Pseudoepitheliomatous Hyperplasia Resembling Multiple Keratoacanthomas Arising in a Tattoo

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Abstract
Tattoo-associated reactions are well-recognized in the literature, including granulomatous, lichenoid, pseudolymphomatous, sarcomatous, and eczematous. There are rare reports of pseudoepitheliomatous hyperplasia and keratoacanthoma arising in tattoos. We report a case of a 28-year-old woman who presented with three growths confined to a tattoo placed one year prior. Clinical and histologic features were suggestive of a differential diagnosis that would include keratoacanthoma, pseudoepitheliomatous hyperplasia secondary to chronic wound healing or trauma, and, less likely, infection. Distinguishing between these entities can be a subject of histopathologic debate. Overlap of histologic features requires excisional biopsy with culture for comprehensive analysis and diagnosis, and close follow-up is necessary.

Introduction
Dermatologic conditions associated with tattoo placement are a well-recognized complication seen in dermatology practices. They have been reported to occur within hours to over 45 years after tattoo placement.5,8 The reported histologic patterns include foreign-body granulomatous, lichenoid, pseudolymphomatous, sarcomatous, and eczematous, such as allergic contact dermatitis or photoallergic dermatitis.1,6 Within the last decade, there have been rare reports of eruptive keratoacanthomas presenting in tattoos as well as pseudoepitheliomatous hyperplasia, particularly in the setting of red tattoo pigment or infection.4 Distinguishing between these entities requires careful clinicopathologic correlation, often necessitating surgical excision.4 Herein, we describe a case that demonstrates histologic features suggestive of pseudoepitheliomatous hyperplasia (PEH) or squamous cell carcinoma of the keratoacanthoma (KA) type.

Case Report
A 28-year-old female presented to the
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dermatology clinic for evaluation of three growths on her left foot. The patient reported getting a tattoo of three stars on her left foot one year prior to presentation and stated that the tattoo never healed well. Over the course of six months she noticed development of the aforementioned growths confined to the tattoo. A thorough review of systems was performed and was negative except for localized tenderness over the growths. Past medical history was noncontributory, and medications consisted of ibuprofen as needed. She denied tobacco, alcohol, or illicit drug use.

Physical exam was exceptional for three 2.4 cm round verrucous plaques, two with an erythematous halo, on the dorsolateral aspect of the left foot contained within the boundaries of the tattoo (Figure 1). Of note, the tattoo did not contain any red pigment. Differential diagnosis included keratoacanthoma, foreign-body reaction, or infection, such as coccidioidomycosis or mycobacteria. Two 4-mm punch biopsies were obtained; one specimen was submitted for hematoxylin-eosin (H&E) analysis and the other for fungal, bacterial, and atypical mycobacterial culture. The patient was also given a course of doxycycline on initial presentation for signs of secondary impetiginization.

Histologic examination of the biopsy disclosed a central, keratin-filled crater surrounded by marked epidermal hyperplasia with irregular, epidermal tongues extending deep into the reticular dermis (Figures 2 and 3). A brisk and diffuse inflammatory infiltrate occupied most of the dermis, which had histiocytic, lymphocytic, and neutrophilic components, and displayed marked, focal exocytosis into the epidermis (Figure 4). Occasional deposits of black and green pigment corresponding to tattoo ink were noted in the dermis as well as degeneration of collagen bundles (Figure 5). Higher magnification of the epidermis revealed very focal cytologic atypia of the keratinocytes in the follicular infundibulum (Figure 6), whereas the majority of the remaining keratinocytes were eosinophilic, contained glassy cytoplasm, and lacked atypia (Figure 3). In addition, viral cytopathic effects were absent.

The constellation of histologic features in the biopsy specimen can be seen in both keratoacanthoma and pseudoepitheliomatous hyperplasia. Given the symmetric, keratin-filled, cup-like crater with epithelial proliferation and prominent infiltrates, keratoacanthoma was high on the differential. However, the relative lack of major cytologic atypia, abundant mitoses, and frank architectural abnormalities seemed to distinguish this lesion as pseudoepitheliomatous hyperplasia. Besides the histologic characteristics favoring this entity, the lack of spontaneous involution of the lesion also favored pseudoepitheliomatous hyperplasia as the diagnosis.

Finally, there was an extensive histiocytic, acute and chronic inflammatory infiltrate occupying the dermis in our specimen, signifying a possible fungal or mycobacterial cutaneous infection. Given the widespread inflammation and the presence of a few ill-defined granulomas, the possibility of an atypical mycobacterial infection arising in a tattoo and resulting in extensive pseudoepitheliomatous hyperplasia was a diagnostic consideration; however, a biopsy sent for bacterial and fungal cultures showed no growth.

The clinical and histopathologic exam as well as negative cultures in this case favored a diagnosis of tattoo-associated pseudoepitheliomatous hyperplasia. The lesions were treated by electrodessication and curettage, with no evidence of recurrence.

Discussion

Tattoos are widely popular, both in the United States and internationally, for decorative, religious, cosmetic, or cultural purposes. Some tattoos are accidental, such as occurs from deposition of exogenous pigment substances in puncture wounds; or iatrogenic, such as occurs from Monsel’s solution when used for hemostasis. Commonly reported tattoo reactions include allergic and hypersensitivity reactions. Reports of pseudoepitheliomatous hyperplasia or keratoacanthoma-like eruptions are rare. Distinguishing between these reactions is difficult due to similar histologic features and often requires complete excision for diagnosis.

Pseudoepitheliomatous hyperplasia is a reactive pattern showing benign, irregular, epidermal hyperplasia characterized by prominent acanthotic downgrowths and keratinocytes with abundant cellular cytoplasm. It can be seen in chronic healing wounds, chronic irritation, trauma, and infection. Histologically, it can mimic keratoacanthoma or squamous cell carcinoma. Fraga et al. detail a series of 11 tattoo-associated keratoacanthomas arising in eight patients, the majority of which were initially diagnosed as invasive squamous cell carcinoma or pseudoepitheliomatous hyperplasia. They note that 82% of the keratoacanthomas occurred in areas of red tattoo pigment, with half of these showing displacement of red tattoo ink into the overlying keratin through transepidermal elimination, suggesting a foreign-body reaction to the tattoo pigment. They acknowledge that there is considerable overlap of histologic
features seen in pseudoepitheliomatous hyperplasia and keratoacanthomas, but conclude that the features noted are likely describing a single reactive pattern better grouped under the classification of keratoacanthoma. Kluger et al. and Balfour et al. collectively describe four similar presentations, and describe histologic findings of pseudoepitheliomatous hyperplasia, the majority seen in areas of red tattoo pigment. They note the lack of abundant mitosis, major architectural disruption and cytologic atypia in pseudoepitheliomatous hyperplasia, distinguishing it from keratoacanthoma. Balfour et al. also note that a regressing keratoacanthoma could not be excluded in their particular case. These reports underscore the challenging distinction between keratoacanthoma and pseudoepitheliomatous hyperplasia, and the need for full-thickness biopsies or excision to rule out a neoplastic process.

Pseudoepitheliomatous hyperplasia can be a reactive process seen in the setting of infection as well, and such etiologies must not be overlooked. Of note, the Centers for Disease Control reported an outbreak of 22 cases of tattoo-associated non-tuberculous mycobacterial skin infections in 2011-2012 from gray tattoo ink. There are no explicit regulations by the Food and Drug Administration requiring sterility of tattoo inks; contamination can occur through use of nonsterile water, contaminated ink products or poor manufacturing processes. Therefore it is essential that cultures and tissue stains are performed for tattoo-associated reactions suspicious for infection.

**Conclusion**

Pseudoepitheliomatous hyperplasia in a tattoo is rarely reported, and it has marked histologic similarity to keratoacanthoma. It can be distinguished from keratoacanthoma by lack of abundant cellular atypia, frequent mitoses, and abnormal architecture. Still, distinguishing between pseudoepitheliomatous hyperplasia and keratoacanthoma is a challenge and likely requires a complete excision to rule out a neoplastic process.

**References**


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