

Urticaria and Angioedema Secondary to Methylphenidate Exposure in a Young Child

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To The Editor:

ALLERGIC ADVERSE REACTIONS TO METHYLPHENIDATE are exceedingly rare, and even rarer with the oral formulation of methylphenidate. Few cases of contact dermatitis secondary to transdermal formulations of methylphenidate have been reported (Warshaw et al. 2010; Vashi et al. 2011). A PubMed search produced only a handful of reports (case reports) of allergic adverse reaction to oral methylphenidate (Weil 1968; Rothschild and Nicol 1972; Sverd et al. 1977; Cohen et al. 1992; Coskun et al. 2009; Heinzerling et al. 2011). We present a case involving hypersensitivity allergic adverse reaction to methylphenidate and dexamethylphenidate. Notably, our patient developed urticaria and angioedema secondary to methylphenidate and dexamethylphenidate, which has been reported only once before (Sverd et al. 1977).

Case Report

A 6-year-old Hispanic boy came to our outpatient clinic with his mother with complaints of hyperactivity, poor attention, and disruptive behavior. His school also reported that he was having difficulty sitting at his desk when expected to, was disruptive to the whole class, and had poor attention. Past medical history was significant for severe eczema and current mild asthma. One first degree and four second degree relatives of the patient had allergic skin problems, including eczema. The patient was using an albuterol inhaler daily on an as-needed basis for asthma. His mother denied his having any known drug or food allergy. Results of laboratory tests including complete blood count, basic metabolic profile, and electrocardiogram (ECG) were within normal limits. The patient was diagnosed with attention-deficit/hyperactivity disorder (ADHD) combined type, and was prescribed methylphenidate 2.5 mg daily as a starting dose. Approximately 5 days after he started methylphenidate therapy, his mother noticed that there was swelling and redness in his left eyelid and all around his left eye (Fig. 1). He complained of discomfort over the same area and was constantly rubbing it with his hand, which led to mild erythema and watering from the eyes. There was no swelling or erythema of the conjunctiva. There was no involvement of the right eye or the rest of his face, but he itched all over his body. When examined, he also had a rash that was distributed over his trunk and both arms. His rash consisted of raised, edematous, circular-oval shaped lesions from 1 mm to 2 cm in size, which were highly pruritic (Fig. 2). Per the patient's mother, his body rash developed at approximately the same time as the swelling

around the left eye. Swelling around the eye was nonpitting and nontender. He did not have any fever, difficulty in breathing, or dizziness. He was not taking any medications other than methylphenidate and the as-needed albuterol inhaler (which he had been taking for many months). There was no history of application of any medication to the eyes. Methylphenidate was immediately discontinued. The child was evaluated and was diagnosed to be having an allergic hypersensitivity reaction in the form of urticaria and angioedema, possibly caused by methylphenidate. He was treated with antihistaminic medications, and his symptoms fully subsided in next few days. One week later, after discussion with his mother, dexamethylphenidate was introduced at a dose of 2.5 mg daily. This time the patient again developed a similar adverse reaction, but it was in the other (right) eye and developed relatively quickly. Within 24 hours of taking the first dose of dexamethylphenidate, he developed swelling and redness of the right eyelid and around the right eye (Fig. 3) and a similar rash to the one he had had previously. Again there was no fever, difficulty in breathing, or dizziness. He was treated with antihistaminic medications and his symptoms completely resolved within next 1 week. At the time of writing this report, the patient has been taking guanfacine 0.5 mg b.i.d. for 1 month without any adverse reaction.

Discussion

The package insert of methylphenidate (Ritalin) and dexamethylphenidate (Focalin) mentions an allergic reaction and/or skin rash as possible adverse reactions, but any report of allergic adverse reaction has been exceedingly rare with methylphenidate or dexamethylphenidate. Our PubMed search, with no time period limit, for allergic reaction to oral methylphenidate/dexamethylphenidate, produced only handful of cases (Weil 1968; Rothschild and Nicol 1972; Sverd et al. 1977; Cohen et al. 1992; Coskun et al. 2009; Heinzerling et al. 2011). The age of the patients in these cases ranged between 4 years 9 months (Rothschild and Nicol 1972) and 9 years (Sverd et al. 1977; Heinzerling et al. 2011). Allergic adverse reactions reported in these case reports included some kind of skin eruptions (Weil 1968; Cohen et al. 1992; Coskun et al. 2009; Heinzerling et al. 2011), swelling of one side of face and penis (Sverd et al. 1977), and allergic conjunctivitis (Rothschild and Nicol 1972). Swelling of one side of face and penis described in an earlier report (Sverd et al. 1977) was probably a case of angioedema similar to our case. The time period for developing the allergic adverse reaction ranged between a few hours to few weeks in these cases. In our case, the first episode of allergic



FIG. 1. Angioedema of the left eye. A color version of this figure is available in the online article at www.liebertpub.com/cap

reaction developed after approximately 5 days, and the second episode developed within 1 day.

Our patient developed urticarial rash and angioedema around the eyes, but only one eye at a time was affected. Angioedema typically accompanies urticaria, is unilateral, and occurs where connective tissue is loose, such as on the eyelids and around the eye. Mostly, acute urticaria is a hypersensitivity reaction to foods, drugs, or insect stings (Amar and Dreskin 2008). This patient developed an allergic adverse reaction in close proximity and subsequent to introduction of methylphenidate, and a similar adverse reaction was reproduced after rechallenge with dexmethylphenidate. There was no history of unusual food ingestion or environment changes. The abovementioned facts make methylphenidate and dexmethylphenidate the most likely cause. Dexmethylphenidate is a dextrorotatory enantiomer of methylphenidate, with a similar chemical structure, which can explain why the patient showed sensitivity to both of abovementioned medications.



FIG. 2. Urticarial rash on the arm. A color version of this figure is available in the online article at www.liebertpub.com/cap



FIG. 3. Angioedema of the right eye. A color version of this figure is available in the online article at www.liebertpub.com/cap

Mast cells are the primary effector cells in urticaria and in most cases of angioedema. In the majority of cases, mast cells are activated by immunoglobulin E (IgE) antibodies produced in response to the allergen (Amar and Dreskin 2008). The child described here had never been exposed to methylphenidate earlier in his life. His first episode of allergic adverse reaction happened after ~5–6 days, but the second one occurred within hours to 1 day. The likely explanation is that initially, his body took some time to get sensitized to methylphenidate. Once sensitized, he developed an allergic adverse reaction rapidly on re-exposure.

Notably, a strong past and family history of severe eczema points toward allergic diathesis in this child. Possibly this allergic diathesis made him more susceptible to having a hypersensitive reaction to methylphenidate/dexmethylphenidate. At times, angioedema and anaphylaxis can be life threatening, with involvement of the larynx and throat. Considering this, we want to emphasize that the prescribing physician should be mindful of the possibility of allergic adverse reactions to methylphenidate/dexmethylphenidate, especially in patients with known allergic diathesis.

Disclosures

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