

Immediate Allergic Reaction to Methylprednisolone with Tolerance of Other Corticosteroids

Marina Atanasković-Marković^{1,2}, Marija Gavrović-Jankulović³, Srdja Janković²,
Gordan Blagojević⁴, Tanja Ćirković-Veličković³, Irina Milojević², Dušica Simić^{1,2},
Branimir Nestorović^{1,2}

¹School of Medicine, University of Belgrade, Belgrade, Serbia;

²University Children's Hospital, Belgrade, Serbia;

³Faculty of Chemistry, University of Belgrade, Belgrade, Serbia;

⁴Institute of Immunology and Virology "Torlak", Belgrade, Serbia

SUMMARY

Introduction In spite of the wide usage of corticosteroids for the treatment of a plethora of diseases, sometimes they can induce immediate hypersensitivity reactions, which are however uncommon.

Case Outline We report a case of immediate allergic reaction induced by intravenous methylprednisolone given before operation for surgical repair of an arm contracture as a sequel of burns, which the child had tolerated a month before. Six weeks later the patient repeated the anaphylactic reaction during skin testing to methylprednisolone. In addition, basophile activation test with methylprednisolone (BAT) was positive.

Conclusion This case report describes a patient who experienced intraoperative anaphylaxis and anaphylactic reaction induced by skin testing. This is the first report on induction of both anaphylactic reactions by methylprednisolone in the same child. Clinical findings, positive BAT and positive skin tests with methylprednisolone imply that the child developed type-I hypersensitivity. The lack of cross-reactivity with other corticosteroids emphasizes that the reactions were caused by the steroid molecule.

Keywords: corticosteroids; children; immediate allergic reaction; hypersensitivity; methylprednisolone

INTRODUCTION

Corticosteroids are widely used for the treatment of asthma, other allergic, autoimmune and neoplastic diseases. Despite their clinical efficacy, they can induce immediate or delayed hypersensitivity reactions [1, 2]. Immediate allergic reactions such as generalized coetaneous eruption (urticaria), severe respiratory distress or collapse are less frequent but may also occur [1]. Allergic reactions after parenteral administration of corticosteroids have rarely been reported in literature and most of them were isolated cases [2, 3]. Only a few reports have shown evidence of IgE antibodies to culprit corticosteroids [4, 5, 6].

Because of their low molecular mass, corticosteroids probably act as haptens. The allergic reactions may be caused by the steroid molecule itself, its ester or the excipients in preparation [1].

Corticosteroids have been classified according to Coopman [7] in four reactivity groups (A, B, C and D) based on their structural and chemical characteristics. Different patterns of cross-reactivity have been reported [8, 9]. Some authors report allergy to corticosteroids belonging to the A group of Coopman classification [1]. Others describe cross-reactivity between different succinate esters [4] or between steroids with similar chemical structure, although they belong to different groups of Coopman classification [10].

In patients allergic to one or more corticosteroids, it is very important to establish those which patients can tolerate, because these drugs represent the most effective treatment for different diseases and sometimes they are the only possible drug to use in daily medical practice [1].

CASE REPORT

We report a case of immediate allergic reaction induced by methylprednisolone with tolerance of other corticosteroids. A 12-year-old boy had an anaphylactic reaction within a few minutes after intravenous injection of 60 mg methylprednisolone given before operation for surgical repair of his right arm contracture as a sequel of burns, which he had tolerated one month before. Symptoms included generalized urticaria, drop in blood pressure, cold sweats, dyspnoea and wheezing (respiratory distress). After treatment with epinephrine and chloropyraminum, his symptoms were considerably reduced within one hour and completely resolved after 6 hours. Tryptase level (ImmunoCAP, Phadia, Uppsala, Sweden, cut-off >6.6 µg/l) was 35 mg/l, five times higher than the referent value, which was rapidly reversed by epinephrine.

The patient had allergic rhinitis and used intranasal steroids mometasone furoate, but had no family history of allergic disease.

Correspondence to:

Marina ATANASKOVIĆ-MARKOVIĆ
University Children's Hospital
Tiršova 10, 11000 Belgrade
Serbia
marinaa@eunet.rs

Six weeks later the child was referred to our department in order to study drug reactions and to determine safe alternative drugs for the future.

The child underwent prick and intradermal skin tests with the commercial preparation of methylprednisolone which were diluted in saline solution (1:10 to 1:1000), as well as with prednisolone, prednisone, hydrocortisone, budesonide, betametasone, dexamethasone and betametasone dipropionate. Saline solution and histamine dihydrochloride (0.1 mg/mL) were used as negative and positive controls, respectively.

Skin tests were performed in accordance with the general ENDA/EAACI guidelines for evaluating and diagnosing subjects with a suspicion of immediate allergic reactions to drugs [11]. In case of positive skin tests further examinations were interrupted and the child was considered allergic to that drug, as previously described. If negative, a drug provocation test (DPT) was done to confirm the diagnosis and assess cross-reactivity [12, 13].

The patient responded positively to intradermal testing with methylprednisolone (wheal 15×25 mm) at a dilution of 1:100. Ten min after application urticarial rash appeared on his arm, face and neck, with drop in blood pressure, which required immediately the administration of epinephrine and cetirizine. Intradermal tests with other above mentioned corticosteroids, belonging to the same or to another group of the Coopman classification were negative. Skin prick and intradermal testing was negative in three control subjects.

The presence of type I hypersensitivity to methylprednisolone was assessed by a basophile activation test (Flow2CAST, Bühlman, Switzerland). Briefly, the patient's whole blood was incubated for 30 minutes with methylprednisolone (0.1 µg/mL), and the percentage of activated basophiles was thereafter determined by measuring the expression of CD63 on a flow cytometer using an appropriate monoclonal antibody. The drug induced activation in 20.2% of basophiles. Since 6.0% of basophiles were activated in the control sample, the stimulation index (the

ratio between percentages of CD63⁺ basophiles in the test sample to that in the control sample) was 3.4.

The methylprednisolone ImmunoCAP (Phadia) was not performed because it was not available in our country.

DISCUSSION

This is the first report describing a child who experienced intraoperative anaphylaxis to methylprednisolone and six weeks later repeated the anaphylactic reaction during skin testing to the same drug. It is widely accepted that patients allergic to one corticosteroid usually shows cross-reactivity to other molecules, because they have common chemical structures [9]. French authors [14] have described cross-reactivity between methylprednisolone and hydrocortisone, two drugs which belong to the A group of corticosteroids. The patient tolerated prednisolone, the corticosteroid which belongs to group A. However, in our case, the child tolerated corticosteroids which belong to group B, C and D, but also other corticosteroids belonging to group A, according to Coopman. Thus, we did not demonstrate any cross-reactivity among different corticosteroids.

Positive skin tests and positive BAT revealed an immediate type I hypersensitivity to methylprednisolone in the case presented in this report. The lack of cross-reactivity with other corticosteroids emphasizes that the reactions were isolated to methylprednisolone.

We believe that our observation is important, because we demonstrated a relationship from the clinical point of view, with skin testing and BAT as a diagnostic tool for the diagnosis of IgE mediated allergy to corticosteroids.

ACKNOWLEDGMENTS

The study was supported by Grants 172049 and 172024 from the Ministry of Education and Science, Republic of Serbia.

REFERENCES

- Venturini M, Lobera T, Del Pozo MD, Gonzalez I, Blasco A. Immediate hypersensitivity to corticosteroids. *J Investing Allergol Clin Immunol*. 2006; 16:51-6.
- Baeck M, Marot L, Nicolas J-F, Pilette C, Tennstedt D, Goossens A. Allergic hypersensitivity to topical and systemic corticosteroids: a review. *Allergy*. 2009; 64:978-94.
- Aranda A, Mayorga C, Ariza A, Dona A, Blanca-Lopez N, Canto G, et al. IgE-mediated hypersensitivity reactions to methyl-prednisolone. *Allergy*. 2010; 65:1376-80.
- Burgdorff T, Venelmalm L, Vogt T, Landthaler M, Stoly W. IgE-mediated anaphylactic reaction induced by succinate ester of methylprednisolone. *Ann Allergy Asthma Immunol*. 2002; 89:425-8.
- Rasanen L, Tarvainen K, Makinen-Kijunen S. Urticaria to hydrocortisone. *Allergy*. 2001; 56:352-3.
- Deruaz CA, Spertini F, Souza Lima F, Du Pasquier RA, Schlupe M. Anaphylactic reaction to methylprednisolone in multiple sclerosis: a practical approach to alternative corticosteroids. *Multiple Sclerosis*. 2007; 13:559-60.
- 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.
- Escribano-Rodriguez MM, Gonzalez-Pol J, Munoz-Bellido FJ, De La Calle-Toral A, Velazques-Amor E, Conde-Hernandez J. Immediate reaction to methylprednisolone with tolerance of other corticosteroids. *Allergy*. 1997; 52:677-8.
- Nucera E, Buonomo A, Pollastrini E, De Pasquale T, Del Ninno M, Roncallo Ch, et al. A case of cutaneous delayed-type allergy to oral dexamethasone and to betamethasone. *Dermatology*. 2002; 204:248-50.
- Lopez-Serrano MC, Moreno-Ancillo A, Contreas J, Ortega N, Cabanas R, Barranco P, et al. Two cases of specific adverse reactions to systemic corticosteroids. *Invest Allergol Clin Immunol*. 1998; 6(5):324-7.
- Brochow K, Romano A, Blanca M, Ring J, Pichler W, Demoly P. General considerations for skin test procedures in the diagnosis of drug hypersensitivity. *Allergy*. 2002; 57(1):45-51.
- Aberer W, Bircher A, Romano A, Blanca M, Campi P, Fernandez J, et al; ENDA EAACI. Drug provocation testing in the diagnosis of drug hypersensitivity reactions: general considerations. *Allergy*. 2003; 58(9):854-63.
- Brockow K, Romano A. Skin tests in the diagnosis of the drug hypersensitivity reactions. *Curr Pharm Des*. 2008; 14(27):2778-91.
- Ben Said B, Larey V, Nicolas JF, Rozieres A, Berard F. Methylprednisolone-induced anaphylaxis: diagnosis by skin test and basophil activation test. *Allergy*. 2010; 65:531-2.

Рана алергијска реакција на метилпреднизолон са толеранцијом других кортикостероида

Марина Атанасковић-Марковић^{1,2}, Марија Гавровић-Јанкуловић³, Срђа Јанковић², Гордан Благојевић⁴, Тања Ћирковић-Величковић³, Ирина Милојевић², Душица Симић^{1,2}, Бранимир Несторовић^{1,2}

¹Медицински факултет, Универзитет у Београду, Београд, Србија;

²Универзитетска дечја клиника, Београд, Србија;

³Хемијски факултет, Универзитет у Београду, Београд, Србија;

⁴Институт за имунологију и вирусологију „Торлак“, Београд, Србија

КРАТАК САДРЖАЈ

Увод Упркос широкој примени кортикостероида у лечењу од различитих болести, они понекад могу изазвати рану алергијску реакцију.

Приказ болесника Код дванаестогодишњег дечака дошло је до ране алергијске реакције изазване интравенском применом метилпреднизолонa непосредно пре хируршке интервенције, тачније, корекције контрактуре шаке која се јавила као компликација опекотине. Месец дана пре појаве алергијске реакције дете је примало метилпреднизолон и добро га подносило. Шест недеља после операције поново се јавила анафилактичка реакција током кожног тести-

рања метилпреднизолоном. Примењен је и тест активације базофила (*BAT*) овим леком, чији је налаз био позитиван.

Закључак Ово је први приказ две врсте анафилактичке реакције изазване метилпреднизолоном код исте особе. Клиничка слика, позитивни налаз *BAT* и позитивне кожне пробе на метилпреднизолон показују да се код детета развио први тип хиперсензитивне реакције. Недостатак унакрсне реактивности с осталим кортикостероидима указује на то да је алергијска реакција изазвана стероидним молекулом.

Кључне речи: деца; хиперсензитивне реакције; кортикостероиди; метилпреднизолон; рани тип алергијске реакције

Примљен • Received: 01/12/2010

Прихваћен • Accepted: 14/07/2011