrated or associated with systemic involvement. Systemic corticosteroids remain first-line therapy but are limited by adverse effects.⁷ Methotrexate has been extensively studied as an effective steroid-sparing agent for both cutaneous and systemic sarcoidosis.⁸ Other immunosuppressive agents, such as azathioprine and mycophenolate mofetil, are viable alternatives, particularly for long-term maintenance.⁹ Biologic therapies targeting TNF- α , including infliximab and adalimumab, are reserved for refractory or severe organ involvement.¹⁰

In this case, the patient exhibited partial and transient responses to corticosteroids and several topical and systemic therapies. Methotrexate provided substantial clinical improvement, allowing corticosteroid tapering, and subsequent transition to azathioprine enabled long-term disease control.

This case highlights the importance of recognizing granulomatous reactions in cosmetic tattoo sites as potential markers of systemic sarcoidosis. Early diagnosis through dermatological assessment can facilitate timely systemic investigation and intervention, potentially improving patient outcomes.

Conclusion

This case highlights the importance of recognizing granulomatous reactions in cosmetic tattoo sites as potential markers of systemic sarcoidosis. Early diagnosis through dermatological assessment can facilitate timely systemic investigation and intervention, potentially improving patient outcomes.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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