Urticaria due to pentoxyfylline

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Key words: pentoxyfylline; urticaria; xanthines.

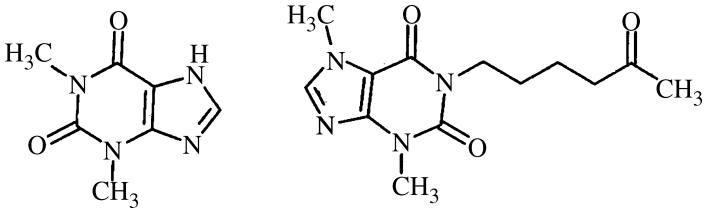

Figure 1. Molecular structure of theophylline and pentoxyfylline respectively.

Pentoxyfylline is a purine derivative. The purines include adenine, guanine, and alkaloids-like caffeine and theophylline. Uric acid is the metabolic end-product of purine metabolism.

We report the first case of urticaria due to pentoxyfylline.

Pentoxyfylline is used as a vasodilator to relieve symptoms in some cases of intermittent claudication. No immediate hypersensitivity reactions have been described with this product to date.

We report the case of a 60-year-old man who had been treated for 2 days with Hemovas® (Gupo Ferrer, Division Robert, Barcelona, Spain) 400 mg and consulted for the appearance of red macules that developed into highly pruriginous papules that spread until becoming generalized and led the patient to seek emergency care.

One month later, administration of the medication was renewed. Immediately after taking the first tablet of pentoxyfylline 400 mg, the patient presented generalized wheals that remitted within hours of taking antihistamines.

The patient gave written consent to undergo hypersensitivity studies. Skin prick and intradermal tests were performed with pentoxyfylline, euphylline, theophylline, allopurinol, azathioprine, and 6-mercaptopurine. Results were positive for intradermal pentoxyfylline, 0.2 mg/ml, in the immediate reading. In 10 controls, the readings were uniformly negative. In response to oral challenge with theophylline 200 mg, the patient reached a cumulative dose of 350 mg with good tolerance.

When given therapeutic doses of pentoxyfylline 400 mg, the patient presented within 1 h of the last dose (cumulative dose of 540 mg) generalized, highly pruriginous erythematous papules that remitted with outpatient oral treatment. He was diagnosed of immediate hypersensitivity to pentoxyfylline.

In the literature we found reports of the pentoxyfylline use as a modulator of immune activity through the production of cytokines with anti-inflammatory effects. Among the xanthine derivatives, there are studies of theophylline, which also has immunomodulator activity (1–3).

We found no published reports of immediate hypersensitivity reactions to pentoxyfylline, and few reports of reactions to methylxanthines, including caffeine and cola products (4, 5).

The responsible mechanism appears to be immunoglobulin E (IgE)-mediated hypersensitivity in view of the results of allergy tests. In addition, as has been reported by other authors, the patient showed tolerance to oral theophylline exposure, thus excluding pharmacologic cross-reactions because of molecular similarity to pentoxyfylline (Fig. 1).

Consequently, we report what we believe is the first case in the literature of acute urticaria triggered by pentoxyfylline and confirmed by skin tests and an oral challenge.

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Anaphylaxis to macrogol 4000 after a parenteral corticoid injection

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Key words: anaphylaxis; betamethasone; hypersensitivity; intradermal tests; macrogols; polyethylenes.

Polyethyelene glycols (PEGs, or macrogols in the European pharmaceutical industry) are used in numerous food, cosmetic and pharmaceutical preparations because of their solvent power

We report the first case of a grade III alergic hypersensitivity reaction because of macrogols.

for substances otherwise sparingly soluble in water. We report the first case of a severe immunoglobulin (Ig)E-mediated hypersensitivity reaction (1) because of betamethasone (Diprostène®) (Scheringh Plough, Levallois-Perret France) in which the allergenic determinant involved was macrogol 4000.

A 45-year-old man was scheduled in a rheumatologist office for a shoulder infiltration with betamethasone (Diprostène®). He denied any allergy to food, drugs or latex. Within 2 min following the intra-articular injection, a nasal pruritus and a conjonctivis appeared while the patient had to lie down because of dizziness. At the same time, a dyspnoea associated to a tongue's oedema and a generalized urticaria were observed while a drop in blood pressure occurred. No epinephrine was injected by the practitioner. The paramedics' service was called to rescue. When they arrived, arterial blood pressure was 65/30 mmHg associated to a tachycardia (135 b/min). All the symptoms relieved by volume loading and methylprednisolone (Solumedrol®). Hopefully, his clinical condition improved and he could be discharged home the day after without sequelae.

Six weeks later, with the patient's consent, cutaneous tests to latex, to betamethasone, and to the excipients (carboxymethylcellulose, macrogol 4000) and the conservatives (parabens) of Diprostène® (kindly provided by the laboratory) were performed. Cutaneous tests were performed according to the standardized procedures recommended by the French Society of Anesthesiology and Critical Care Medicine (2). Prick-tests (PTs) and intradermal tests (IDTs) to betamethasone, carboxymethylcellulose and parabens remained negative as PTs to latex. The PT and IDT since 10^{-2} dilution to Diprostène® were positive in 15 min. Prick-test to macrogol 4000 was found to be positive. Intradermal tests since 10^{-2} dilution to macrogol 4000 was positive and triggered in 2 min a facial erythema and a periorbital oedema.

Taken together, clinical symptoms and allergological assessment results confirm the onset of an anaphylactic reaction to macrogol 4000. The clinical arguments were the onset delay of the reaction between the Diprostène® injection and the reaction, the clinical symptoms belonging to the triad of hypersensitivity reactions: cutaneous-mucous signs, cardiovascular and respiratory manifestations and their severity which evoked a grade III allergic hypersensitivity reaction (1). The allergological arguments were: the positivity of the cutaneous tests to Diprostène®; the negativity of the cutaneous tests to betamethasone, carboxymethylcellulose and parabens; the positivity of the cutaneous tests to macrogol confirming, therefore, its responsibility and the IgE-mediated mechanism of the reaction; the IDT with macrogol triggering a grade II reaction.

Allergic reactions to PEGs have been mostly reported with lavage solutions before coloscopies. In these previous cases, the presumptive diagnosis was determined on clinical arguments, with no further tests performed to establish the mechanism of the reaction (3–5). However, to our knowledge, the present anaphylactic reaction to Diprostène® because of macrogols, is the first case supported by an allergological assessment. This confirms the need for systematic allergological investigation with all conservatives and excipients to identify the allergenic determinant. However, macrogol testing might be dangerous and we speculate that IDT with macrogol should be performed only if the PT is negative.

In our patient, the supine position (6) and the endogenous sympathetic activation were probably lifesaving in absence of exogenous epinephrine injection which remains the drug of choice in case of anaphylaxis. Hopefully, the Solumedrol® injected by the paramedics did not contain macrogol. We consider necessary to emphasize that excipients or conservatives must be taken into account as a potential source of adverse reactions to drugs. Physicians should be aware of the possibility of hypersensitivity reaction with macrogols.

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An unusual pattern of meat allergy

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Key words: immunoblot; meat allergy; skin-prick tests; urticaria.

Allergy to meat is very uncommon. It has been described most frequently in children in association with cow's milk and beef allergy (1). Occasional case reports have described acute onset of allergy in adulthood (2).

We report a rare case of adult onset allergy to multiple cross-reacting meats.

A 61-year-old female presented with an 18-month history of acute urticarial reactions. All the reactions occurred following the consumption of meat or meat products. She had the most severe reaction after the consumption of a stew containing veal, potatoes and tomatoes.