

and an indirect enzyme immunoassay was performed by incubating for 1 h and after washing with our patient sera, IgG against human IgE and human IgG peroxidase, respectively, obtaining defined bands of 115, 150 and 199 kDa (Fig. 1). The immunoblot with 10 random-selected control patients serum was negative.

In conclusion, the positive oral challenge and the finding of bands in the immunoblotting suggest a type I IgE-mediated immunologic mechanism as being responsible for the patient's anaphylactic symptoms. It has been described that IgE symptoms with other infusions like coffee (2), cacao (3), tea (4) and chamomile tea (5) causes urticaria, occupational asthma and anaphylaxis respectively, but we have not found any case described in the literature with boldo.

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A case of urticaria due to sulpiride

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Key words: drug allergy; skin prick test; sulpiride.

We report the case of a male patient with a generalized urticaria because of

hypersensitivity to sulpiride. Sulpiride is a selective dopaminergic antagonist for D2 receptors that belongs to the group of benzamids or ortopramids, with neuroleptic, antidepressive, antiemetic, and antivertigo effects. It has been rarely associated with cutaneous adverse effects (1).

A 31-year-old man without any personal or familiar history of atopy, was referred to our department for allergologic evaluation because he had presented a cutaneous eruption 20 min after taking 100 mg of sulpiride (Dogmatil®, Sanofi-Synthelabo, Barcelona, Spain) p.o. on day 3 of treatment for dizziness. The reaction began with palmoplantar itching, progressing to generalized urticaria. The patient was treated with parenteral administration of corticosteroids and antihistamines in the Emergency room. Sulpiride was discontinued and tiethylperazine (Torecan®, Novartis Pharmaceutica, Barcelona, Spain) was used instead. Twenty-four hours later he returned to the Emergency room because dizziness and itching had not disappeared. When treatment with β -histine (Serc®, Solvay Pharma, Barcelona, Spain) was started itching increased and urticaria reappeared. The patient was admitted to hospital in the ORL department and after treatment with diazepam (Valium®, Roche Pharma, Madrid, Spain), dimenhydrinate (Biodramina®, Uriach-Biohorm, Barcelona, Spain), and dexchlorfeniramine (Polaramine®, Schering Plough, Madrid, Spain), his symptoms were completely resolved in 4–5 days.

After obtaining informed consent for the drug study, a skin prick test with sulpiride (5 mg/ml) and β -histine (8 mg/ml) was performed. It was positive for sulpiride (4×4 mm) and negative with β -histine with a wheal 5×5 mm for histamine. Skin prick tests with sulpiride were negative in 20 control subjects.

Single-blind oral tolerance exposure tests with tiethylperazine and β -histine were performed. In both cases, we reached the highest therapeutic dose with good tolerance.

Suspected IgE-mediated reaction to sulpiride was confirmed by positive skin prick test.

We decided to attempt an oral challenge with sulpiride in order to confirm the diagnosis. Within 24 min of receiving the first dose of the drug (5 mg equivalent to one of 20 therapeutic dose) he began to experience intensive palmoplantar itching. The oral challenge was stopped and the patient was immediately treated with endovenous dexchlorfeniramine with complete resolution of itching.

We describe a case of drug-induced eruption because of sulpiride by a type I hypersensitivity mechanism. Suspecting an IgE-mediated mechanism, carried us to perform a skin prick test with sulpiride to the patient and to 20 control subjects with the above-mentioned results, which confirmed our initial hypothesis. The fact that the skin prick test result fits in with the oral challenge result, makes the prick test with sulpiride a useful diagnostic tool (2).

Clinical findings and positive skin prick test, as well as positive challenge with sulpiride imply that the patient developed type I hypersensitivity. To our knowledge, this is the first case of immediate hypersensitivity to sulpiride.

The cutaneous exacerbation that followed the β -histine administration was probably because of the fact that this drug is an histamine analog (3, 4). Tiethylperazine is a fenothiazine with antidopaminergic and antihistaminic H1 with antiemetic and antivertigo effects. This drug did not resolve the dizziness but did not aggravate the skin eruption.

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Successful combined therapy for refractory chronic urticaria in a 10-year-old boy

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Key words: chronic urticaria; ϵ aminocaproic acid; montelukast; ranitidine.

Urticaria lasting more than 6 weeks is defined as chronic, and in the majority of cases its etiology remains unknown. Chronic idiopathic urticaria is usually quite frustrating for the patient, as it heavily impairs the quality of life, and for the physician, as it is difficult to

Chronic idiopathic urticaria is a difficult to treating disease, therefore we describe a combination therapy which may be considered an useful treatment.

treat. H1-antihistamines are the first-line treatment (1), and in those patients with an unsatisfactory response to antihistamines, the addition of other antimediator (e.g. leukotriene modifiers or anti-H2 antihistamines) can be of benefit. For refractory cases, long-term treatments with systemic steroid or immunosuppressants are used as second choice (1, 2), whereas the role of intravenous gammaglobulins or plasmapheresis is controversial. We describe the case of a child with severe and refractory chronic urticaria (CU), successfully treated with a new combination therapy.

A 10-year-old boy was referred for severe chronic urticaria. He had been well until the age of 8, when episodes of generalized urticaria began to occur. His clinical history was negative for allergic diseases: asthma, atopic dermatitis, hay fever. A detailed study for the possible common causes of urticaria was under-

Table 1. Posology of the combined regimen

Drugs			
Month 1	ϵ -Aminocaproic acid (100 mg/kg/day)	Montelukast (5 mg/day)	Ranitidine (6 mg/kg/day)
Month 2		Montelukast (5 mg/day)	Ranitidine (6 mg/kg/day)
Month 3			Ranitidine (6 mg/kg/day)

taken. Routine laboratory parameters (including blood cell counts, clinical chemistry and urinalysis) were all within the normal range, as well as thyroid hormones and thyrothrin. Erythrocyte sedimentation rate was 16 mm/h. Antinuclear autoantibodies and rheumatoid factor were negative and complement fractions and circulating immune complexes were normal. Repeated stool assays for parasites and eggs gave negative results. A detailed allergologic study was also carried out, but skin prick tests and radioallergosorbent test with aeroallergens and common food allergens were negative; total serum IgE was 179.5 U/ml. No local reaction after intradermal injection of autolog serum could be demonstrated. Additional studies included hepatitis B surface antigen and antibody, and paranasal sinuses CT, that provided negative results as well. The C1qINH, measured by radial immunodiffusion, resulted within the normal range. The patient was repeatedly treated with H1 and H2 antihistamines in various combinations, with only marginal benefit. A satisfactory, although not full, control of symptoms could be obtained only with repeated courses of prednisone (1 mg/kg/day). Nevertheless, when the systemic steroid was tapered, urticaria invariably relapsed within 1–2 weeks. During 2 years, the patient underwent nine courses of systemic prednisone.

Before giving immunosuppressant agents we attempted an empirical therapeutic approach, combining an anti-fibrinolytic agent (ϵ aminocaproic acid) plus montelukast plus the H2 antihistamine ranitidine. This regimen induced a full remission of urticaria in about 48 h. The treatment was gradually tapered in the subsequent months, and no relapse of symptoms occurred (Table 1). At present, after about 13 months, the patient still remains completely symptom-free.

Treating chronic idiopathic urticaria represents a challenge for physicians, as no avoidable cause can be detected. Therefore, the therapy can only have the goal of controlling symptoms. Nevertheless, in several patients the recommended first-line drugs are not effective, and the second-line drugs (steroids, cyclosporine) provoke severe systemic effects. These problems are of major relevance in the pediatric age. These are the reasons why numerous empirical attempts have been proposed and described. For instance, antiprotease drugs (e.g. tranexamic acid or ϵ -aminocaproic acid) that are commonly used for prophylaxis of hereditary angioedema are effective in chronic urticaria (3, 4). In children, these anti-fibrinolytic agents are always of first choice for long-term treatments, because they are safer than attenuated androgens (5). On the contrary, the efficacy of leukotriene receptor antagonists has been demonstrated in several studies, although the role of leukotrienes in urticaria is not completely clarified. Finally, H2 antihistamines are often considered as useful adjuncts in the treatment of urticaria (1).

In the case herein described, our main aim was to avoid, if possible, the use of long-term corticosteroids or cyclosporin A (6). For this reason we carried out an exploratory attempt with a combination of relatively safe drugs which, in turn, seldom are effective when used alone.

This case report suggests the described combination therapy may be considered as an alternative to standard medications.

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