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Aquagenic Urticaria: A Case Report

Sir,

Aquagenic urticaria is a rare form of physical urticaria, characterized by small follicular wheals, with an erythematous halo upon exposure to aqueous solutions. We describe here a case of this disorder, whose lesions were maximally reproduced by a combination of pretreatment with acetone and contact with saline.

CASE REPORT

A non-atopic 19-year-old man had noticed the development of small wheals accompanied by itching when he took bath. This reaction had occurred since the age of 13 years. The wheals also appeared when he got wet in the rain, went swimming, or sweated. They disappeared spontaneously about 30 min later. More wheals were induced by seawater than by tap water, and by hot water than cold water, but the wheals failed to appear upon exposure to sunlight or cold air. No enhanced dermatographic reaction was observed. A general physical examination showed no abnormal findings. No similar episode has been observed in his family.

Laboratory investigations, including complete blood cell count, liver and renal function tests, serum protein electrophoresis, immunoglobulins (IgG, A, M, and E), serum complement components of C3 and C4, anti-nuclear antibody and serological test for syphilis, were all negative or within normal limits. Serum and whole blood histamine concentrations were 4.7 nM and 34.0 ng/ml, measured by enzyme immunoassay (Immunotech, Marseille, France) and HPLC, respectively. Skin tests showed a somewhat large erythema for 0.2 µg histamine (50 × 30 mm), but no exaggerated reaction was observed with physiological saline (1 × 1 mm).

The immersion of his forearm in tap water at 35°C for 15 min caused the development of 2 small erythemas with itching. Consequently, 4 conditions of aqueous challenges were applied to his back at room temperature. Sites 1–3 were directly challenged by compresses with distilled water (site 1), 99.5% ethanol (site 2) and 5% saline (site 3), respectively. Site 4 was wiped with a compress with acetone, then applied with 5% saline. After 15 min, when the compresses were removed, 3 pinhead-sized wheals were observed, corresponding to hair follicles at site 4 (Fig. 1a). After a further 15 min, additional wheals appeared especially at site 4 (Fig. 1b). No eruption or itching was induced at sites 1 and 2.

Oral anti-histamines, terfenadine 60 mg and mequitazine 6 mg per day partially reduced the symptoms. This combination, with topical application of 1% diphenhydramine ointment, prevented further wheal formation to some extent.

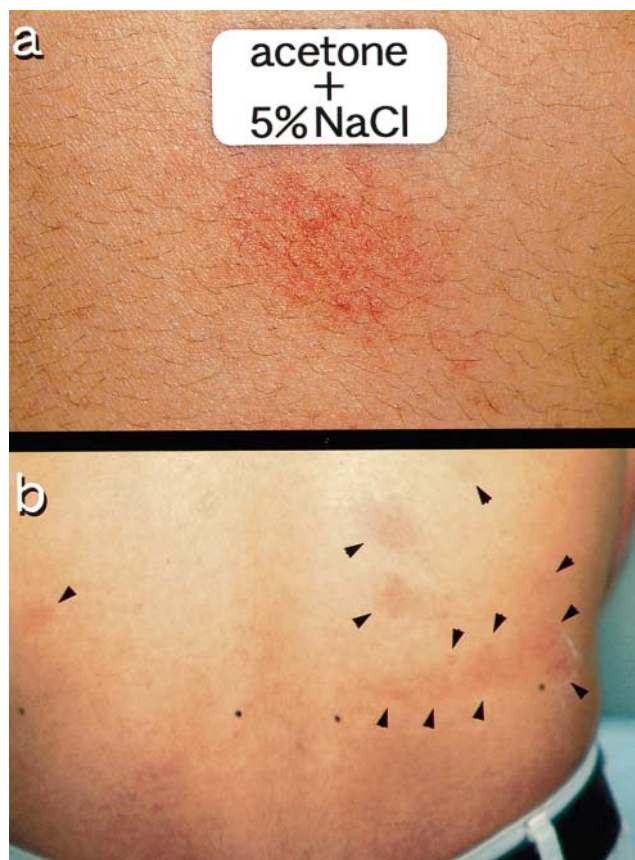


Fig. 1. Wheal-and-flare reactions induced by contact with 5% saline on the back. (a) After 15 min a wheal with flare appeared at a hair follicle. (b) After 30 min acetone pretreatment induced more wheals and flares (site 4, right) than control (site 3, left).

DISCUSSION

Since the first report by Shelly & Rawnsley (1), 26 cases with aquagenic urticaria have been described or mentioned in the literature (2). The effectiveness of histamine H₁-antagonists and the increase in plasma histamine upon provocation (3) indicate the degranulation of mast cells in association with the symptoms. The mechanism of mast cell activation is a matter of debate. Sibbald et al. suggested the involvement of a cholinergic mechanism, because of the resemblance of the eruption with cholinergic urticaria, association with sweating and the inhibitory effect of topical scopolamine (3). However, no inhibitory effect of scopolamine or atropine, and no reactions with methacholine have been reported in other cases. Moreover, Czarnetzki et al. (4) reported that even vigorous exercises did not induced wheals, suggesting that the mechanism of wheal formation in aquagenic urticaria is different from that in cholinergic urticaria.

Although water is apparently more critical than organic solvent, a skin test or prick test with saline did not induce an enhanced reaction, suggesting that water plays a role as a vehicle rather than as a mast cell secretagogue itself. Shelley & Rawnsley suspected sebum or sebaceous glands produced a toxic substance (1). However, Sibbald et al. argued against this possibility, since complete removal of the stratum corneum enhanced the reaction (3). On the other hand, Tkach described a 30-year-old female who did not develop eruptions when swimming in the ocean, and suspected sudden change in osmotic pressure as the triggering event (5). Czarnetzki et al. (4) reported the reproduction of a burning sensation on intradermal injection of the extract from human callus, but not that from psoriatic scale, and suspected the presence of a pathological antigen in the epidermal horny

layer. In the case presented here, 5% saline is more effective in producing wheal-and-flare than is distilled water, which is in agreement with the report of Shelley & Rawnsley (1); the pretreatment with acetone further enhanced this reaction in agreement with the report of Sibbald et al. (3). These findings support the hypothesis that the secretagogue is a polar substance located around hair follicles under the sebum, rather than the sebum itself.

The identification of such a substance may enable us to develop better treatment for this unique type of urticaria.

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