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Desmoplastic intradermal spitz nevi arising within red tattoo ink

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Abstract
Tattoos present a diagnostic challenge for dermatologists. Various reactions to tattoo have been identified in the literature ranging from allergic, to infectious, to neoplastic. Of the neoplastic cases identified, it is unclear whether the tattoo ink was directly causative, or if the cases were merely coincidence, as the number of cutaneous malignancies has also been on the rise. We present a novel case of two desmoplastic intradermal Spitz nevi arising within red tattoo ink.

Keywords: tattoo reaction, Spitz nevus, desmoplastic Spitz, red ink

Introduction
Tattoos have become increasingly popular in the past several decades in both the U.S. and abroad; in fact, nearly 25% of the U.S. population has at least one tattoo [1, 2]. This increase in the number of tattooed individuals at younger ages in the U.S. population is of particular importance to dermatologists, underscoring the need for proper diagnosis and treatment of potential complications, both neoplastic and otherwise. In this report, we describe two desmoplastic intradermal Spitz nevi arising within red tattoo ink.

Case Synopsis
A 28-year-old woman with a known family history of melanoma presented to the dermatology clinic for evaluation of two small, raised lesions within the red ink of her multi-colored left arm sleeve tattoo. She reported that the tattoo was completed in 2013 and the first of the two raised areas developed approximately 8-12 months later. She did not recall any lesions in the areas involved prior to obtaining the tattoo. At that time, she sought the evaluation of a dermatologist who believed the area was a scar and did not suggest any further follow-up. She remained asymptomatic and without obvious indication of inflammation, drainage, or swelling. However, three years later, she developed a second raised area nearby, also within red ink, prompting her to return to the dermatology clinic for re-evaluation.

Examination revealed a 2cm oval-shaped, firm plaque within an area of red ink on her left forearm (Figure 1A, B, white box and arrow) with an adjacent 0.5cm papule of similar texture in a neighboring area of red ink (Figure 1B, black box and arrow). No overlying epidermal changes were noted. Punch biopsy was performed of the larger plaque (Figure 1A, both biopsy sites outlined in marker within white box) for both histologic evaluation and culture to rule out infectious etiology. Histologic examination revealed a dermal storiform proliferation of spindled mononuclear cells in association with thickened collagen fibers (Figure 2A, B). Gram, periodic acid-Schiff (PAS), and acid-fast bacilli (AFB) stains were negative, and culture was likewise negative. The cells were positive for the melanocytic markers microphthalmia-associated transcription factor (MiTF), S100 and SRY-related HMB-box 10 (Sox10).
Additionally, immunostaining for p16 demonstrated preserved expression, consistent with a melanocytic nevus versus desmoplastic melanoma [3]. Subsequent biopsy of the smaller papule on the left arm showed remarkably similar findings (Figure 2C, D). A final diagnosis of desmoplastic intradermal Spitz nevus was reached and the patient was referred for excision of both sites with 0.5cm margins.

**Discussion**

Lesions arising within tattoos can present quite the diagnostic challenge to dermatologists as tattoo ink can mask color changes and make changes more difficult to detect. As such, biopsy of all suspected tattoo reactions is recommended to evaluate for systemic disease or infection [4]. To our knowledge, this is the first case of a Spitz nevus arising within a tattoo. Both lesions were an unusual desmoplastic variant of Spitz nevus. Given the timing and distribution of these atypical, non-contiguous lesions, it is suspicious that the tattoo played a role their development.

In the setting of tattoo, exogenous pigments, dyes, and metallic salts remain in the dermis for the lifetime of the patient and the potential local and carcinogenic effects have yet to be fully elucidated [5]. Many reactions to tattoo have been identified, including transient inflammatory reactions secondary to trauma, superficial and deep local infections, systemic infections, granulomatous and lichenoid reactions, and both Koebner and isotopic responses (psoriasis, lichen planus, pseudolymphoma, and morphea), [6]. Although the pathogenesis of the various reactions differ, the majority of allergic reactions occur in red ink in which a component of the tattoo pigment acts as a hapten in a type IV hypersensitivity reaction. In papulonodular reactions occurring in black ink, clusters of pigment are seen as foreign bodies and induce an inflammatory response, potentially leading to granulomatous inflammation or sarcoid granulomas in predisposed individuals [7]. The pathogenesis of cutaneous neoplasms arising in tattoos is less clear. Although tattoo ink is comprised of various potential carcinogens, the associated cutaneous malignancies could be the result of lesions present prior to tattoo placement or from other exposures such as ultraviolet radiation.

The concept of the “immunocompromised cutaneous district” may also partially explain the propensity of nevi and other cutaneous malignancies to arise within tattooed areas. This concept describes the phenomenon of cutaneous reactions and malignancies arising at altered sites in the skin; the isomorphic response or Koebner phenomenon being one such example of reactions occurring in compromised skin [8].
Figure 2. A, B) Dermal storiform proliferation of spindled mononuclear cells in association with thickened collagen fibers from the larger plaque (A, 40×; B, 100×). C, D) and smaller papule (C, 40×; D, 100×) on the left arm. H&E stain. Dark brown-black dermal staining represents tattoo pigment.

A recent literature review identified 64 cases of cutaneous neoplasms arising in tattoos diagnosed between 1938 and 2017, including squamous cell carcinoma, basal cell carcinoma, melanoma, and less-common cutaneous malignancies; the review described the characteristics of each case (Table 1), [9]. Of the neoplasms arising within tattoos, squamous cell skin cancer and keratoacanthomas are most common, possibly secondary to the trauma involved in the act of tattooing [5, 10, 11]. Seventeen cases of melanoma arising within tattoo ink have been reported, with time of tattoo to diagnosis of melanoma ranging from 3 months to over 40 years [5, 12]. The majority of melanomas reported to arise within tattoo ink arise in black, blue, or green ink [5]. There was a single case of melanoma arising in red tattoo ink diagnosed 3 years after tattoo placement in which the patient was found to have in-transit metastases, all within the red tattoo ink [12]. To date, there has been no reported case of Spitz nevi arising within tattoo ink. 

Spitz nevi are melanocytic proliferations of spindled and/or epithelioid melanocytes. They were first described in 1948 by Sophie Spitz as “juvenile melanomas” based on their histologic findings similar to that of melanomas, though they were noted to have less aggressive behavior [13]. Whereas they are largely considered benign lesions, rare instances of metastasis and death have been
Table 1. Cutaneous neoplasms arising within tattoo ink *adapted from Paprottka et al.[9].

<table>
<thead>
<tr>
<th>Type of skin cancer</th>
<th>Number of Cases</th>
<th>Date of Publication</th>
<th>Gender</th>
<th>Median Age</th>
<th>Ink Color</th>
<th>Location</th>
<th>Skin Color</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant Melanoma [12, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35]</td>
<td>22</td>
<td>1938-2018</td>
<td>m = 17; f = 3; unknown = 2</td>
<td>45y</td>
<td>Black/Dark blue = 15; Red = 2; Green = 2</td>
<td>Arm = 10; Chest = 4; Leg = 2; Back = 5; Abdomen = 1; Face = 1</td>
<td>White = 10</td>
</tr>
<tr>
<td>Squamous Cell Carcinoma [9, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47]</td>
<td>13</td>
<td>1966-2017</td>
<td>m = 7; f = 5; unknown = 1</td>
<td>48y</td>
<td>Black/Dark blue = 4; Red = 7; Multicolor = 1</td>
<td>Arm = 6; Chest = 1; Leg = 3; Back = 1; Face = 2</td>
<td>White = 8</td>
</tr>
<tr>
<td>Basal Cell Carcinoma [23, 48, 49, 50, 51, 52, 53, 54]</td>
<td>11</td>
<td>1976-2009</td>
<td>m = 6; f = 5</td>
<td>56y</td>
<td>Black/Dark blue = 10; Red = 1; Green = 1</td>
<td>Arm = 2; Back = 4; Face = 5</td>
<td>White = 4</td>
</tr>
<tr>
<td>Keratoacanthoma [41, 55, 56, 57, 58, 59, 60]</td>
<td>16</td>
<td>1973-2009</td>
<td>m = 9; f = 5; unknown = 2</td>
<td>50y</td>
<td>Black = 1; Red = 10; Yellow = 1</td>
<td>Arm = 6; Leg = 7; Back = 1</td>
<td>White = 9; Black = 1</td>
</tr>
<tr>
<td>Leiomyosarcoma [61]</td>
<td>1</td>
<td>2009</td>
<td>m = 1</td>
<td>41y</td>
<td>Black = 1</td>
<td>Arm = 1</td>
<td>–</td>
</tr>
<tr>
<td>Dermatofibroma [62]</td>
<td>2</td>
<td>2008</td>
<td>m = 2</td>
<td>35y</td>
<td>Black = 1</td>
<td>Arm = 1; Leg = 1</td>
<td>–</td>
</tr>
<tr>
<td>Dermatofibrosarcoma protuberans [63, 64]</td>
<td>2</td>
<td>2005, 2011</td>
<td>m = 2</td>
<td>44y</td>
<td>Black = 1; Red = 1</td>
<td>Arm = 1; Back = 1</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>1938-2018</td>
<td>m = 66% (n = 44); f = 27% (n = 18); unknown = 7% (n = 5)</td>
<td>9-79y</td>
<td>Black/Dark blue = 33; Red = 21; Multicolor = 1; Green = 3; Yellow = 1</td>
<td>Arm = 27; Chest = 5; Leg = 13; Back = 8; Abdomen = 1; Face = 8</td>
<td>–</td>
</tr>
</tbody>
</table>

reported [14]. Spitz nevi exist on a histologic spectrum, ranging from common Spitz nevi that are frequently seen in children and are thought of as benign to “spitzoid melanoma,” which is more accurately considered melanoma with Spitz-like features, than a Spitz nevus [13]. Desmoplastic Spitz nevi share histologic features with dermatofibroma, desmoplastic blue nevi, and desmoplastic melanoma [14]. They differ from desmoplastic melanoma histologically with better circumscription and maturation, and more frequently involve adnexal structures [15]. Excision of Spitz nevi is recommended in adults, with wide local excision recommended for atypical lesions [14].

In this case, two separate intradermal desmoplastic Spitz nevi arose within red ink of a tattoo and both lesions were subsequently excised.

**Conclusion**

We present a case of two intradermal desmoplastic Spitz nevi arising within the red ink that highlights need for thorough malignancy screenings at the site of tattoos.
References