CASE REPORT

Treatment of a refractory allergic reaction to a red tattoo on the lips with methotrexate and Q-switched Nd-Yag laser

Sebastiaan A. S. van der Bent, MD, PhD,a and Martijn B. A. van Doorn, MD, PhDb
Leiden and Rotterdam, The Netherlands

Key words: adverse reaction; allergy; complication; cosmetic; permanent makeup; pigment; tattoo.

INTRODUCTION

Tattoos, including permanent makeup, are a popular and increasing form of body art. However, complications such as allergic reactions can occur and are difficult to treat.

CASE REPORT

A 51-year-old, otherwise healthy, woman was referred to the Tattoo Clinic with a painful and pruritic swelling of her recently red-tattooed lips. The cosmetic tattoo was placed 6 months prior to her visit to the patient clinic, and her first symptoms occurred 2 months after the tattooing procedure. Because of the painful swelling, she had difficulty eating and talking, which had a significant impact on her quality of life. On physical examination, both the entire upper and lower lip showed erythematous-plaques, sharply confined to the red-tattooed mucosa (Fig 1, A and B). After follow-up weeks later, the reaction had evolved into ulcerative plaques (Fig 1, C). There was no lymphadenopathy. Histopathology of a skin biopsy specimen revealed a lymphohistiocytic, nonsarcoïd, granulomatous infiltrate surrounding the red tattoo pigment. Ziehl-Neelsen and periodic acid–Schiff–diastase stains were negative. Serum angiotensin-converting enzyme was within the normal range. Chest X-ray showed no signs of sarcoidosis or other abnormalities. Repeated cultures for bacteria and fungi were negative. Polymerase chain reactions for herpes simplex virus and varicella-zoster virus were also negative, as was serology for HIV.

On the basis of the clinical and histologic findings, we diagnosed her with a delayed allergic reaction to the red tattoo pigment. No patch testing was performed because no reliable patch tests for tattoo allergies are currently available.

Previous unsuccessful treatment included topical corticosteroids (clobetasol propionate 0.05%), topical antifungals, topical antibiotics, oral amoxicillin-clavulanate, oral ciprofloxacin, and prednisolone 30 mg/day for 2 weeks. Because of potential cutaneous atrophy, our patient was reluctant to receive therapy with intralesional corticosteroids. Therefore, and because of previous good results in other cases, treatment with hydroxychloroquine 200 mg twice daily was initiated. However, after 4 months of treatment, there was no clinical improvement. Consequently, hydroxychloroquine was discontinued, and treatment with cyclosporine 175 mg twice daily (3–4 mg/kg) was initiated. Unfortunately, after 3 months, no clinical improvement was observed. Because of her ongoing severe symptoms, she agreed to a single session of intralesional corticosteroid injections, but this only resulted in a minimal reduction of the ulceration and swelling. Because of the severe pain she experienced from the intralesional corticosteroid treatment and potential risk of skin atrophy, further treatment was rejected by the patient. As the next anti-inflammatory treatment, oral methotrexate 15 mg per week was started in combination with folic acid 5 mg per week. After 2 months, significant clinical improvement was observed, and after 3 months, the

From the Tattoo Clinic (Tattoo poli), Department of Dermatology, Alrijne Hospital, Leiden and Department of Dermatology, Erasmus Medical Center, Rotterdam.

Funding sources: None.
IRB approval status: Not applicable.
Correspondence to: Sebastiaan A. S. van der Bent, MD, PhD, Tattoo poli, Department of Dermatology, Alrijne Ziekenhuis, Houtlaan 55, 2334 CK, Leiden, The Netherlands. E-mail: sasvanderbent@alrijne.nl.

JAAD Case Reports 2022;21:109-11.
2352-5126 © 2022 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
https://doi.org/10.1016/j.jdcr.2022.01.004
swelling and ulceration had completely disappeared (Fig 2, A). Despite this good clinical result, a permanent treatment was desired because the symptoms were likely to recur if the methotrexate was discontinued. In order to establish this, complete removal of the tattoo pigments from the skin is needed. Surgical procedures, such as treatment with ablative CO2 laser, dermatome shaving, or excision with mucosal transposition, could be employed; however, they were not advised because of the potential extensive scarring that could occur, which would lead to permanent physical disability. Therefore, after 6 months of continuous therapy with methotrexate, treatment with Q-switched Nd-Yag laser was initiated. Before starting this therapy, the patient was extensively counseled about the possible side effects and, more specifically, the risk of a generalized type IV allergic reaction.3

After 4 treatment sessions with a single pass Q-switched Nd-Yag laser (532 nm; 2 J/cm², 3-mm spot size, 6-ns pulse duration) (Q-plus C, Quanta Systems) with 4-weekly intervals, the red pigment was completely removed from the skin (Fig 2, B and C). During each treatment, extensive ecchymoses occurred, which resolved spontaneously within 1 week after each treatment. No allergic reaction or other adverse reactions occurred. After the final laser treatment, the methotrexate dosage was tapered and later discontinued, and after 3 months of follow-up, her symptoms were still in remission (Fig 2, B and C).

**DISCUSSION**

Although tattooing of the skin is generally regarded as safe, serious complications can occur.4 Allergic reactions to red tattoo ink are the most frequently encountered complications in dermatologic practice.5 These reactions are characterized by chronic pain and itch associated with swelling and hyperkeratosis, sometimes leading to ulceration and crusting, which is sharply confined to the red-tattooed skin.6 The histopathology is predominated by histiocytes, sometimes in granulomatous formation, and frequently in combination with an interface dermatitis.7 These reactions are thought to be a delayed type IV allergic reaction to components of the tattoo ink, but the exact allergen remains unknown. A recent study demonstrated the presence of several red azo pigments in allergic red-tattoo reactions.8 In the culprit tattoo ink of our case (LaBina
Mars Red, LaBina Permanent-Line, GmbH & Co KG), several of these azo pigments are present.

Unfortunately, the allergen causing the allergic reaction is permanently residing in the mid-to-reticular dermis. Therefore, a curative treatment for these red-tattoo reactions is difficult to achieve. First-line therapy includes anti-inflammatory drugs, such as topical or intralesional corticosteroids. However, clinical improvement is often insufficient and only temporary. Unfortunately, only few reports describing alternative therapies to treat these allergic reactions, including hydroxychloroquine and allopurinol, have been published.1-3,9,10

Moreover, for a permanent treatment result, (complete) removal of the red pigment is usually necessary. Treatment modalities that may be considered include full surface and fractional ablative CO2 laser therapy, surgical excision, or dermatome shaving.11,12 However, these therapies may lead to undesirable permanent scars, especially in permanent makeup. As an alternative, targeted treatment with a Q-switched nanosecond or picosecond laser at 532 nm (matching the red pigment chromophore) can be considered as a therapeutic option with a low scarring potential. However, this treatment should be performed with caution because a generalized type IV allergic reaction caused by the photomechanical breakdown of the tattoo pigments has previously been described after Q-switched laser treatment.3

In this case, treatment with various local and systemic immunosuppressive therapies had already been attempted. Because of the severe and persisting symptoms, new alternative therapies were sought. To our knowledge, this is the first report describing successful treatment of a recalcitrant allergic red-tattoo reaction with methotrexate and Q-switched Nd:Yag (532nm) laser therapy. This new combination treatment can be considered as a promising treatment option for patients with severe refractory allergic reactions to (cosmetic) red tattoos.

Conflicts of interest
None disclosed.

REFERENCES
1. de Winter RW, van der Bent SAS, van Esch M, Wolkerstorfer A, Rustemeyer T. Allergic reaction to red cosmetic lip tattoo treated with hydroxychloroquine. Dermatitis. 2019;30(1):82-83. https://doi.org/10.1097/DER.0000000000000437
2. Patrizi A, Raone B, Savoia F, et al. Tattoo-associated pseudolymphomatous reaction and its successful treatment with hydroxychloroquine. Acta Derm Venereol. 2009;89(3):327-328. https://doi.org/10.2340/00015555-0639
3. Ashinoff R, Levine VJ, Soter NA. Allergic reactions to tattoo pigment after laser treatment. Dermatol Surg. 1995;21(4):291-294. https://doi.org/10.1111/j.1524-4725.1995.tb00175.x
4. Ortiz AE, Alster TS. Rising concern over cosmetic tattoos. Dermatol Surg. 2012;38(3):424-429. https://doi.org/10.1111/j.1524-4725.2011.02202.x
5. van der Bent SAS, Rauwerdink D, Oyen EMM, Maijer KI, Rustemeyer T, Wolkerstorfer A. Complications of tattoos and permanent makeup: overview and analysis of 308 cases. J Cosmet Dermatol. 2021;20(11):3630-3641. https://doi.org/10.1111/jocd.14498
6. van der Bent SAS, de Winter RW, Wolkerstorfer A, Rustemeyer T. Red tattoo reactions, a prospective cohort on clinical aspects. J Eur Acad Dermatol Venereol. 2019;33(10):e384-e386. https://doi.org/10.1111/jdv.15677
7. van der Bent S, Oyen E, Rustemeyer T, Jaspar L, Hoekzema R. Histopathology of red tattoo reactions. Am J Dermatopathol. 2021;43(5):331-337. https://doi.org/10.1097/DAD.0000000000001751
8. Serup J, Hutton Carsen K, Dommershausen N, et al. Identification of pigments related to allergic tattoo reactions in 104 human skin biopsies. Contact Dermatitis. 2020;82(2):73-82. https://doi.org/10.1111/cod.13423
9. Godinho MM, Aguinaga F, Grynszpan R, et al. Granulomatous reaction to red tattoo pigment treated with allopurinol. J Cosmet Dermatol. 2015;14(3):241-245. https://doi.org/10.1111/jocd.12149
10. Martin JM, Revert A, Montecujo C, Villalón G, Godoy R, Jordá E. Granulomatous reactions to permanent cosmetic tattoos successfully treated with topical steroids and allopurinol. J Cosmet Dermatol. 2007;64(4):229-231. https://doi.org/10.1111/j.1473-2165.2007.00338.x
11. van der Bent SAS, Huisman S, Rustemeyer T, Wolkerstorfer A. Ablative laser surgery for allergic tattoo reactions: a retrospective study. Lasers Med Sci. 2021;36(6):1241-1248. https://doi.org/10.1007/s10103-020-03164-2
12. Ibrahimi OA, Syed Z, Sakamoto FH, Avram MM, Anderson RR. Treatment of tattoo allergy with ablative fractional resurfacing: a novel paradigm for tattoo removal. J Am Acad Dermatol. 2011;64(6):1111-1114. https://doi.org/10.1016/j.jaad.2010.11.005