CASE REPORT AND LITERATURE REVIEW

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ANAKINRA-INDUCED PARADOXICAL PSORIASIS AND A CASE REPORT AND REVIEW OF LITERATURE

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Abstract

Familial mediterranean fever (FMF) is the most common inherited autoinflammatory disease and is characterized by recurrent episodes of fever and serositis. Anakinra, an interleukin (IL)-1 antagonist, is commonly used in patients with FMF who are resistant or intolerant to colchicine. In this case, the FMF patient who developed paradoxical psoriasis after the use of anakinra will be discussed. Paradoxical psoriasis is a side effect of drug treatment that results in the formation of psoriasis-like plaques. Paradoxical reactions have been reported with many biological drugs (anti-tumor necriosis factor, IL17, IL-23 inhibitors, etc.) or other classes (e.g. tocilizumab). The etiology of paradoxical psoriasis is not fully understood. Paradoxical psoriasis may be caused by an exaggerated interferon response without T-cell induction. Herein, we describe a rare case that used anakinra and developed palmoplantar psoriasis after a while and evaluate the literature.

Keywords: Anakinra, paradoxial psoriasis, familial mediterranean fever, classical psoriasis

INTRODUCTION

Familial mediterranean fever (FMF) is the most common inherited autoinflammatory disease and is characterized by recurrent episodes of fever and serositis. Anakinra, an interleukin (IL)-1 antagonist, is commonly used in FMF patients who are resistant or intolerant to colchicine. An injection site reaction is the most common side effect of anakinra. It can cause headaches (1), decreased blood cell (2) or platelet counts, headaches, and increased cholesterol levels. There is limited data in the literature about anakinra causing paradoxical psoriasis. Paradoxical psoriasis is a side effect of drug treatment that results in the formation of psoriasis-like plaques on the skin. Although it was initially reported that paradoxical reactions developed only against anti-tumor necriosis factor (TNF) drugs, paradoxical psoriasis has also been shown to develop with all other biological classes. For example: anti-TNF, secucinumab, baricitinib (3), risankizumab (4), ustekinumab, rituksimab, abatacept, tocilisumab, anakinra (5-8). Herein, we describe a rare case that used anakinra and developed palmoplantar psoriasis after a while and evaluate the review of the literature.

CASE REPORT

We present a 33-year-old female patient who was diagnosed with FMF in 2010. In the patient's medical history, it was learned that she had many recurrent peritonitis and arthritis attacks that started 13 years ago, and she was diagnosed with FMF and colochicine treatment was started. There was a good response to colchicine at first. She had no illnesses in her

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medical history. She stated that there was no rheumatological or other disease in his family history, his mother, father, and siblings. Because of the severe abdominal attacks that occurred some time after starting colchicine treatment, a diagnosis of resistant FMF was made and anakinra treatment was initiated. She stated that she benefited from the treatment and that her abdominal pain attacks were gone. There were no problems with the laboratory tests performed after starting anakinra. At the patient's 2-month follow-up visit, there was a pustular psoriasis rash only in the palmar region of the hand. No past personal or familial history of psoriasis was recalled. With dermatological consultation, a biopsy was not needed, and it was decided to discontinue the treatment, considering paradoxical psoriasis developing secondary to anakinra treatment. Blood tests revealed fibrinogen: negative, C-reactive protein: 5 mg/L, and erythrocyte sedimentation rate (ESR): 18 mm/h. Proteinuria was not found. No pathology was detected in the complete blood count and biochemistry tests. Hepatitis markers were negative. The respiratory system, cardiovascular system, and abdominal examination were normal. There were no abnormalities in other rheumatological examinations. With dermatological consultation, a biopsy was not needed, and it was decided to discontinue the treatment, considering paradoxical psoriasis developing secondary to anakinra treatment. The patient was followed closely and canakinumab treatment was initiated. At the outpatient clinic visit 1 month later, rashes in the palmar region of the hands regressed. Paradoxical psoriasis did not develop again. The patient has been receiving canakinumab treatment for several years and has never experienced episodes of abdominal pain.

DISCUSSION

Here we describe a rare case of cutaneous side effects of anakinra, which induced paradoxical psoriasis. This side effect is a well-established phenomenon. Paradoxical psoriasis is a condition that results in the formation of scaly, red, psoriasis-like plaques on the skin after a period of treatment with certain medications. In paradoxical psoriasis, the palmoplantar area is often affected and it also has many forms. For example, it can be found in plaque type, guttate, pustular forms, and eczematiform forms. Paradoxical psoriasis is caused by the absence of TNF and represents an ongoing IFNα-driven acute immune inflammation independent of T-cells (6). Anakinra exhibited a higher rate of skin reactions than placebo in the clinical trial. The pathomechanism underlying paradoxical psoriasis due to anakinra treatment is difficult to explain. It showed overexpression of IL-1ra, whose action was mimicked by anakinra, in the psoriatic epidermis compared with the normal epidermis (7).

Furthermore, this resulted in a 10-fold increase in the amount of IL-Ira relative to IL-Ia in psoriatic lesions compared with normal skin (9). The increased expression of IL-1ra protein in the lower level of the lesional psoriatic epidermis may represent activation of IL-1ra in concert with other terminal differentiation-associated proteins. Alternatively, a possible explanation would be that, considering that IL-1 is a control point in the regulation of the immune response, reduction in the level of IL-1 signaling may have effects on other cytokines or regulatory cells involved in the pathogenesis of psoriasis (5).

It is unusual for it to cause paradoxical psoriasis. The estimated prevalence of paradoxical psoriasis in patients taking anakinra is unknown. Studies are needed to understand it better. There are few epidemiological data on paradoxical psoriasis in the literature. Table 1 shows a summary of the published cases of IL-1 inhibitor-associated paradoxical psoriasis in the literature (5,8).

As mentioned above, this is a very common side effect, but it has been observed to regress with discontinuation of the drug. Studies in the literature have reported that approximately 50% of cases improve or disappear after discontinuation of the biological drug. In the other 50%, these lesions persisted or appeared again. Discontinuing the medication causing paradoxical psoriasis, taking a break, or switching to another

Table 1. Literature review of IL-1 inhibitor-associated paradoxical psoriasis

Year, author	Age (years), gender	Disease	Location	Onset	Treatment	Outcome
Our study	33, female	FMF	Hands	2 months	Discontinuation of anakinra	Psoriatic lesions improved significantly
2022, Bauer-Alonso et al. (8)	74 , female	Schnitzler's syndrome	Lower limbs	1 month	Acitretin 35 mg/day) was added to anakinra	Psoriatic lesions improved significantly
2008, González-López et al. (5)	75, female	Rheumatoid arthritis	Elbows	9 months	Discontinuation of anakinra, topical steroids, and vitamin D	Psoriatic lesions improved significantly

FMF: Familial mediterranean fever

agent is an option that should be considered on a case-by-case basis. Although there is not strong evidence, there is a risk of paradoxical psoriasis development with the administration of the same biological. For cutaneous paradoxical reactions, symptom-based scores such as severity of involvement, itching, pain, and patient-reported quality of life indexes should also be evaluated. Topical or systemic treatments that are effective on the skin should be planned. Topical corticosteroids, keratolytic agents, and immunomodulators may be preferred among topical treatment options. In cases of severe paradoxical reactions (body psoriasis area >10%), traditional agents such as phototherapy and methotrexate, cyclosporine, retinoids, and oral corticosteroids may be considered.

CONCLUSION

Paradoxical psoriasis should definitely come to mind in inflammatory skin lesions that develop while using biological or other drugs. Skin biopsy should be considered in terms of differential diagnoses and should be evaluated together with dermatology. As mentioned in this case, it should not be forgotten that paradoxical psoriasis develops as a side effect of anakinra.

Ethics

Informed Consent: Written consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.A., Concept: F.A., Design: F.A., Data Collection or Processing: I.I., Analysis or Interpretation: I.I., Literature Search: I.I., Writing: I.I.

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