Multiple Lentigines Arising in Sites of Resolving Psoriatic Plaques after Treatment with Ustekinumab

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Dear Editor:

The patient was a 32-year-old man of Fitzpatrick skin type IV with plaque psoriasis of 20 years' duration. He had been previously treated with topical corticosteroids and calcipotriol, phototherapy, systemic cyclosporin, and methotrexate, but with limited efficacy. When his psoriasis area severity index (PASI) reached 52.8, he was switched to ustekinumab (45 mg, every 12 weeks), and 9 months later a marked improvement was observed (to PASI 90). However,

after 1 year of ustekinumab therapy, multiple, asymptomatic, brownish hyperpigmented macules were observed on his face, neck, trunk and both extremities regardless as to whether the region sun-exposed (Fig. 1). Histological examination showed basal layer hyperpigmentation (Fig. 2). Because of the inadequacies of previous treatments and after consultation with the patient, ustekinumab was continued for psoriasis control. The development of lentigines in association with psoriasis treatment has been fre-

Fig. 1. (A~C) Multiple lentigines confined to resolving psoriatic plaques and one of the lentigines (indicated by arrows) was biopsied.

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Fig. 2. Photomicrograph showing basal layer hyperpigmentation (H&E, $\times 200$).

quently reported¹⁻⁴. In most cases lentigines development occurred after phototherapy, and thus, it has been suggested lentiginous proliferation is associated with a reaction to ultraviolet light¹. Topical calcipotriol has also been reported to induce lentigines². Martí et al.² suggested an unusual form of postinflammatory hyperpigmentation underlies lentigines formation. Recently, many biologic agents used to treat psoriasis have been associated lentigines. Costa et al.¹ reported two patients developed multiple lentigines after the etanercept-induced resolution of psoriatic plaques, and suggested lentiginous proliferation is a characteristic of psoriasis and not of the therapy used. Three months of infliximab therapy was also reported to induce lentiginous eruption in areas of resolved psoriatic plaques³. In our case, lentigines were not appeared after treatment with phototherapy for 6 months 8 years ago. However after 12 months of treatment with ustekinumab, multiple lentigines were developed in sites of resolving psoriatic plaques instead of sun-exposed area. Therefore we thought that lentigines were developed by ustekinumab. Some authors have argued the melanocyte inhibitory effects of psoriasis-related inflammatory cytokines are compromised by biologic agents. Interleukin (IL)-1 α , IL-6 and tumor necrosis factor (TNF)- α are suggested to inhibit melanocytes and have an inhibitory effect on tyrosinase

activity. Effective suppression of TNF- α and other cytokines with melanocyte inhibitory effects triggers lentiginous eruption in a patient-dependent manner³. Others have suggested these lentigines are the result of a type of post-inflammatory hyperpigmentation⁴. We favor a pathogenesis involving post-inflammatory hyperpigmentation, because ustekinumab is an anti-IL-12/23 inhibitor not a TNF- α inhibitor, and used to treat other inflammatory diseases, such as, rheumatoid arthritis, Crohn's disease, and a rare case of severe refractory atopic dermatitis⁵, in addition a literature search failed to reveal any mention about lentigines formation after treating these diseases with ustekinumab. Although interestingly, multiple lentigines in resolving psoriasis lesions were reported after treatment with topical calcipotriol². Inevitably, biologic agents will be increasingly used to treat psoriasis, and thus, further study about this phenomenon is needed.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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