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Methotrexate does not impede the development of contact allergy

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Methotrexate (MTX) is a folic acid analogue with immunosuppressive and anti-inflammatory properties. It is used in the treatment of numerous inflammatory skin diseases, including moderate to severe atopic dermatitis (AD) (1). Evidence is scarce regarding the reliability of patch testing during immunosuppressive treatment. We report a case of strongly positive epicutaneous test results in an AD patient receiving high doses of MTX.

Case Report

A 39-year-old woman with a known history of AD was referred to the dermato-allergology department for persistent, painful, hyperkeratotic palmoplantar eczema, despite local treatment with betamethasone dipropionate ointment 0.05% and emollients. Therefore, systemic treatment with intramuscular injections of methotrexate (25 mg weekly) was initiated, with substitution of folic acid. Three months later, improvement was marked, although incomplete. Therefore, patch tests with the European baseline series with allergens from Chemotechnique (Vellinge, Sweden) and Finn Chambers[®] were performed to exclude allergic contact dermatitis. On day 3, the patch tests showed extreme positive reactions (+++) to both nickel sulfate and hydroperoxides of linalool. These findings were considered to be clinically relevant, as the patient had a known history of allergic contact dermatitis caused by imitation jewellery and fragrances. After 1 year of systemic treatment, and given

the dramatic improvement of AD lesions (DLQI 7/30 instead of 30/30), MTX treatment was stopped.

Discussion

Evidence concerning the performance of patch testing during immunomodulating treatments is scarce, because investigations are usually postponed, with the rationale that these drugs could impair elicitation reactions. However, positive patch test reactions in patients receiving MTX have already been reported (2, 3). Indeed, patients receiving low doses of MTX tend to have strong eczematous reactions, whereas those receiving doses of ≥ 15 mg weekly seem to have weaker, mainly erythematous reactions. In the present case, however, patch test reactions were extreme positive, indicating that high doses of MTX had no anti-inflammatory action on the development of allergic contact dermatitis in a previously sensitized patient. This observation is in line with previous studies using experimental models of allergic contact dermatitis (contact hypersensitivity), in which the effect of MTX was evaluated (4). The results showed that MTX could block the afferent phase of contact hypersensitivity, but had no effect on the elicitation phase, resulting in the development of eczema following contact allergen challenge in already sensitized animals.

The fact that MTX improves AD without impeding the development of allergic contact dermatitis strongly supports the existence of different pathophysiological processes in the two types of eczema, mediated by type 2/Th2 and type 1/Th1 immunity, respectively (5, 6).

In conclusion, our results highlight the fact that positive and clinically relevant patch test reactions can be observed during high-dose MTX treatment. Nevertheless, it remains uncertain in which way and to what extent immunosuppressive drugs may affect cutaneous immune reactions, making the interpretation of patch tests extremely challenging.

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