Clinicopathological reaction patterns to tattoo pigments: a report of 13 cases from the south of Iran

Fatemeh Sari Aslani, MD [1]
Mozhdeh Sepaskhah, MD [2]
Mojgan Akbarzadeh Jahromi, MD [1*]

1. Maternal-Fetal Medicine Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
2. Molecular Dermatology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

**Corresponding author:*
Mojgan Akbarzadeh Jahromi, MD
Maternal-Fetal Medicine Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
Email: mojganakbarzadeh@yahoo.com

Received: 1 November 2020
Accepted: 22 January 2021

The rate of cosmetic tattooing in Iran is increasing as in many other countries, with concomitant rises in tattoo-associated complications, including inflammatory (infectious and non-infectious) and neoplastic reactions. We reviewed clinical and pathology features of a series of 13 cases of adverse reactions to tattoo pigments. The participants included 11 women and 2 men aged between 22 and 58. The histopathologic reaction patterns were seven granulomatous (four sarcoid, with heavy tattoo pigments in the superficial dermis, and three tuberculoid, with scanty tattoo pigments in the superficial dermis), three cases of pseudoepitheliomatous hyperplasia, one cutaneous lupus erythematosus-like reaction, one pseudolymphomatous reaction, and one case of mild superficial perivascular inflammation. More than two-thirds of the reactions were to brown tattoos on the eyebrows. The lag in lesion development after tattooing varied from five days to two years.

Keywords: tattooing, pathology, granulomatous, tuberculoid, sarcoidosis

Iran J Dermatol 2022; 25: 183-189

DOI: 10.22034/ijd.2021.255394.1256

INTRODUCTION

Histopathologic reaction patterns are detected secondary to delayed hypersensitivity reactions, infections, systemic diseases, or cutaneous malignancies [1]. Various tattoo pigments contain different elements and chemical compounds in different proportions, such as mercury salts (red ink), cadmium sulfide (yellow ink), iron oxide (brown ink), carbon (black ink), cobalt chloride (blue ink), and manganese (purple ink) [2,3]. Cutaneous complications of tattooing include allergic reactions (mainly to red tattoos and their shades), non-allergic reactions (mainly to black tattoos), and bacterial infections [4].

This study presents retrospective findings of 13 cases of tattoo pigment reactions. From 2013 to 2019, these patients were managed at the Dermatology Clinic of Shahid Faghihi Hospital, affiliated with Shiraz University of Medical Sciences, Shiraz, Iran. The histopathologic reaction patterns and clinical features are reviewed.

CASE PRESENTATION

There were 13 patients aged from 22 to 58. The female to male ratio was 11 to 2. The site of involvement was the eyebrow in nine cases, vermilion in two, and forearm in two. The reactions were caused mainly by brown tattoos (9 cases), with papule or plaque patterns. The time lag between tattooing and the reaction varied between five days to two years.

Three dermatopathologists reviewed H&E stained slides of the patients' punch biopsies with a triple head microscope. The microscopic examination showed different histopathological reaction patterns. Seven (53.8%) cases with granulomatous patterns (three tuberculoid-type and four sarcoid-type) (Figure 1), three (23%) cases with pseudoepitheliomatous epidermal hyperplasia (Figure 2), one cutaneous lupus erythematosus-

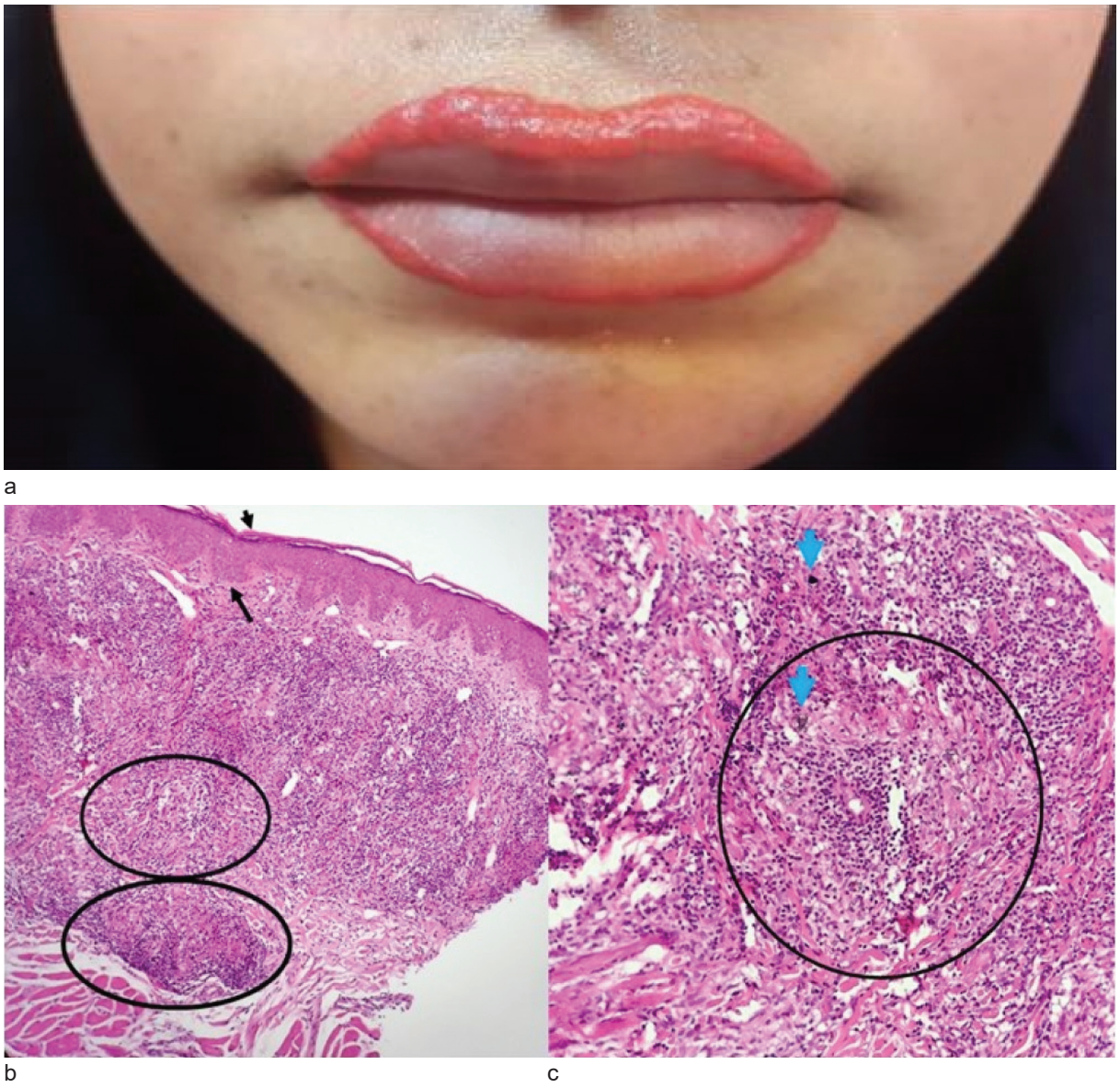
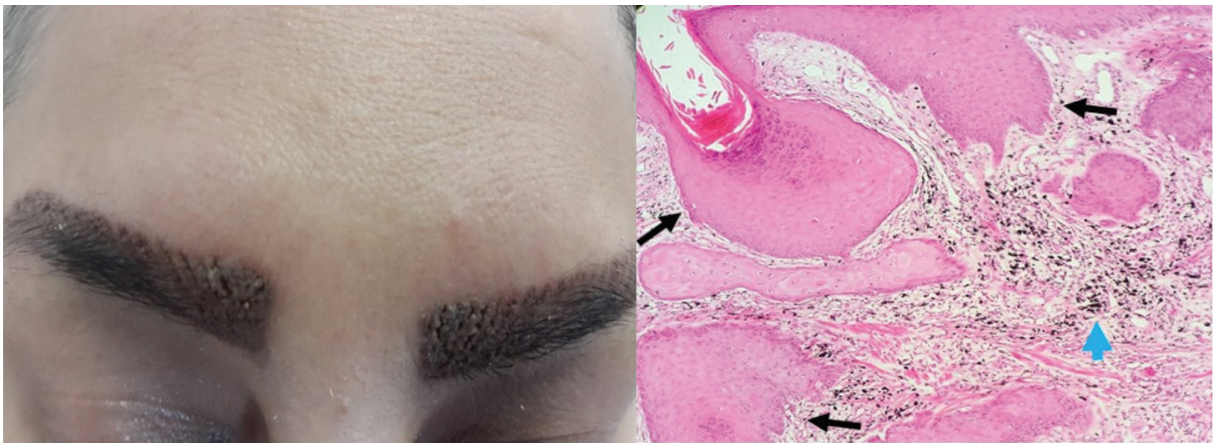


Figure 1. Case No. 6 (a), Indurated red plaque on the vermilion. (b) Tuberculoid-type granulomatous inflammation (circles) with hyperkeratosis (arrowhead) and acanthosis (arrow) (H&E, ×100). (c) Tuberculoid-type granulomatous inflammation (circle) and scanty focal tattoo pigment deposition (arrowheads) (H&E, ×400).

like reaction (Figure 3), one with heavy pigment deposition and mild perivascular lymphocytic infiltrate, and one with pseudolymphomatous reaction (Figure 4). Tattoo pigments were present in the macrophages and free within the dermis. All cases with sarcoid-type reaction and pseudoepitheliomatous hyperplasia showed heavy tattoo pigments in the dermis, while all tuberculoid reactions showed scanty tattoo pigments in the superficial dermis. Demographic and clinicopathologic features are presented in Table 1.

DISCUSSION

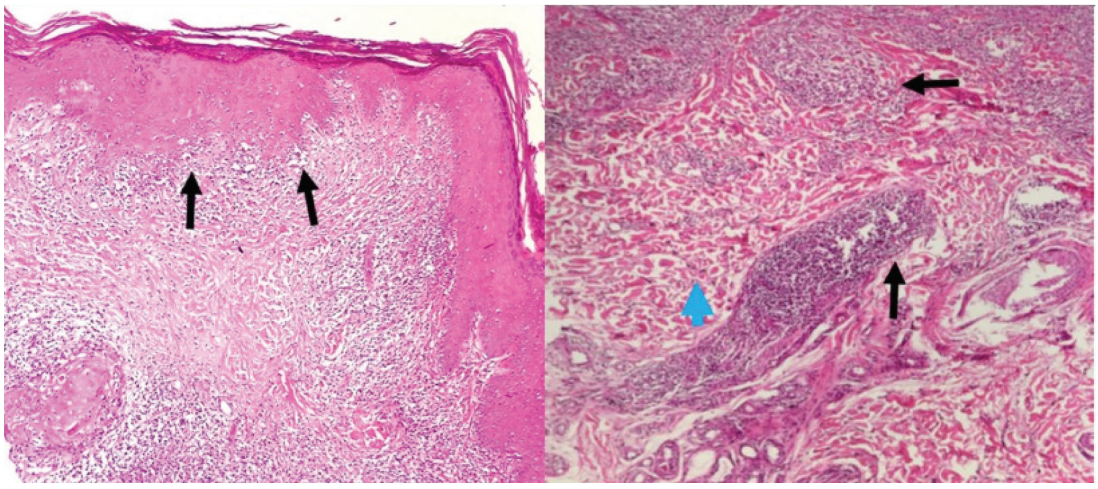
Among the inflammatory complications of tattooing, hypersensitivity reactions to pigments injected into the skin are relatively frequent [5]. A study of adverse reactions in 405 tattoo patients revealed allergic reactions were primarily detected



a b

Figure 2. Case No. 4 (a) Verrucous plaque on the eyebrow. (b) Pseudoepitheliomatous hyperplasia (arrows) and heavy tattoo pigment deposition (arrowhead) (H&E, ×200).

a



b c

Figure 3. Case No. 9. (a) Hyperkeratotic nodules on the forearm. (b) Lupus erythematous-like reaction (lichenoid reaction) (arrows) (H&E, ×200). (c) Deep dermal dense lymphocytic infiltrate (arrows) and tattoo pigment deposition (arrowhead) (H&E, ×400).

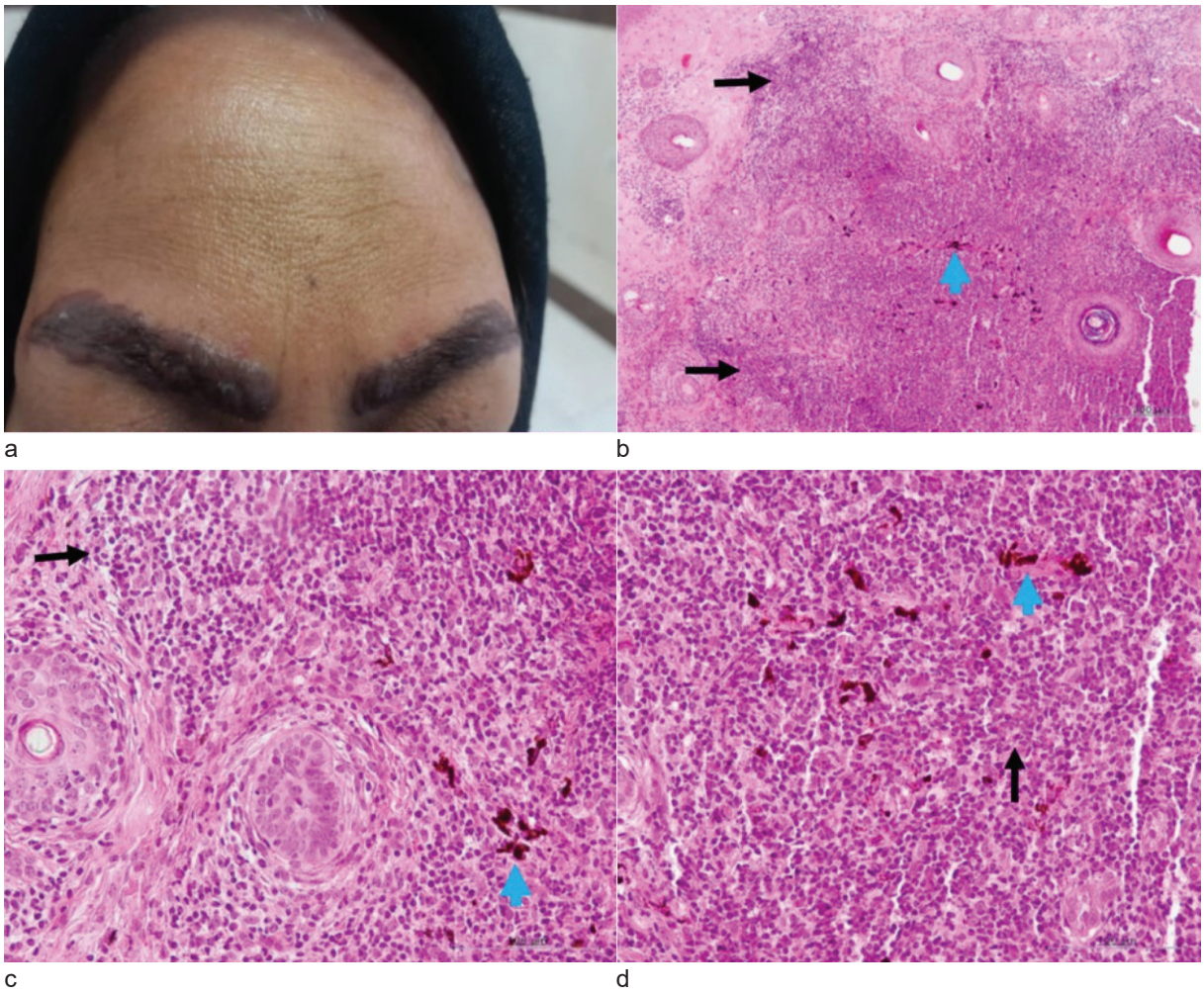


Figure 4. Case No.13 (a) Indurated brown plaque on the eyebrow.(b) Dense lymphoid infiltrate (arrows), perivascular and perifollicular, in the superficial and deep dermis, tattoo pigment deposition (arrowheads) with mild hyperkeratosis and acanthosis (×40). (c, d) Dense lymphocytic infiltrate and tattoo pigment deposition (H&E, ×200 & ×400).

in tattoos that were red or had shades of red, while non-allergic papulonodular reactions were mostly seen in black tattoos [4]. Sanghavi SA *et al.* classified the histopathological types into lichenoid, eczematous, pseudolymphomatous, photoallergic, morphea-like, and granulomatous [6].

In our study, most cases presented as brown or red-brown plaque lesions, mostly due to brown tattoos. The most common patterns in this study were granulomatous (53.8%) and pseudoepitheliomatous hyperplasia (23%). However, lichenoid and granulomatous reactions were another study's most commonly reported patterns, frequently associated with colored tattoo inks, particularly red [7].

Sepehri *et al.* reported 92 reactions to black tattoos with a papulonodular pattern. Twenty-seven (29%) reactions were diagnosed as cutaneous or systemic sarcoidosis, supported by histology. They concluded that black tattoos with papulonodular reactions should be considered a marker of sarcoidosis [8]. Also, in our study, 31% of cases showed sarcoidal-type granuloma on histologic examination without clear evidence of systemic sarcoidosis. Skin lesions or sarcoidosis involving tattoos may occur even decades after tattooing, possibly due to chronic antigenic stimulation from the ink in a genetically predisposed person [9].

In our report, the lag in lesions development

Table 1. Clinical and histological features of tattoo reactions

Case	1	2	3	4	5	6	7
Age	48	51	39	31	31	32	37
Sex	F	F	F	F	F	F	F
Location	Eyebrow	Eyebrow	Eyebrow	Eyebrow	Eyebrow	Lip vermilion	Eyebrow
Color reaction	Brown	Brown	Brown	Brown	Brown	Red	Brown
Clinical presentation	Red-brown plaque	Red-brown plaque	Verrucous weeping plaque	Verrucous plaque	Red-brown plaque	Indurated red plaque	Verrucous plaque
Interval between tattoo & reaction	NA	NA	7 days	NA	NA	5 months	5 days
Epidermal changes	-HK, flat epidermis lymphocyte exocytosis	HK, flat epidermis -lymphocyte exocytosis	Pseudoepitheliomatous	Pseudoepitheliomatous	HK, intermittent thin & thick epithelium. Spongiosis Lymphocyte exocytosis	HK, intermittent thin & thick epithelium. Lymphocyte exocytosis	Pseudoepitheliomatous
Composition of dermal infiltrate	Lymphocytes, epithelioid cells and histiocytes	Lymphocytes, epithelioid cells and histiocytes	lymphocyte & eosinophil infiltrate	Lymphocyte infiltrate	Lymphocytes, epithelioid cells and histiocytes	Lymphocytes, epithelioid cells and histiocytes	lymphocyte & eosinophil infiltrate
Density & Location of tattoo pigment	Heavy, Superficial dermis	Heavy, Superficial dermis	Heavy, Superficial dermis	Heavy, Superficial dermis	Heavy, Superficial dermis	scanty, focal Superficial dermis	Heavy, Superficial dermis
Final histopathologic diagnosis	Sarcoidal type granulomatous inflammation	Sarcoidal type granulomatous inflammation	Pseudoepitheliomatous hyperplasia	Pseudoepitheliomatous hyperplasia	Sarcoidal type granulomatous inflammation	Tuberculoid type granulomatous inflammation	Pseudoepitheliomatous hyperplasia

Table 1. Continued

Case	8	9	10	11	12	13
Age	58	22	32	49	25	45
Sex	F	M	F	F	M	F
Location	Eyebrow	Forearm	Lip vermilion	Eyebrow	Forearm	Eyebrow
Color reaction	Brown	Dark blue	Red	Brown	Dark blue	Brown
Clinical presentation	Red-brown plaque	HK nodule	Papules	Crusted plaque	NA	Indurated brown plaque
Interval between tattoo & reaction	NA	6 months	2 years	NA	NA	5 months
Epidermal changes	HK, PK, - atrophic epidermis	HK, intermittent thinning & thickening	HK, -acanthosis	HK, intermittent thin & thick epithelium.	Unremarkable	HK, acanthosis
Composition of dermal infiltrate	Lymphocytes, epithelioid cells and histiocytes	Perivascular & perifollicular lymphocyte	Lymphocytes, epithelioid cells and histiocytes	Diffuse Dense perivascular/ perifollicular lymphoplasma cell infiltration	Upper & mid dermal perivascular mild lymphocytic infiltration	Dense perivascular & perifollicular, mainly lymphocytes
Density & Location of tattoo pigment	Heavy Superficial & deep dermis	Focal scanty Superficial & deep	Focal scanty superficial dermis	Focal scanty superficial dermis	Heavy around the vessels	Heavy Superficial & deep dermis
Final histopathologic diagnosis	Sarcoid type granulomatous inflammation	Cutaneous lupus erythematosus-like reaction	Tuberculoid type granulomatous inflammation	Tuberculoid type granulomatous inflammation	Nonspecific superficial mild perivascular inflammation	Pseudolymphomatous reaction

Abbreviations: F, Female; HK, hyperkeratotic; M, Male; NA, Not Avilable; PK: Parakeratosis

after tattooing was not more than two years, which happened in one of the cases with granulomatous reaction. However, lag time information was unavailable for all cases. Some authors reported long lag times, such as 30–40 years [10,11]. Valbuena *et al* reported two cases with sarcoidal granulomatous reactions, one after 1.5 years and another after 16 years [12]. Remarkably, all cases of sarcoid type were associated with heavy tattoo pigments, but the tuberculoid type had scanty tattoo pigments, which were not reported in other studies.

Pseudoepitheliomatous hyperplasia is an uncommon histological reaction pattern reported with either red, purple, or black tattoos [7,13]. In our review, 3 cases (23%) of pseudoepitheliomatous hyperplasia were seen in brown tattoos, and the time lag was within one week. However, the lag time was reported as four days to one year in a previous study on red pigment tattoos [14]. Delayed-onset pseudoepitheliomatous hyperplasia was reported within a preexisting red tattoo after ten years while being recolored with blue ink two years back [15].

Granuloma annulare-like pattern reactions to tattoo pigments have been reported from India and Iran [16,17]. Vellaisamy *et al.* presented five patients with tattoo reactions. The site of involvement in all cases was the upper limb. The age of the tattooing ranged from 3 months to 1.5 years. Black tattoos caused all the reactions. Two cases showed granulomatous patterns, one with a palisading granuloma mimicking granuloma annulare and another with a tuberculoid granuloma [18]. The third case showed pseudoepitheliomatous epidermal hyperplasia with a dense nodular, dermal lymphoid infiltrate, similar to our study. Another case showed minimal dermal inflammation [18], similar to one of the cases in our study. The fifth case had a lichenoid pattern with lymphocytes, presenting with a raised, pruritic erythematous plaque [18].

In our study, there was one case of lupus erythematosus-like lichenoid reaction with a hyperkeratotic nodule on the forearm. In a previous study, the lag time between tattooing and onset of symptoms in lichenoid reactions was reported as low as two days or so long as some years, with most reactions occurring within the first year [19]. The lag time was six months in our case of lupus erythematosus-like lichenoid reaction.

Mycobacterial infections were reported in another study [20]. None of our cases with tuberculoid-type granulomas showed positive PCR for tuberculosis. A pseudolymphomatous reaction may unusually occur after tattooing, with a lag time between less than 2 months to 20 years [21]. This reaction is mostly related to the intradermal injection of red tattoo pigments [20], though we had one case of pseudolymphomatous reaction to brown tattoos five months after tattooing.

The limitation of this study was a lack of information on lag times in some cases. The total number of cases was limited in this review. The possibility of observing more cases in this area is expectable considering the lag times of even decades for adverse reactions to tattooing.

CONCLUSION

In the cases of this study, the most common histopathologic patterns were granulomatous reactions to brown tattoos with a lag period from 5 months to 2 years. Therefore, any plaque or papulonodular growth within the tattoo pigment should be biopsied for further evaluation to rule out granulomatous inflammation. All lesions observed after tattooing should undergo biopsies in spite of the time of occurrence, given the variety of reactions. Pseudoepitheliomatous hyperplasia should be considered among the very early reactions, even within the first week.

Acknowledgments

The authors of the present study would like to thank the lab staff working at Shahid Faghihi Hospital.

Funding Sources

No funding was received for this work.

Conflict of interest: None declared.

REFERENCES

1. Vangipuram R, Bull L, Tarbox M, et al. Histopathologic reaction patterns in decorative tattoos. Pigmentary Disorders. 2016;3(1):1-4.

2. Barua S. Laser-tissue interaction in tattoo removal by Q-switched lasers. J Cutan Aesthet Surg. 2015;8(1):5-8.
3. Jones B, Oh C, Egan CA. Spontaneous resolution of a delayed granulomatous reaction to cosmetic tattoo. Int J Dermatol. 2008;47(1):59-60.
4. Serup J, Sepehri M, Hutton Carlsen K. Classification of tattoo complications in a Hospital Material of 493 adverse events. Dermatology. 2016;232(6):668-78.
5. Morales-Callaghan AM Jr, Aguilar-Bernier M Jr, Martínez-García G, et al. Sarcoid granuloma on black tattoo. J Am Acad Dermatol. 2006;55(5 Suppl):S71-3.
6. Sanghavi SA, Dongre AM, Khopkar US. Tattoo reactions--an epidemic on the surge: a report of 3 cases. Indian J Dermatol Venereol Leprol. 2013;79(2):231-4.
7. Thum CK, Biswas A. Inflammatory complications related to tattooing: a histopathological approach based on pattern analysis. Am J Dermatopathol. 2015;37(1):54-66.
8. Sepehri M, Hutton Carlsen K, Serup J. Papulo-nodular reactions in black tattoos as markers of sarcoidosis: study of 92 tattoo reactions from a Hospital Material. Dermatology. 2016;232(6):679-86.
9. De Cuyper C. Permanent makeup: indications and complications. Clin Dermatol. 2008;26(1):30-4.
10. Ghorpade A. Sarcoidosis detected due to tattoo swellings in an Indian female. Indian J Pathol Microbiol. 2015;58(3):362-4.
11. Ohtsuka M, Natsuko M, Toshiyuki Y. Sarcoidal granuloma presenting on tattoo: a report of a Japanese female patient and a review of Japanese published work. Sarcoidosis Vasc Diffuse Lung Dis. 2016;33(1):83-9.
12. Valbuena MC, Franco VE, Sánchez L, et al. Sarcoidal granulomatous reaction due to tattoos: report of two cases. An Bras Dermatol. 2017;92(5 Suppl 1):138-41.
13. Balfour E, Olhoffer I, Leffell D, et al. Massive pseudoepitheliomatous hyperplasia: an unusual reaction to a tattoo. Am J Dermatopathol. 2003;25(4):338-40.
14. Kazlouskaya V, Junkins-Hopkins JM. Pseudoepitheliomatous hyperplasia in a red pigment tattoo: a separate entity or hypertrophic lichen planus-like reaction? J Clin Aesthet Dermatol. 2015;8(12):48-52.
15. Andrew P. Sauvageau, Jacob Mojeski, Michael J. Bax, Paul N. Bogner. Delayed-onset pseudoepitheliomatous hyperplasia reaction to red tattoo pigment resembling squamous cell carcinoma. JAAD Case Rep. 2019; 5(3):222-4.
16. Shashikumar BM, Harish MR, Shwetha B, et al. Hypersensitive reaction to tattoos: a growing menace in Rural India. Indian J Dermatol. 2017;62(3):291-6.
17. Kamyab K, Jamshidi S, Hamed G, et al. A rare type of reaction to tattoo materials: A granuloma annulare like reaction. Iran J Dermatol. 2011;14: 35-6.
18. Vellaisamy G, Tirumalae R, Inchara Y. Histopathologic spectrum of reactions to black tattoo pigment: a report of five cases from India. Egypt J Dermatol Venerol. 2018;38(1):18-22.
19. De Argila D, Chaves A, Moreno JC. Erbium:Yag laser therapy of lichenoid red tattoo reaction. J Eur Acad Dermatol Venereol. 2004;18(3):332-3.
20. Forbat E, Al-Niaimi F. Patterns of reactions to red pigment tattoo and treatment methods. Dermatol Ther. 2016; 6(1):13–23.
21. Saulite I, Pekar-Lukacs A, Kerl K, et al. Pseudolymphomatous reaction to red tattoo pigment. Case Rep Dermatol. 2018;10(2):162-8.