SHORT COMMUNICATION

A Case of Systemic Sarcoidosis Revealed by Tattoo Associated Granuloma and Uveitis

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Granulomatous inflammation against tattoo pigments is a rare cause of intraocular inflammation and commonly referred to as tattoo-associated granulomatous uveitis (TAGU). Although its pathophysiology is not fully understood, TAGU is thought to involve a delayed hypersensitivity reaction to tattoo ink antigens, including metallic components such as chromium, cobalt, copper, and nickel. Another hypothesis proposes that tattoo pigments may act as a persistent antigenic stimulus, contributing to immune dysregulation and systemic granulomatous inflammation, which may explain its frequent association with cutaneous or systemic sarcoidosis (1). With the prevalence of tattoos in Western populations estimated at 10–30% and steadily increasing, TAGU is likely underdiagnosed. We describe a case of TAGU associated with confirmed pulmonary sarcoidosis, successfully treated with topical prednisone and oral methotrexate.

CASE PRESENTATION

A 34-year-old Tamil male presented with a one-week history of acute bilateral ocular redness, pain, photophobia, and blurred vision. Ophthalmological examination revealed conjunctival and ciliary injection and mild non-pathological conjunctival melanosis. Both eyes demonstrated severe anterior intraocular inflammation with residual pigment on the lens surface due to posterior synechiae in the left eye (Fig. 1B and D). The vitreous, retina and choroid showed no signs of inflammation.

The patient reported no rheumatologic, gastrointestinal, or respiratory symptoms, and his family and medical history were unremarkable. On targeted questioning, he described swelling, pain, and flaking skin over a 13-year-old tattoo on his right upper arm and an 11-year-old tattoo on his lower right leg for the past month. Both tattoos appeared elevated and papulous, with induration and desquamation, while an adjacent tattoo on the lower right leg appeared normal (**Fig. 2**A and B).

A systemic checkup included a complete differential blood count, liver and kidney enzymes, C-reactive protein, angiotensin-converting enzyme, soluble interleukin-2 receptor (sIL-2R), serum calcium, antinuclear antibodies, anti-neutrophil cytoplasmic antibodies as well as an infectious checkup including syphilis serology and interferon-gamma release assay (QuantiFERON®-TB Gold Plus). All results were unremarkable except for an elevated sIL-2R level of 795 pg/ml (upper limit 477 pg/ml).

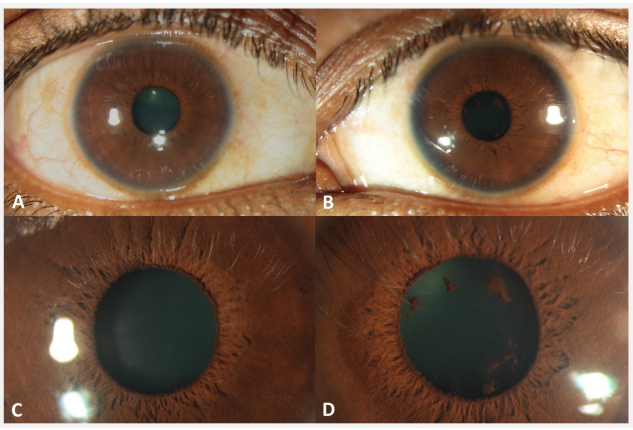

Fig. 1. Anterior segment photography showing mild conjunctival injection with perilimbal melanosis. The left eye demonstrates little residual pigment on the lens surface caused by posterior synechiae.

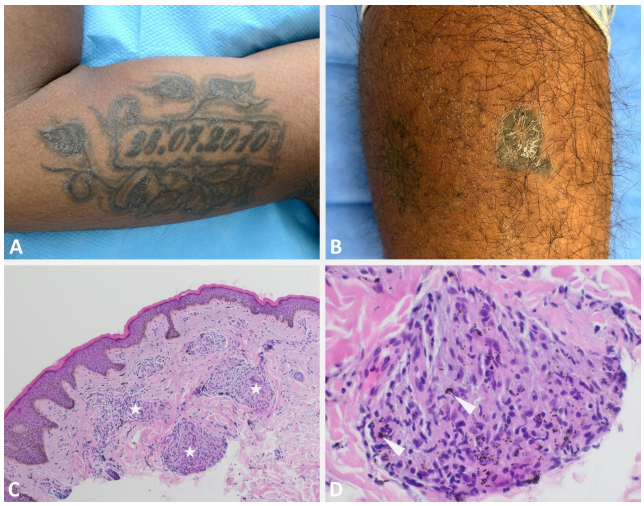

Fig. 2. Photograph of the skin tattoos on the right upper arm (A) and lower right leg (B), presenting firm papules with desquamation. Histopathological imaging of a skin punch biopsy obtained from the inflamed tattoo on the right upper arm (haematoxylin and eosin staining at 100× (C) and 200× (D) magnification) showing granulomatous non-caseating inflammatory infiltrates (asterisks) composed of epithelioid histiocytes and multinucleated giant cells with abundant exogenous tattoo pigment present in the cytoplasm (arrowheads), consistent with sarcoid-type granulomatous inflammation.

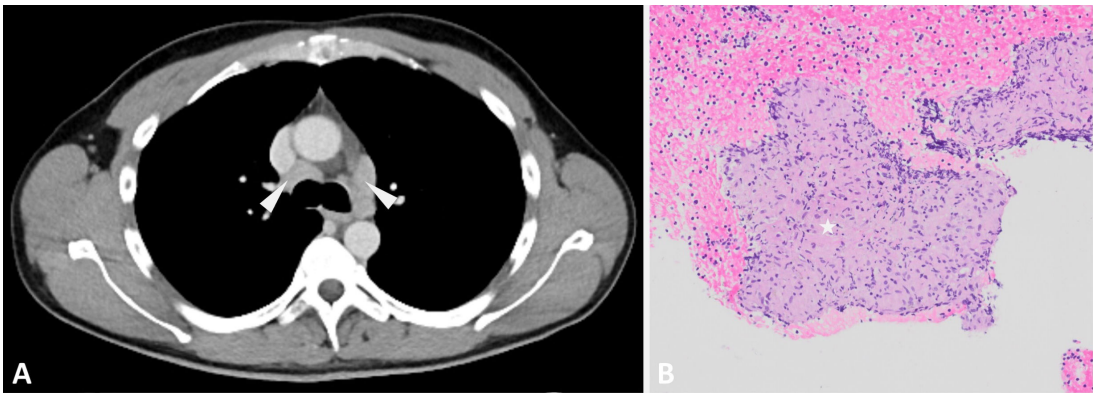

Fig. 3. Chest computed tomography showing bihilar and mediastinal lymphadenopathy. (A) Histopathological imaging of a punch biopsy obtained from the thoracic lymph node (haematoxylin and eosin staining at 100× (B) magnification) showing granulomatous non-caseating inflammatory infiltrates (asterisk) composed of epithelioid histiocytes and multinucleated giant cells consistent with sarcoid-type granulomatous inflammation.

A chest X-ray showed no signs of pulmonary sarcoidosis or tuberculosis. The patient was subsequently referred to the department of Dermatology for detailed examination, including a punch biopsy of the inflamed tattoo on the right upper arm. Histopathology revealed granulomatous infiltrates of epithelioid histiocytes and multinucleated giant cells containing abundant exogenous tattoo pigment in the cytoplasm (Fig. 2C and D). Neither non-caseating granulomas without pigment deposits nor infectious granulomas were detectable, consistent with sarcoid-type granulomatous foreign body reaction to tattoo pigment. However, histopathology alone did not allow definitive distinction from cutaneous sarcoidosis. Due to suspicion of systemic involvement, a chest computed tomography (CT) scan was obtained in addition to the previously unremarkable X-ray. The CT showed bihilar and mediastinal lymphadenopathy with micronodular pulmonary involvement (Fig. 3A). Bronchoscopy with biopsies of the enlarged lymph nodes was then performed. Histopathology demonstrated non-caseating epithelioid cell granulomas (Fig. 3B), confirming systemic sarcoidosis with cutaneous, pulmonary and ocular involvement.

Anti-inflammatory treatment with prednisolone acetate eye drops was initiated and resulted in significant reduction in inflammation. Corticosteroids were tapered over 8 weeks. After discontinuation, however, the uveitis recurred, and steroid-sparing immunosuppressive therapy was initiated, and the patient is currently managed on oral methotrexate.

DISCUSSION

In a 2018 systematic review, Kluger et al. proposed a TAGU categorization into three groups: (1) in the context of systemic sarcoidosis, (2) without evidence of systemic sarcoidosis and (3) cases in which uveitis occurs shortly after tattooing without granulomas in the tattoo or evidence of systemic sarcoidosis. (2) The exact pathophysiology of granulomatous tattoo reaction remains unclear, but it is hypothesized to be caused by a delayed hypersensitivity reaction triggered by specific antigens from tattoo ink, including metallic substances such as chromium, cobalt, copper and nickel.

Nevertheless, some therapy-refractory and chronic cases require long-term steroid-sparing immunosuppressive therapy (3–5). For therapy-resistant or recurrent inflammation, laser and surgical tattoo removal have been proposed. While surgical tattoo excision can effectively reduce inflammation, its practicality is limited due to the frequent presence of multiple tattoos, making surgical excision and subsequent skin grafting unfeasible. (6–8) Laser treatment, on the other hand, only removes the visible portions of the tattoo but disperses ink pigment into the surrounding skin, potentially exacerbating the inflammation (9, 10).

In suspected TAGU, a systematic evaluation for cutaneous or systemic sarcoidosis is essential. This should include a dermatologic examination, laboratory testing according to the 2017 International Workshop on Ocular Sarcoidosis criteria, and radiological chest imaging, preferably CT to identify inflammatory foci. (11) If uncertainty remains, positron emission tomography can be used to identify areas of increased metabolic activity and guide biopsy site selection. (12, 13) Biopsies should be obtained from the inflamed tattoo and from any accessible lesions identified on imaging. As no single conclusive test for sarcoidosis exists, the diagnosis must be based on a combination of clinical findings, imaging, histopathology, and laboratory results. TAGU has been proposed as a diagnosis of exclusion no systemic or cutaneous sarcoidosis are present; otherwise it should be classified as ocular sarcoidosis. At present, it is still unclear whether TAGU represents a distinct entity separate from sarcoidosis. (2)

Cutaneous granulomatous tattoo inflammation is an uncommon cause of intraocular inflammation. (3) Clinically suspicious tattoos should be biopsied to exclude cutaneous sarcoidosis. However as histopathological differentiation between cutaneous sarcoidosis and sarcoid-type foreign body reaction to tattoo pigment is not always possible, additional evaluation for systemic sarcoidosis is recommended. This should include a complete dermatological examination as well as radiological imaging and supportive laboratory tests. Anti-inflammatory therapy depending on the localization of the uveitis remains the mainstay of therapy. In therapy-refractory or recurrent cases, long-term steroid-sparing immunomodulatory therapy or tattoo removal may be necessary.

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Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

The authors have no conflicts of interest to declare.

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