

Anaphylaxis to 6- α -methylprednisolone in an eight-year-old child

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Corticosteroids are widely used in the treatment of several diseases, including allergic or pseudoallergic reactions. It is therefore somewhat ironic that they may be responsible for adverse events and provoke allergic or allergic-like reactions.

Allergic reactions to hydrocortisone have been reported since the 1950s.^{1,2} These reactions may be immunologic or nonimmunologic in nature, and they are very rare. Allergic contact dermatitis caused by corticosteroids, however, seems to be more common, and prevalences near 4% have been reported in recent studies of patients who have undergone patch testing.³

Hydrocortisone and methylprednisolone are the most common drugs involved in systemic adverse reactions. Prednisone, betamethasone, and dexamethasone are reported less frequently as causative agents.^{1,2,6} Allergic or pseudoallergic reactions to systemic corticosteroid therapy include bronchospasm,^{1,2,4,5} urticaria with or without angioedema,^{1,2,6} and anaphylaxis.^{1,2,7}

Previous contact dermatitis resulting from topical corticosteroid therapy may occasionally predispose the patient to a generalized reaction after systemic corticosteroid therapy.⁶ We report a case of anaphylaxis resulting from an intramuscular injection of 6- α -methylprednisolone. Type 1 hypersensitivity was proved by a positive skin test response. Other corticosteroids were tolerated.

CASE REPORT

An 8-year-old boy with mild cat dander-induced asthma consulted us because he had had an adverse reaction to Urbason (6- α -methylprednisolone hemisuc-

inate, monosodium phosphate, disodium phosphate, and distilled water). He had been treated with this drug before and had shown good tolerance. No other diseases were reported.

After the boy spent the night at the house of a friend who kept several cats, cough and wheezing developed. He was seen at our hospital's emergency department where he was treated with nebulized albuterol. When symptoms remitted and before he was sent home, 20 mg of Urbason was administered intramuscularly. Immediately after the injection, sneezing, severe generalized erythematous urticaria, and a marked increase of wheezing with dyspnea developed. Further administration of nebulized albuterol, intravenous aminophiline, and epinephrine was necessary to reverse this reaction. Complete resolution of symptoms was observed in 4 days.

METHODS

Skin prick tests with Urbason, 10 mg/ml, and pure 6- α -methylprednisolone dissolved in water at a concentration of 10 mg/ml were performed. Skin prick tests with additives at 10 mg/ml and several other corticosteroids (hydrocortisone at 10 mg/ml and 50 mg/ml; prednisone, prednisolone, betamethasone, dexamethasone, and deflazacort at 10 mg/ml and 20 mg/ml; and budesonide at 0.5 mg/ml) were performed.

Epicutaneous patch tests with hydrocortisone, methylprednisolone, budesonide, tixocortol, and prednisolone 10% in petrolatum and 10 mg/ml in dimethylsulfoxide-ethanol (1:1) were performed to obtain more information regarding the mechanism of the reaction. The patient tolerated the additives in other pharmacologic preparations, so challenges were not deemed necessary. Challenges with corticosteroids, theophylline, sulfites, and aspirin were carried out. The total amount of IgE (IMX System; Abbott Laboratories, Diagnostic Div., Chicago, Ill.) was estimated, but RAST system (Pharmacia, Uppsala, Sweden) failed to measure serum-specific IgE.

RESULTS

Results of skin prick tests with both Urbason (wheal, 6 $\times$ 6 mm; flare, 10 $\times$ 13 mm) and pure 6- α -methylprednisolone (wheal, 6 $\times$ 7 mm; flare, 12 $\times$ 13 mm) were positive. Tests were repeated

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twice with same result (histamine control wheal, 5 × 5 mm; flare, 11 × 10 mm; saline solution, 0 mm). Skin prick tests were also performed on 10 atopic patients and on 10 nonatopic control subjects, and in both cases results were negative.

Results of skin prick tests performed on our patient with the other corticosteroids and additives were negative. All patch test results were negative at 24, 48, and 72 hours. Total IgE was 346 IU/ml. Haematologic and biochemical findings were within the normal range.

Our patient was challenged with the most commonly prescribed corticosteroids (except methylprednisolone), beginning with the most structurally different drugs. Therapeutic doses of deflazacort, budesonide, hydrocortisone, prednisone, and prednisolone were tolerated. All drugs were given on different days. Aspirin, sulfites, and aminophylline were also tolerated.

DISCUSSION

Cases of allergic and pseudoallergic reactions resulting from systemic corticosteroid therapy have been reported in the literature.^{1,2,4-7} Severe allergic reactions caused by corticosteroids, however, have not been described in childhood.

We report on an 8-year-old boy who had an anaphylactic reaction to 6- α -methylprednisolone, which he had used and tolerated to treat his asthma before. We did not perform a challenge test with 6- α -methylprednisolone because of the risk of a new anaphylactic episode. A positive skin test response to the pure 6- α -methylprednisolone shows a type 1 immunologic hypersensitivity mechanism. We made an attempt to link the drug to different solid phases in order to quantify serum-specific IgE by RAST, but results were negative. It was very important to determine which corticosteroid could be tolerated by this patient, because he would need corticosteroid therapy for his asthma; thus, it was necessary to perform challenges with other corticosteroids.

The structure of methylprednisolone differs from that of the other corticosteroids in its six-carbon methyl group. This structure is quickly broken down in the body, and most corticosteroids share a common metabolic pathway; thus, a true allergic reaction to one specific corticosteroid should probably be based on the allergenic properties of the original, unmetabolized compound. Because of this, it is really difficult to define patterns of cross-reactivity in adverse reactions to systemic corticosteroids. Thus the recent classifica-

tion of topical corticosteroids on the basis of patterns of cross-reactivity in patients who have undergone patch testing⁸ is not completely useful in adverse reactions resulting from systemic treatments.

Three main adverse reactions have been reported in the literature: anaphylaxis, urticaria/angioedema, and bronchospasm. Anaphylactic reactions often occur after intravenous therapy with hydrocortisone or methylprednisolone.^{1,2} There are few cases with positive skin test results showing allergic reactions.^{1,2,6,7}

Urticaria (with or without angioedema) is often reported as a late adverse reaction to oral or parenteral corticosteroids.^{1,2,6} Some cases show late positive intradermal skin test results (range, 4 to 12 hours), and positive patch test results. This shows that cutaneous delayed sensitization might predispose the patient to generalized cutaneous reactions after systemic corticosteroid therapy in certain cases.⁶ In our opinion, in cases of urticaria or angioedema reactions with negative skin test results, challenges are necessary to establish a diagnosis, because corticosteroids are commonly prescribed and very useful drugs.

Bronchospasm caused by systemic corticosteroid therapy usually occurs immediately after intravenous administration of hydrocortisone.^{4,5} Most of these reactions appear in nonatopic patients with aspirin-sensitive intrinsic asthma. This shows an idiosyncratic mechanism.^{1,2} Tolerance to other corticosteroids must be determined by challenge. True allergic reactions resulting from systemic corticosteroid therapy are not frequent; nevertheless, they should be kept in mind, because this kind of therapy is a potential cause of allergic or pseudoallergic reactions.

We report a new case of anaphylaxis caused by 6- α -methylprednisolone. A positive skin prick test response shows a type 1 immunologic hypersensitivity mechanism. We do not know which part of the molecule caused our patient's reaction, but in this particular case, no cross-reactive mechanism with other corticosteroids seems to be involved.

Further studies are needed to establish the allergenicity and cross-reactivity of systemic corticosteroids.

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Successful desensitization for treatment of a fixed drug eruption to allopurinol

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Fixed drug eruption is the term used to describe a lesion of the skin or mucous membranes that occurs with administration of a drug, subsides when the drug is withdrawn, and recurs at the same location when the drug is reintroduced.¹ We report the case of a man who had a fixed drug eruption on several previous occasions when given allopurinol for treatment of hyperuricemia. In an attempt to readminister this drug without recurrence of the lesion, a desensitization protocol was followed. This protocol was previously described for a more generalized rash caused by allopurinol.²

CASE REPORT

The patient is a 71-year-old man with multiple medical problems including diabetes, coronary artery

disease, hypertension, atrial fibrillation, chronic renal insufficiency, and polyarticular, tophaceous gout. He had been treated for hyperuricemia for several years with allopurinol without side effects. About 5 years ago, the medication had been discontinued briefly. When it was restarted, a red, raised, weeping lesion developed on the glans penis. The allopurinol was discontinued, and the lesion resolved. On at least two subsequent occasions, most recently about 1 year ago, the allopurinol had been readministered, and a lesion of the same description occurred in exactly the same location within about 2 days. It resolved over several days after the medication was stopped.

The patient's gout remained poorly controlled, requiring frequent bursts of prednisone, as well as long-term prophylaxis with prednisone at a dose of 10 mg/day. Therefore an additional attempt was made to administer allopurinol according to a desensitization schedule, with the hope that the drug could be reintroduced without recurrence of the fixed drug eruption.

The patient began receiving allopurinol at a dose of 50 µg/day for 3 days. The dose was then increased to 100 µg and, at subsequent 3 day intervals, to 200 µg, 500 µg, 1 mg, 5 mg, 10 mg, 25 mg, 50 mg, and finally 100 mg. He continued to receive prednisone, 10 mg/day, during the desensitization and for about a month after achieving his maintenance allopurinol dose of 100 mg/day. The prednisone was subsequently discontinued. The patient had no recurrence of his fixed drug eruption during or after the allopurinol desensitization.

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