Lymphomatoid papulosis responding to topical methotrexate

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INTRODUCTION

Lymphomatoid papulosis is a nonaggressive cutaneous T-cell lymphoma characterized by recurrent, asymptomatic, papulonodular lesions featuring $CD30^+$ T cells on histology. The prognosis is excellent, but treatment can prove to be difficult. The disease has a chronic course of years to decades, with patients often becoming significantly affected cosmetically.[1] Commonly prescribed first-line treatments for lymphomatoid papulosis are topical corticosteroids, phototherapy, and systemic methotrexate.[2]

We report a patient who had complete resolution of her lesions with the use of topical methotrexate. This is, to our knowledge, the second case described in the literature.

CASE DESCRIPTION

The patient was a 36-year-old Caucasian woman with no pertinent past medical history. The only medications she was taking were escitalopram and naproxen, as needed. She was a smoker. The initial reason for consultation was to "rule out allergic contact dermatitis." Upon questioning, the patient reported a many-year history of asymptomatic, red-brown papules appearing and disappearing over the course of a few weeks, mainly on her limbs. The papules occasionally became crusted. They tended to resolve as brownish macules that eventually faded away. She rarely had periods without lesions. The patient noticed a slight improvement with the daily use of a commercially available moisturizer and 0.1% mometasone furoate cream applied twice daily on the papules. She did not identify any precipitating factors and denied any associated systemic symptoms.

On physical examination, grouped reddish papules were noted on the patient's forearms and thighs, along with sparse brownish macules (Fig 1). The rest of the mucocutaneous examination was normal. An incisional punch biopsy confirmed the diagnosis of lymphomatoid papulosis (type A, more specifically). Her complete blood count, flow cytometry, and lactate dehydrogenase levels were all normal. Sézary cells were not detected in the peripheral blood smear.

The patient was started on narrowband UV-B plus UV-A1 phototherapy twice weekly and asked to continue the twice-daily application of 0.1% mometasone furoate cream. Improvement was noted at the follow-up appointment 2 months later. Replacing the 0.1% mometasone furoate cream with 0.05% clobetasol propionate cream led to further improvement. After a few months of treatment, the only refractory region was the left forearm. The decision was made to stop the 0.05% clobetasol propionate cream and instead try a 0.25% methotrexate cream applied daily (approximately 1 fingertip unit over a 10-cm^2 area); the patient wished to avoid systemically administered agents. The vehicle used was a stable, hypoallergenic oil-in-water-type cream. The twice-weekly phototherapy was continued concurrently, without shielding the region treated with topical methotrexate. Complete resolution was noted after 1 week (Fig 2). Two months later, the patient is still lesion-free and continues phototherapy, but on a weekly basis only. An attempt will eventually be made to stop the phototherapy.

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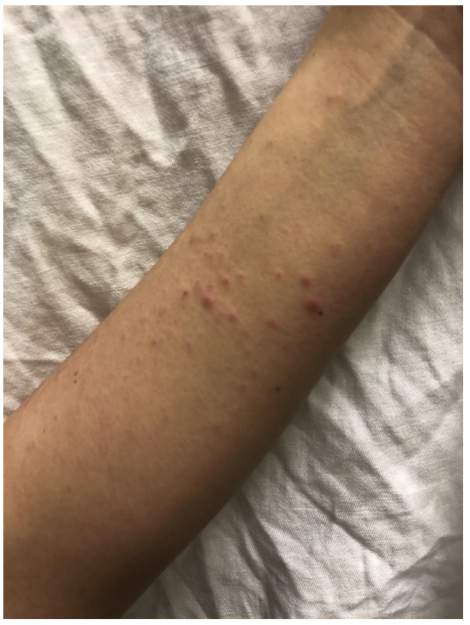

Fig 1. Grouped reddish papules noted on the patient's left forearm.

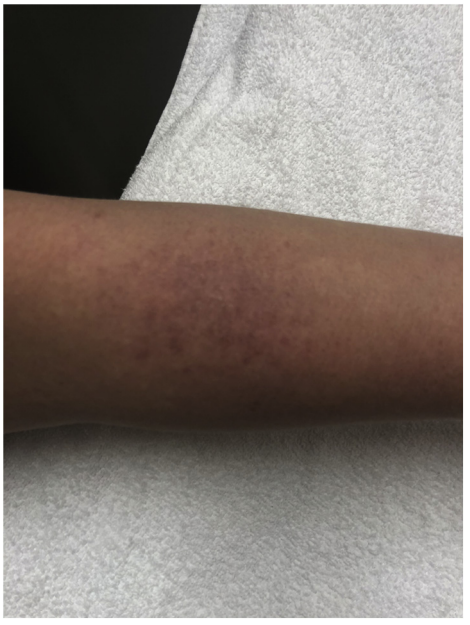

Fig 2. Complete resolution of the grouped papules after 1 week of 2.5% methotrexate cream applied daily.

DISCUSSION

Systemic methotrexate is a commonly used agent in dermatology for its antiproliferative, anti-inflammatory, and immunosuppressive properties. Its most important side effects are hepatotoxicity and pancytopenia. When considering methotrexate for the treatment of debilitating dermatologic conditions, the potential risks are usually small compared to the expected clinical benefits. However, the risks may outweigh the benefits in patients with minimal or localized diseases. Topically applied methotrexate gained interest in the 1960s to 1980s for the treatment of localized psoriasis. Poor cutaneous absorption, however, limited its efficacy and usage. Since then, topical methotrexate has been tried in several cases of mycosis fungoides and oral precancerous lesions and in 1 case of lymphomatoid papulosis.[3]

Bergstrom et al[4] reported the case of a patient who moistened a 2.5-mg tablet of methotrexate with tap water and rubbed it onto a gauze, which he then applied daily on the newly formed papules. The treated lesions regressed within 2 to 3 days, whereas the untreated ones persisted for more than 3 weeks. In the case of our patient, the use of topical methotrexate (0.25% cream) also led to faster resolution—the papules resolved within a few days instead of a few weeks.

These 2 cases underscore topical methotrexate as a potential alternative with few side effects in the symptomatic treatment of limited lymphomatoid papulosis. In the case of our patient, knowing the natural course of the disease, the question remains as to whether the papules would have resolved without the methotrexate cream being applied (with or without the continued application of a potent topical corticosteroid). Moreover, the treated region was not shielded during the phototherapy, adding a confounding factor. Nonetheless, it still raises the interesting possibility of topical methotrexate being an effective, innocuous treatment for limited lymphomatoid papulosis. Controlled studies are needed to demonstrate its efficacy and safety as a monotherapy. Stable compounds with known bioavailability and optimized transcutaneous absorption also need to be formulated and made commercially available. Ongoing studies are directed at this goal.[5,6] All in all, topical methotrexate is an avenue to explore in the management of many skin diseases, including lymphomatoid papulosis.

Conflicts of interest

None disclosed.

REFERENCES

1. Di Raimondo C, Parekh V, Song JY, et al. Primary cutaneous CD30+ lymphoproliferative disorders: a comprehensive review. *Curr Hematol Malig Rep*. 2020;15(4):333-342. https://doi.org/10.1007/s11899-020-00583-4
2. Fernández-de-Misa R, Hernández-Machín B, Servitje O, et al. First-line treatment in lymphomatoid papulosis: a retrospective multicentre study. *Clin Exp Dermatol*. 2018;43(2):137-143. https://doi.org/10.1111/ced.13256
3. Aickara D, Bashyam AM, Pichardo RO, Feldman SR. Topical methotrexate in dermatology: a review of the literature. *J*

Dermatolog Treat. 2020:1-6. https://doi.org/10.1080/09546634.2020.1770170

4. Bergstrom JS, Jaworsky C. Topical methotrexate for lymphomatoid papulosis. *J Am Acad Dermatol*. 2003;49(5):937-939. https://doi.org/10.1016/s0190-9622(03)00470-5
5. Javadzadeh Y, Hamishehkar H. Enhancing percutaneous delivery of methotrexate using different types of surfactants. *Colloids Surf B Biointerfaces*. 2011;82(2):422-426. https://doi.org/10.1016/j.colsurfb.2010.09.015
6. Wohlrab J, Neubert RHH, Michael J, Naumann S. Methotrexate for topical application in an extemporaneous preparation. *J Dtsch Dermatol Ges*. 2015;13(9):891-901. https://doi.org/10.1111/ddg.12622