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Urticaria Associated With the Pilocarpine Iontophoresis Sweat Test

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INTRODUCTION

The quantitative pilocarpine iontophoresis sweat chloride test is used to confirm the diagnosis of cystic fibrosis. In this test sweat glands are stimulated by pilocarpine, a cholinergic agonist. Pilocarpine is delivered into the skin by a low-voltage electric current through the process of iontophoresis. Pilocarpine nitrate in either a gel or moistened pad is placed under the positive electrode; an electrolyte solution in a gel or moistened pad is placed under the negative electrode, and a current of 2–4 mA is applied for a maximum of 5 min.[1] Following iontophoresis, it is expected that the skin corresponding to the area under the positive electrode be slightly erythematous. From this site sweat is then collected and quantitatively analyzed for chloride.

Pharmacologically, pilocarpine is used in the treatment of xerostomia and glaucoma. There are reports of delayed allergic contact dermatitis in patients using ophthalmic pilocarpine solutions.[2–4] To our knowledge, pilocarpine has not been previously reported to cause urticaria in the setting of sweat testing. We describe a case of urticaria that was successfully prevented upon retesting using an H_1 antihistamine.

CASE REPORT

A 6-year-old girl with a history of recurrent cough and wheezing associated with viral upper respiratory infections was referred to the pediatric pulmonary clinic for evaluation. The history was significant for prolonged coughing after viral upper respiratory tract infections that were not responsive to antibiotics, cough suppressants, or decongestants. Between episodes she was asymptomatic. Past history was negative for urticaria. Her physical examination was completely normal. Pulmonary function by spirometry revealed values in the normal range based on predicted values standardized according to height and gender. A chest radiograph demonstrated normal lungs and resolution of a previously noted left lower lobe atelectasis. An abbreviated panel of aeroallergen skin tests was negative.

A sweat test was performed. Immediately following iontophoresis on the right arm, localized urticarial lesions were observed corresponding to the area of pilocarpine stimulation. The patient did not display symptoms of generalized urticaria or an anaphylactic response. Due to the appearance of the lesions, sweat was not collected from the right arm, nor was the test initiated on the left arm. The patient was treated with 25 mg of oral diphenhydramine hydrochloride elixir. The lesions resolved within hours, and the patient was rescheduled for a second sweat test in 7 days. Hydroxyzine hydrochloride (0.5 mg/kg/dose) was administered orally for three doses every 8 hours in the 24 h before her sweat test was repeated.

The sweat test was repeated, and the patient showed no signs of urticaria following iontophoresis. Sweat was successfully collected and analyzed with the following results: right arm, 9 mmol/L chloride with a 225 mg sample; left arm, 9 mmol/L chloride with a 219 mg sample. Having ruled out cystic fibrosis on the basis of clinical presentation and a negative sweat test, a diagnosis of mild asthma was made. She was treated with daily inhaled beclomethasone, 2 puffs three times a day, and with albuterol (2 puffs) as needed for breakthrough symptoms of cough and wheezing. She has responded well to this regimen and maintains normal lung function.

DISCUSSION

Contact urticaria can be classified as immunological, nonimmunological, or combined etiology, depending on

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whether or not the response is IgE mediated. A variety of chemicals, drugs, foods, toxins, and physical stimuli can produce contact urticaria, presumably through nonimmunological mechanisms.[5] In the case described, pilocarpine appears to have caused contact urticaria directly, without requiring an IgE-mediated reaction. Presumably, during iontophoresis, pilocarpine penetrates the epidermis and acts directly on mast cells, causing the release of histamine and other vasoactive agents. Because pilocarpine is a cholinergic agent, it may also act directly on nerve cells in the skin, which then mediate the development of urticaria. The result is vascular dilatation, increased vascular permeability, and edema, giving rise to the wheal-and-flare response observed in urticaria. Hydroxyzine hydrochloride has been reported to be the most effective H_1 antihistamine for blocking wheal and flare response.[6,7]

The procedure of pilocarpine iontophoresis could also trigger physical urticaria through thermal or electrical current stimulation. In these situations, urticaria would appear on the skin corresponding to both the negative and positive electrodes. In a report of electrical current-stimulated urticaria associated with pilocarpine iontophoresis, urticaria occurred at both electrode sites and was reproducible by the iontophoresis when the chemicals were replaced with deionized water.[6]

The frequency of contact urticaria associated with pilocarpine iontophoresis is unknown but is probably very rare. In the Cystic Fibrosis Center at the University of North Carolina at Chapel Hill 7 of 2,059 patients (0.3%) tested over a 6-year period were reported to have pilocarpine urticaria. In all cases, the reaction was localized and did not cause anaphylaxis. Three of the seven patients were predosed with antihistamine prior to retesting and displayed no signs of urticaria on repeat testing. The remaining four patients were lost to follow up.

The implication of pilocarpine urticaria is significant to clinicians and laboratory personnel performing sweat tests. Sweat should not be collected over any area of diffuse inflammation such as urticaria or eczema because of the concern of potential contamination of the sweat sample with extravascular fluid from such lesions.[1] However, patients susceptible to pilocarpine urticaria can be successfully retested by pretreating them with hydroxyzine hydrochloride.

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