Letter

Eruptive lentiginosis in resolving plaque psoriasis associated with methotrexate therapy

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To the Editor

Eruptive lentiginosis in resolving psoriatic plaques is a rare condition reported only in a small subset of patients, including children.[1,2] It was initially described with psoralen and ultraviolet A phototherapy, but other therapeutic modalities such as topical corticosteroids, calcipotriol, and apremilast have been reported. Recently, cases with antitumor necrosis factor (infliximab, adalimumab, and etanercept), anti-IL12/23 (ustekinumab), anti-IL23 (guselkumab), and anti-IL17A (secukinumab and ixekizumab) agents have been published.[3-6] The association with methotrexate (MTX) is rarely reported.[7]

We describe a 59-year-old woman, Fitzpatrick phototype II, with a medical history of hypertension, dyslipidemia, obesity, and osteoporosis. The patient was diagnosed with psoriasis at the age of 18, which was initially controlled with topical therapies and then psoralen and ultraviolet A phototherapy; she received psoralen and ultraviolet A phototherapy for four weeks at the age of 43 with a cumulative dose of 63.5J/cm^2. At the age of 44, she developed psoriatic arthritis and commenced treatment with oral MTX at doses ranging from 15-25mg/week. Adalimumab was later added but discontinued after three months owing to primary failure. Over the past few years, the patient experienced several interruptions of MTX, mainly related to irregular follow-up. Recently, she had resumed the MTX treatment, now at a dose of 15mg/week, and for the first time through subcutaneous route and without interruptions.

Three months after the sustained restart of MTX, the patient was referred to our dermatology department because of the appearance of brownish macules clustered in areas previously affected by psoriatic plaques, elbows, forearms, and knees (Figures 1-2). Based on the clinical history and examination, the diagnosis of eruptive lentiginosis in resolving plaque psoriasis associated with MTX was made.

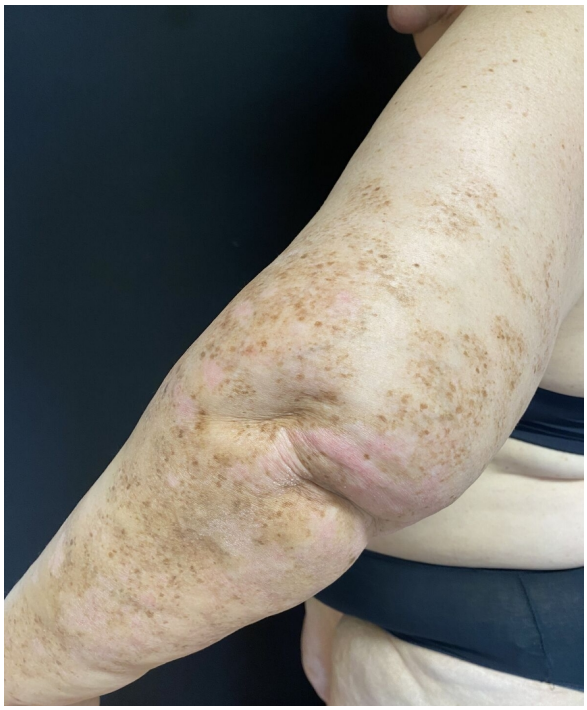

Figure 1. *Brown macules clustered in areas previously affected by psoriatic plaques on the elbows and forearms.*

The pathophysiology of this condition is still not well understood, mainly because it occurs related to different types of therapeutic modalities.[1] In the case of MTX, it is thought that its suppressive effect on T cells and inflammatory cytokines, including tumor necrosis factor, may interfere with the immune response targeted to melanocytes, reducing the inhibition of melanogenesis and resulting in hyperpigmentation.[7] To the best of our knowledge, this association with MTX is very unusual, with only 2 cases described in the literature to date.[7]

According to the literature, lentigines usually appear in the first six months of treatment,[1] but in this case, they only developed after several years of treatment with

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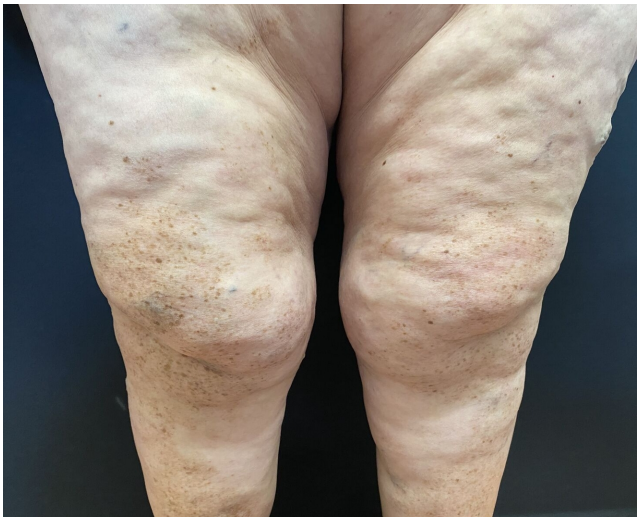

Figure 2. *Brown macules clustered in areas previously affected by psoriatic plaques on knees.*

intermittent MTX. Although the patient had been medicated with MTX for a long period, she only recently started taking the drug subcutaneously and on a regular basis, which may explain why the lentigines only appeared at this stage. The bioavailability of oral MTX is rather variable (50%–80%) and several trials have demonstrated that the bioavailability of subcutaneous MTX is superior.[8]

Suspension of the drug is not necessary, but the appearance of pigmented lesions is a condition that requires vigilance.[3] With the widespread use of biological therapy and the emergence of new therapeutic targets, this dermatosis may become more frequently seen in clinical practice.[3]

Potential conflicts of interest

The authors declare no conflicts of interest.

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