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Secukinumab-induced paradoxical palmoplantar pustular psoriasis

Sekukinumabın tetiklediği paradoksal palmoplantar püstüler psoriazis

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To the Editor,

A paradoxical adverse effect (PAE) is an unexpected drug reaction that is opposed to the expected pharmaceutical effect of the drug. The most frequently reported PAE to biologic therapies is psoriasis, presenting as de novo development, exacerbation of existing disease, or development of a different morphological variant[1]. Herein, we present a patient who developed paradoxical palmoplantar pustular psoriasis after receiving secukinumab and responded well to treatment with ustekinumab.

A 45-year-old woman presented with severe, chronic plaque psoriasis vulgaris [psoriasis area and severity index (PASI) = 25.4]. Treatment with secukinumab 300 mg by subcutaneous injection (standard dose) was initiated after the patient did not respond to topical agents, narrow-band ultraviolet light, or methotrexate therapy. After the fifth dose, she responded well, with PASI of 100. In week 11 of treatment, she presented again to the outpatient clinic with complaints of pain and itching on both palms and soles. Dermatological examination revealed multiple pustules on an erythematous base on the palmoplantar region bilaterally (Figure 1a, b). Her palmoplantar pustulosis (PPP) PASI was 13.2. She denied any previous history of similar disease, smoking, or stress. Potassium hydroxide mount, gram

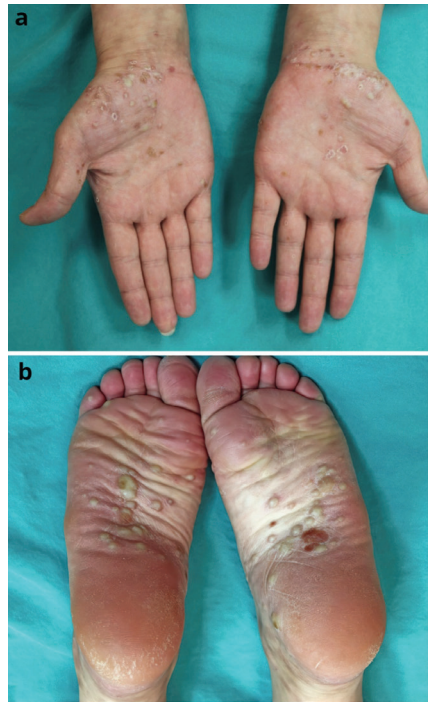

Figure 1. (a, b) Paradoxical palmoplantar pustular psoriasis during secukinumab treatment

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staining, and swab cultures yielded negative results. Histopathological examination revealed hyperkeratosis, parakeratosis, focal worsening of spongiosis, and lymphocyte exocytosis associated with spongiosis (Figure 2). She was switched from secukinumab to ustekinumab 45 mg by subcutaneous injection (weight, 50 kg, standard dose) combined with topical steroids. In the fourth month of treatment, she showed good response, and her PPP PASI score decreased to 1.8 (Figure 3a, b).

Although PAE is considered a class effect of anti-tumor necrosis factor (TNF) agents, cases caused by other biologics such as ustekinumab and anti-interleukin-17 (IL-17) agents are increasingly common in recent years[1]. Several recent reports have described the development of PAE after significant initial improvement in refractory plaque psoriasis with secukinumab[2-4].

Recently, an imbalance between TNF and type 1 interferon (IFN) was confirmed to result in PAE. TNF blockade reduces the maturation of plasmacytic dendritic cells (PDC) and thus increases type 1 IFN production. Unlike classical psoriasis, T-cell-mediated autoimmunity triggered by type I IFN does not occur in PAE. In parallel, since T-cell-mediated memory cells do not develop in PAE, relapse is not observed[5]. However, the factors leading to the activation of PDC cells are unclear. Despite attempts at explaining the etiopathogenesis of PAE that occurs after the use of anti-TNF agents as caused by infections and genetic predisposition, the recent occurrence of PAE also after the use of ustekinumab and anti-IL-17 agents suggests there may be other mechanisms in etiopathogenesis[1,5].

The underlying mechanism is believed to be related to an imbalance in the cytokine pathway following progressive hyperexpression of early proinflammatory cytokines (TNF-α, IL-12/23) after IL-17A blockade[2,3]. Thus, it contributes to the new disease form, which has a predominantly pustular character[1]. Although paradoxical reactions can be resolved by switching or discontinuing the causative drug, additional topical or systemic treatments may be required in some cases[1,5]. In our case, after discontinuing secukinumab, we both changed the biologic agent to ustekinumab and initiated topical therapy, after which the patient's paradoxical psoriasis lesions regressed.

In this case, the dilemma is that such episodes can also occur in the natural course of psoriasis[1]. Considering the report by Mylonas and Conrad[5], we believe that our patient had PAE for several reasons: 1) She exhibited a different clinical presentation, 2) PAE more commonly involves the palmoplantar region, 3) histopathology was accompanied by spongiotic dermatitis, and 4) a good response was obtained with ustekinumab. Awareness of this potential effect of anti-IL-17 agents can provide guidance during the course of biologic therapy for psoriasis. Informed consent was obtained.

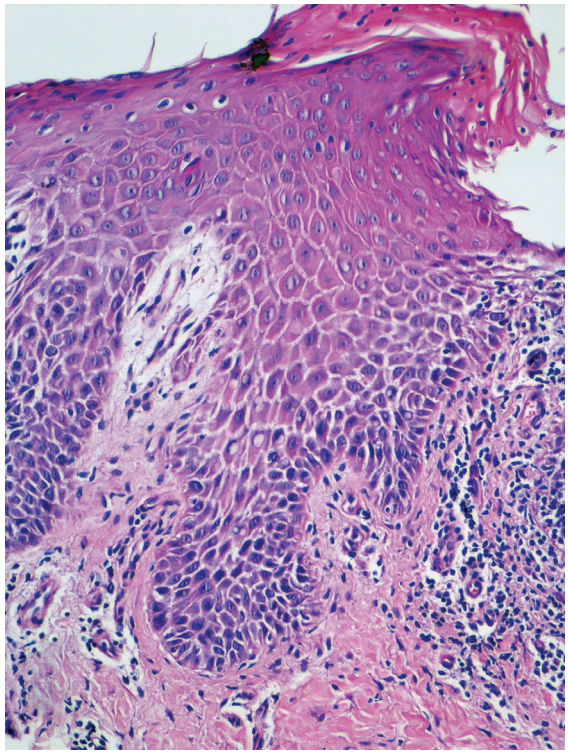

Figure 2. Histopathological findings consistent with spongiotic and psoriasiform reactions. Skin biopsy specimen was obtained before treatment with ustekinumab (hematoxylin and eosin staining, x400)

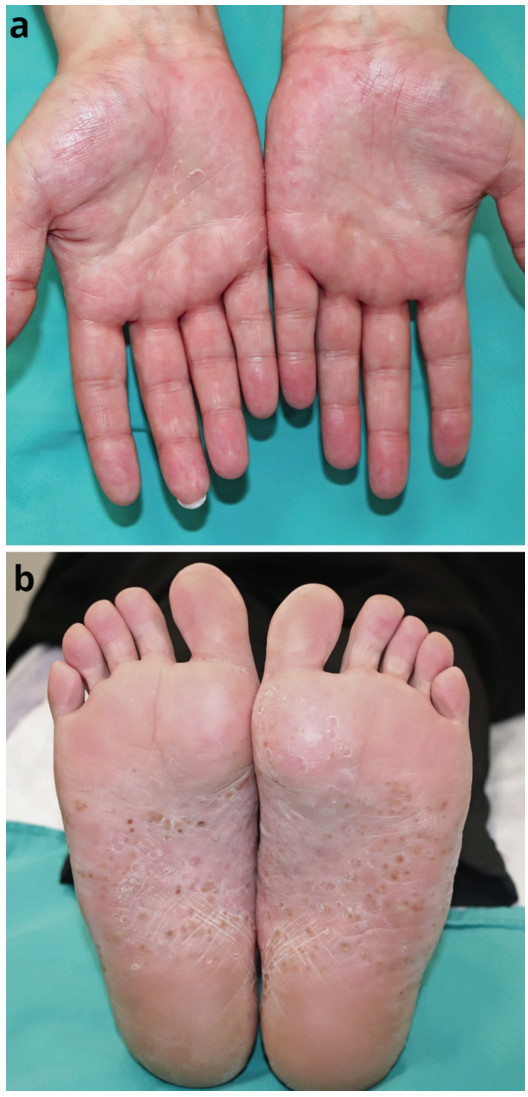

Figure 3. (a, b) Dramatic improvement achieved within 4 months after ustekinumab treatment

Ethics

Informed Consent: It was obtained.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.G.Ü., H.Y., M.Ü., N.C., Concept: Y.G.Ü., H.Y., M.Ü., N.C., Design: Y.G.Ü., H.Y., M.Ü., N.C., Data Collection or Processing: Y.G.Ü., H.Y., M.Ü., N.C., Analysis or Interpretation Y.G.Ü., H.Y., M.Ü., N.C., Literature Search: Y.G.Ü., H.Y., M.Ü., N.C., Writing: Y.G.Ü., H.Y., M.Ü., N.C.

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