ASTHMA ALLERGY IMMUNOLOGY
ASTIM ALLERJİ İMMÜNOLOJİ

doi: 10.21911/aai.346
Asthma Allergy Immunol 2019;17:111-114

CASE REPORT

Received: 17/01/2017 • Accepted: 16/06/2017
Online Published: 30/06/2019

Hypersensitivity Reaction Due to Oral Methylprednisolone in a Patient with Nonsteroidal Anti-Inflammatory Drug-Exacerbated Respiratory Disease

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ABSTRACT

Hypersensitivity reactions caused by corticosteroids are rarely seen, despite widespread use of these medications. Sensitization to corticosteroids can occur through many routes such as nasal, aerosol, parenteral, oral and topical. Delayed allergic reactions may be observed after topically applied glucocorticoids, but IgE-mediated type 1 (immediate) allergic reactions, which occur after systemic application of glucocorticoids, are very rare. When case-based publications were examined, it was noticed that corticosteroid-associated IgE-mediated type 1 hypersensitivity reactions were more common in patients with nonsteroidal anti-inflammatory drug-exacerbated respiratory diseases (NERD). We present a 32-year-old patient with nonsteroidal anti-inflammatory drug-exacerbated airway disease and a hypersensitivity reaction due to methylprednisolone.

Keywords: Methylprednisolone, hypersensitivity, drug allergy, corticosteroids, Samter's triad (nonsteroidal anti-inflammatory drug-exacerbated respiratory disease)

INTRODUCTION

Corticosteroid use is common in many diseases like asthma, allergic diseases, autoimmune diseases, post-transplantation regimens, and immunologically mediated diseases due to their anti-inflammatory and immunosuppressive effects (1-4). Although corticosteroids are one of the indispensable drugs for the treatment of asthma and allergic diseases, they may cause unexpected hypersensitivity reactions. Hypersensitivity reactions are divided into two subgroups as early and late types. Delayed type hypersensitivity reactions usually occur after topical steroid administration with a rate of 0.5-5%. Early hypersensitivity reactions usually occur after systemic administration and are IgE-mediated type 1 reactions, with a rate of 0.3-0.5% (5-7).

We share a case of hypersensitivity reaction caused by oral methylprednisolone tablet given for asthma attack.

CASE REPORT

A 32-year-old male patient had been followed up for asthma and rhinitis for 5 years. The patient had history of allergic reaction to methylprednisolone and was evaluated in our clinic since he needed systemic corticosteroids due to asthma attacks.

The patient had no additional disease in his medical history and did not report food allergy when food and drug allergy was questioned. He had developed swelling, itching, redness in the tongue and lips, and shortness of breath that appeared 15-30 minutes after taking acetylsalicylic acid, metamizol and diclofenac sodium tablets.

His respiratory system examination showed bilateral prolonged expiration, and ear, nose & throat examination showed posterior nasal drip; there was tenderness upon pressing on the face. Examination of other systems was

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unremarkable. Posteroanterior chest x-Ray was normal. Waters radiography showed mucosal thickening and closure in both maxillary sinuses. Skin prick test was negative. Other laboratory tests were unremarkable.

Anamnesis was obtained from the patient, and the file was retrospectively examined: the patient had first used methylprednisolone tablet 48 mg once daily because of an asthma attack 4 years ago. On the 7th day of the treatment, there was widespread itching, redness, swelling, swelling on the face and feet, in addiction to diarrhea and nausea. Methylprednisolone-dependent drug allergy was considered, treatment was discontinued, and tests were performed after four weeks. Blood tests showed eosinophilia (11.3%; 0.0-7.0), AST: 91 U / L (5-34), and ALT: 245 U / L (3-55). Although liver enzymes were high, hepatitis markers and abdominal USG were normal. Improvement was achieved with symptomatic treatment. No systemic corticosteroid treatment had been administered to the patient for 4 years because of the history of methylprednisolone hypersensitivity, despite need.

We performed prick, intradermal (ID), and oral drug provocation tests (DPT) with methylprednisolone, inhaled budesonide, and other corticosteroids. Skin tests were performed in accordance with the European Network for Drug Allergy (ENDA) guide. When the prick test was negative, the patient underwent intradermal testing. Oral drug provocation was performed as single blind placebo-controlled test with skin test-negative drugs in accordance with ENDA guidelines (8).

Test results are shown in Table I and prick test with methylprednisolone was positive (10x9 mm) (9). The prick and intradermal tests with dexamethasone were performed in order to find alternative corticosteroids that could be used safely. Dexamethasone skin tests were negative. Subsequently, oral drug provocation test was performed, and there was no reaction to dexamethasone. Oral drug provocation test with deflazacort was performed without skin tests due to the lack of an intravenous form and it was negative. The prick and intradermal tests with budesonide were negative (Table I). The drug provocation test with budesonide was performed in inhaled form. During the follow up with PEFmeter, the basal PEF values did not change. Therefore, the patient did not have a reaction against budesonide.

As the patient had history of reactions with acetylsalicylic acid and other nonsteroidal anti-inflammatory drugs, aspirin provocation test was performed and lip swelling, facial rash, and rhinorrhea symptoms were observed with aspirin at the dose of 40 mg. The diagnosis of nonsteroidal anti-inflammatory drug-exacerbated respiratory disease (Samter's triad) was confirmed.

DISCUSSION

Corticosteroids, which have very important place in the clinic and used widely, have common side effects. However, hypersensitivity reactions are rarely seen in the general population. In our patient, there was history of IgE-mediated type 1 hypersensitivity reaction due to methylprednisolone and the skin test was positive. Coopman and Goossens corticosteroid classification was used to select safe and alternative corticosteroids. In 1989, based on steroid allergy, corticosteroid compounds were divided into four groups according to cross-reactivity by Coopman et al. (10). This classification was validated using a larger cohort study based on patch test results by Goosseen et al. (11) (Table II).

This classification is mostly defined for reactions occurring after topical administration of corticosteroids, and the ability of this classification to detect cross-reactivity to systemic corticosteroids is less known. In our patient, according to this classification, methylprednisolone sensitivity in Group A was present. Alternatively, in order to find a safe corticosteroid that can be used safely based on the preparations in our country, skin tests and DPTs were performed using budesonide from Group B,

Table I. Prick / intradermal test doses and results with corticosteroids

Corticosteroid	Prick test dose	ID test dose	Prick test	ID test	DPT
Methylprednisolone	40 mg/dl	4 mg/dl	Positive	Not applied	Not applied
Budesonide	0,25 mg/dl	0.025mg/dl	Negative	Negative	Negative
Dexamethasone	4 mg/dl	0.4 mg/dl	Negative	Negative	Negative
Deflazacort			Not applied	Not applied	Negative

ID: Intradermal test, **DPT:** Drug provocation test

Table II. Coopman and Goossens Corticosteroid Classification

Group	Compound	Example
A	Hydrocortisone	Hipocord cream® / Locoid cream®
	Methylprednisolone	Prednol tab-amp-cream® / Depomedrol amp®
	Tixocortol pivalate	—
	Prednisolone	Deltacortril tab® / Norsol drops®
	Prednisone	—
B	Triamcinolone acetonide	Kenacort amp-pomade® / Nasacort spray®
	Fluocinolone acetonide	—
	Halcinonide	—
	Desonide	Prenacid drops®
	Fluocinonide	—
	Budesonid	Pulmicort nebul-inhaler® / Inflacort nasal spray®
C	Betamethasone	Celestone amp®
	Dexamethasone	Dekort tab-amp®
	Desoximetasone	—
	Fluocortolone	Ultralan tab-cream®
D1	Clobetasone-17-butyrate	Eumavate cream ®
	Clobetasol-17-propionate	Psovate cream ®
	Beclomethasone dipropionate	Diprospan amp® / Rinoclenil nasal spray®
	Betamethasone valerate	Betnovate cream ®
	Betamethasone dipropionate	Foster inhaler®
D2	HC-17-propionate	—
	HC-17-butyrate	Lokoid cream®
	Methylprednisolone aceponate	Advantan cream®
	Prednicarbate	Dermatop cream®
	Difluprednate	—

dexamethasone from Group C, and deflazacort without any group classification. It was observed that the other group of corticosteroids could be used safely. There was no cross-reaction between the groups.

Some risk factors associated with corticosteroid allergy have been identified. The ability of the corticosteroids to bind to arginine was suggested as a drug-induced factor, and increase in the alkalinity of the skin (sweat, skin infections, venous stasis, anti-inflammatory drug, atopic dermatitis, irritant contact dermatitis), nonsteroidal hypersensitivity, and conditions requiring repeated high-dose corticosteroid intake (asthma, nephritis, renal transplantation) are factors related to the individual (12). There are case reports suggesting that early-type corticosteroid allergy is more common in asthmatic patients with nonsteroidal anti-inflammatory drug allergy (13-16). This finding is supported in our case, since our case had nonsteroidal anti-inflammatory drug-exacerbated respiratory disease.

Sensitization to corticosteroids can occur by nasal, aerolizer, parenteral, oral, and topical applications. The incidence of corticosteroid hypersensitivity is unclear, with a limited number of case reports and small clinical trials. Clinicians should take this possibility into consideration when evaluating patients, although corticosteroid allergy is observed rarely.

REFERENCES

1. Mumtaz IM, Hoyer BF, Panne D, Moser K, Winter O, Cheng QY, et al. Bone marrow of NZB/W mice is the major site for plasma cells resistant to dexamethasone and cyclophosphamide: Implications for the treatment of autoimmunity. J Autoimmun 2012;39:180-8.
2. Chang C, Gershwin ME. Drugs and autoimmunity a contemporary review and mechanistic approach. J Autoimmun 2010;34:266-75.
3. Hansel A, Gunther C, Baran W, Bidier M, Lorenz HM, Schmitz M, et al. Human 6-sulfo LacNAc (slan) dendritic cells have molecular and functional features of an important pro-inflammatory cell type in lupus erythematosus. J Autoimmun 2012;40:1-8.

4. Cornec D, Devauchelle-Pensec V, Tobon GJ, Pers JO, Jousse-Joulin S, Saraux A. B cells in Sjogren's syndrome: From pathophysiology to diagnosis and treatment. J Autoimmun 2012;39:161-7.
5. Matura M, Goossens A. Contact allergy to corticosteroids. Allergy 2000;55:698-704.
6. Baeck M, Marot L, Nicolas JF, Pilette C, Tennstedt D, Goossens A. Allergic hypersensitivity to topical and systemic corticosteroids: A review. Allergy 2009;64:978-94.
7. Borja JM, Galindo PA, Feo F, Gomez E. Urticaria to methylprednisolone sodium hemisuccinate. Allergy 2001;56:791-2.
8. Kowalski ML, Asero R, Bavbek S, Blanca M, Blanca-Lopez N, Bochenek G, et al. Classification and practical approach to the diagnosis and management of hypersensitivity to nonsteroidal anti-inflammatory drugs. Allergy 2013;68:1219-32.
9. Ek-ilaç allerjileri tanısında kullanılan protokoller. İçinde: Çelik GE (ed). İlaç Aşırı Duyarlılık Reaksiyonlarına Yaklaşım Ulusal Rehber. 1. Baskı. Ankara: Bilimsel Tıp Yayınevi, 2014; 185.
10. Coopman S, Degreef H, Dooms-Goossens A. Identification of cross-reaction patterns in allergic contact dermatitis from topical corticosteroids. Br J Dermatol 1989;121:27-34.
11. Goossens A, Matura M, Degreef H. Reactions to corticosteroids: Some new aspects regarding cross-sensitivity. Cutis 2000;65: 43-45.
12. Ventura MT, Calogiuri GF, Muratore L, Di Leo E, Buquicchio R, Ferrannini A, et al. Crossreactivity in cell-mediated and IgE-mediated hypersensitivity to glucocorticoids. Curr Pharm Des 2006;12:3383-91.
13. Partridge MR, Gibson GJ. Adverse bronchial reactions to intravenous hydrocortisone in two aspirin-sensitive asthmatic patients. BMJ 1978;1:1521-2.
14. Preuss L. Allergic reactions to systemic glucocorticoids: A review. Ann Allergy Asthma Immunol 1985;55:772-5.
15. Judson MA, Sperl PL. Status asthmaticus with acute decompensation with therapy in a 27-year-old woman. Chest 1995;107:563-5.
16. Dajani BM, Sliman NA, Shubair KS, Hamzeh YS. Bronchospasm caused by intravenous hydrocortisone sodium succinate (Solu-Cortef) in aspirin-sensitive asthmatics. J Allergy Clin Immunol 1981;68:201-4.