

Immediate and Delayed Hypersensitivity to Systemic Corticosteroids: 2 Case Reports

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Background: Both immediate, type I reactions and delayed hypersensitivity, type IV reactions to systemic corticosteroid preparations have been reported. Type I reactions are rare, with delayed hypersensitivity reactions being slightly more common.

Cases: A 33-year-old woman presented repeatedly to the emergency department with asthma attacks. She developed pruritus and hives approximately 30 minutes after the administration of parenteral corticosteroids. Her respiratory status deteriorated approximately 6 hours after she received the corticosteroids. An acute eczematous dermatitis on her face, neck, and upper body appeared 24 hours after administration of the corticosteroids. The dermatitis peaked at 72 hours. Intradermal testing to Solu-Medrol, Solu-Cortef, prednisone, and Decadron confirmed a type I, anaphylactoid reaction. The dermatitis that presented 24 hours after administration of the parenteral corticosteroids is consistent clinically with a type IV delayed hypersensitivity reaction to the corticosteroids. A second patient, a 51-year-old woman, developed urticarial lesions that lasted approximately 30 minutes, immediately after intralesional triamcinolone injections for keloid scars. Intradermal testing was performed. She showed a positive reaction to triamcinolone confirming a type I allergy to this steroid.

Conclusions: It is important to consider an allergy to corticosteroids in patients with worsening anaphylactic symptoms after administration of systemic corticosteroids.

CASE 1

A 33-year-old woman with an atopic diathesis, fragile high-risk asthma, and ulcerative colitis developed both type I and type IV allergic reactions to systemic corticosteroids.

This patient presented on several occasions with a history of an acute eczematous dermatitis on her face, neck, and upper body after receiving either intravenous (IV) Solu-Medrol (methyl prednisolone sodium succinate; Pfizer Labs), IV Solu-Cortef (hydrocortisone sodium succinate; Pfizer Labs), or oral prednisone for treatment of an asthma exacerbation. All 3 medications are group A steroids. Eczematous dermatitis started 24 hours after steroid administration, peaked at 72 hours, and lasted several weeks. Episodes were associated with intense burning and itching. The patient also reported a similar milder burning of the skin associated with a low-grade eczema after repetitive use of her Pulmicort (budesonide; AstraZeneca) inhaler, usually within 24 to 72 hours. Pulmicort is a group B corticosteroid.

She presented to the emergency department on multiple occasions for asthma attacks. After receiving parenteral corticosteroids in the emergency department, her respiratory status

deteriorated, at approximately 6 hours after drug administration, necessitating transfer to the intensive care unit. On 4 occasions, intubation was required. Initially, there was no perceived association between the deterioration in respiratory status and a possible steroid allergy.

To confirm the diagnosis of a type IV hypersensitivity reaction after systemic corticosteroids manifesting as dermatitis, this woman was patch tested twice to the chemotechnique topical corticosteroid series (Chemotechnique Diagnostics, Malmö, Sweden), European standard series, cosmetic series, and textile series. Patch testing was performed with a standardized technique using the Finn Chambers (Epitest, Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster A/S, Vennesla, Norway). The patches were evaluated at 48 and 96 hours after initial placement according to the North American Contact Dermatitis Group guidelines, and the results were all found to be negative, including the screening agents for steroid allergy.¹

Later, intradermal testing was done to confirm a type I allergy to systemic corticosteroids, to explain the deterioration of her respiratory status after administration of corticosteroids. One milligram each of Solu-Medrol, Solu-Cortef, and prednisone in 0.25 mL of sterile water were sequentially injected into the patient's arms at 5-minute intervals. Benzyl alcohol was also injected as a control. Benzyl alcohol was a preservative in the sterile water. At 15 minutes, the patient developed a headache, tachycardia, and shakiness. After 30 minutes, the patient deteriorated with wheezing and bronchospasm, and she was transferred to the

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The authors have no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0b013e318277ca22

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emergency department. She was treated with IV Benadryl (diphenhydramine; McNeil Consumer & Specialty Pharmaceuticals), Atrovent (ipratropium bromide; Boehringer Ingelheim Pharmaceuticals), and Intal (cromolyn sodium inhalation aerosol; King Pharmaceuticals) via nebulizer. She settled and was discharged at 4 hours after intradermal testing. At 72 hours, she returned to the clinic with an acute eczematous reaction on her head, neck, and upper extremities. She had a flare, showing a 3+ reaction at 72 hours at the Solu-Cortef site of intradermal testing, as well as the Solu-Medrol site. There was a milder 2+ reaction at the site where crushed prednisone mixed with sterile water was injected.

The patient was electively admitted to the respiratory service to determine whether she could be treated with group C corticosteroids in the future for her asthma. One milligram of Decadron (dexamethasone; Merck & Co, Inc) in 0.25 mL of sterile water was injected intradermally into her right arm. At 15 minutes, she developed tachycardia and shakiness and was treated with IV Benadryl. At 40 minutes, she became short of breath and developed brochospasm. She stabilized with Intal and Atrovent nebulizers. At 6 hours, her respiratory status deteriorated suddenly, and she was transferred to the intensive care unit where she was treated with 2 doses of IV adrenaline and racemized adrenaline via a nebulizer and stabilized over a few hours. At 72 hours, a widespread eczematous reaction developed on her face, trunk, and extremities associated with a marked localized reaction at the site of intradermal testing on her arm of dexamethasone.

This patient has a true allergy to systemic corticosteroids. She developed reactions to corticosteroids in group A (Solu-Cortef, Solu-Medrol, and prednisone), group B (budesonide), and group C (dexamethasone). She has both a type I immediate hypersensitivity reaction (proven by intradermal testing) and a type IV delayed hypersensitivity reaction, which was clinically manifested as dermatitis at 72 hours. Type IV hypersensitivity reaction could not be confirmed by patch testing. One reason for this might be that a delayed reading was not done. She did not react to the control, benzyl alcohol, a preservative in the sterile water.

CASE 2

We present a case of a 51-year-old woman. She received intralesional triamcinolone injections on 3 separate occasions for the treatment of keloid scars. On the third exposure to triamcinolone, she developed urticarial lesions on her arms immediately after the injections. The urticaria lasted approximately 30 minutes and then cleared. She had no associated respiratory complaints. The clinical history was consistent with an immediate type I reaction to intralesional triamcinolone, a group B steroid. She was referred for testing to various corticosteroids to confirm this.

Prick testing was done in the clinic to confirm a type I allergy to corticosteroids to explain her urticaria after intralesional triamcinolone. Testing was done to triamcinolone (40 mg/mL), hydrocortisone (250 mg/mL), solumedrol (40 mg/mL), and celestone (5 mg/mL). Results to the prick testing were negative.

Intradermal testing was then performed to try to confirm a type I allergy. She was tested to triamcinolone (4 mg/mL), hydrocortisone (25 mg/mL), solumedrol (4 mg/mL), and celestone (0.5 mg/mL). She had a strong reaction to the triamcinolone only, presenting as a wheal at the site of injection as well as diffuse hives. This confirmed an immediate type I reaction to triamcinolone. Unlike our first patient, she did not have any evidence clinically of a delayed, type IV hypersensitivity reaction manifesting as dermatitis.

DISCUSSION

The possibility of an allergic reaction to systemic corticosteroids is often not considered and may result in severe complications, for example, in the treatment of status asthmaticus or anaphylactic reactions. This, unfortunately, was the scenario with the patient in our first case. She repeatedly presented in acute respiratory distress to the emergency department.

Type I and type IV allergic reactions are both observed with systemic corticosteroids with type IV reactions being much more common than type I. Allergic contact dermatitis after application to topical corticosteroids is by far the most common type of type IV, delayed hypersensitivity reaction.²

Sensitization to topical corticosteroids is not rare, occurring in 0.2% to 5% of the population. Corticosteroids can cause sensitization when used orally, parenterally, or intralesionally as well; however, these modes of sensitization are rare.³ The prevalence of IgE-mediated anaphylactic (type I) reactions to systemic corticosteroids is reported to be approximately 0.3%.⁴

Immediate, type I allergic reactions after oral, intravenous, intramuscular, subcutaneous, and intra-articular administration of corticosteroids can cause sneezing, angioedema, generalized urticaria, bronchospasm, hypotension, and anaphylactic shock.⁴ Methylprednisolone and hydrocortisone are the steroids most commonly reported to cause an immediate reaction when used systemically. These immediate allergic reactions to systemic corticosteroids have been reported to occur more frequently in asthma patients, patients with renal transplants, and patients with a history of aspirin allergy.^{5,6} One of the earliest reports of an immediate, type I reaction to systemic corticosteroids described urticaria and bronchospasm after the injection of corticosteroids in 20 of 2256 patients.⁷

Systemic corticosteroids may be associated with delayed, type IV hypersensitivity reactions as well. Type IV hypersensitivity reactions to systemically administered steroids may present as a generalized dermatitis, an exanthematous eruption, or occasionally, with blistering or purpura.⁸ Different groups of corticosteroids (groups A to D) can trigger the reaction. Bircher et al reported a delayed hypersensitivity reaction to the oral administration of prednisone, although this is rare. The patient presented with a generalized exanthem. The patient had a history of contact allergy to topical prednisone acetate.⁹

Type I immediate hypersensitivity reactions can be identified by prick tests and early intradermal readings (30 minutes). If prick test results are negative, then intradermal testing at progressively higher concentrations of the prick solution are carried out. Type IV hypersensitivity reactions can be identified by patch testing.² The steroid screening agents for patch testing are tixocortol-21-pivalate 1% in petrolatum (group A steroids), budesonide 0.1% in petrolatum (group B steroids), desoximetasone 1% in petrolatum (group C steroids), clobetasol-17-propionate 1% in petrolatum (group D1 steroids), and hydrocortisone-17-butyrate 1% in alcohol (group D2 steroids).

Rasanen and Hasan (1993) were able to document delayed hypersensitivity reactions to oral or intralesional corticosteroids by challenging 5 patients with suspected allergy to corticosteroids orally and/or intralesionally. Oral or intralesional betamethasone caused skin reactions in 3 of the 5 patients, methylprednisolone in 2 of the 5 patients, and hydrocortisone in 1 of the 5 patients. All 5 patients developed a diffuse erythema, predominantly on the face or trunk within a few to 24 hours. The erythema faded in 24 to 72 hours. There was no anaphylactoid reaction.

Patients sensitized to a systemic corticosteroid often exhibit positive tests to other systemic corticosteroids. Evidence to date does not support the classification and patterns of cross-reactivity used for topical corticosteroids being useful in predicting adverse reactions to systemic corticosteroids.²

CONCLUSIONS

Type I allergic reactions to systemic corticosteroids are rare. Type IV allergic reactions are not as rare. It is important to consider an allergy to corticosteroids in patients with worsening anaphylactic

symptoms after administration of corticosteroids. The most common systemic corticosteroids causing anaphylactic reactions, according to the literature, are hydrocortisone and methylprednisolone. To properly identify a type I allergic reaction, skin prick tests, intradermal tests, and oral challenges of different corticosteroids are necessary.⁴ Type IV reactions to parenteral corticosteroids can sometimes be confirmed by patch testing, although in our first case, patch test results were negative.

REFERENCES

1. Marks JG, Belsito JV, Deleo VA, et al. North American Contact Dermatitis Group standard tray patch test results (1992–1994). *Am J Contact Dermat* 1995;6:160–165.
2. Baek M, Marot L, Nicolas J-F, et al. Allergic hypersensitivity to topical and systemic corticosteroids: a review. *Allergy* 2009;64:978–994.
3. Matura M, Goosens A. Contact allergy to corticosteroids. *Allergy* 2000;55:698–704.
4. Comaish S. A case of hypersensitivity to corticosteroids. *Br J Dermatol* 1969;81:919–925.
5. Mathias CGT, Maibach HI, Ostler HB, et al. Delayed hypersensitivity to retrobulbar injections of methylprednisolone acetate. *Am J Ophthalmol* 1978;86:816–819.
6. Sheath A, Reddymasu S, Jackson R. Worsening of asthma with systemic corticosteroids. A case report and review of literature. *J Gen Intern Med* 2006;21:C11–C13.
7. Kilpio K, Hannuksela M. Corticosteroid allergy in asthma. *Allergy* 2003;58:1131–1135.
8. Browne F, Wilkinson SM. Effective prescribing in steroid allergy: controversies and cross-reactions. *Clin Dermatol* 2011;29:287–294.
9. Burgdorff T, et al. IgE-mediated anaphylactic reaction induced by succinate ester of methylprednisolone. *Ann Allergy Asthma Immunol* 2000;89:425–428.