CASE REPORT

Eruptive lentiginosis in resolving psoriatic plaques

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INTRODUCTION
Eruptive lentiginosis confined to areas of resolving psoriatic plaques (ELRP) is a rare occurrence. Several previous reports described this phenomenon after the use of different treatment modalities to resolve psoriatic plaques, including topical, ultraviolet light, and biologic therapies. We present a case of ELRP after treatment with ustekinumab. We completed a review of the literature synthesizing all available reports describing lentiginous macules at the site of resolving psoriatic plaques to describe the patient population, treatments, and clinical characteristics associated with this entity.

CASE REPORT
A 29-year-old man with Fitzpatrick skin type III-IV presented with a 6-year history of chronic plaque psoriasis. His psoriasis was not previously treated, and he was not on any other medications. He had no other significant medical history. On physical examination, the patient had diffuse psoriatic plaques on the trunk and extremities with scalp and nail involvement covering roughly 20% body surface area. Treatment with ustekinumab was initiated at a psoriasis-scheduled dose. Resolution of the psoriatic plaques started 3 weeks after initiation of ustekinumab with complete clearance after 3 months. However, at 3 months, the patient presented with multiple 2- to 5-mm light to dark brown fairly symmetrical macules located on the upper extremities and trunk that were confined to previous sites of psoriatic plaques (Fig 1). Lentigines appeared in all areas of resolution; however, some areas had a higher density of lentigines relative to others. The patient did not have a history of lentigines, no phototherapy was performed, and the patient denied sun exposure on the affected areas during the treatment period. A punch biopsy of a macule found elongation of the rete ridges with mild acanthosis and hyperpigmentation of the basal layer compatible with lentigo (Fig 2). Treatment continued, and follow-up at 3 months found no change in the macules.

DISCUSSION
Our case report describes ELRP after anti-interleukin (IL)-12/23 treatment and adds to the growing body of literature describing this phenomenon. A MEDLINE, EMBASE, and PubMed search, and review of the references, found that ELRP is described in 12 studies (10 case reports, 2 case series) for a total of 18 patients (Table I). Patients with a history of phototherapy were excluded. These lentiginous eruptions have been most commonly reported after treatment with biologics, which was the case for 6 reports representing a total of 7 patients (39%).

Biopsy results of the pigmented macules, when reported, were consistent with lentigo. Based on the published reports, these lentigines appear within the first 6 months of treatment initiation, appearing as early as 3 months in some cases. All patients, with the

Abbreviations used:
ELRP: eruptive lentiginosis in resolving psoriatic plaques
IL: interleukin
TNF: tumor necrosis factor

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exception of the one in our case described above, received prior treatment for their psoriasis that included one or a combination of topical and systemic therapies. Although follow-up was only reported for 4 patients, it appears the lentigines persist with little to no improvement for several years after onset. For instance, in one case report, minimal improvement was found in the lentigines over 5 years. However, treatment with a Q-switched ruby laser led to partial clearance of the pigmented lesions in 1 patient.6

The age of the patient population for which ELRP was described ranged from 7 to 74 years with an average age of 48. Two of these patients were younger than 18 years. Gender was reported for only 12 of the patients, of which, 7 were male and 5 were female. Furthermore, patients had a prolonged history of psoriasis ranging from 6 to 40 years before the onset of lentigines. This phenomenon was described in 2 patients with Fitzpatrick skin type 2 and in 8 patients with skin types 3 or 4. Skin type was not stated for the remaining 8 patients.

The pathophysiology of ELRP is not well understood. Because these pigmented lesions appeared after several different treatment modalities, a common pathway affecting melanocytes is potentially implicated. A previous study by Wang et al11 provides some insight into this mechanism. They found high levels of cytokines IL-17 and tumor necrosis factor (TNF) in psoriatic plaques. These cytokines, in addition to others, help stimulate melanocytic growth such that psoriatic lesions have almost twice as many melanocytes as nonlesional skin. The high levels of these cytokines also contribute to the suppression of those genes responsible for pigment production. Consequently, therapeutic neutralization of TNF and IL-17 with biologics reduced the inhibition of melanogenesis and led to a rapid recovery in pigment production in all patients that were treated with anti-TNF (etanercept) and anti–IL-17 (ixekizumab). The increased number of melanocytes combined with a recovery in pigment production led to an abundant production of melanin in resolving psoriatic plaques, potentially explaining the lentigines observed in this study. Although Wang et al11 only focused on IL-17 and TNF, there may be several other cytokines and factors that help regulate melanogenesis12 and melanocytic growth that are targeted by other biologics and treatments described in this study. Previous reports of eruptive lentiginosis after chemotherapy in cancer patients13-15 provides further support that immune modulation may be responsible for these eruptions.

ELRP has only been reported in a small subset of patients. Perhaps ELRP represents a more exaggerated recovery in pigment production, associated with greater disease severity or greater inhibition of cytokines with treatment. Supporting this is the fact that in some patients, ELRP appeared after the resolution of thick psoriatic plaques and not thin ones. As well, it has been suggested that certain mutations in signaling proteins may predispose certain individuals to developing lentigines, as immune modulation may be greater in these individuals.14,16 Overall, it seems that the rapid clearance of psoriatic plaques with new targeted therapies may contribute to the appearance of ELRP.

Fig 1. Eruptive lentiginosis in previous sites of psoriatic plaques on the right shoulder (A) and right arm (B).

Fig 2. Punch biopsy of a macule shows elongation of the rete ridges with mild acanthosis and hyperpigmentation of the basal layer compatible with lentigo.
| Treatment class | Reference | Most recent treatment before lesions | Patient details | Lesion details | Time to onset of lesions | Histopathology | Prior psoriatic treatment | Follow-up |
|-----------------|-----------|--------------------------------------|-----------------|---------------|-------------------------|----------------|--------------------------|-----------|
| Biologics       | Santos-Juanes et al<sup>1</sup> | Adalimumab (40 mg once every 15 days) | 55-y woman, 25-y history of psoriasis | Light and brown regular lentigines over the previous sites of the psoriatic plaques | 2 mo after treatment | Confirmation of lentigines | Topical steroids, tacalcitol, calcipotriol, methotrexate | NS        |
|                 | Alman-Fernandez and Fernandez-Crehuet<sup>2</sup> | Etanercept (50 mg twice weekly) | 53-y woman, 30-y history of psoriasis | Multiple small pigmented lesions in areas previously affected by psoriasis. On forearms, legs, and buttocks. | NS | Consistent with lentigines. No actinic damage. | Topical treatments, methotrexate, acitretin | NS        |
|                 | LaRosa et al<sup>3</sup> | Etanercept (50 mg weekly) | 16-y Hispanic boy, 9-y history of severe plaque psoriasis covering 40% of body surface area, skin type 3 | Speckled lentiginous macules within dark-tan hyperpigmented patches, resembling nevus spilus in resolving plaques on chest and back | Appeared before Etanercept treatment and 3 mo after treatment | NS | Triamcinolone, calcipotriene, acitretin, methotrexate | 28 mo; development of additional macules |
|                 | Dogan and Atakan<sup>4</sup> | Infliximab (5 mg/kg IV per 8 weeks after 0 and 2 week infusions) | 55-y white woman, 12-year history of psoriasis, skin type 3 | Small, 2- to 3-mm light and dark brownish hyperpigmented macules were found on each resolved psoriatic plaque | NS | NS | Topical corticosteroids, emollients, systemic methotrexate, adalimumab | NS        |
| Current study | Ustekinumab | 29-yo, 6-y history of plaque psoriasis, skin type 3-4 | Multiple 2- to 5-mm light to dark brown fairly symmetrical macules located on the upper extremities and trunk that were confined to previous sites of psoriatic plaques | 3 mo after treatment | Elongation of the rete ridges with mild acanthosis and hyperpigmentation of the basal layer compatible with benign lentigo | None | 3 mo; lentigines still present without improvement |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Gutierrez-Gonzalez et al | Ustekinumab (45 mg every 12 weeks) | 40-yo, 15-y history of plaque psoriasis, skin type 4 | Multiple grouped but not confluent, brown macules of 2-3 mm over well-defined slightly hyperpigmented areas previously affected by psoriasis on trunk and extremities | 6 mo after treatment | Not performed | Topical corticosteroids, calcipotriol, systemic acitretin, methotrexate | NS |
| Ultraviolet light ( +/- other treatments) | Mitra et al | Dithranol + UVB phototherapy (cumulative dose 6.73 J/cm²) | 55-yo man, 28-y history of psoriasis, skin type 2 | Light and dark-brown macules around the periphery of the cleared psoriasis plaques | 6 mo after treatment | Small areas of epidermal basal layer hyperpigmentation | NS | 4 y; macules still present without improvement |
| Dawn et al | Coal tar, dithranol, topical steroids, UVB | 67-yo man, 20-y history of psoriasis | Dark lentigines on psoriasis plaques on thigh | NS | Confirmed presence of lentigines | NS | NS |
| Other | Sfecci et al | Apremilast (30 mg) | 4 of 21 pts (19%) treated had lentigines. Age range, 39-74 y and Fitzpatrick skin type 3 or 4 | Lentigines only in areas of resolving psoriatic plaques Most occurred in sun protected areas | 0-4 mo after treatment | Not performed | 3 pts, methotrexate 1 pt, NS | 5 y; lentigines still present |
| Marti et al | Calcipotriol | 65-yo man, 30-y history of psoriasis, skin type 2 | Small dark brown macules within light brown macules on his | 3 mo after treatment | Basal cell hyperpigmentation and elongation of the rete ridges | Topical corticosteroids | NS |

Continued
| Treatment class | Reference | Most recent treatment before lesions | Patient details | Lesion details | Time to onset of lesions | Histopathology | Prior psoriatic treatment | Follow-up |
|-----------------|-----------|-------------------------------------|-----------------|---------------|------------------------|---------------|--------------------------|-----------|
| Prior psoriatic | Rogers¹⁰  | Liquor picis carbonis 4% in aqueous | 7-yo boy        | Lentigines at sites of very thick resolving plaques. No lentigines at other less thick resolving psoriatic lesions | NS           | NS                       | No phototherapy | NS        |
| treatment       |           | cream and a fluorinated topical      |                 |               |                        |               |                          |           |
|                 |           | steroid                              |                 |               |                        |               |                          |           |
|                 | Dawn et al⁷ | Coal tar, dithranol, topical steroids | 74-yo woman, 40-year history of psoriasis mainly on elbows, knees, and hands | Dark irregular lentigines on the hands. | NS           | Confirmed presence of lentigines | NS         | NS        |
|                 |           | Topical steroids, crude coal tar     | 56-yo man, 15-y history of psoriasis limited to hands (including palms) | Dark lentigines that have increased in number but remain limited to areas affected by psoriasis. | NS           | Confirmed presence of lentigines | NS         | NS        |
|                 |           | Coal tar, dithranol, topical steroids, calcipotriol | 41-yo woman, 25-y history of plaque psoriasis | Dark irregular 3- to 5-mm macular pigmentation limited to psoriasis plaques on the elbows and knuckles of the right hand for 15 years | NS           | Features of lentigo         | NS         | NS        |

NS, Not stated; Pts, patients; UVB, ultraviolet B; yo, years old.

*One patient who had lentigines was omitted because of a history of phototherapy.
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