CASE REPORT

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A Case of Paradoxical Acneiform Eruption Triggered by Ixekizumab

Fidan YEGİN BENER[a]

[a]Darıca Farabi Training and Research Hospital, Clinic of Dermatology, Kocaeli, Türkiye

ABSTRACT As a humanized monoclonal antibody targeting interleukin-17A, ixekizumab is increasingly used for the treatment of psoriasis vulgaris. Here, we present a male patient who developed acneiform eruption after using ixekizumab for psoriasis vulgaris. We described acneiform eruption without comedones on the anterior and posterior trunks of a 35-year-old patient with an estimated psoriasis area and severity index score of 32 at the sixth month of treatment. We successfully treated the patient within 1 month with benzoyl peroxide/clindamycin gel and oral azithromycin. Here, acneiform eruption represents a negative event that does not cause discontinuation of ixekizumab. We felt the need to write this case report to raise awareness of the association of this dermatological side effect, which we accept as a paradoxical reaction, with ixekizumab.

Keywords: Ixekizumab; acneiform eruption; paradoxical reaction

Biological agents such as interleukin (IL)-23, IL-12/23, and IL-17 inhibitors, and tumor necrosis factor alpha (TNF-α) are preferred increasingly in psoriasis vulgaris.[1] Although they have an admissible reliability profile as a group, some patients develop unexpected adverse reactions with respect to their mechanism of effect.[2] These reactions are referred to as paradoxical reactions.[3] Paradoxical reactions include a de novo or deteriorating condition that will respond to the same therapeutic agent.[3] Skin diseases considered paradoxical reaction are hidradenitis suppurativa, inflammatory bowel disease, psoriasis and psoriasiform reactions, vitiligo, acneiform reactions, and alopecia areata.[2]

Ixekizumab, which is a humanized monoclonal antibody targeting IL-17A, reduces the signs and symptoms of moderate to severe plaque psoriasis at significant levels.[4] Since this agent was recently released, the data on related side effects are not extensive.[5] The most common side effects reported were nasopharyngitis, upper respiratory tract infections, headache, and arthralgia.[4] Here we present a male patient who developed acneiform eruption after using ixekizumab for psoriasis vulgaris. We felt the need to report this case to raise awareness about the association of this dermatological side effect, which we accept as a paradoxical reaction, with ixekizumab.

CASE REPORT

A 35-year-old male patient had psoriasis vulgaris for 10 years. There were no other significant problems in his medical history. No comorbidity was recorded. Phototherapy, acitretin and methotrexate had previously been used for his disease, and the patient was unresponsive to these treatments. The patient who had an estimated psoriasis area and severity index

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Correspondence: Fidan YEGİN BENER
Darıca Farabi Training and Research Hospital, Clinic of Dermatology, Kocaeli, Türkiye
E-mail: fidanyegin@yahoo.com

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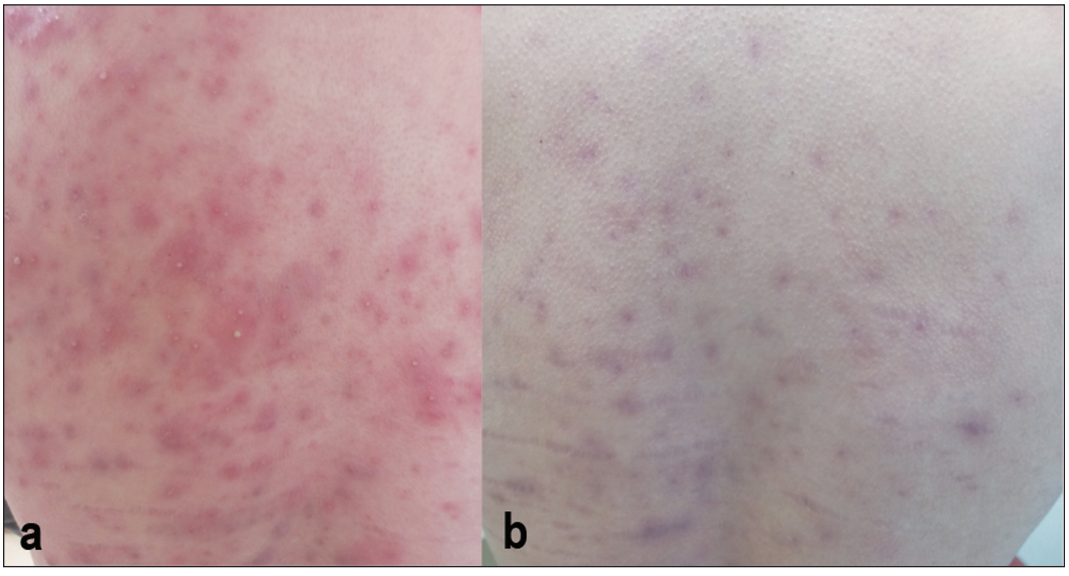

FIGURE 1: a) Acneiform eruption without comedones on the back triggered by ixekizumab therapy; **b)** Postinflammatory hyperpigmentation on the back after treatment.

(PASI) score of 32 was started on ixekizumab treatment in the standard regimen. In this respect, he received 160 mg of ixekizumab in the first week, and 80 mg of ixekizumab at 2nd, 4th, 6th, and 8th weeks, and then every 4 weeks. After the sixth injection, the psoriatic rash completely disappeared and achieving a PASI 100 response. The patient did not complain of any side effects during these periods. However, in the sixth month of the treatment, acneiform eruption without comedones was detected on the anterior and posterior trunks (Figure 1a). The patient did not give a history of other triggers that would explain his eruption, such as acute stress, dietary change, overexertion, or use of other medications. There was no pathology in biochemical and hormonal parameters. A direct potassium hydroxide smear from a pustule was negative for pityrosporum folliculitis. Normal skin flora grew on the swab sample. A combination of oral azithromycin 500 mg 3 times a week and benzoyl peroxide/clindamycin gel was started for 4 weeks as the treatment. If the lesions did not regress or increased further, it was considered that ixekizumab treatment would be stopped and acitretin started, but it was decided to continue the treatment with close control. The patient's lesions completely regressed after 1 month of treatment, leaving postinflammatory hyperpigmentation (Figure 1b).

Informed consent was obtained from the patient.

DISCUSSION

In the case presented here, we defined acneiform eruption during ixekizumab treatment is. We could not find any evidence of acneiform eruption developing during ixekizumab treatment in the literature. However, acneiform reactions were reported in a small number of cases during treatment with TNF-α inhibitors.[6-9] In these cases, the onset duration of lesions was reported to be approximately 2 months after the start of treatment.[2] However, paradoxical reactions can occur at any time from the beginning of treatment.[2] In a retrospective review of 216 and 222 cases, the average induction time of psoriatic lesions caused by TNF-α inhibitors was reported as 14 months.[10,11] In our case, the rash developed in the sixth month of treatment. As in the reported cases, there was no other factor that triggered the development of the lesion in our patient. According to the Naranjo Adverse Drug Reaction Probability Scale, with which we assessed causality, our patient was in the "probable" range with 5 points.[12] When part of the immune pathways are blocked, cytokines imbalance and autoantibodies production occur, which leads to the inflammatory process.[2] These are the hy-

potheses suggested to clarify the pathogenesis of paradoxical reactions.[2] Although most of the reported paradoxical reactions are related to the use of TNF-α inhibitors, cases related to more recently emerging biological agents such as ixekizumab are becoming more frequent.[13] Retrospectively, 2,049 paradoxical reactions caused by biological agents were examined in 313 articles.[14] 246 paradoxical reactions thought to occur due to ixekizumab have been reported as sarcoidosis-like reactions, eczema, vitiligo, hidradenitis suppurativa, alopecia areata and psoriasis, respectively.[14] If the causative agent of the inflammatory disease is the drug used to treat the disease, a paradoxical reaction is accepted to occur.[2] Since infliximab and adalimumab are used successfully off-label in the treatment of the synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome and acne conglobate, the acneiform eruption that occurs as a side effect is considered paradoxical reaction by authors.[15] Similarly, the previous experience that ixekizumab is effective in the SAPHO Syndrome strengthens the causality of the side effect in our case.

Regarding the management of paradoxical reactions, it is recommended in the literature to discontinue the drug or switch to another biological agent.[2] However, in our case, the lesions were controlled in 1 month with the treatment without the need for discontinuation of the treatment. For this reason, the emergence of a paradoxical reaction may not always require the discontinuation of the agent. As in our case, it may be sufficient to administer topical or systemic treatment for the reaction. This case is important as it was the first case to develop an acneiform eruption with the use of ixekizumab and its prognosis was very good. Although this experience is limited to the current case, it represents an adverse event that did not cause the discontinuation of acneiform eruption ixekizumab.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

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