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Cutaneous Adverse Reactions after Intra-articular Injection of Triamcinolone Acetonide

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A patient is described with a disseminated morbilliform and partially persistent urticarial dermatitis following intra-articular injections of triamcinolone acetonide.
A delayed-type hypersensitivity to triamcinolone acetonide was observed after patch and intradermal testing. However, an immediate-type hypersensitivity to this drug was not observed.
A delayed-type sensitization to betamethasone, dexamethasone and prednisolone, but not to hydrocortisone was also observed after patch testing. Intradermal tests with these representatives of corticosteroids were all negative.
Although little is known yet about the relationship between immediate and delayed-type hypersensitivity and the side-effects of oral use of corticosteroids, the absence of positive skin tests to corticosteroids other than triamcinolone acetonide may indicate a safe use of these drugs orally or via injection. ***Key words: drug eruption; corticosteroids; delayed-type allergy; delayed-type hypersensitivity; patch testing***

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Allergy to corticosteroids presents either as a systemic or a cutaneous reaction after an injection of a corticosteroid or as contact dermatitis following the topical application of such a drug. Allergic reactions after injection of hydrocortisone were described by Kendall (1) who observed generalized urticaria (0.12%), broncho-spasms and angioedema (0.015%) and local urticaria (0.16%) among 2,256 patients. A respiratory arrest was described by Partridge & Gibson (2) after an intravenous injection of hydrocortisone. An urticarial rash following an injection of hydrocortisone was observed by O'Gara (3), and also sudden death was reported (4). The reported incidence of contact hypersensitivity to topical corticosteroids ranges from 0.5% to 8.5% (5–7). Recently, the association of delayed-type hypersensitivity reactions to different corticosteroids has been investigated to establish "classes" of related corticosteroids and representative corticosteroids with a highly predictive positive test result (6, 8, 9). In this case report, we present a patient with cutaneous side-effects due to intra-articular injection of triamcinolone acetonide and the results of intradermal and patch testing using a representative panel of corticosteroids.

CASE REPORT

A 45-year-old man received intra-articular injections of triamcinolone acetonide (Kenacort A 10® and A 40®) and procaine injections into the right shoulder to alleviate the painful arthritis that had existed for a year. In November 1991, 10 days after an injection with procaine and 2 days after the last injection with triamcinolone acetonide, a red, predominantly morbilliform, but partially urticarial skin eruption beginning at the feet and spreading over the body without affecting the face developed. No other drugs had been used. A week later, the skin eruption with the clinical appearance of a drug reaction still persisted, although the patient was taking 1 mg clemastine twice. He was given 20 mg prednisone orally but this had no effect. The patient was admitted for clinical observation, since the skin reactions persisted. His condition slowly improved, but small areas of erythema persisted for over a month. Hypersensitivity to one of the injected drugs (triamcinolone acetonide – Kenacort® or procaine) was suspected as the cause of the skin reactions.

Allergologic studies

Patch tests with the involved and related drugs in addition to the European standard routine (ESR) series and certain local anaesthetics according to the methods of the ICDRG were performed to establish the drug that was responsible. Three months later, corticosteroid test materials were prepared as published before (Table I) (6). The test results were graded as follows: – = negative (no reaction or a dubious reaction); + = positive (erythema, mild oedema); 2+ = positive (erythema, oedema and papules); 3+ = strongly positive (erythema, induration, papules, vesicles). Patch tests were read at 48 and 72 h after application. A positive reaction (2+) to fragrance mix was observed when tested with the ESR series. The patch tests with 5% procaine, 15% lidocaine and 5% cinchocaine, all in white petrolatum, were negative. The results of patch testing with different corticosteroids are shown in Table I. Of the corticosteroids tested, all were reactive except hydrocortisone acetate. Patch tests with other constituents of Kenacort® (2% carboxymethylcellulose in petrolatum and 10% polysorbat-80 in petrolatum) were negative. In addition, a panel of corticosteroids: hydrocortisone acetate, hydrocortisone butyrate, triamcinolone acetonide (Kenacort®), prednisolone, dexamethasone, betamethasone, histamine and phosphate-buffered saline (PBS) as control were investigated by intradermal tests (Table II). The corticosteroids tested were dissolved in saline in increasing concentrations. Test results were read after 20 min, 48 and 72 h. All intradermal tests were negative except for an erythematous patch with slight induration of 2 cm diameter after 72 h following intradermal injection of triamcinolone acetonide (Kenacort®). No flare-up reaction at other sites on the skin was observed during patch testing.

Table I. *Results of patch testing with corticosteroid series at different concentrations*

Corticosteroid	48 h	72 h
Betamethasone dipropionate 1% in ethanol	2+	3+
Betamethasone-17-valerate 2% in ethanol	2+	3+
Clobetasol-17-propionate as is	2+	2+
Clobetasone-17-butyrate as is	2+	2+
Clobetasone-17-butyrate 1% in ethanol	2+	3+
Dexamethasone 1% in ethanol	+	3+
Hydrocortisone acetate 2% in petrolatum	–	–
Hydrocortisone-17-butyrate as is	2+	2+
Prednisolone 2% in ethanol	+	3+
Prednisone 1% in ethanol	+	2+
Triamcinolone acetonide 0.1% (Kenacort A 10®)	–	3+
Triamcinolone acetonide 0.4% (Kenacort A 40®)	–	3+
Triamcinolone acetonide 2% in ethanol	+	3+
Triamcinolone acetonide 2% in petrolatum	–	3+

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Table II. *Results of intradermal tests with corticosteroid series at different concentrations*

Corticosteroid	mg/ml*	20 min	48/72 h
Betamethasone di-Na-phosphate	0.1	–	–
	1	–	–
	10	ND	–
Dexamethasone di-Na-phosphate	0.1	–	–
	1	–	–
	10	ND	–
Hydrocortisone acetate	0.1	–	–
	1	–	–
	10	ND	–
Hydrocortisone-17-butyrate	0.1	ND	–
	1	ND	–
	10	–	–
Prednisolone Na-succinate	0.1	–	–
	1	–	–
	10	–	–
Triamcinolone acetonide (Kenacort A 10®)	0.1	ND	+**
	1	ND	
	10	–	

–: negative skin reaction
*: ml of phosphate buffered saline
**: indurated erythematous and papular patch of 2 cm diameter
ND: not read

DISCUSSION

In this patient, a delayed-type hypersensitivity to triamcinolone acetonide was established both by patch testing (Table I) and intradermal testing (Table II). These observations strongly support the assumption that the drug eruption was caused by the intra-articular Kenakort® injections. Clinically, procaine as the cause of the skin eruption was suspected to a lesser extent. Procaine had been given 10 days before the eruption developed and sensitization to procaine could not be established by patch testing.

Furthermore, a relationship between the skin lesions and the observed sensitization to Fragrance mix was highly unlikely.

The patient showed positive patch tests to all corticosteroids but one: hydrocortisone acetate (Table II). Patch tests, however, are considered to be poor detectors of hydrocortisone hypersensitivity in comparison with intradermal tests (10). It is also of interest that by intradermal testing no delayed-type hypersensitivity to hydrocortisone was observed. No immediate-type hypersensitivity to hydrocortisone (concentration up to 10 mg/ml in PBS) or other corticosteroids summarized in Table II was detected.

Both tests (patch test and intradermal test) revealed a delayed-type hypersensitivity to triamcinolone in the patient. Patch testing was positive with several corticosteroids but intradermal tests only with triamcinolone acetonide. This discrepancy in intradermal test-reactivity cannot easily be explained, but it can be speculated that this discrepancy might be related to the particular chemical structures of the immunogens or be due to the fact that the previous (intra-articular) injections resulted in facilitation of direct T cell stimulation in the dermis. The sensitization to several different corticosteroids observed in this patient makes it difficult to advise on the therapeutic use of topical corticosteroids. In the test series used by us, representatives from all classes of corticosteroids according to their potency for sensitization as proposed by Coopman et al. (8) were included. Group allergy between different corticosteroids has been described (11).

In this patient, oral prednisone (20 mg/day), prescribed shortly after the onset of the skin eruptions, was not effective, but on the other hand it did not aggravate the eruptions. As yet, little is known on the relationship between immediate- and delayed-type hypersensitivity reactions and the risk of side-effects by the oral use of corticosteroids. It may be proposed that the absence of positive intradermal skin tests to corticosteroids other than triamcinolone acetonide (Table II) may indicate a safe use of these drugs orally or via injection. However, it has been reported that corticosteroid allergy may be dose-related, and therefore corticosteroids should only be administered to the patient with great caution.

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