

### Systemic IgE-mediated hypersensitivity reaction to topical polymyxin B

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#### Clinical Implications

- We present a novel case of a systemic reaction to a topical formulation of polymyxin B that highlights the importance of considering topical antibiotics as a cause of systemic reactions, especially as the class of polymyxin antibiotics gain wider clinical use.

#### TO THE EDITOR:

Topical antibiotics are frequent causes of allergic contact dermatitis. Two commonly implicated antibiotics include neomycin and bacitracin, which had a prevalence of allergic contact dermatitis in North America over the past 20 years of 7.2% to 13.1% and 1.5% to 9.1%, respectively.<sup>1</sup> Recently, there has been increasing literature demonstrating allergic contact dermatitis to polymyxin B.<sup>2,3</sup> However, we could find only 1 reported case of a systemic reaction to topical polymyxin B in our literature review.<sup>4</sup> We present a case of systemic IgE-mediated reaction to topical polymyxin B.

A 12-year-old boy with no significant medical history presented to the emergency room with angioedema of the tongue, face, eyes, hands, and feet; coughing; and pruritus of the eyes, fingers, and feet. The patient was given epinephrine, antihistamines, and systemic steroids with improvement and discharged several hours later. Swelling resolved over the next few days. Of note, the patient had the reaction after playing outside that afternoon and approximately 3 hours after having eaten cookie dough ice cream. Fifteen minutes before the reaction he had applied a generic neosporin containing polymyxin B, bacitracin zinc, neomycin, and pramoxine with a Band-Aid to an abrasion on his knee from a fall. He had not taken any over-the-counter medications including nonsteroidal anti-inflammatory drugs. The patient reported no previous history of allergic reactions or anaphylaxis, and there was no family history of urticaria or angioedema. At the time of the evaluation, he had subsequently tolerated peanut and a few tree nuts. Serum specific IgE testing for latex, tree nuts, and aeroallergens was unremarkable. C4 was normal. Skin prick testing to aeroallergens revealed positive reactions to ragweed, dust mites, alternaria/hormodendrum, penicillium mix, aspergillus mix, and dog. He was initially diagnosed with idiopathic urticaria and angioedema. He remained asymptomatic until 1 year later; after application of generic neosporin to abrasions on the right face, shoulder, and wrist, he complained of tingling and swelling of his face, fingers, and toes. He developed a facial rash and periorbital swelling, which was worse on the right side, with no laryngeal edema, respiratory distress, or gastrointestinal symptoms. Symptoms improved with diphenhydramine at the time of the reaction; he also started cetirizine twice daily for 1 week. At this time, the patient and his mother recalled an incident when the same topical antibiotics were applied to an abrasion on his left elbow.

The lesion remained red and was pruritic for weeks following application of topical neosporin; it also did not heal well per the mother. Three months after the systemic reaction, percutaneous skin testing was performed to bacitracin/polymyxin (500 units bacitracin, 10,000 units polymyxin per 28 g), bacitracin 500 units per 28 g (in duplicate), neomycin sulfate 3.5 mg per 28 g, and Sarna antiitch cream (pramoxine HCl) 10 mg per 28 g. The patient had a positive skin prick test result to bacitracin/polymyxin ointment with a wheal and flare reaction of  $5 \times 8$  mm (saline control  $1 \times 3$  mm), and negative skin test result to bacitracin ointment (in duplicate,  $1 \times 3$  mm and  $2 \times 3$  mm, respectively), neomycin ointment ( $2 \times 3$  mm), and Sarna antiitch cream containing pramoxine ( $2 \times 3$  mm) (Figure 1). Polymyxin alone was unavailable at the time of testing. Although the wheal and flare to the combined bacitracin/polymyxin ointment was relatively small, when taking into consideration the patient's history of several systemic reactions to triple antibiotic ointment and the negative skin testing results to all other components of the ointment, it was concluded that the patient had a systemic hypersensitivity reaction to topical application of polymyxin B. The patient was instructed to avoid all medications containing polymyxin B as well as any vaccines that contain polymyxin B.

Recently, increased reports of allergic contact dermatitis to polymyxin B have led to greater recognition that polymyxin B is a more common contact allergen than once thought.<sup>2</sup> A study analyzing patch testing data from 2 hospitals showed a 2.3% prevalence of reactivity to polymyxin B among 795 tested participants.<sup>3</sup> As a result of this growing awareness, polymyxin B has since been added to the American Contact Dermatitis Society Core Allergen Series for patch testing in 2017.<sup>5</sup> However, literature search revealed only 1 case of a systemic reaction linked directly to polymyxin B. Henao and Ghaffari<sup>4</sup> reported a 2-year-old patient with anaphylaxis after the second course of treatment with polymyxin B and trimethoprim (Polytrim) ophthalmic solution for bacterial conjunctivitis with a positive skin prick test result to polymyxin B and negative skin prick test result to trimethoprim.<sup>4</sup> Our particular case provides additional evidence for the potential for a systemic reaction to polymyxin B through topical application to an open skin wound.

Bacitracin has been frequently implicated in cases of allergic contact dermatitis as well as anaphylaxis.<sup>6,7</sup> There have also been cases in which there is concomitant hypersensitivity to both bacitracin and polymyxin B.<sup>3</sup> In multiple cases of patients reacting to topical combination bacitracin and polymyxin B formulations, when further workup was not pursued, it was assumed that bacitracin was the culprit because there was much more literature to support bacitracin causing anaphylaxis.<sup>6</sup> In such cases, the allergic reaction may have instead been secondary to polymyxin B or both agents, and thus the incidence for systemic reaction to polymyxin B may be underestimated.

It is important to recognize the risks of polymyxins, as they are gaining more use because of the emergence of more multidrug-resistant organisms. Polymyxin is a class of antibiotics with narrow antibacterial spectrum, targeting primarily gram-negative rods. Isolated from *Paenibacillus polymyxa*, there are 5 groups of polymyxins, labeled A-E, with only polymyxin B and polymyxin



**FIGURE 1.** Photo of patient's percutaneous skin testing to components of generic neosporin. Testing was done from top to bottom to bacitracin 500 units per 28 g, bacitracin/polymyxin (500 units bacitracin, 10,000 units polymyxin per 28 g), neomycin sulfate 3.5 mg per 28 g, and Sarna antiitch cream (pramoxine HCl) 10 mg per 28 g. Positive skin prick test result is noted to bacitracin/polymyxin, with negative skin prick test result to bacitracin alone.

E having clinical utility. Polymyxin B is a common component of topical, ophthalmic, and otic preparations, often in combination with other antibiotics, used to treat superficial infections. Polymyxin E, also known as colistin, is most commonly found in

a parenteral formulation that has become a last-line agent for treating multidrug-resistant gram-negative rods such as *Pseudomonas aeruginosa*, *Aceinobacter baumannii*, and *Klebsiella pneumoniae*.<sup>8</sup> Literature review reveals very few cases of systemic reaction to colistin.<sup>9</sup> To our knowledge, potential cross-reactivity patterns among polymyxins are unknown and would be an area for further research. With a growing interest in developing new generations of polymyxins to combat the increasing threat of multidrug-resistant organisms, particularly for parenteral use, it would be important to recognize the risk of hypersensitivity to polymyxin drugs, even in the topical form.

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