Systemic contact allergy to corticosteroids revisited

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Hypersensitivity to corticosteroids has been known among dermatologists since the late 1980s, but other specialists may still be unaware of it and the difficulties of suspecting it in the single case. Allergic contact dermatitis is the most common sign but systemic contact dermatitis can also occur.

Case 1

A 49-year-old woman without personal atopy suffered from external otitis since the age of 20, treated with Kenacort®-T comp. solution (containing triamcinolone acetonide 1.8 mg/ml; Bristol-Myers Squibb AB, Stockholm, Sweden) intermittently but her otitis never cleared. Some 20 years later, a generalized papular eczema with severe pruritus erupted on several occasions on the trunk, arms, and legs and lasted for 3–4 weeks during a 2-year period. A general practitioner had given her Betapred tablets (betamethasone, dose not specified in file) (Swedish Orphan AB, Stockholm, Sweden) per orally and Celeston® valerate cream (betamethasone valerate 0.1%; Schering-Plough AB, Stockholm, Sweden) without much effect, and the patient even experienced worsening from the topical medication. She was eventually sent to a general dermatologist who patch tested her with a standard series (containing budesonide and tixocortol pivalate) and some additional substances and a reading on day (D) 3 showed positive reactions to nickel sulfate 0.2 mg/cm^2 (True test, Pharmacia, Sweden) (++), benzoylperoxide 1% pet (++), and benzalkonium chloride 0.1% aqua (++), the latter a component of the external ear preparation. This therapy was stopped and the dermatitis cleared all over, resulting in normal ear canals since then. 5 years later, a new papular dermatitis appeared on the dorsal hands, feet, and ankles where systemic and topical corticosteroids were given, Betapred tablets (dose not specified in file) and Apolar cream (desonide 0.1%; Dumex-Alpharma AB, Stockholm, Sweden), resulting in a flexural eczema with spreading to the body, i.e. systemic contact dermatitis.

She was again seen by the dermatologist, given Betapred tablets and Flutivate® cream (fluticasone propionate 0.05%; GlaxoSmithKline AB, Solna, Sweden), and 5 months later patch tested to a standard [nickel sulfate 0.2 mg/cm^2 (++), Kathon CG 0.004 mg/cm^2 (True test) budesonide 0.1% (Table 1)] and a corticosteroid series (Table 1). To further elucidate her contact allergy to corticosteroids, she was referred to us 3 years later, where a new patch test with a standard and our corticosteroid series was performed (Table 1). She then suffered intermittently from hand and foot eczema thought to be atopic and was treated with topical tacrolimus with good benefit.

Case 2

A 30-year-old woman of Asian descent suffered from a blocked nose since 4 years, treated at the ear/nose/and throat (ENT) clinic of our hospital with nose decongestants such as Rhinocort® Aqua nose spray (budesonide 32 μg/dose; AstraZeneca AB, Södertälje, Sweden) without much success, why a conchotomy was performed. Already then, she had a history of pain in the nose and papules around it from the use of Rhinocort Aqua. The operation cleared her nose and sinuses temporarily, but 2 years later, new symptoms emerged rendering new treatment with antibiotics, nose decongestants, and per orally the corticosteroids prednisolone and betamethasone (doses not specified in file). Rhinocort Aqua was started again 2 years after the operation (lowest dose possible, 1–2 times/day) and within 1 week similar symptoms appeared as before, i.e. pain and pruritus in the nose and an acneiform facial rash. Treatment was therefore changed to Nasacort® nose spray (triamcinolone acetonide 55 μg/dose; Aventis Pharma AB, Stockholm, Sweden) after 2 months, but within 2 days lesions reappeared in the face. Despite this, treatment with both corticosteroids continued intermittently for another 0.5 year resulting in exacerbation of the facial rash with papules resembling acne according to the patient file. In the end, the patient sought help 2–3 times a week at the ENT Clinic. The patient was eventually referred to us. A patch test with a standard, rhinitis, and a corticosteroid series plus Rhinocort 'as is' was performed (Table 1); she reacted to budesonide, amcinonide, and Rhinocort Aqua as is, and a new corticosteroid not cross-reacting with budesonide was given, viz. Nasonex® nose spray (mometasone furoate 50 μg/dose, Schering Plough AB, Stockholm, Sweden). This corticosteroid did not give any skin symptoms but she was not pleased with the efficacy. 3 years later, she was again seen by us because of a flexural eczema, and it turned out and she was again using Nasacort, containing triamcinolone acetonide that cross-reacts with budesonide. By changing to Nasonex, her systemic contact dermatitis cleared.

Discussion

Case 1 illustrates that occasional patients may have a very broad contact allergy to corticosteroids that precludes corticosteroid treatment (1). She reacted to all corticosteroids available on the Swedish market, both topical and systemic (Fig. 1). The mechanism behind is however not clear and may be a contact allergy to the basic corticosteroid structure or a common metabolite. The case is also interesting because contrary to many corticosteroid-allergic patients, she reacted to all corticosteroids in the series (diluted in ethanol 99.5% v/v or dimethyl sulphoxide/ethanol 99.5% (DMSO/EtOH) 50/50 v/v as vehicle) but not to ethanol or

Table 1. Patch tested corticosteroids with concentrations and vehicles in the 2 cases and test results

Substance	Concentration %	Vehicle	Case 1		Case 2	
			Day 3/4	Day 7	Day 3	Day 7
Tixocortol pivalate[a]	1.0	Pet	—	NR	NA	NA
Tixocortol pivalate[b]	1.0	Pet	—	—	NA	NA
Tixocortol pivalate[c]	0.01	Pet	—	—	—	—
Budesonide[a]	0.1	Pet	—	NR	NA	NA
Budesonide[b]	0.1	Pet	+++	+++	NA	NA
Budesonide[c]	0.01	Pet	+++	++	++	+
Betamethasone valerate[b]	1.0	Pet	+	NR	NA	NA
Betamethasone valerate[c]	1.0	Eth	++	+	—	—
Betamethasone[c]	0.01	Eth	(+)	—	—	—
Betamethasone dipropionate[c]	1.0	Eth	++	+	—	—
Triamcinolone acetonide[b]	1.0	Pet	++	NR	NA	NA
Triamcinolone acetonide[c]	0.01	Eth	(+)[d]	(+)[e]	—	—
Alclomethasone-dipropionate[b]	1.0	Pet	—	NR	NA	NA
Alclomethasone-dipropionate[c]	1.0	D/e	++	+	—	—
Clobetasol-17-propionate[b]	1.0	Pet	++	NR	NA	NA
Clobetasol-17-propionate[c]	1.0	Eth	++	+	—	—
Dexamethasone-21-phosphate[b]	1.0	Pet	+	NR	NA	NA
Dexamethasone-21-phosphate[c]	0.1	Eth	++	+	—	—
Hydrocortisone-17-butyrate[b]	1.0	Eth	++	NR	—	—
Hydrocortisone-17-butyrate[c]	1.0	Eth	++	+	NA	NA
Amcinonide	1.0	Eth	NA	NA	+	++
Beclomethasone dipropionate[c]	1.0	Eth	++	+	—	—
Clobetasone butyrate[c]	1.0	Eth	++	+	—	—
Desonide[c]	0.1	Eth	+++	+	—	—
Desoximethasone[c]	0.01	Eth	++	+	—	—
Diflorasone diacetate[c]	1.0	D/e	++	?	—	—
Flumetasone[c]	1.0	Eth	(+)	(+)	—	—
Flupredniden acetate[c]	0.01	Eth	(+)	(+)	—	—
Fluticasone propionate[c]	1.0	D/e	++	+	—	—
Fluocinolone acetonide[c]	1.0	Eth	++	+	—	—
Fluocortolone[c]	1.0	Eth	++	+	—	—
Hydrocortisone[c]	1.0	D/e	++	+	—	—
Methylprednisolone aceponate[c]	1.0	Eth	++	++	—	?
Mometasone furoate[c]	0.01	Eth	++	+	—	—
Prednicarbate[c]	1.0	Eth	++	++	—	—
DMSO/EtOH[c]	50/50	NA	—	—	—	—
Ethanol[c]	99.5	NA	—	—	—	—
Nasacort as is	NA	NA	NA	NA	?	—
Rhinocort Aqua as is	NA	NA	NA	NA	++	++

eth, ethanol; D/e and DMSO/EtOH, dimethyl sulphoxide/ethanol 50/50; NR, not read; NA, not applicable.
[a]First test session.
[b]Second test session.
[c]Third test session; [a–c]only pertains to case 1.
[d]Erythematous circle.
[e]Infiltrated circle (edge reaction).

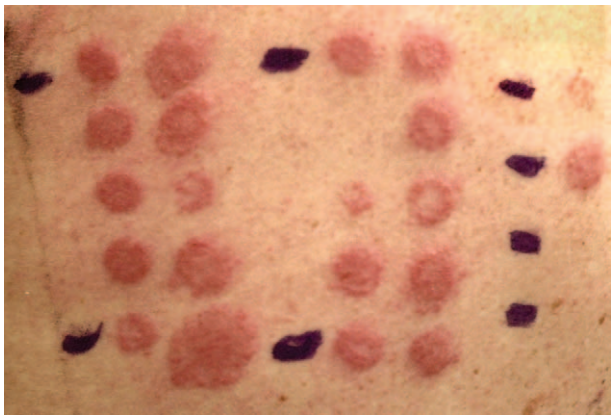

Fig. 1. Case 1 reacted to all patch-tested corticosteroids available on the Swedish market but not to fusidic acid.

DMSO/EtOH as such. Corticosteroid-allergic patients often react to ethanol, which is considered to be an irritant reaction (2). When you see positive reactions both to the corticosteroid diluted in ethanol and the vehicle as such, the reaction to the corticosteroid may also be toxic and consequently a false positive. This is the main reason why one always should patch test with ethanol as is when using this vehicle. Our patient also reacted to several corticosteroids dispersed in pet, so her contact allergy to corticosteroids was undoubtedly real (and not false positive) and relevant. She rapidly improved when systemic and topical corticosteroids

were replaced with emollients. At the time of testing, we had added fusidic acid sodium salt 2.0% pet to our corticosteroid series to see whether there were simultaneous reactions as a sign of cross-reactivity, but she did not react to fusidic acid.

Case 2 emphasizes that we dermatologists must expand the knowledge of corticosteroid contact allergy and potential cross-reactivity between different corticosteroids to other physicians treating patients with these drugs, not only topical but also systemic corticosteroids, i.e. for inhalation, per orally, and injections (3). The patient had symptoms suggestive of corticosteroid contact allergy for at least 2 years before she was referred. Even when her corticosteroid contact allergy was known, she was given a corticosteroid she did not tolerate, leading to a systemic contact dermatitis.

Of the 17 parenteral corticosteroid preparations on the Swedish market in 2006 (including 7 different glucocorticosteroids), all but 3 data sheets inform that allergic reactions can (if rarely) occur, contrary to the findings of English et al. (1)in 1990, when only 1/13 preparations had the warning. In Sweden, it is parenteral preparations containing prednisolone and hydrocortisone that lack the warning.

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