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ADALIMUMAB DESENSITIZATION AFTER ANAPHYLACTIC REACTION

Adalimumab (Humira) is a recombinant human monoclonal antibody that inhibits tumor necrosis factor α , a substance that plays an important role in the genesis of inflammation.¹ It is used for the treatment of rheumatoid arthritis, ankylosis spondylitis, Crohn disease, psoriatic arthritis, and moderate-severe chronic plaque psoriasis.^{2,3}

The most commonly reported adverse effects are headache, rash, and nausea. In 20% of patients edema, itching, and erythema appear at the injection site.

In addition, hypersensitivity reactions have been reported. According to clinical studies, hypersensitivity reactions to adalimumab have been reported in approximately 1% of treated patients at the recommended therapeutic dose of 40 mg every 2 weeks. There have been rare postmarketing reports of anaphylaxis and/or angioedema.⁴

We report the case of a 50-year-old woman with rheumatoid arthritis. She was initially treated with steroids and nonsteroidal anti-inflammatory drugs, with no improvement in symptoms. Then she began treatment with leflunomide, with the appearance of hives in the late phase. The same symptoms appeared after administration of etanercept. The treatment was discontinued and then replaced with adalimumab.

Initially, the drug was well tolerated, but after 20 minutes from the 10th injection on, erythematous rash and urticaria appeared, which were successfully treated with intramuscular corticosteroids and antihistamines. Within a few minutes of the next dose of adalimumab, the patient experienced the same symptoms, with asthma, facial angioedema, generalized itching, and severe hypotension. She required treatment with intramuscular corticosteroids and antihistamines. Adalimumab therapy was discontinued, and the arthritis worsened.

The patient was referred by rheumatologists to our outpatient department 2 weeks after the reaction to adalimumab. Reports from the emergency department did not indicate the use of adrenaline.

Table 1. Protocol for Rapid Desensitization to Adalimumab

Dose	Concentration	Time	Volume, mL	Administered dose, mg	Cumulative dose, mg
1	1/1	0	0.1	5	5
2	1/1	30'	0.2	10	15
3	1/1	30'	0.2	10	25
4	1/1	30'	0.3	15	40

Tryptase during the reaction were not administered. The baseline tryptase test result was negative.

Skin prick tests with adalimumab were performed at least 3 weeks after the initial adverse reaction to minimize false-negative results. Monoclonal antibody was obtained as a full-strength solution or reconstituted per the manufacturer's instructions and was diluted further in normal saline for intradermal testing. Histamine prick (10 mg/mL) was used a positive control. For epicutaneous skin testing, a drop of adalimumab (50 mg/mL) was applied and pricked to the volar surface of the forearm. It elicited an unclear response because of dermographism. Then we proceeded with intradermal injections of 0.03 mL of a 1:100 and 1:10 dilution of the adalimumab strength solution, which produced negative results.

Given the clinical success of adalimumab, the patient, in agreement with the rheumatologist, agreed to be re-treated with this drug. Because of the severity of the initial reaction, despite the negative skin test results, we decided to proceed with the readministration using a desensitization protocol, as reported by Brennan et al in 2009.⁵

After informed consent was obtained from the patient, desensitization was performed in the outpatient department. The patient was monitored for vital signs, and the intensive unit care was alerted in case of anaphylactic reactions. She was premedicated with cetirizine, 10 mg, and montelukast, 10 mg, 30 minutes before the protocol.⁶ The protocol began with an initial subcutaneous dose of 5 mg (1/1), which was gradually increased until a cumulative dose of 40 mg was reached (Table 1). Dose escalation occurred every 30 minutes. The complete process took 2 hours, and the patient did not develop local or systemic reactions.

In the second week, the patient received 20 mg plus 20 mg after 30 minutes, with premedication, and then she received the full dose at once in the third and fourth weeks. She experienced a significant clinical improvement during the following weeks. The patient continued the treatment every 2 weeks, as suggested by her rheumatologist. Currently, she has been receiving therapy for 2 years without any adverse effects.

Our desensitization protocol provided for the attainment of the therapeutic dose in only 2 hours, with premedication (antihistamines and antileukotrienes) for the first 4 sessions.

In patients with moderate to severe reactions, suggestive of IgE-mediated reactions, even if doubt or negative skin test results occur, induction or tolerance is a recommended option. In the literature, there are some reports of desensitization protocols with other biological drugs but only 1 report with adalimumab for generalized urticaria and rhinitis. In this case, the desensitization was performed with a standard protocol, with achievement of the maximum dose in 6 hours.⁷

We report the first case, to our knowledge, of anaphylactic shock with adalimumab, with inconclusive skin test results. The

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rush desensitization protocol, preceded by premedication, was well tolerated by patients and successfully completed.

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Erratum

In the article “Autologous Plasma Skin Test” by Núñez-Acedvedo et al (*Ann Allergy Asthma Immunol* 2011;106:175-176), the last three authors’ last names were missing

hyphens. The corrected names are as follows: María Luisa González-Gutiérrez, MD; Consuelo Martínez-Cócera, MD, PhD; Montserrat Fernández-Rivas, MD.