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.

Anamnestic 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>
<thead>
<tr>
<th>Corticosteroid</th>
<th>Prick test dose</th>
<th>ID test dose</th>
<th>Prick test</th>
<th>ID test</th>
<th>DPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylprednisolone</td>
<td>40 mg/dl</td>
<td>4 mg/dl</td>
<td>Positive</td>
<td>Not applied</td>
<td>Not applied</td>
</tr>
<tr>
<td>Budesonide</td>
<td>0.25 mg/dl</td>
<td>0.025 mg/dl</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>4 mg/dl</td>
<td>0.4 mg/dl</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Deflazacort</td>
<td>Not applied</td>
<td>Not applied</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ID: Intradermal test, DPT: Drug provocation test
Sensitization to corticosteroids can occur by nasal, aerosolizer, 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