

Urticaria to hydrocortisone

E. Nettis*, L. Muratore, G. Calogiuri, A. Ferrannini, A. Tursi

Key words: allergic contact dermatitis; cutaneous reactions; hydrocortisone sodium succinate; IgE-mediated reactions.

• We describe two systemic immediate-type cutaneous reactions to hydrocortisone sodium succinate (HC-SS).

Case 1 was that of a 36-year-old woman with a history of allergic contact dermatitis since 1991; furthermore, the use of the corticosteroid/antibiotic ointments Gentilyn Beta (gentamycin/betamethasone) and Aureocort (aureomycin/triamcinolone acetone) had caused worsening of the dermatitis in different episodes. In summer 1995, after the topical use of an insect-repellent spray, the patient exhibited erythematous reactions with pruritus over the areas of spray application. For that reason, she was admitted to her local hospital

Two cases of possibly allergic systemic reactions.

emergency room and was administered 100 mg Solucortef (HC-SS) I.M. Fifteen minutes after the administration of this therapy, the patient developed generalized urticaria with facial angioedema and conjunctival congestion. Those symptoms spontaneously faded within 30 min.

Case 2 was that of a 47-year-old woman affected by pruritus sine materia. During a climax of itching, she presented to the emergency room, where she was treated with 10 mg clorphenamine maleate and 500 mg Solucortef (HC-SS) intravenously. The patient exhibited extensive urticaria within a few minutes, which faded and disappeared 1 h later without any further administration of drugs.

At the Department of Allergy and Clinical Immunology of Bari University Hospital, skin prick tests (SPT) and intradermal tests (IT) were performed with either the commercial HC-SS and methylprednisolone sodium succinate (MP-SS) powders or the pure powders of them (without preservatives), provided by Pharmacia & Upjohn (Milan, Italy), diluted with 0.9% saline solution at 0.1 and 1 mg/ml. The SPT gave negative results, but the IT showed a positive reaction at 0.1 mg/ml for all four diagnostic reagents (pure and commercial powders of HC-SS and MP-SS), whose papules were measured in mm histamine chloride (0.1%), and the allergen diluents were used as positive and negative controls. Furthermore, the patients were patch-tested with the European standard series, Gentilyn Beta ointment (as in case 1), Aureocort ointment (as in case 1), pure HC-SS, and pure MP-SS (both at 20% pet.). Patch preparations were applied with Finn chambers on Scampor, according to the IRDGC recommendations. Patch test reading was performed at 48 h and 96 h, confirming the nickel contact allergy only in case 1. Patch tests with pure HC-SS and pure MP-SS and skin tests for GCSs, at the same concentrations, were also executed on a control group of 10 people with negative history of adverse reactions to drugs and foods, and their results were negative, as expected.

Finally, SPT and IT with halogenated corticosteroids (dexamethasone, betamethasone, and triamcinolone), at the same concentrations of 0.1 and 1 mg/ml, gave negative results in both our subjects.

Everything in the two patients indicates a possible IgE-mediated reaction to GCSs, and the skin tests seem to confirm this hypothesis. Doooms-Goossens & Degreeef (1) suggest that patients who suddenly developed an immediate-type reaction to systemic administration of GCSs had

previously experienced allergic contact dermatitis caused by topical corticosteroids, in which the transcutaneous route might represent the path of sensitization. In fact, dermatologic studies confirm the possibility of a systemic absorption of GCS through the cutaneous route (2). Patient 1 in our paper reported a worsening of dermatitis after application of ointments containing corticosteroids. Nevertheless, patch tests with HC-SS and MP-SS 20% pet. proved to be negative, but other authors have postulated that it could depend on the difficulties in performing correct patch tests with anti-inflammatory drugs such as corticosteroids (3, 4). Both the patients reacted to systemic administration of the HC-SS, but their IT were positive to MP-SS; thus, it is very difficult to establish whether this was a cross-reaction or a concomitant sensitization, due to previous use of MP, in the topical or systemic way. Analysis of the literature (5) shows simultaneous positivity to skin tests for both molecules (HC-SS and MP-SS) to be quite frequent; yet, isolated skin positivity to HC-SS or MP-SS has sometimes been evidenced (5). It could depend on a subsequent sensitization, as shown by Wilkinson et al. (6) in 96 patients with allergic contact dermatitis to HC. They documented that changes operated on carbon rings of the steroid's structure influenced the immune response and consequent cutaneous immunoreactivity to the steroid allergen. Since HC was the sensitizing base molecule, most reactions occurred to other non-C6 and non-C9 substituted corticosteroids, followed, respectively, by those substituted at C6, C9, and C6 and C9. Thus, even in the IgE-mediated response, as well as in the cellular-mediated one, the modification of C9 is probably sufficient to change the immunogenicity of the carbon rings structure, by allowing the tolerance of halogenated GCSs in patients with immediate-type reactions to HC-SS and/or

MP-SS. Data from a general review of literature confirm that hypothesis (5).

Acknowledgments We thank Dr Giovanni F. M. Strippoli and Maria Cristina Colanardi for their expert cooperation and the Pharmacia-Upjohn Co. for their collaboration. This work was presented in part at the Italian Congress "Anafilassi in ambiente ospedaliero" in Ancona, Italy, 4 October 1996.

*Cattedra di Allergologia e Immunologia Clinica
Padiglione Chini – Policlinico
Piazza Giulio Cesare, 70124 Bari
Italy
Tel. 0039 080 5592821
Fax: 0039 080 5478780
E-mail: e.nettis@allergy.uniba.it

Accepted for publication 17 April 2001
Allergy 2001; 56:802–803
Copyright © Munksgaard 2001
ISSN 0105-4538

References

1. DOOMS-GOOSSENS A, DEGREEF H. Clinical aspects of contact allergy to corticosteroids. *Dermatology* 1994;**189 Suppl 2**:54–55.
2. KECSKES A, JALUS P, MATTHES H, KUHLMANN RK, LANGE L. Systemic effects of topically applied methylprednisolone aceponate in healthy volunteers. *J Am Acad Dermatol* 1993;**28**:789–792.
3. WILKINSON SM, BECK MH. Corticosteroid contact hypersensitivity: what vehicle and concentration? *Contact Dermatitis* 1996;**34**:308–308.
4. ISAKSSON M, BRUZE M, GOOSSENS A, LEPOITTEVIN JP. Patch testing with budesonide in serial dilutions: the significance of dose, occlusion time and reading time. *Contact Dermatitis* 1999;**40**:24–31.
5. KAMM GL, HAGMEYER KO. Allergic type reaction to corticosteroids. *Ann Pharmacother* 1999;**33**:451–459.
6. WILKINSON SM, HOLLIS S, BECK MH. Reactions to other corticosteroids in patients with allergic contact dermatitis from hydrocortisone. *Br J Dermatol* 1995;**132**:766–771.

Meloxicam in hypersensitivity to NSAIDs

E. Nettis*, R. Di Paola, A. Ferrannini, A. Tursi

Key words: angioedema; meloxicam; NSAID; tolerance; urticaria.

● CUTANEOUS adverse reactions to drugs are a common problem in clinical practice. Among them, the urticaria/angioedema syndrome is the most frequent. The drug categories responsible for the majority of cases are antimicrobials and nonsteroidal anti-inflammatory drugs (NSAIDs) (1). A patient with a history of allergic or pseudoallergic reaction to NSAIDs needs an alternative NSAID to take if necessary. The peroral challenge with an alternative NSAID is the most

common way to achieve this goal.

At the moment, there are no NSAIDs absolutely free of adverse reactions. The drugs that are the best tolerated are acetaminophen (paracetamol) and nimesulide. Meloxicam, floctafenine, and benzydamine seem to be tolerable as well (2–5).

Over a period of two and a half years (2 February 1998 to 25 June 2000), some of the patients referred to our outpatient department for unequivocal clinical history of urticaria with or without angioedema to NSAIDs were enrolled in the study. All subjects underwent single-blind, placebo-controlled peroral challenge with meloxicam after giving informed written consent. They presented a forced expiratory volume after 1 s (FEV₁) of >80% of predictive value. Antihistamines and other drugs had been discontinued 1 week (2 weeks for patients with chronic urticaria and 4 weeks for those treated with astemizole) before challenge.

Table 1. NSAIDs causing urticaria with or without angioedema in 148 patients

Drug	No. of patients	Percentage of patients
ASA	36	24.3
Pyrazolone derivatives	25	16.9
Propionic acid derivatives	25	16.9
Arylacetics	7	4.7
Others*	18	12.1
ASA + pyrazolone derivatives	13	8.8
ASA + propionic acid derivatives	6	4.0
ASA + arylacetics	1	0.7
ASA + others	3	2.0
Propionic acid derivatives + arylacetics	3	2.0
Propionic acid derivatives + others	1	0.7
Pyrazolone derivatives + propionic acid derivatives	1	0.7
Pyrazolone derivatives + arylacetics	1	0.7
Pyrazolone derivatives + others	3	2.0
Arylacetics + others	1	0.7
Arylacetics + propionic acid derivatives + others	1	0.7
Pyrazolone derivatives + ASA + others	1	0.7
ASA + propionic acid derivatives + others	1	0.7
ASA + propionic acid derivatives + arylacetics	1	
Total	148	100

*Others: nimesulide, paracetamol, morniflumate, niflumic acid, bromelain, and mefenamic acid.