

Successful subcutaneous desensitization in a patient with allergy to ixekizumab

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Clinical Implications

- We report a patient diagnosed with psoriasis treated with ixekizumab (anti-IL-17A antibody), who developed an immediate local site injection reaction with positive skin test results. A successful desensitization protocol to this drug enabled the patient to receive the best therapeutic treatment.

TO THE EDITOR:

Ixekizumab is a humanized IgG₄ that binds to and neutralizes IL-17A, and is indicated as a treatment line for moderate to severe plaque psoriasis. Injection-site reactions are reported as a frequent adverse reaction (25% in a phase III trial with ixekizumab 80 mg every 2 weeks).¹

We present a 25-year-old woman who had plaque psoriasis with severe involvement of scalp, which developed into scarring alopecia. She was resistant to multiple systemic treatments.² Since 2011, she has received the following drugs as treatment: methotrexate, cyclosporine, etanercept, ustekinumab, infliximab, adalimumab, and secukinumab. Because of a partial response to the treatment and the continued negative effect on the patient's quality of life, all treatments were interrupted.

For this reason, treatment with ixekizumab 80 mg subcutaneously (containing polysorbate 80 as excipient) was prescribed. One hour after the administration of the first injection, she developed local pruritus, redness, and swelling (16 × 8 cm) at the site of injection that increased during the following 24 hours to 18 × 10 cm. Treatment with dexchlorpheniramine, ibuprofen, and topical methylprednisolone aceponate was prescribed for 10 days and resulted in remission of the lesion on fifth day. No other symptoms, desquamation, or residual lesions were observed. Skin biopsy showed the presence of perivascular lymphocytes infiltration associated with neutrophils and eosinophils in the reticular dermis compatible with lupus-like reaction. Laboratory findings ruled out autoimmune diseases. Ixekizumab was interrupted and her dermatologist referred her to our outpatient clinic for an assessment. The medical history did not show any evidence of latex allergy or atopy. The patient also had redness and swelling of 1 cm in diameter at the site of injection with the last 2 doses of secukinumab, a fully human IgG₁ anti-IL-17 mAb containing polysorbate 80 as excipient. Written informed consent was obtained before skin testing, which was performed 3 weeks after the reactions in order to avoid false-negative results. For skin testing, ixekizumab, diluted in saline

concentrations, was prepared by the Pharmacy Department. Epicutaneous tests to ixekizumab (80 mg/mL) and secukinumab (150 mg/mL) with readings at 48 and 96 hours were performed with negative results. Skin prick test (SPT) result to ixekizumab (80 mg/mL) was negative and intradermal test (IDT) result to ixekizumab (0.08 and 0.8 mg/mL) was positive in the immediate and delayed readings (24, 48 hours). Seven healthy controls had negative results on IDTs to all dilutions including full-strength concentration. SPT (150 mg/mL) and IDTs (15 mg/mL and 1.5 mg/mL) to secukinumab were performed. IDT with secukinumab at 15 mg/mL showed a positive reaction. As control, skin tests to secukinumab were also performed in 1 patient with ixekizumab hypersensitivity reaction, with negative results. SPT to polysorbate 80 (undiluted) and IDTs to polysorbate 80 (1/100 and 1/10) showed negative results, suggesting that allergy to this excipient was not involved. Despite the local skin reaction due to ixekizumab, the dermatologist decided that the patient should continue receiving the same drug, because no other therapies had been effective. She was admitted to the Allergy Department to perform a desensitization protocol. The procedure was carried out in the outpatient medical infusion center by a specialized nurse and an allergist. A 3-solution, 7-step desensitization protocol^{3,4} to ixekizumab was performed (Table I). Doses were subcutaneously administered in the abdomen, legs, and arms, every 15 minutes, starting from 0.8 mg dose. Pretreatment with cetirizine 10 mg and ranitidine 50 mg was administered 30 minutes before the procedure. After 1 hour of first and second doses, she presented local reactions consistent with erythema 3.5 cm and 2 cm in diameter, respectively. No pruritus or any other symptoms were observed. Finally, the cumulative dose of 79.55 mg was reached without any other reaction. Antihistamines and topical corticosteroids were prescribed for the following 5 days.

Two weeks later a second desensitization protocol was performed with the same pretreatment without any breakthrough reactions. The interval of 14 days used does not go over 2 times the half-life usually followed for drug desensitization. So, for the third administration, the full dose was administered, divided between both arms, following previous recommendations to avoid high local deposits of the drug,⁵ without any local reactions. Since then, she has tolerated 80 mg of ixekizumab every 2 weeks.

Pretreatment and/or posttreatment could have helped to avoid local reactions, but the positive skin test result to ixekizumab indicated an immune mechanism as well as the possibility of systemic reaction. Therefore, in the absence of therapeutic options to improve the patient's quality of life, desensitization to ixekizumab was the most effective therapeutic treatment.

Hypersensitivity reactions with the first administration of other drugs like adalimumab and etanercept have been reported,⁴ all of them with a positive skin test result, not knowing the moment of drug sensitization. However, our patient could have been sensitized during treatment with secukinumab (anti-IL-17), reinforced by the positive skin test result to secukinumab.

To our knowledge, this is the first case of desensitization to ixekizumab reported. Positive skin test results suggest that an IgE mechanism is involved, although histopathological findings also

TABLE I. Subcutaneous desensitization protocol used

Step	Time (min)	Concentration (mg/mL)	Dose (mg)
1	0	0.8	0.8
2	30	8	1.25
3	60	8	2.5
4	90	8	5
5	120	80	10
6	150	80	20
7	180	80	40

suggest that delayed hypersensitivity mechanism could also be implicated, as has been previously reported.⁶

The desensitization procedure is a well-documented technique for both immediate^{3,4,7,8} and delayed reactions,^{4,9} enabling allergic patients to receive the drug responsible if it is the best therapeutic option.

Because there were no other alternative therapies available, desensitization was carried out successfully.

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Conflicts of interest: R. Rivera-Díaz has received fees as an advisory board member, speaker, and investigator from Abbvie, Almirall, Celgene Corporation, GSK, Janssen-Cilag, Lilly, LEO Pharma, MSD, Novartis, and Pfizer. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication October 16, 2017; revised December 20, 2017; accepted for publication December 27, 2017.

Available online February 10, 2018.

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<https://doi.org/10.1016/j.jaip.2017.12.036>

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