

Delayed-onset pseudoepitheliomatous hyperplasia reaction to red tattoo pigment resembling squamous cell carcinoma



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INTRODUCTION

Introduction of exogenous pigment into the dermis for cosmetic purpose (tattoo) is a common presentation encountered in clinical practice. The procedure, however, is not without risk. Complication rates are reported to be as high as 7%, and some associated adverse reactions may have a considerable delay in onset.¹ Examples include infection; hypersensitivity reactions with granulomatous, lichenoid, and pseudoepitheliomatous characteristics; and neoplasms such as lymphoma, squamous cell carcinoma, and keratoacanthoma.^{2,3} In particular, pseudoepitheliomatous hyperplasia (PH) is a rare benign reaction often associated with red tattoo pigment.^{2,4} It is characterized by hyperplasia of the epidermis and adnexal epithelium and can resemble squamous cell carcinoma both clinically and pathologically.^{3,4} We report a PH and granulomatous reaction to red tattoo pigment with a verrucous clinical appearance arising 8 years after a tattooing procedure.

CASE HISTORY

A 73-year-old man presented to Roswell Park Comprehensive Cancer Center (Roswell Park) with a 2-year history of a growing lesion on his inferior, left lateral knee within a buffalo-shaped tattoo. The tattoo was acquired 10 years before presentation and originally colored with red ink. Eight years after the original tattoo was acquired, and 2 years before presentation, the patient underwent a recoloring of the tattoo with blue ink. It was after this revision that

Abbreviations used:

PH: pseudoepitheliomatous hyperplasia
SCC: squamous cell carcinoma

a slowly enlarging verrucous growth developed within the tattooed area. There was no associated pruritus, pain, or drainage, apart from mild tenderness to applied pressure. Because of continued growth and cosmetic disfigurement, he presented to Roswell Park for treatment.

Clinical examination found a 10- × 7-cm well-circumscribed, tan-colored, verrucous plaque with surrounding inflammation on the inferior, lateral left knee located within a dark blue tattoo (Fig 1, A). Initial clinical differential included squamous cell carcinoma, verrucous type, so a punch biopsy was obtained. The biopsy results were consistent with PH and granulomatous reaction to exogenous red tattoo pigment, and the patient subsequently underwent a shave removal procedure of the entire lesion for cosmesis (Fig 1, B).

Histologic examination of the specimens (punch and subsequent removal) found marked epidermal hyperplasia and hyperkeratosis with mixed papillomatous/verrucous and endophytic growth patterns. Within the dermis, a brisk inflammatory reaction consisting of lymphocytes, eosinophils, and sheets of histiocytes (granulomas) to both black and red tattoo pigment was observed. Although the epithelial proliferation was exuberant, no markedly infiltrative

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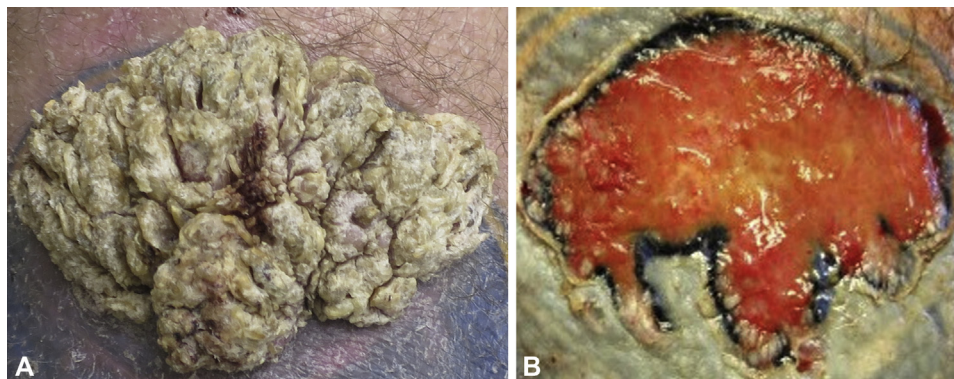


Fig 1. **A**, PH reaction to tattoo ink resembling SCC, verrucous subtype. **B**, Postexcision of pseudoepitheliomatous hyperplasia reaction.

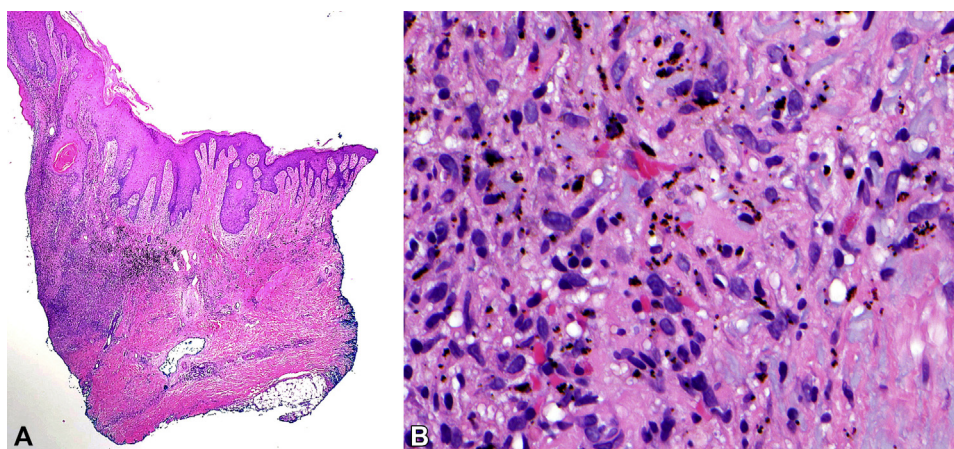


Fig 2. **A**, Punch biopsy results show epidermal hyperplasia over a granulomatous reaction to exogenous tattoo pigment. **B**, The dermis contains sheets of histiocytes with oval nuclei and abundant cytoplasm. Both red and dark tattoo pigment are present in this granulomatous inflammation. (Hematoxylin-eosin stain; original magnifications: **A**, $\times 20$; **B**, $\times 400$.)

or deep growth was identified, and cytologic atypia was minimal (Fig 2, A and B).

DISCUSSION

The development of PH in response to red pigment was first reported by MB Sulzberger in 1937 and further characterized by HI Goldberg in 1959 as multiple verrucous papules within an area of red ink.⁵ To date, multiple other cases have been described in the literature.⁵⁻⁸ Because of its characteristic verrucous growth pattern, it is often mistaken for squamous cell carcinoma (SCC). Making this distinction is important, as rare cases of SCC arising within tattoos have been reported.^{5,9} SCC has also been seen arising within existing PH.^{2,6}

The development of tattoo-associated PH most often occurs days to months after a tattoo procedure.^{1,5,8,10} Our case is unique in that our patient's PH reaction presented within a preexisting red tattoo

only after being recolored with blue ink. Red and blue tattoo inks contain different pigment compounds, but it is not possible to know the precise composition of the inks in this patient. We feel there are several potential explanations for this peculiar timing and presentation. The simplest possibility is that the patient's reaction is solely related to introduction of the newer blue ink pigments. However, because blue ink is rarely associated with PH tattoo reactions in the literature, we believe that the epidermal hyperplasia is less likely to be a direct result of that blue pigment. Another possibility is that there was cross-reactivity between antigens in the original red tattoo ink and the newer blue ink, or re-exposure to a common substance, such as a carrier material, to which the patient was previously sensitized during the original tattoo procedure.^{1,5,8} The last possibility is that reintroduction of red pigment into the epidermis during the second tattoo

procedure elicited a delayed immune response. Although rare, delayed hypersensitivity to repeated exposures of a specific coloring agent has been reported.^{1,2} This may be because needles used by tattoo artists introduce antigens directly into the dermis. By bypassing the epidermis, where most immune presenting cells reside, antigens and hap- tens within the dermis may avoid the first phase of innate immunity.²

Topical steroids are generally considered first-line treatment for tattoo reactions, with intralesional corticosteroids, surgery, and laser reserved for recalcitrant cases.¹ Compared with smaller lesions, larger PH lesions are often less responsive to both topical and intralesional corticosteroid treatment and may require alternative therapy.¹⁰ Surgical removal of large PH lesions has well documented success and low recurrence rates; however, scarring is frequent and can be disfiguring. Laser therapy, although not well documented for PH reactions, may be an alternative to surgery if cosmesis is desired. For example, one study reported complete disappearance of a tattoo-associated PH lesion subjected to Q-Switched neodymium-doped yttrium aluminum garnet (Nd:YAG) laser, with better aesthetic results compared with surgery.²

The varied appearance and often delayed onset of PH reactions can make clinical diagnosis difficult for both general practitioners and dermatologists. Similarly, histologic diagnosis can be challenging. Distinguishing PH from SCC is particularly important, as SCC has been reported to arise both spontaneously within tattoos and within existing PH.^{2,6,9,11} Helpful clues to a diagnosis of PH include confinement of the lesion to the tattoo margins and onset of the lesion shortly (weeks to months) after a tattoo procedure. Compared with PH, SCC typically

has a later onset, will not stay confined to tattoo borders, has the potential for metastasis, and, if left untreated, will infiltrate underlying and adjacent tissue. Although to our knowledge no fatalities have been reported from tattoo-associated SCC, early diagnosis and treatment are pivotal to prevent potential morbidity and cosmetic disfigurement.

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