

A case of aquagenic urticaria successfully treated with omalizumab

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Clinical Implications

- We report a case of aquagenic urticaria refractory to antihistamines.
- Aquagenic urticaria is a rare form of physical urticaria occurring after contact with various forms of water.
- Omalizumab may be considered in patients who do not adequately respond to antihistamines.

TO THE EDITOR

Aquagenic urticaria is a rare form of physical urticaria described as distinct perifollicular urticaria, 1 to 2 mm in size arising after contact with water.¹ Symptoms occur within 20 to 30 minutes of water exposure, regardless of temperature, and resolve within 30 to 60 minutes after water is eliminated from the skin. Most of the reported cases are sporadic, though there have been familial cases documented and recently described in monozygotic twins.² There is a similar condition termed “idiopathic aquagenic pruritus” in which intense itching occurs after dermal contact with water; however, there are no visible skin changes separating it from aquagenic urticaria.³

Here, we report a case of a 34-year-old white woman with a 2-year history of aquagenic urticaria and possible idiopathic aquagenic pruritus. She described intense pruritus with and without small wheal formation immediately after every water exposure of any kind. The urticaria and pruritus were limited only to the body surface area that was exposed to water, though she could tolerate drinking water, as is often the case. Her symptoms were not associated with water temperature or food ingestion before water contact, and trials with city water, well water, and distilled water yielded the same symptoms. Further history was not suggestive of other coexisting physical urticaria, specifically cold or cholinergic urticaria. There was no associated angioedema, hypotension, or respiratory difficulty. The patient reported a significant reduction in her quality of life because showering and bathing resulted in excruciating pruritus. A general physical examination was benign, and there was a notable absence of dermatographism. The patient elected not to proceed with a water challenge in the clinic because of refusal to discontinue antihistamines for 1 week before testing. Our diagnosis was aquagenic urticaria, with obvious wheals occurring on most occasions on the basis of historical description. Previous simultaneous treatment with montelukast 10 mg daily, cetirizine 10 mg daily, loratadine 10 mg daily, ranitidine 150 mg twice daily, diphenhydramine 50 mg every night, and hydroxyzine 25 to 50 mg 30 minutes before bathing and frequently up to 3 times daily was ineffective. A laboratory evaluation was notable for normal thyroid-stimulating hormone, antithyroperoxidase antibody, antithyroglobulin antibody, cryoglobulins, complete blood cell count with differential, comprehensive metabolic profile,

C-reactive protein, and tryptase. After her initial visit with us, she was instructed to continue her current medications and begin propranolol 10 mg daily on the basis of case reports of successful management of aquagenic pruritus.⁴ There was no improvement in her urticaria despite titration of propranolol to 30 mg daily; however, she did perceive mild improvement in the pruritus associated with water exposure. She was then started on omalizumab 300 mg every 28 days and after 2 injections reported complete resolution of her aquagenic pruritus and urticaria. She has been able to go swimming for the first time in many years without urticaria or pruritus and successfully discontinued cetirizine, loratadine, ranitidine, and hydroxyzine without symptom recurrence.

The etiology of this physical urticaria has not been well understood. It is difficult to explain how the human body that is largely constituted of water can trigger some individuals to develop severe urticaria and pruritus upon dermal contact with water. The authors who first described this condition proposed the formation of a toxic substance by the combination of water and sebum that causes mast cell degranulation.¹ Further support for this hypothesis developed when Chalamidas and Charles⁵ reported that patch testing with a patient’s own sweat did not produce urticaria while patch testing with the patient’s own sweat and sebum produced marked perifollicular urticaria. Later, Czarnetzki et al⁶ reported that a water-soluble antigen located in the epidermis may cause mast cell degranulation upon diffusion into the dermis. There have since been a number of differing hypotheses; however, no widespread agreement on etiology has been established.

The development of evidence-based pharmacologic interventions has been hindered because of the rarity of aquagenic urticaria and pruritus, paired with a poor understanding of the pathophysiology. Upon review of the literature, there are variable responses to different treatments. Some patients have documented complete resolution of symptoms with antihistamines.⁷ Other antihistamine refractory cases have used ultraviolet monotherapy alone or in combination with antihistamines with some efficacy.⁸ It has been hypothesized that the ultraviolet therapy induces thickening of the epidermis, which may prevent water penetration and further interaction in the epidermal milieu. Other therapeutic options have included topical barrier creams and acetylcholine antagonists.⁹

Aquagenic urticaria is a rare type of physical urticaria with fewer than 50 case reports published in the literature. A number of treatment options have been described. However, despite these pharmacologic measures, the symptoms are frequently refractory to therapy. Because these patients have distressing symptoms affecting activities of daily living such as showering, they have a significant reduction in quality of life. To our knowledge, this is the first report in the literature of treating aquagenic urticaria with omalizumab. In the setting of aquagenic urticaria that is refractory to antihistamine therapy, a trial of omalizumab as a safe and possibly effective treatment option should be considered.

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