Doxylamine Allergy in a Pregnant Woman: Suitability of the Basophil Activation Test

Rial MJ1,2, Fernández-Nieto M1,2, Rodrigo-Muñoz JM1, Sastre B2,3, Sastre J1,2, del Pozo V2,3
1Allergy Department, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain
2Immunology Department, Instituto de Investigación Sanitaria Fundación Jiménez Díaz, Madrid, Spain
3CIBER de Enfermedades Respiratorias (CIBERES)

doi: 10.18176/jiaci.0311

Keywords: Drug allergy. Doxylamine. Basophil activation test. Pregnancy. Antihistamines.


Nausea and vomiting are very common in pregnancy, affecting 75%-80% of pregnant women. The most serious type of nausea and vomiting, known as hyperemesis gravidarum, is much less frequent and affects 0.3%-3% of all pregnant women [1]. Hyperemesis gravidarum can be treated using 3 options [2]: doxylamine 10 mg + pyridoxine 10 mg (Cariban, Inibsa Ginecología S.A.), dimenhydrinate, and metoclopramide. The development of allergy to the first treatment option (doxylamine + pyridoxine) requires the prescription of second-line drugs with a higher rate of adverse effects in a particularly sensitive group. Because of their rarity, these hypersensitivity reactions may be misdiagnosed. We present the first report of a case of hypersensitivity to doxylamine demonstrated using the basophil activation test (BAT).

A 34-year-old primigravida was referred to our allergy clinic with intractable vomiting that started 4 weeks after becoming pregnant. Since the vomiting did not resolve with dietary measures, her obstetrician prescribed 4 tablets daily of doxylamine succinate 10 mg + pyridoxine hydrochloride 10 mg. After less than 60 minutes of taking the first 2 tablets, the patient experienced dizziness, shortness of breath, and generalized pruritus. Consequently, she went to the emergency department, where she was diagnosed with hypotension (70/52 mmHg) and urticaria on the trunk and extremities, although oxygen saturation was appropriate. She received intravenous hydrocortisone and dextchlorpheniramine, and her symptoms resolved within 2 hours. When the patient came to our allergy clinic, she was diagnosed with anaphylaxis caused by Cariban. Intraepidermal tests were performed using the prick-by-prick technique with oral doxylamine 25 mg (Dormidina sachets, Laboratorios Pensa). No tests were performed with pyridoxine (Benadon, Teofarma), because the drug was not available in our clinic. A positive result was obtained with doxylamine (8×6 mm) in the patient and a negative result (2×1 mm) in a nonatopic control. As the results of the skin tests were positive and the reaction under study was very serious, we decided not to carry out an oral challenge test to confirm the diagnosis, preferring a BAT instead. The BAT has previously proven useful for confirming the involvement of a drug in cases of anaphylaxis [3-7]. It was performed with the patient’s blood sample and blood from a nonatopic healthy control. The population of basophils was defined as CD63+/SSClow by flow cytometry. The results are expressed as the percentage of CD63+ basophils (activated basophils). The BAT result was positive, with >10% of the patient’s basophils activated after stimulation with the second smallest dose of doxylamine (10 ng). Activation increased in a dose-dependent manner to levels of over 40%, similar to those of the positive control (10 μL) with the highest dose of doxylamine (10 μg) (Figure). No activation of basophils was observed in the nonallergic control after stimulation with the allergen, yet the control basophils were activated in the patient with the positive stimulation control (Figure). We also tested whether the commercial drug activated basophils from the patient and observed that when we incubated the patient’s basophils with 200 μg of Cariban, activation was over 10% in the patient (12%), that is, higher than the nonallergic control basophils stimulated with the same amount of Cariban (3.6%).

Taken together, our results enable us to confirm that the patient in the present case is allergic to doxylamine, both in the pure form and as Cariban.

Diagnosis of drug allergy is difficult, because the underlying mechanisms are not yet clear and the allergenic structures are mostly unknown. Although challenge testing is the gold standard for the diagnosis of drug allergies, there are potential risks of systemic reactions. In the case of the patient we report, the reaction after exposure to doxylamine was a life-threatening reaction. BAT has several advantages over conventional diagnostic tools, namely, safety, specificity, and the possibility of evaluating multiple drugs at the same time. BAT has been validated for the diagnosis of hypersensitivity to β-lactams, aspirin/nonsteroidal antiinflammatory drugs, contrast media, and fluoroquinolones [8]. To our knowledge, this is the first time BAT has been used for the diagnosis of allergy to doxylamine. In conclusion, we suggest that BAT is a useful diagnostic tool when deciding on the clinical approach to patients with hypersensitivity to medications.
Manuscript received July 2, 2018; accepted for publication August 27, 2018.

Manuel Rial Prado
Allergy Department
Hospital Universitario Fundación Jiménez Díaz
Madrid, Spain
E-mail: manuel.rial@quironsalud.es

Funding

The authors declare that no funding was received for the present study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References


Moderate Asymptomatic Subacute Eosinophilia Secondary to Simvastatin Therapy

de las Marinas Alvarez MD 1, López Calatayud V 1, Solaz Garrido B 2, Catalá Bauset M 3, Montesinos Carbonell M 4, Albert Sánchez P 5
1Department of Allergology, Policlínico Valencia, Valencia, Spain
2Digestive Medicine Department, Policlínico Valencia, Valencia, Spain
3Endocrinology Department, Policlínico Valencia, Valencia, Spain
4Gynecology Department, Policlínico Valencia, Valencia, Spain
5Clinical Analysis Laboratory, Policlínico Valencia, Valencia, Spain

In allergological practice, we often see patients with serum eosinophil counts above normal. These elevations are generally mild and are easily related to an atopic background. We also see patients requiring a differential diagnosis owing to eosinophilia of indeterminate origin. The present case seeks to alert clinicians to the need to investigate the etiology of casually identified eosinophilia, particularly with the purpose of diagnosing underlying disorders that are not clinically manifest at the time (eg, proliferative syndromes, parasitoses, drugs, autoimmune diseases) and could cause collateral damage owing to eosinophilic infiltration of various tissues if not adequately treated. In general, all cases of moderate to severe eosinophilia persisting for over 6 months should be monitored through laboratory tests and echocardiography, with administration of adequate corrective treatment, even cytoreductive medication [1-3].

We present the case of a 28-year-old woman who consulted owing to the casual identification of marked eosinophilia (3000/µL, 40%) in a blood count requested by her gynecologist for the evaluation of an ovarian cyst that was casually detected during a routine annual ultrasound exploration. The blood count was repeated 1 week later, with a manual reading of the blood smear, and confirmed persistent eosinophilia of similar magnitude (2980/µL, 36.6%). The case history showed that the eosinophil counts had always been under 200/µL in previous years. The patient therefore consulted the allergology clinic, where a detailed history was taken, with assessment of the most common possible causes (especially atopic disease and parasitic infestation). She reported having had mild symptoms of nonseasonal rhinitis for several years and mild dyspepsia, with no malaise, altered bowel habit, weight loss, fever, or other signs or symptoms of systemic disease or abnormalities associated with infiltration of organs by eosinophils. The...