

Urticaria to carisoprodol

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Key words: carbamates; carisoprodol; drug allergy; meprobamate.

● CARISOPRODOL (isopropylmeprobamate) is a skeletal muscle relaxant belonging to the carbamate group which includes meprobamate, methocarbamol, and mebutamate. It is used alone or in association with analgesics (1). We report an exceptional case of urticaria induced by carisoprodol in which reactivity to the related meprobamate was also demonstrated.

A 53-year-old woman received, for sciatica, carisoprodol 350 mg (Mio-Relax[®], Belmac S.A., Madrid, Spain) and diclofenac 50 mg (Voltaren[®], Novartis, Barcelona, Spain). Four hours after the first dose of both drugs (taken together) she developed a generalized itching erythema which resolved with intramuscular methylprednisolone and dexchlorfeniramine. The patient had previously tolerated diclofenac but she had not taken any nonsteroidal anti-inflammatory drug after the reported reaction.

The patient gave written consent to the following allergological study performed in our Allergy Unit following a single-blind placebo-controlled procedure. The administration of aspirin (up to 1000 mg) was well tolerated. Skin prick tests (SPT) (25 mg/mL), intradermal tests (IDT) (0.25 mg/mL) and patch tests (10% in petrolatum) with diclofenac and carisoprodol were negative. The patient tolerated increasing doses of diclofenac up to 50 mg. Eight hours after the administration of 175 mg of carisoprodol, a pruritic erythema and hives appeared in the forearms, inguinal area, and abdomen, which resolved with oral dexchlorfeniramine and prednisone. As meprobamate is a related carbamate and one of the metabolites of carisoprodol (1), reactivity to this drug was investigated. SPT and IDT (25 and 0.25 mg/mL, respectively) with meprobamate were negative, as well as

patch test (10% in petrolatum). Five hours after the administration of 100 mg of meprobamate, urticarial lesions appeared in forearms and abdomen, which subsided with ebastine.

Carisoprodol is an old (>40 years) and widely used drug which has been very infrequently involved in skin adverse reactions (1,2,3). There is one reported fixed drug eruption induced by both carisoprodol and meprobamate (2). In the present urticaria to carisoprodol, we have demonstrated reactivity to meprobamate by means of an oral provocation. These two drugs have similar chemical structures (Fig. 1) and might give rise to the same metabolite(s) which could induce the immunologic response leading to the urticaria. This would also explain the negativity of the skin tests performed with the native drugs.

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FDE to macrolides

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Key words: cross-reactivity; erythromycin; fixed drug eruption; macrolides; patch test.

● MACROLIDES are among the safest antibiotics; their low indices of toxicity

make them useful agents for the treatment of upper respiratory tract and skin and soft-tissue infections caused by susceptible organisms.

Adverse reactions to macrolides appear to be very rare (1). Only a few cases of fixed drug eruption (FDE) (2–4) and urticaria (5,6), due to the administration of different antibiotics from this group, have been reported. All cases of FDE do not show any evidence of cross-reactivity among macrolides on the basis of the patch test results (2–4).

However, in a unique patient with proven IgE-mediated hypersensitivity due to erythromycin, we have documented a partial cross-reactivity with midecamycin through RAST-inhibition experiments (5).

We report a case of a 64-year-old man, who had been treated for respiratory tract infection with erythromycin 500 mg, and developed pruritic blisters on the penis, with local hyperpigmentation, 6 h after the intake of this antibiotic. The cutaneous lesions disappeared after approximately 15 days. Previously he also referred two similar episodes upon administration of erythromycin, at the same localization.

One month later, after the patient had given written informed consent, epicutaneous patch tests were carried out on unaffected skin using different macrolides (erythromycin, clarithromycin, roxithromycin, midecamycin and azithromycin). The drugs were prepared at 10% concentration in dimethylsulfoxide. Positive (3+) results to all drugs (except azithromycin) were noted at 48 h (Table 1). Controlled oral challenges with increasing doses of

Table 1. Patch-test results with different macrolide antibiotics

Agent	Results*
Erythromycin	3+
Clarithromycin	3+
Roxithromycin	3+
Midecamycin	3+
Azithromycin	–

*. Epicutaneous patch tests were read at 48 h intervals.

azithromycin (to 500 mg p.o.) were carried out with good tolerance.

The basic structure of macrolides is characterized by a lactonic cycle with 2 osidic chains. They are classified by the number of carbon atoms in the cycle. For example: 14-membered macrolides such as erythromycin, roxithromycin, and clarithromycin; 15-membered macrolides such as azithromycin; and 16-membered macrolides such as midecamycin (7). Whether these differences in chemical structure form the basis of the different cross-reactivities among macrolides is largely unknown. However, we have documented the use of topical provocation tests and a controlled oral challenge in the first reported case of FDE caused by a macrolide showing cross-reactivity with other antibiotics from the same group. Thus, it seems reasonable to perform patch testing with macrolides that have different numbers of carbon atoms in patients with FDE due to this specific antibiotic group.

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Immediate pressure urticaria

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Key words: nonallergic urticaria; pressure urticaria; wheal.

● PRESSURE urticaria is typically delayed in nature such that pressure applied to the skin leads to hives and/or swelling some 4–8 h later (1). The histology of the lesion is strikingly similar to that seen with chronic idiopathic urticaria (1) or, using the new terminology, chronic nonallergic urticaria (2). Dermatographism, on the other hand, is an immediate wheal and flare reaction occurring within a few minutes of stroking the skin. A delayed form with linear wheals occurring hours after stroking the skin (so-called delayed dermatographism) may represent an alternative manifestation of delayed pressure urticaria (3).

We have encountered an unusual form of physical urticaria in which pressure applied to the skin for 1 min leads to immediate hive formation, yet the subject was not dermatographic. The case is described herein and the literature reviewed.

The patient was a 44-year-old male who presented with nonallergic urticaria of 10 years' duration. He had had hives on a daily basis which could occur on virtually any part of his body, including his scalp, face, trunk, and all four extremities. On occasion, hives had presented on his palms and soles. He was extremely pruritic even when hives were not present, although scratching himself did not cause urticaria.

He presented to us taking Prevacid (30 mg/day), Pepcid (20 mg/day), Zyrtec

(10 mg/day), Singulair (10 mg/day), Atarax (25 mg HS), doxepin (10 mg HS) and occasionally methylprednisolone. A number of years ago he had taken prednisone on a regular basis with significant diminution of the hives but developed ulcer symptoms as a result. He has used corticosteroids for occasional relief and in these instances has found the Medrol dose pack to be very helpful.

It was thought that the patient had systemic mastocytosis for which he was evaluated at the National Institutes of Health. The results of a bone marrow biopsy performed in 1999 were negative. He had a tonsillectomy and adenoidectomy two years previously and was diagnosed one year previously with degenerative disc disease. There was no history of cardiac disease, hypertension, diabetes, liver or kidney disease, thyroid disease, arthritis or colitis. The patient worked as a carpenter, did not smoke and drank about 24 beers per week.

There were no remarkable findings on physical examination, including no evident urticaria or angioedema. Of note, however, was the appearance of hives in the area where the blood pressure cuff had been inflated. Direct pressure applied to his back by pressing with a thumb for 1 min caused immediate urticaria in the shape of a thumbprint to appear in 4 min, and although still evident an hour later it appeared to be fading. Tests for dermatographism were repeatedly negative. Laboratory data included a normal CBC, sedimentation rate, thyroid function tests and absence of antibodies to thyroglobulin microsomal antigens.

The various types of physically induced hives can, at times, be difficult to distinguish from each other. There is, for example, a variant of cholinergic urticaria in which hives occur only upon exercise in a cold environment (4) that is easily confused with patients who have both cold urticaria and cholinergic urticaria.

Dermatographism can be confused with chronic urticaria because, when it is unusually severe, clothing that rubs on the skin can be sufficient to induce hives so that occurrences appear to be 'spontaneous'. Another variant is dermatographism that is inducible only when the skin has been chilled (5).

Pressure urticaria is considered to be synonymous with 'delayed' pressure urticaria because the rash typically occurs 4–6 h after the stimulus is applied. The sole

An unusual case of physical urticaria.