

Anaphylaxis to Topically Applied Sodium Fusidate

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Fusidic acid is a bacteriostatic antibiotic that is effective primarily on gram-positive bacteria, such as *Staphylococcus* and *Corynebacterium* species. It is often topically applied to the skin, but is also given systemically as a tablet or injection. Allergic contact dermatitis, or urticaria, has been reported as a side effect of fusidic acid treatment, whereas anaphylaxis to topically administered fusidic acid has not been reported previously. A 16-year-old boy visited an outpatient clinic for further evaluation of anaphylaxis. He suffered abrasions on his arms during exercise, which were treated with a topical ointment containing sodium fusidate. Within 30 minutes, he developed urticaria and eyelid swelling, followed by a cough and respiratory difficulty. His symptoms were relieved by emergency treatment in a nearby hospital. To investigate the etiology, oral provocation with fusidate was performed. After 125 mg (1/2 tablet) of sodium fusidate was administered, he developed a cough and itching of the throat within 30 minutes, which was followed by chest discomfort and urticaria. Forced expiratory volume in 1 second (FEV1) dropped from 4.09 L at baseline to 3.50 L after challenge, although wheezing was not heard in his chest. After management with an inhaled bronchodilator using a nebulizer, chest discomfort was relieved and FEV1 rose to 3.86 L. The patient was directed not to use fusidate, especially on abrasions. Here we report the first case of anaphylaxis resulting from topical fusidic acid application to abrasions.

Key Words: Anaphylaxis; fusidic acid; ointment

INTRODUCTION

Fusidic acid is a bacteriostatic antibiotic that is obtained from the fungus *Fusidium coccineum* that is primarily effective on gram-positive bacteria. It has a steroid structure and displays very high activity against *Staphylococcus aureus*, including methicillin-resistant strains, and *Staphylococcus epidermidis*. It is also active against some *Corynebacterium* species, when it is used via oral, intravenous, and topical application routes. Fusidic acid has commonly been used for the treatment of mild to moderate skin and soft-tissue infections for more than 30 years.^{1,2}

Despite the wide use of fusidic acid, it presents few serious side effects. Occasional allergic reactions associated with allergic contact dermatitis have been reported.^{3,4} Most of these cases had underlying stasis dermatitis or atopic dermatitis.⁵ However, anaphylaxis to topically administered fusidic acid has not been reported previously. Here, we report a case of a 16-year-old boy who showed anaphylactic reactions after topical administration of fusidic acid ointment to abrasions on his arms.

CASE REPORT

A 16-year-old boy visited an outpatient clinic for further eval-

uation of anaphylaxis. He presented to the school nurse after acquiring abrasions on his arms during exercise. The nurse applied a topical ointment containing sodium fusidate to the abrasions. Within 30 minutes, the patient began experiencing eyelid swelling and urticaria with pruritus of his whole body. He then began coughing and had difficulty breathing. He was taken to the nearby hospital and received emergency treatment. Two years earlier, he had been brought to the emergency department with symptoms of urticaria, eyelid edema, a cough, and dyspnea after taking medications containing acetaminophen, tiropamide, domperidone, and trimebutine. However, drug allergy was not confirmed at that time. No past medical history of asthma or allergic rhinitis or family history of allergic diseases was found.

We performed an oral provocation test with 125 mg (1/2 tablet) of fusidic acid. Thirty minutes after the first dose, the patient

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presented with a cough and an itching sensation on his neck followed by chest discomfort and urticaria on the forehead and right arm. Forced expiratory volume in 1 second (FEV1) dropped from 4.09 L at baseline to 3.50 L after challenge, although wheezing was not heard in his chest. The provocation test was terminated and an inhaled bronchodilator was given using a nebulizer. Chest discomfort was relieved and FEV1 rose to 3.86 L following management. His skin lesions improved with oral administration of antihistamine. Oral provocation tests with acetaminophen, amoxicillin, and cefadroxil were all negative. However, he showed conjunctival injection and itchy throat 30 minutes after a challenge test with 100 mg tiropramide. His final diagnosis was drug allergy to fusidic acid and tiropramide. We recommended that these drugs should not be administered systemically and not to use topical fusidic acid on abrasions.

DISCUSSION

Fusidic acid is metabolized mainly in the liver. Adverse reactions to fusidic acid are associated with intravenous administration, and have been related to the gastrointestinal tract and liver. Oral fusidic acid has also been shown to cause adverse reactions, which were classified as gastrointestinal (58%), constitutional (6.1%), neurologic (3.3%), allergic (4.6%), and other (27%).⁶ These occurred most commonly within 6-10 days.

With regard to adverse reactions, 29 cases involving allergic contact dermatitis to topical fusidic acid have been reported.⁷ However, the incidence of hypersensitivity to topical fusidic acid is very low in most studies. In a study that performed patch tests with 26 commercially available antiseptic, antibacterial, and antifungal ointments, 45 out of 200 subjects (22%) showed one or more positive tests, but none was sensitive to fusidic acid.⁸ A study investigating the comparative frequency of patch test reactions to topical antibiotics found a low incidence of positive reactions to fusidic acid (0.3%) as compared with 3.6% for neomycin and 0.7% for clioquinol.⁹ It was also reported that there has been no increase in the frequency of allergic reactions to fusidic acid since the 1980s, despite its increasing use. The reason for fusidic acid being an inappropriate contact allergen may result from its large molecular weight (>500 kDa) and its unique structure, which is different from that of other antibiotics.

To support the diagnosis of allergy to topically applied fusidic acid in our patient, we needed to exclude allergic reactions to other components of the ointment. The components of fusidic acid ointment are 2% sodium fusidate, lanolin, liquid paraffin, Vaseline, and cetyl alcohol. A study in the UK revealed that most fusidic-acid-allergic patients were also allergic to lanolin (52%), one of the constituents of Fucidin[®] ointment.⁹ However, our patient also manifested anaphylactic reactions in the provocation test with the fusidic acid tablet, which did not contain any of the additives present in the Fucidin[®] ointment. This indicates that anaphylaxis was triggered by fusidic acid itself and not by any

of the additives, including lanolin.

In our study, the patient displayed anaphylactic reactions, including a cough and chest discomfort, following the application of fusidic acid ointment. When trying to establish the cause of anaphylactic reactions, materials that were previously injected or ingested are generally considered, but agents applied to the skin may be easily overlooked. However, it should be considered that systemic absorption of topically applied substances is possible, especially through a defective skin barrier.¹⁰⁻¹² Because we suspected anaphylaxis caused by systemic absorption of fusidic acid through abrasions, an oral provocation test was performed using a fusidic acid tablet. Although rare, anaphylactic reactions have been reported after application of bacitracin ointment, and the presence of specific IgE antibodies to bacitracin has been suggested.^{10,13,14} Unfortunately, we did not examine the presence of IgE antibodies specific to fusidic acid in our patient.

Conclusively, we report the first case of anaphylaxis following topical administration of fusidic acid. Specifically, fusidic acid ointment was applied to abrasions on the arms of a 16-year-old boy. This rare, life-threatening adverse event is clearly worth the attention of practitioners.

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