

Letters

POSITIVE BASOPHIL ACTIVATION TEST RESULT IN A PATIENT WITH ACUTE URTICARIA INDUCED BY CETIRIZINE AND DESLORATADINE

Antihistamines are safe and effective drugs widely used to treat allergic diseases. Occasionally, skin reactions to antihistamines occur, the cause of which remains unknown. Several studies have suggested mechanisms for these reactions, including type IV reactions, malfunction of the histamine₁ (H₁)-receptor, and on rare occasions IgE-mediated reactions.^{1,2} Because in cases of acute urticaria mistakes can lead to misdiagnosis and incorrect treatment, treating this condition remains a challenge for allergologists.

We describe a 32-year-old woman diagnosed as having rhinitis and asthma with sensitization to *Artemisia vulgaris* pollen and cat dander and also nonsteroidal anti-inflammatory drug intolerance. Desloratadine, a previously tolerated drug, was used to treat a cold. Five hours after its ingestion, the patient developed erythema and pruritic 4- to 5-mm hives on the scalp, face, neck, thorax, and legs. This clinical profile improved within hours after administration of intramuscular methylprednisolone. Several days later she first ingested generic cetirizine and developed the same cutaneous profile 5 hours later.

Skin prick tests were performed with desloratadine (5 mg/mL), cetirizine (10 mg/mL), loratadine (10 mg/mL), levocetirizine (5 mg/mL), ebastine (10 mg/mL), fexofenadine (40 mg/mL), dexchlorpheniramine (6 mg/mL), and hydroxyzine (25 mg/mL) tablets crushed and diluted in saline³ and with levocabastine and azelastine eye drops undiluted; the results of all these tests were negative. After informed consent was obtained, double-blind, placebo-controlled, oral or ocular challenge tests were performed with those drugs in the Drug Allergy Unit of our department. Oral challenges were started with one-quarter of the therapeutic dose and increased every 30 minutes to reach the full dose or until reaction occurred. Ocular challenges were performed with full-strength drug. Negative results

for placebo, dexchlorpheniramine, and levocabastine were obtained, whereas the patient developed a urticarial reaction 5 to 6 hours after the administration of the other drugs.

The basophil activation test (BAT) measures the expression of markers such as CD63 or CD203c proteins at the surface of the basophils when they are activated in the presence of drugs. These molecules can be detected by flow cytometry using monoclonal anti-IgE antibodies.⁴ BATs were performed with all previously listed antihistamines except fexofenadine and also with hydroxyzine and azelastine. The results of all these tests were negative except for the implicated drugs desloratadine, cetirizine, ebastine, and hydroxyzine (Table 1).

Histamine is a chemical mediator of inflammation produced and stored in mast cells and basophils, and it is composed of a heterocyclic aromatic ring connected to an ethylamine group. Antihistamines are pharmacologic inverse agonists of histamine at the H₁-receptor sites trying to shift the equilibrium toward the inactive state, preventing an H₁ response.¹

Few cases of urticaria due to multiple antihistamines have been previously reported.^{1,2,5,6} Skin prick,^{1,2,5,6} intradermal,⁵ and epicutaneous^{1,2,6} tests were performed; the results of most of these results were negative. Even though skin prick test results were positive to some antihistamines,^{1,2} in other cases² and in our case, positive oral challenge results were found with negative skin prick test results.

In vitro tests are useful to reduce the potential risks of in vivo tests (skin and/or challenge). There are different methods for detecting IgE antibodies to drugs involved in type 1 reactions, such as immunoassay, radioimmunoassay, enzyme-linked immunosorbent assay, fluorescent enzyme immunoassay, BAT, and tests of mediator release (histamine, tryptase, and leukotrienes).⁴ In previous reports, in vitro enzyme-linked immunosorbent assay,⁵ lymphocyte transformation test and human basophil degranulation test,⁷ and histamine release test¹ were performed with some antihistamines, with negative results. These tests are not available in our hospital.

In our case, BAT results were positive in half of the cases in which the challenge test result was positive. Thus, we conclude

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Table 1. Results of Controlled Challenges and Basophil Activation Tests

Antihistamine	Classification		Dose	Challenge			Basophil activation test result
	Family	Generation		Route	Reaction	Time until onset	
Desloratadine	Piperidine	2	5 mg	Oral	+	4 h	+
Loratadine	Piperidine	2	10 mg	Oral	+	7–8 h	–
Cetirizine	Piperazine	2	10 mg	Oral	+	3 h 30 min	+
Levocetirizine	Piperazine	2	5 mg	Oral	+	5 h	–
Ebastine	Piperidine	2	10 mg	Oral	+	5 h	+
Fexofenadine	Piperidine	2	120 mg	Oral	+	8–9 h	NP
Dexchlorpheniramine	Alkylamine	1	6 mg	Oral	–	–	–
Levocabastine	Piperidine	2	0.05%	Ocular	–	–	–
Hydroxyzine	Piperazine	1	25 mg	NP	–	–	+
Azelastine	Phtalazinone	2	140 µg	NP	–	–	–

Abbreviation: NP, not performed.

Symbols: +, positive (urticaria); –, negative.

that the mechanism is IgE mediated and that the sensitization route was the previous intake of desloratadine to treat the patient's rhinitis. Sensitivity and specificity would be similar to other drugs (approximately 50% and 93.3% for β -lactams, 91.7% and 100% for muscle relaxants, and 42.3%-56.7% and 83%-100% in selective allergy to nonsteroidal anti-inflammatory drugs, respectively).⁴

In summary, we present a case of acute urticaria due to multiple antihistamines regardless of family and/or generation. To our knowledge, we also communicate for the first time the usefulness of BAT in hypersensitivity to antihistamines. Because of the limited diagnostic value of skin tests, BAT may be considered as a complementary tool and a challenge is essential to reach a definitive diagnosis. However, a larger number of patients should be studied in the future to reach conclusions.

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TRIMMING CYPRESS TREE HEDGES AND ITS EFFECTS ON SUBSEQUENT POLLINATION

Cypress pollen allergy causes major pollinosis around the Mediterranean basin¹ and affects both atopic and nonatopic individuals.² Primary prevention of cypress pollinosis aims at lowering the population exposure. Cutting or trimming trees is sometimes suggested to reduce pollen emission. To validate this approach, we compared pollen counts from traps located near trimmed and nontrimmed parts of a cypress hedge.

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A 10-m-high *Cupressus sempervirens* hedge, located in a school in Montpellier, France, was chosen for this study. The hedge, oriented southeast-northwest, was 66 m long and up to 6 m wide and located on the wind side of the school building that was located 20 m away. During fall 2004 (before cypress pollination), half of the hedge was trimmed 1.5 m away from the trunk. A total of 25 m³ of cut foliage was removed. The other half of the hedge was trimmed during May 2005.

For methodologic and practical reasons, pollen counts at the foot of the hedge and in the classroom were made with Cour pollen receptors frequently used in agronomy and pollen allergy studies.^{3,4} Like pluviometers, Cour traps, situated 1.2 m above the ground, allow pollen sedimentation through a horizontal filter made of hydrophilic gauze with a 400-cm² sampling surface. During weeks 9 to 13 in 2005 and 2006, 2 Cour pollen receptors were set approximately 10 m away from the nontrimmed (trap A) and the trimmed (trap B) parts of the hedge. A third pollen trap (trap C) was installed in a classroom, in front of the uncut part of the hedge, approximately 20 m away from the hedge. Pollen counts were performed on a weekly basis from February 28 to April 4, 2005, and from March 1 to April 18, 2006. Results were expressed in number of pollen grains per day and per square centimeter of filter. The weekly regional pollen counts (grains per cubic meter) in Montpellier were estimated by averaging daily observations from a Lanzoni volumetric spore trap^{5,6} set up 400 m away from the hedge on the top of a 5-floor building. To test for a significant effect of trimming, pollen counts from traps A and B were analyzed with the R statistical software package⁷ according to the following generalized linear model: $\log(\text{count}) \sim \text{pollenTrap} + \text{year} + \text{pollenTrap} \times \text{year} + \text{week-within-year}$. We used the quasi Poisson link function to account for overdispersion ($\Phi = 16$).

Cypress pollen counts are presented in Figure 1. During 2005, pollination lasted for 3 weeks. The peak pollination occurred on trap A and equaled 2,037 pollen grains/cm² daily during week 11. The curves for the 4 traps showed the same trend. The cumulated pollen counts on trap A reached 6,241 grains/cm², whereas on trap B (in front of the cut hedge) only 4,702 pollen grains/cm² were counted. Only 11 grains/cm² were monitored in the classroom.

In 2006, the peak pollination also occurred during week 11, and all 4 curves demonstrated a similar overall trend with lower differences among traps. The generalized linear model statistical analysis of pollen counts during the 2 years revealed a significant effect of weeks ($P < .001$) and a significant interaction between year and traps ($P = .005$) but no trap effect. The within-year subanalysis showed that in 2005 pollen counts in trap A were lower than the pollen counts in trap B ($P = .01$), whereas no differences were observed in 2006 ($P = .10$). No statistical test was performed for trap C because the pollen counts were too low.

In 2005, pollen counts collected downwind of the nontrimmed part of the hedge (6,241 grains/cm²) were 33% greater than pollen counts under the trimmed part of the same hedge (4,702 grains/cm²). This significant difference is attributable to the removal of part of the male cones by trimming. Because of the proximity of the trimmed and nontrimmed hedge parts, it is likely that some pollen in trap B came from the nontrimmed part, underestimating the effect of trimming. Other pollen grains would come from the male cones and from the regional airborne pollen as suggested by the Lanzoni trap counts. During the 2006 pollination season, pollen counts on both