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LETTER TO THE EDITOR

Cholinergic urticaria with angioedema successfully treated with omalizumab

Dear Editor,

Cholinergic urticaria (CholU) is a condition characterized by pinpoint-sized, highly pruritic wheals and typically provoked by stimulation such as exercise, warmth, and emotional distress, which promotes sweating.[1] Since acetylcholine (Ach) is known to induce both sweating and wheals when injected intradermally, it has been considered that this perspiration-associated, syringeal orifice-coincident wheal is mediated by Ach. Meanwhile, angioedema is a sudden-onset localized swelling affecting the skin and/or mucosa and occasionally associated with CholU.[2] Here, we report a case of CholU with angioedema, which was successfully treated with omalizumab.

A 27-year-old Japanese woman was referred to us for evaluation of a 4-year history of pinpoint wheals occurring upon sweating. She also suffered from a number of episodes of swelling of the lips, some of which were accompanied by dyspnea. Her past history included atopic dermatitis. She was treated by a physician with antihistamines at a twice more dose than usual, H2 receptor antagonist, and prednisolone at 20 mg daily. However, her condition did not respond efficiently to any of these drugs.

Blood examination showed high levels of total IgE (1471 U/mL; normal, <200 U/mL), and specific IgE to *Dermatophagoides pteronyssinus* and *Malassezia*. Perspiration was examined by exercise-induced sweating, which was detected by iodine-starch test. There was no hypohidrotic or anhidrotic area on the neck, trunk, limbs, or palms (Figure 1). Ach (Ovisot; Daiichi Pharm. Co., Tokyo, Japan) was diluted to 100 μg/mL with physiological saline, and 0.1 mL of the diluted one was intradermally injected. It induced satellite wheals and sweating around the injection site, as assessed by the iodine-starch technique. Intradermal injection of the patients' own diluted sweat was not performed. We diagnosed her as having CholU with angioedema.

We treated her with omalizumab at 300 mg. After the initial treatment, CholU and angioedema were improved almost completely, as Urticaria Control Test[3] was increased from four (before treatment) to 14 (4 weeks after treatment; more than 12 are evaluated to be well controlled). The patients received omalizumab therapy every 4 weeks, and currently every 6 weeks, with a good therapeutic efficacy.

CholU has two major types.[4] One is the sweat allergy type, in which Ach indirectly acts on mast cells via sweat allergens.[5] The

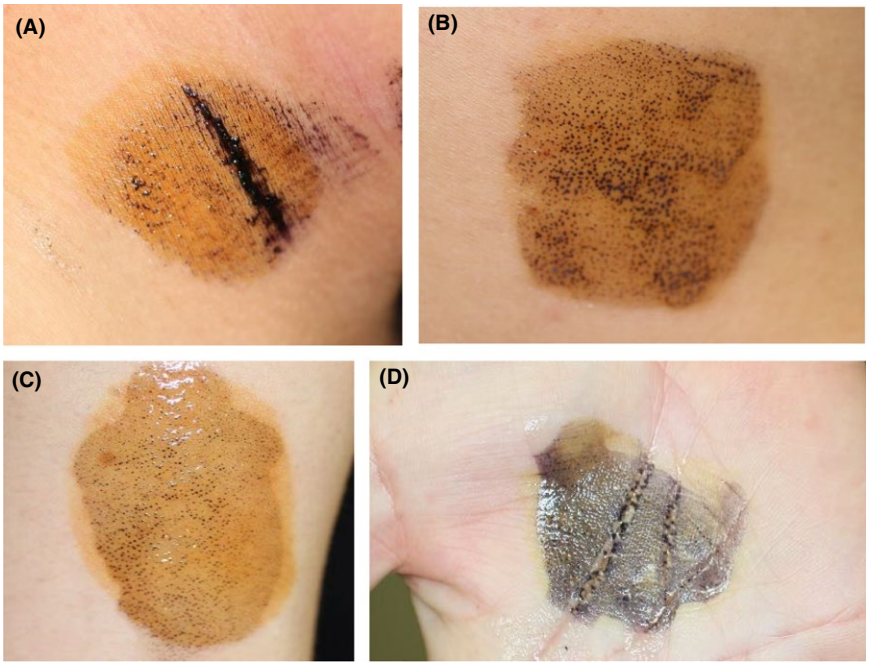

FIGURE 1 No disturbed sweating in this case. Normal sweating on the A, neck, B, trunk, C, forearm, and D, palm

other one is the depressed sweating type, in which Ach directly acts on mast cells.[6] In the former type, patients develop wheals in response to sweat substance leaking from the syringeal ducts to the dermis. In the latter type, we found that CholU with anhidrosis and hypohidrosis (CUAH) lacks cholinergic receptor M3 expression in eccrine gland epithelial cells.[6] CholU with angioedema is characterized by sweat allergy, female dominancy, concomitant presence of atopic dermatitis, and high frequency of anaphylaxis.[2] Instead of palpebral swelling, lip swelling was prominent in our case.

Antihistamines are mostly ineffective in CholU. In several cases, omalizumab has been reported as useful therapy for CholU.[7–9] Our case also documented the effectiveness of omalizumab for both CHolU and the associated symptom of angioedema.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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