GRANULOMATOUS REACTION TO RED PIGMENT, AFTER PERMANENT DECORATIVE TATTOO – CLINICAL CASE

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Abstract

Tattoos have been used for over 2000 years. Nowadays, the frequency of tattoos has been growing, especially among young people. In many countries, more than 25% of the population has a tattoo. Lately, the medical world is trying to increase the awareness concerning tattoos and the multiple risks they carry, like allergic reactions, lichenoid reactions, sarcoidosis, scleroderma-like reactions, viral, bacterial and fungal infections, benign tumors, pseudolymphomas, chronic lymphoid hyperplasia. Rarely, malignant tumor can develop on the tattoo surface.

Clinical case: A 25 year old male has been admitted in our clinic presenting infiltrative, erythematous, scaly plaques, with yellow crusts on the surface, placed on the left arm and right leg, on the surface of two tattoos, only on the areas with red pigment. The patient had these symptoms for over one year. The tattoos were made two years before coming to the hospital. The cutaneous lesions were surgically removed and a histopathological exam was performed, revealing chronic granulomatous inflammatory infiltrate, with giant cells and eosinophilic necrosis areas.

Discussions: In order to make a tattoo, body artists use multiple pigments, by themselves or in different combinations. The red pigment used in tattoos can be organic (santal wood, Caesalpinia echinata – both vegetal dyes) or inorganic (cadmium, mercury, selenium, sienna, the last one is an iron hydrate). There are several cutaneous reactions to the pigments found in tattoos: inflammatory reactions, allergic reactions, granulomatous reactions, lichenoid reactions and pseudolymphomatous reactions.

Conclusions: 1) The granulomatous reaction is a complication that occurs frequently after red pigment tattoos; and 2) The patients need to be thoroughly investigated in order to rule out a foreign body reaction, sarcoidosis, an infectious disease (tuberculosis, mycobacteria infections, leprosy, leishmaniasis, and fungal infections), granuloma annulare, and iatrogenic granulomatous disease after the use of ribavirin, interferon, anti-TNF α medication, ipilimumab.
Introduction
Tattoos have been used for over 2000 years. Nowadays, the frequency of tattoos has been growing, especially among young people. Demographic studies show that in Germany, 8.5% of the population with ages between 14 and 90 has a tattoo, in France, the percentage is 10% and among young people, in many countries, more than 25% of them are tattooed. Most of them see it as a form of body art. However, 14% of the people that had a tattoo regret it at some point.

Tattoos can be interpreted as an initiation practice used in some communities (the evolution from childhood to adulthood), sacred sign (protection or magic sign), and decorative element (especially for women), virility sign (for men), seduction sign, a deprivation of liberty sign (1).

Although right after a tattoo is done, the site exhibits erythema, edema, exudation and crusts, these are not considered side effects and most of them disappear in three weeks.

Lately, the medical world is trying to increase the awareness concerning tattoos and the multiple risks that they carry, such as allergic reactions, lichenoid reactions, sarcoidosis, scleroderma-like reactions, viral infections (HPV, HVB, HVC, HIV, molluscum contagiosum), bacterial infections (impetigo, ecthyma) and fungal infections, benign tumors, pseudolymphomas, chronic lymphoid hyperplasia. Rarely, malignant tumors (squamous cell carcinoma, basal cell carcinoma, melanoma, dermatofibrosarcoma, leiomyosarcoma, cutaneous lymphomas) can develop on the tattoo surface (2). Infections like leprosy, tuberculosis, syphilis, erysipelas are rarities nowadays.

Also, cutaneous diseases like psoriasis, vitiligo, and lichen planus have been documented as tattoo complications.

We present the case of a granulomatous reaction determined by the red pigment found in a tattoo.

Clinical case
A 25 year old male has been admitted in our clinic presenting infiltrative, erythematous, scaly plaques, with yellow crusts on the surface, placed on the left arm and right leg, overlying two tattoos, only on the areas with red pigment (Figures 1 & 2). The patient has had these symptoms for over one year and tattoos were done two years before the patient came to the doctor. Family history and personal history showed no significant pathology. The clinical exam was normal.

The blood work showed a high white blood cells number (11.610/μL), hematocrite (50.8%), hemoglobin (17.55 g/dL). The tests for B and C type hepatitis were negative and the erythrocyte sedimentation rate was normal.

The cutaneous lesions were surgically removed (Fig. 3) and a histopathological exam was performed, which revealed: epithelioid and giant cells, epidermal detachment areas, acanthosis and hyperkeratosis (Fig. 4), intense chronic granulomatous inflammatory infiltrate with epithelioid cells (Fig. 5) and multiple eosinophilic necrosis areas, which affect the entire dermis (Fig. 6) and focally affect the hypodermis too (Fig. 7).

The paraclinical investigations ruled out sarcoidosis and other granulomatous diseases. The evo-
The black pigment is made of numerous toxic compounds, like black carbon or aromatic polycyclic hydrocarbon that can generate genetic mutations. These substances absorb UV radiations and form new compounds, releasing oxygen radicals, which affect the cellular integrity.

**Discussions**

In order to make a tattoo, body artists use multiple pigments, by themselves or in different combinations. If each pigment, by itself, can cause various allergic reactions that are easy to manage, the pigment combinations can generate various reactions, making the incriminated compound more difficult to discover.

The black pigment is made of numerous toxic compounds, like black carbon or aromatic polycyclic hydrocarbon that can generate genetic mutations. These substances absorb UV radiations and form new compounds, releasing oxygen radicals, which affect the cellular integrity.
Colored tattoos are made with various pigments (e.g., nitric pigments) which will be decomposed after sun exposure and will release aromatic amines, very harmful for the human body. In numerous situations, the decomposing compounds of the pigments used in tattoos have been discovered in the lymph nodes (3).

There are several cutaneous reactions to the pigments found in tattoos: inflammatory reactions, allergic reactions, granulomatous reactions, lichenoid reactions and pseudolymphomatous reactions (4).

We will discuss the cutaneous reactions determined by the red pigment in tattoos, used in our patient’s case.

The red pigment used in tattoos can be organic (santal wood, Caesalpinia echinata – both vegetal dyes) or inorganic (cadmium, mercury, selenium, sienna; the last one is an iron hydrate).

The mercury used in tattoos determines a delayed hypersensitivity reaction, but it can also determine lichenoid reactions and epiteliomatos hyperplasia.

Besides mercury, the red pigment can also contain other toxic products like aluminium, iron, calcium, titanium, silicone and cadmium. All of those compounds can generate cutaneous allergic reactions (5).

A study made in 2015 by Hogsberg, Thomsen and Serup, which included 19 patients with post-tattoo reactions, revealed that the incriminated pigments in those tattoo reactions were red/pink (15 patients), and purple/bordeaux (four patients). Of these patients, 78% had dermatitis, 32% an overlapping granulomatous reaction and another 32% an overlapping pseudolymphomatous reaction. The patients also had hyperkeratosis (89%) and red pigment passage at the level of the dermis and inflammatory infiltrate composed of T lymphocytes, histiocytes, plasmocytes and polymorphonuclear cells. Hystopathological changes suggestive for lichen were found in the epidermis and the saw-tooth image, specific for lichen planus, was found in the dermal-epidermal junction. Mercury is the first to be incriminated in these types of reactions, especially in the presence of red pigment. After mercury, cadmium is the next one to blame (9).

3. Pseudolymphomatous reactions – represent a benign lymphocytes proliferation, which mimic a malignant lymphoma. In the case of tattoos, the pigment acts as an antigen which stimulates lymphocytic proliferation. They usually appear after a few months or years after the pigment is introduced inside the body. Most cases appear due to red pigment, as a delayed hypersensitivity reaction to Cinnabar (mercury sulfate).

Although they are considered benign, pseudolymphomas must be kept under observation, as they can transform in a malignant lymphoma after a long evolution.

In 1992, Sangueza and his collaborators described a benign T cell pseudolymphoma, with 10-20% B lymphocytes, which turned in a B cell malignant lymphoma after some time (10).

4. Granulomatous reactions – just like the previous reaction, granulomatous reactions are most frequently determined by the red pigment. The granulomatous reaction is a foreign body reaction, frequently associated with the presence of sun exposure. Sixty of them complained about cutaneous reactions after sun exposure, which included edema (58%), pruritus/pain/burn (52%) and erythema (26%) (8). In literature, contact dermatitis after a „fake” Henna tattoo has also been described. The leaves of this tree, used as a powder, produce shades of red, yellow and orange, which are used mainly for textile dyeing, but they are also used for temporary tattoos. It is difficult to say if the contact dermatitis was totally due to henna, because of the fact that paraphenylene-diamine is often added to highlight the henna color.

2. Lichenoid reactions – are the next most frequent after eczematous reactions. According to some authors, (9) lichenoid reactions are actually more common than eczematous reactions. Lichenoid reaction appears more frequently due to the red pigment in tattoos, possibly because of the immunogenic properties of the dye.

The clinical aspect resembles the one in lichen planus, but the lesions appear on the surface of the tattoo. There have been some case reports of cutaneous and mucous lichen planus which appeared far from the tattoo surface.

The histopathological exam revealed irregular grains and amorphic masses of pigment in the dermis and inflammatory infiltrate composed of lymphocytes, histiocytes, plasmocytes and polymorphonuclear cells. Hystopathological changes suggestive for lichen were found in the epidermis and the saw-tooth image, specific for lichen planus, was found in the dermal-epidermal junction. Mercury is the first to be incriminated in these types of reactions, especially in the presence of red pigment. After mercury, cadmium is the next one to blame (9).
of mercury, chrome, cobalt and manganese. It is usually limited to the colored areas of the tattoo and it is considered an allergic reaction to the compounds of the pigment.

The clinical aspect is of red and pruriginous nodules, placed on the sun exposed areas.

Sarcoidosis, as an adverse tattoo reaction, is rare and usually appears after the use of a silicone-based pigment (11). It is usually determined by multi colored tattoos.

In both cases, the histopathological exam reveals granulomatous reaction, with areas containing pigment grains. Histopathologically, limited post-tattoo sarcoidosis granuloma contains epithelioid cells with small amounts of pigment, a few or no giant cells and a lymphocytes crown.

The cases of tattoo-induced sarcoidosis usually evolve with cutaneous lesions, lymphadenopathy and pulmonary sarcoidosis. So, in the presence of a histopathological exam that reveals granulomatous inflammation, in the absence of a foreign body, the recommendation is to perform a pulmonary X-ray and other investigations to exclude sarcoidosis, because a sarcoidosis granuloma can announce an authentic sarcoidosis (12).

5. Other reactions

a) Pyoderma gangrenosum – there has been described the case of a woman with personal history of enteritis, who presented on the surface of a tattoo, on the areas with red pigment, a painful ulceration, with grey-colored margins. The ulceration appeared approximately 5-6 weeks after the tattoo was made. Two weeks after having the tattoo, the patient had an allergic dermatitis, which represented the posivation of the pathergy test. This led to the diagnosis of pyoderma gangrenosum (13).

b) Granuloma annulare-like, described for the first time in October 2013, by Sweeney et al. They described the case of a granulomatous dermatitis, which appeared on the surface of a tattoo, only in the areas where red pigment was used (14).

Treatment

The treatment of post-tattoo adverse reactions implies most of the times the use of very potent topical corticosteroids (usually under occlusive dressing) or intralesional injection of steroids. In case of failure, Tacrolimus 0.1% has been used 2 times/day, for three months, with good results. In spite of all these, the tattoo removal is required. The surgical excision, which we also practiced, is taken in consideration in the case of small tattoos and the case of tattoos placed on areas with good skin laxity.

In the past, tattoo removal techniques implied dermabrasion, cryosurgery, CO₂ lasers or surgical excision. All these procedures left a permanent scar, which led to the discovery of new tattoo removal techniques that did not leave a scar.

Multiple publications reported the efficiency of Q-switched Nd:YAG 532 nm lasers in the treatment of red tattoo reactions (lichenoid and granulomatous reactions). There has also been reported the efficiency of Erbium:YAG 2940 nm ablative laser, by itself or associated with Nd:YAG 1064 nm and 582 nm laser (15). The necessary amount of sessions is between 5 and 12, performed every six to eight weeks. This tattoo removal technique is not working in all cases and it can cause a permanent scar, structure and pigmentation changes and distant allergic reactions, if the pigment grains are dispersed after the tattoo removal session (16).

In the case of granulomatous reactions, there have been cited cases with favorable evolution after Allopurinol (300-600 mg/day, two months) or minocycline (200 mg/day). In the case of foreign body granulomas, colchicine or imiquimod 5% have proven useful (16).

Conclusions

1. The granulomatous reaction is a complication that occurs frequently after red pigment tattoos.
2. The patients need to be thoroughly investigated in order to rule out a foreign body reaction, sarcoidosis, an infectious disease (tuberculosis, mycobacteria infections, leprosy, leishmaniasis, and fungal infections), granuloma annulare, and iatrogenic granulomatous disease after the use of ribavirin, interferon, anti-TNF α medication, ipilimumab.

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