Unsuccessful Desensitization to Paclitaxel in a Patient With High Basophil Sensitivity

Kopač P[1,2]*, Koren A[1]*, Jošt M[1], Mangaroski D[3], Lainščak M[4], Korošec P[1]

[1]*University Clinic of Respiratory and Allergic Diseases, Golnik, Slovenia*

[2]*Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia*

[3]*Institute of Oncology, Ljubljana, Slovenia*

[4]*Division of Cardiology, General Hospital Murska Sobota, Murska Sobota, Slovenia*

[*]*These authors contributed equally to this article and are joint first authors.*

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Immediate hypersensitivity reactions (HSRs) occur during the administration of taxanes in 10%-30% of patients and are severe in up to 10% [1]. Desensitization has proven to be safe and successful in most cases of HSR, enabling patients to be retreated with taxanes [2]. However, even during desensitization, HSRs can occur in 15% of treated patients regardless of the severity of the initial reaction or skin test results. Reactions during desensitization are severe in 13%, regardless of the initial reaction. Since measurement of specific IgE to taxanes is not commercially available [3], the basophil activation test (BAT) could prove useful for detecting IgE-mediated reactions. The BAT result was already shown to be a relevant biomarker of the outcome of rapid desensitization in allergy to platinum compounds [4]. Data on diagnostic testing for taxane allergy are scarce and often limited to case reports [1,3,5]. To the best of our knowledge, the utility of BAT in taxane allergy has not been fully evaluated. In food and insect venom, the allergic sensitivity of basophils can predict the severity and threshold of allergic reactions to allergens [6], although such experiences in drug allergies are limited [4,7]. We report a case of a highly positive BAT result to paclitaxel in a patient with severe HSR at very low concentrations of paclitaxel during initial treatment and an attempt at desensitization.

A 50-year-old woman with estrogen receptor–positive and HER2-positive breast cancer was treated with adjuvant trastuzumab, pertuzumab, and paclitaxel. The first two 3-weekly applications of both anti-HER-2 drugs were uneventful. During the first 5 minutes of the second weekly infusion of paclitaxel, the patient developed a grade 4 reaction with abdominal cramps, dyspnea, generalized erythema, hypotension (blood pressure, 70/40 mmHg), tachycardia (110 bpm), and reduction in peripheral oxygenation to 80%.

She was treated with methylprednisolone, clemastine, saline, and oxygen. The next day, chemotherapy with paclitaxel was restarted, again 1 hour after premedication with clemastine and dexamethasone. After receiving 15 mL of the paclitaxel infusion, she developed a grade 1 reaction with abdominal cramps, dyspnea, heart rate 120 bpm, and oxygen saturation 95%, blood pressure 120/80 mmHg. The infusion was stopped, and methylprednisolone and clemastine were administered. Tryptase was not measured during either reaction.

The skin prick test with paclitaxel was negative (1 mg/mL); however, the intradermal test was positive at 0.01 mg/mL (but negative at 0.001 mg/mL). Baseline serum tryptase was normal (5.1 µg/L). To confirm the allergenic activity of paclitaxel sensitization, we performed a BAT, in which basophils were identified as CD123-positive and HLA-DR–negative cells, while CD63 was used as a marker of basophil activation. For the controls, the whole blood cells were exposed to stimulation buffer alone (negative control) or to 0.55 µg/mL of anti-FcεRI mAb and 50 µg/mL of fMLP (positive control) [8,9]. An example of the gating strategy used for the flow cytometry basophil analysis is shown in Figure S1. The percentage of CD63+ basophils was 2%, 67%, 62%, 69%, and 80% after stimulation with paclitaxel from 0.005 to 50 µg/mL, respectively. Thus, the BAT result was highly positive, even at low allergen concentrations (Figure). The BAT response to paclitaxel in 3 healthy controls and in 3 paclitaxel-exposed nonallergic controls was negative (all <5% CD63+ basophils; 0.005 to 50 µg/mL). After premedication with montelukast 10 mg, ranitidine 300 mg, clemastine 2 mg, and methylprednisolone 100 mg, we performed a 12-step (3 bags) desensitization protocol. At the cumulative dose of 0.022 mg of paclitaxel, the patient already had a reaction with generalized erythema and pruritus. She was treated with adrenaline and clemastine, and desensitization was stopped.

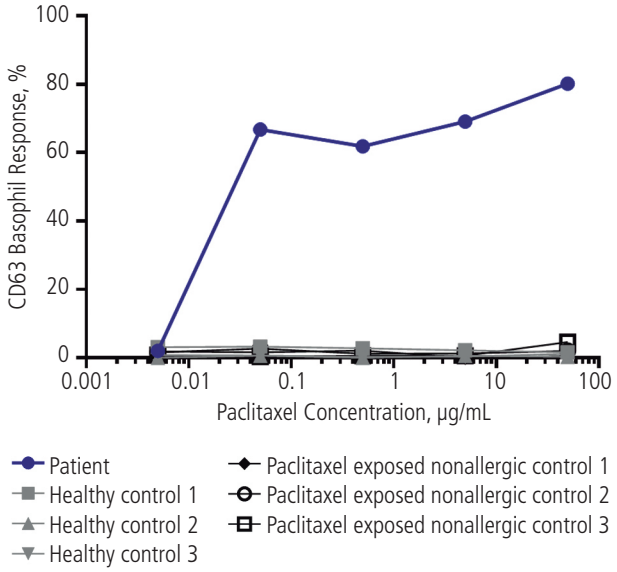

Figure. Results of the basophil activation test in response to stimulation with various concentrations of paclitaxel (0.005-50 µg/mL) in a paclitaxel-allergic patient, 3 healthy controls, and 3 paclitaxel-exposed nonallergic controls.

The next day, a 16-step protocol was started, and she developed generalized urticaria after 0.010 mg of paclitaxel. The infusion was stopped, and the patient was treated with adrenaline and clemastine. After 30 minutes, desensitization was continued, but the patient experienced another reaction with generalized urticaria after a cumulative dose of 0.023 mg paclitaxel, and treatment was stopped. We did consider administering omalizumab, as favorable data have been reported with respect to drug hypersensitivity [10]. However, the patient declined this option, as pretreatment with omalizumab would have postponed her chemotherapy.

In the present case, the BAT provided important additional information on the mechanisms and severity of HSR to paclitaxel. As the reaction occurred during the second application and the BAT result was positive, we believe that the reaction was IgE-mediated, although mast cells could be activated through other mechanisms. High basophil sensitivity at low concentrations of paclitaxel may be associated with a lower threshold and a more severe allergic reaction. Our observations suggest that BAT, if available, could be important in risk stratification procedures before desensitization, as it could help to identify patients at high risk for severe HSRs during desensitization and even failure to desensitize.

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Conflicts of Interest

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Peter Kopač
University Clinic of Respiratory and Allergic Diseases
Golnik 36
4204 Golnik, Slovenia
E-mail: peter.kopac@klinika-golnik

