SKIN

BRIEF ARTICLE

Late Onset Pseudolymphomatous Reaction to Blue Tattoo Pigment Precipitated by Covid Vaccination

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ABSTRACT

Tattoos can lead to a variety of cutaneous conditions such as allergic or contact dermatitis, lichenoid dermatitis, pseudolymphomatous reactions and granulomatous responses such as foreign body granulomas that may have a sarcoidal histology simulating sarcoidosis. Pseudolymphomatous reactions are less common and may clinically and histologically resemble cutaneous lymphomas. Pseudolymphomatous reactions may develop in response to injections, *Borrelia* infections and arthropod bites. Diagnosis of cutaneous pseudolymphoma is usually based on clinicopathologic correlation coupled with skin biopsy and ancillary tests such as immunoperoxidase stains and genetic testing when necessary. Treatment is generally successful with application of topical corticosteroid preparation or injection of intralesional corticosteroids and in some cases, surgical excision. Here, we describe the case of a 61-year-old male who presented with 3-4 mm papules contained within the blue region of a multicolored tattoo on his upper right arm that had been present for several years. The reaction developed shortly following a Covid vaccination.

INTRODUCTION

Pseudolymphoma has been reported to occur as a complication of tattoos and is marked by tissue histology that may simulate cutaneous B-cell lymphoma most commonly.[1,2] The process is benign and can be differentiated by demonstrating polyclonality of lymphocytes versus the monoclonality seen in malignant processes.[3,4]

It has been hypothesized that particles in tattoo pigments, commonly red pigment, serve as dermal antigens and induce lymphoid cell proliferation.[5] This leads to a persistent reactive lymphocytic infiltration seen usually resulting in the development of germinal centers. The exact mechanism of the pathogenesis of the pseudolymphoma has yet to be defined, however.[5,6] In some cases, some factor leads to activation of the immune system resulting in a hyperactive local immune response leading to a pseudolymphomatous reaction in the skin such as exaggerated arthropod assault reactions. This has been observed in patients with hematologic malignant neoplasms and other immunodeficiency states such as HIV infection.[7-10] We herein report a patient who developed a pseudolymphomatous tattoo reaction in a long-standing blue tattoo that

developed shortly after receiving a vaccination for Covid-19.

CASE REPORT

A 61-year-old male with past medical history of type 2 diabetes mellitus, hypertension, hypercholesterolemia, and hypertriglyceridemia presented to an outpatient private practice dermatologist with a chief complaint of papules in a tattoo. The papules occurred only in the blue ink in the tattoo of his right upper arm and developed approximately one year previously after a recent Moderna bivalent mRNA-1273 COVID vaccination (**Figure 1**). The papules were found nowhere else on his body and began 3-4 weeks after receiving the second of both doses of the Moderna COVID-19 Vaccine. The tattoo was 5-6 years old, and the papules spread along the blue ink of the tattoo only (**Figure 2**). They were slightly pruritic. The patient had not used any topical or systemic therapies prior to evaluation. The patient reported no reactions or problems with the original tattoo.

Figure 1. Pseudolymphomatous reaction to tattoo - Large multicolored tattoo with various sized granulomatous-appearing papules.

Figure 2. Papules confined to blue ink - the papules were not found anywhere else in the tattoo, specifically the red or black pigment nearby.

On exam, the eruption was contained within the blue portion a large multicolored tattoo with various sized pink to skin-colored papules. Punch biopsy demonstrated a dense inflammatory cell infiltrate in the upper dermis composed of lymphocytes, histiocytes, eosinophils and plasma cells most consistent with a pseudolymphomatous tattoo reaction (**Figure 3**). The patient was treated with a Class one topical steroid cream and injection of intralesional steroids which resulted in improvement but not disappearance of the lesions.

DISCUSSION

In pseudolymphomatous reactions, the tattoo dye pigments in the dermis act as an antigen stimulating the polyclonal proliferation of lymphoid cells.[3,5,6] The onset can range from a few months to several years after the tattoo placement.[3,5,6] While most cases have been

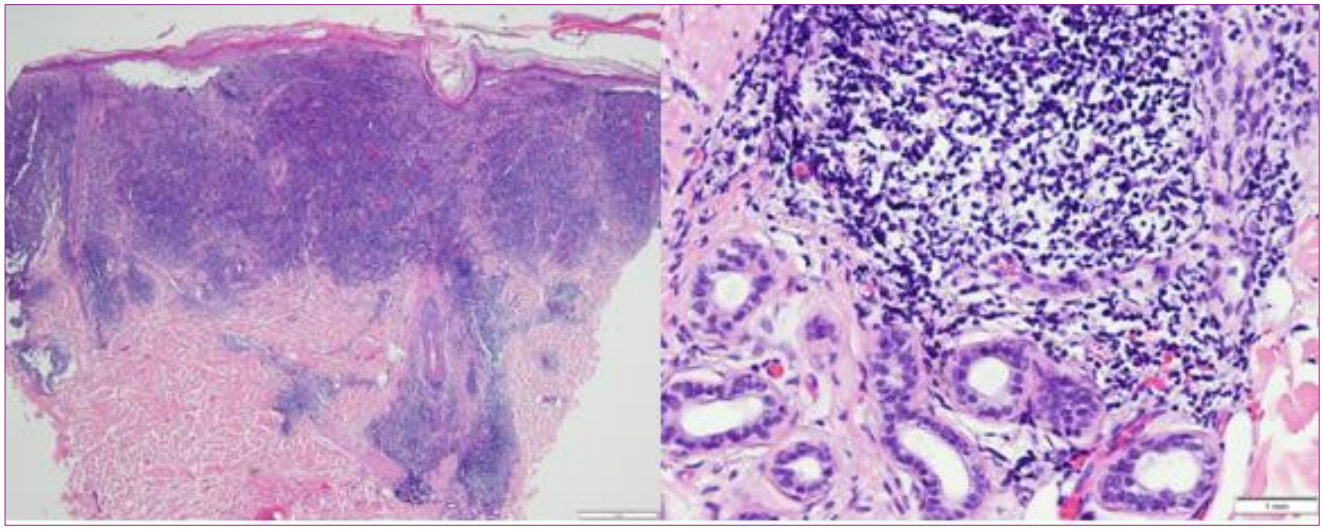

Figure 3. Dense inflammatory infiltrate composed of a mix of lymphocytes, histiocytes, and plasma cells. Infiltrate is distributed as prominent band in the upper dermis (left) and in perifollicular and peri-eccrine locations in the deeper dermis (right).

described following red tattoos in patients with delayed sensitivity to cinnabar (mercuric sulfate), inflammatory reactions can also occur in blue areas, which are mainly cobalt salts, or green areas which are mainly chrome salts.[2,4-7] Here, the Covid vaccination and booster coincided with the appearance of the pseudolymphoma and likely served as a stimulus for its development possibly via a hyperactive immune response.[5,6,10]

Exposure to the Covid 19 spike protein, through vaccination or infection, has been associated with cases of Delayed Inflammatory Reactions in Hyaluronic Acid Dermal Fillers.[11] It's suggested that the Spike protein interaction with dermal ACE2 receptors favors a pro-inflammatory, loco-regional TH1 cascade, promoting a CD8+T cell mediated reaction to incipient granulomas, which previously formed around residual HA particles.[10,11] This reaction resembles our case with a delayed inflammatory reaction post Covid vaccination. Further, a study found an increase in autoimmunity and immune response following infection with Covid-19 due to molecular mimicry between human tissue and viral antigens.[12] Thus, in our patient Covid vaccination may have triggered the inflammatory immune response to tattoo dye.

Although pseudolymphoma is a benign disease, in cases which are persistent, prolonged follow up is important because of rare case reports of progression to cutaneous lymphoma.[8] Tattoo pseudolymphoma can be treated with topical or intralesional corticosteroids, surgical excision, or laser treatment.[7] In our patient, conservative treatment with topical and intralesional steroids resulted in resolution.

CONCLUSION

Allergic reactions may develop in patients with tattoos that may assume several different morphologies, both clinically and histologically. While these may develop spontaneously, Covid-19 vaccination may be a stimulus that leads to development of cutaneous inflammatory disorders in tattoos that were previously well-tolerated. Clinicians should be aware of this rare

phenomenon which should be added to the list of cutaneous reactions that can follow Covid-19 vaccination.

Conflict of Interest Disclosures: None

Funding: None

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