CASE REPORT

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Multiple Lentigines in Resolving Psoriatic Plaques After Treatment with Secukinumab in Two Cases

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ABSTRACT

The development of lentigines in resolving psoriatic plaques has been reported in the literature after different treatment modalities including phototherapy, topical therapeutics, and recently during or after treatment with tumor necrosis factor inhibitors and ustekinumab. Herein we want to report two cases with multiple lentigines developed after healing of the plaques of psoriasis who received treatment with secukinumab for psoriasis. To our knowledge development of multiple lentigines after secukinumab treatment has not been reported in the literature before.

Keywords: Biologic agents, Dermatology, Lentigo, Psoriasis, Secukinumab

Introduction

The development of lentiginous pigmentation confined to resolved psoriatic plaques is a rare phenomenon that has been reported after different treatment regimens in the literature [1,2,3]. The pathogenesis of the melanocytic stimulation and increased melanin production over resolved psoriatic plaques after the treatment is not well-known but it was suggested that this reaction may be explained with post-inflammatory hyperpigmentation and previous history of ultraviolet (UV) light exposure, genetic predisposition, having a fair skin type and disease severity may also have a role [2].

Case Reports

Case 1

A 37-year-old male patient who was under follow-up for chronic plaque-type psoriasis for 2 years in our clinic admitted for a routine control visit. He was taking secukinumab for 6 months due to the side effects and unresponsiveness to conventional antipsoriatic agents. On dermatologic examination, marked remission was detected on hyperkeratotic and desquamating erythematous plaques over the trunk, upper and lower extremities. Also, small, 2-3 mm of light and the dark brownish hyperpigmented lentiginous macular eruption was realized over resolved psoriatic plaques (Figure 1). Patient consent form was taken before the treatment. Histologically these pigmented lesions were consistent with lentiginous proliferation (H&E, x400) (Figure 1b). He was otherwise healthy and he has no history of any other systemic or dermatologic disease and biologic agent used previously. Routine follow-up was recommended.

Case 2

A 38-year-old female patient who was diagnosed as a 4-year history of chronic plaque-type psoriasis presented to our outpatient clinic for her routine control visit. She was unresponsive to conventional therapies and due to the secondary unresponsiveness to etanercept

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and primary unresponsiveness to adalimumab, we initiated secukinumab. On her routine follow up at 3rd month, multiple millimetric brown lentiginous eruption was realized over previously psoriatic plaques on elbows and knees (Figure 2a). There was no similar lentiginous lesion on the normal skin or mucosal surfaces. She has no history of another systemic or dermatological disease. Patient consent form was taken before the treatment. Histologically lentiginous proliferation was noted on the epidermis. (H&E, x200) (Figure 2b). Routine follow-up was recommended.

Discussion

Development of lentigines on resolving psoriatic plaques is a rare phenomenon that has been reported following different topical and systemic antipsoriatic treatment modalities including topical calcipotriol, topical tar, phototherapy, apremilast, methotrexate, and some biologic agents including adalimumab, infliximab, ustekinumab, and recently after guselkumab use [1,2,3,4,5,6,7,8,9]. The occurrence of lentigines was first linked to the phototherapy and implicated as PUVA- or UVB-induced lentigo in most cases, but after they have been noted following different therapy modalities, especially patients who do not have history phototherapy, they were referred to post-inflammatory hyperpigmentation mechanisms [3,5,7]. Most of the cases had skin types of Fitzpatrick I-III and the appearance of the lentiginous lesions usually reported to develop at 2-6 months of the treatments. In some of these observations, the development of lentigines was linked to sun exposure or sunburns. None of our patients have sunburn history previously, the possible effect of biologic agents on melanocytes or melanogenesis is not well-known. Some authors suggested that the effective suppression of tumor necrosis factor (TNF)-a and other psoriasis-related inflammatory cytokines may lead to this reaction by their inhibitory effects on melanocytes and tyrosinase activity [1,8,9,10,11]. Our first patient was biologic naive, and he has also no history of phototherapy or anti-TNF agent use. Our second patient has also no history of phototherapy, she used anti-TNF agents previously but no similar lesions occurred on resolving psoriatic plaques during these therapies. They have skin types of Fitzpatrick type III and PASI scores were between 10-15 in our patients. Dogan and Atakan [1] suggested that the development of lentiginous eruption may be a clinical marker of response to the therapy. They reported almost total clearance with infliximab, which was resulted in multiple lentiginous proliferation within the resolved plaques. As Singh and Beniwal [2] mentioned, this reaction is most probably related to the level of cytokine suppression is responsible for this phenomenon rather than the drug itself.

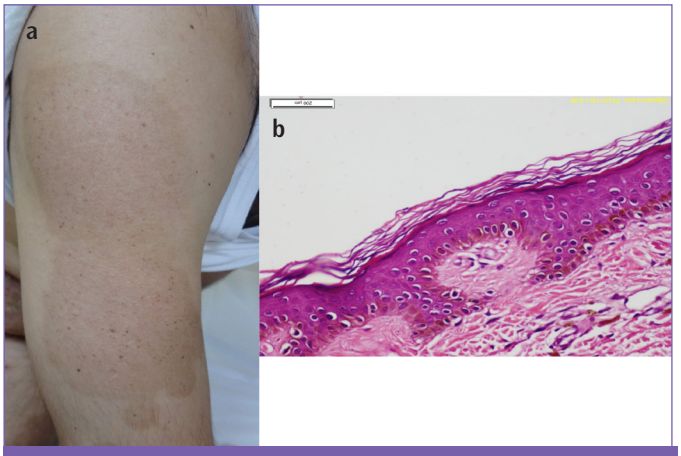

Figure 1. a) Lentiginous macular lesions over healed plaques of psoriasis on the extensor surface of the left arm, **b)** Lentiginous proliferation on basal layer (H&E, x400)

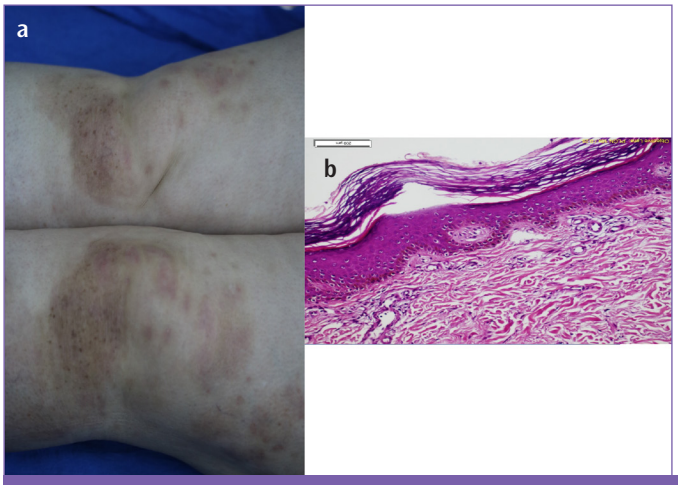

Figure 2. a) Lentiginous macular lesions over healed plaques of psoriasis on the knees (marked with red lines), **b)** Homogenous lentiginous proliferation in the epidermis (H&E, x200)

The effects of proinflammatory cytokines including TNF-alpha and IL-17 on melanocytes were investigated in previous studies and the authors underlined the synergistic stimulation of these cytokines may lead to increased expression of growth factor genes and mitogenic cytokines and seems to downregulate the melanin production and the pigmentation signaling pathway [10,11]. The blockage of IL-17 by secukinumab may be the most probable factor in the development of lentigines in our patients.

Conclusion

The development of multiple lentigines in treated lesions of psoriasis is a rare clinical manifestation that may present following different therapeutic agents. In the literature both anti-TNF agents and anti IL12/23 agents. To our knowledge lentiginous proliferation has not been reported with anti-IL-17 agents previously. The development of lentiginous proliferation with different biologic pathways may support the hypothesis of post-inflammatory hyperpigmentation mechanisms in response to effective therapy in

psoriasis. These lesions are usually permanent and laser therapies may be offered for the patients. Although long term follow-ups have not been reported in the literature, in few cases reports total clearance was reported in 4 weeks - 4 months, and persistence of the lesions for years was reported in some of the cases.

In our patients during routine follow-ups, no clinical regression was detected on the lentiginous eruption. It is also not well-known if this localized pigmentation may be a marker for cutaneous malignancy or progress into a malignancy in long term. Physicians should be aware of this entity and sun protection should be advised to prevent further formation.

Ethics

Informed Consent: Patient consent form was taken before the treatment.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.K.U., Concept: T.K.U., A.S.K., Design: T.K.U., A.S.K., B.Ç.Ş., Data Collection or Processing: T.K.U., B.Ç.Ş., Analysis or Interpretation: T.K.U., A.S.K., B.Ç.Ş., Literature Search: T.K.U., Writing: T.K.U.

Conflict of Interest: No conflict of interest was declared by the authors.

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