



Allergologia et immunopathologia

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RESEARCH LETTERS

Immediate reaction to articaine

To the Editor:

A 50-year-old woman was referred from dental clinic to be evaluated for hypersensitivity for articaine. Previously 3 years ago she had urticaria in 10–15 min after administration of a local anaesthetic agent for a dental procedure. She did not know the name of the local anaesthetic agent. For the last 6 years she had been followed with diagnoses of chronic urticaria and angioedema in dermatology department. She was treated with various antihistamines, systemic corticosteroids, montelukast, azathiopurine and cyclosporine. In her previous examinations she was allergic to house dust mite and autologous serum skin test was found to be negative. She did not report any adverse drug reactions apart from the one she had with local anaesthetic mentioned above. The patient had no family history of allergy. She was on daily levocetirizine therapy for the last 4 months.

Skin tests were planned with articaine after cessation of antihistamines for 5 days and provided informed consent for allergologic workup. Positive (histamine) and negative (normal saline solution) controls were also carried out. Skin prick test was negative for articaine HCl/epinephrine HCl (Ultracaine; Sanofi aventis) (1/1). During intradermal test with articaine (1/100) in the tenth minute 30 mm × 30 mm endurance and redness ensued together with globus hystericus and paraesthesia in tongue and the test was ended. The physical examination did not reveal any systemic sign of allergic reaction and the symptoms resolved completely in a few minutes without any medical intervention. This result suggested the involvement of a type I allergic reaction. Subcutaneous challenge was not performed for ethical reasons since intradermal test with articaine HCl/epinephrine HCl (1/100) was positive. Since no product containing articaine HCl without epinephrine is not available in the market, in order to exclude hypersensitivity to epinephrine, we also performed skin prick and intradermal tests with epinephrine HCl and found negative. Accordingly the patient was evaluated to be allergic to articaine. Afterwards an allergologic workup with prilocaine was planned to determine its safety for the patient. The patient presented negative prick and intradermal test with prilocaine HCl (Citanest; Astra Zeneca). Subcutaneous challenge with prilocaine 0.1 ml and 1 ml was performed and came out to be negative and no adverse reactions were observed. In the following day dental

procedure was performed successfully without any adverse reaction with prilocaine.

Local anaesthetics drugs are widely used since they allow performance of procedures to be safely and comfortably especially in dental and minor surgical interventions. Unfortunately adverse reactions may limit their use although allergic reactions to local anaesthetics are reported to be less than 1% in the literature.¹ The adverse reactions comprise of symptoms unrelated to the local anaesthetic, such as psychomotor reactions, dose-related toxic reactions and idiosyncratic or true allergic reactions in susceptible individuals. A definite diagnosis of drug hypersensitivity requires allergologic workup with the suspected drug.²

Adverse reactions against local anaesthetics present as objective symptoms in 87.6% of the cases; such as urticaria, angioedema, rhinitis, dyspnoea, vomiting, chills, speech disorder, tachycardia, arrhythmia, loss of consciousness and cardiac arrest and as subjective symptoms in 12.4%; such as fear, sensation of heat, headache, vertigo, paraesthesia, nausea, tenesmus and globus hystericus.¹

The general thought about skin tests being not useful with amide-type local anaesthetic agents is recently been changed by some recent studies demonstrating positive skin tests in some local anaesthetic allergy cases.^{3–5} Articaine which belongs to amide-type local anaesthetic group, is the most commonly used local anaesthetic for dental procedures. The studies carried out suggest that there is cross-reactivity among local anaesthetics of the amide group.³ However tolerance to articaine may be possible because of its different chemical structure with thiophene ring, when other amide local anaesthetics are allergic, no matter it should be kept in mind that pattern of cross-reactivity may vary in different patients.^{4,5}

Unfortunately, we were unable to find a marketed product containing articaine without epinephrine to perform skin tests so we also performed skin prick and intradermal tests with epinephrine in order to exclude that the hypersensitivity reaction observed was due to epinephrine. The latter test being negative affirmed that the positive intradermal test implied articaine hypersensitivity. In the case presented subjective symptoms observed following intradermal articaine administration could be more exaggerated if we could have eliminated the probable effect of epinephrine in slowing down the allergic reaction.

With this case we conclude that different amide-group local anaesthetics agents could be used safely after

allergologic workup in hypersensitive patients. Secondly we mention that skin tests are advisable such as in the presented case skin tests may yield positive results thus a generalized allergic reaction could be prevented.

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Urticaria pigmentosa in a female patient with celiac disease: Response to a gluten-free diet

To the Editor,

Systemic mastocytosis (SM) is characterised by the accumulation of neoplastic mast cells in bone marrow and other organs. In contrast with normal mast cells, in SM these cells usually express CD25.¹ Urticaria pigmentosa (UP) constitutes the most common form of cutaneous affectation caused by SM. Urticaria pigmentosa, which is characterised by pruritus and reddish or violet skin lesions usually caused by the release of histamine and other inflammatory mediators, is generally unleashed after exposure to physical stimuli, changes in temperature, anxiety, or medication. Neoplastic mast cells may also infiltrate the gastrointestinal (GI) tract; in fact, GI symptoms in the form of colicky abdominal pain and diarrhoea are common in both SM and UP and may markedly alter patient quality of life. In this context, an increase in mast cells in GI biopsies has been proposed as a helpful criterion to establish the diagnosis of SM. Still, while an increase in mast cells has been reported in various inflammatory diseases, mast cell density has not been systematically evaluated in many GI disorders.

We have had the opportunity to study a female patient diagnosed with SM while also suffering from celiac disease (CD) in whom the establishment and maintenance of a gluten-free diet led to a good response in both diseases.

The subject was a 21-year-old female suffering from recurrent episodes of headache for the past five years and who had contracted infectious mononucleosis at the age of 19. In the family background, several first-degree maternal relatives had been diagnosed with CD, including the patient's mother, grandfather, three uncles, and four cousins. The patient had been presenting a persistent maculopapular rash on the neck and upper chest for the past three years. Armpit skin biopsies demonstrated multifocal and diffuse aggregates of tryptase(+) mast cells with ovoid nuclei in papillary dermis extending into the reticular dermis. CD117/*c-kit* immunostaining also resulted positive.

Bone marrow aspirate resulted normal; subsequently, the *c-kit* D816V activating mutation was found on archived formalin-fixed paraffin-embedded skin tissue, which led to a diagnosis of SM in its childhood form of UP, including systemic manifestations.²

Physical exploration showed neck adenopathies and mild splenomegaly (with a bipolar diameter of 14 cm). Every two or three months the patient had recurrent episodes of oedema in the left eyelid (Fig. 1) associated with increased tryptase serum levels around 30 ng/mL, which resolved with intravenous steroid boluses. She also suffered pain in both legs and frequent episodes of generalised pruritus. Blood cell counts were normal, with the eosinophils count being below 200 cells/ μ L. Liver function tests were normal as were total IgE serum levels (24 kU/L). Grass-allergen specific IgE levels were therefore not determined.

Furthermore, she suffered from repeated episodes of abdominal pain and gastro-oesophageal reflux, along with sporadic diarrhoea. Because of this, she was referred to our Gastroenterology Department.

Analytical studies also showed decreased levels of cholesterol down to 120 mg/dL (normal 150–250); decreased folic acid serum levels (2.2 ng/mL, normal 4.6–18.7) and reduced levels of vitamin B12 (193 ng/mL, normal 211–946) without



Figure 1 Left eyelid oedema in a woman suffering from systemic mastocytosis.