

Familial Aquagenic Urticaria

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Port J Pediatr 2021;52:220-3

DOI: <https://doi.org/10.25754/pjp.2021.21048>

Abstract

Aquagenic urticaria is a rare form of inducible urticaria that is precipitated by water contact with the skin, regardless of its temperature and nature. The pathophysiology is not yet quite clear. There are fewer than 50 cases reported. Most cases are sporadic, but there is a small number of familial cases. We report a case of familial aquagenic urticaria in two children: a brother and sister. To the best of our knowledge, no other case of familial aquagenic urticaria has been reported in Portugal. With these two related cases, the authors wish to emphasize that, although this is a type of inducible urticaria rare in children, it should be recognized because it can cause systemic potentially fatal reactions and an adequate treatment can allow for a better quality of life.

Keywords: Adolescent; Portugal; Siblings; Urticaria/diagnosis; Urticaria/etiology; Water/adverse effects

Introduction

Aquagenic urticaria is a rare form of inducible urticaria (< 1%) that is precipitated by water contact with the skin, regardless of its temperature and nature.¹ There are fewer than 50 cases reported in the medical literature.²⁻⁴ Most cases are sporadic, but familial aquagenic urticaria has been reported.^{2,4-6} In one report, the condition existed across three generations of a single family.⁵ Women seem to have a higher prevalence than men and the affected age is often at or after puberty.^{1-4,6} Aquagenic urticaria was first described in 1964.⁷ The pathophysiology is not yet quite clear, but several mechanisms have been proposed. It was suggested that a reaction of water with sebum or sebaceous glands would form a toxic substance that stimulates mast cell degranulation with the consequent release of histamine, leading to the development of urticarial

lesions.⁷ In 1981, it was hypothesized that hypotonic water sources could lead to osmotic pressure changes, resulting in the indirect provocation of urticaria.⁸ In 1986, it was suggested that there is a water-soluble antigen in the epidermis that, when in contact with water, diffuses more deeply into the dermis with a consequent histamine release from mast cells.⁹ Although histamine plays an important role in aquagenic urticaria pathophysiology, other chemical mediators, such as acetylcholine, serotonin, and bradykinin, are also involved as a histamine-independent mechanism.² We present a rare case of familial aquagenic urticaria in two children: a brother and sister. To the best of our knowledge, no cases of familial aquagenic urticaria have been reported in Portugal.

Case Report

The first case was a 14-year-old girl who was referred to our department due to recurrent episodes of urticaria. She reported a four-year history of multiple small, punctate, perifollicular wheals with erythema and intense pruritus, confined to the trunk that appears 15-20 minutes after contact with various sources of water (tap/distilled/saline water), regardless of the water temperature and time of exposure. No rash developed when she was exercising, under emotional stress, or after water ingestion. Once the water source was removed, the wheals spontaneously disappeared after 30 minutes, with no residual mark. She denied angioedema, hypotension, gastrointestinal symptoms, lipothymia/syncope, wheezing, or dyspnea related to these episodes. She had no personal history of allergies to drugs, food, or any physical stimulus. At the time of the first interview, there was no family history of atopy and, according to them, none of the girl's relatives reported similar skin reactions related to water exposure. Laboratory evaluation, which included complete blood count, C-reactive protein, immunoglobulins (Ig G, A,

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Received: 28/09/2020 | Accepted: 18/02/2020 | Published online: 02/07/2021 | Published: 02/07/2021

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M, thyroid function tests, and anti-thyroid antibodies revealed no abnormalities. Her skin tests were positive for house dust mites and grass pollens. The IgE level was within the normal range. An ice cube test elicited no reaction, excluding cold-induced urticaria. The Fric test was positive over the forearm (Fig. 1). A water challenge test using regional contact with a body temperature (36°C) wet compress on the patient's trunk for 30 minutes was performed, and a few micropapular highly pruritic erythematous eruptions appeared in the contact area. Based on this clinical history and the water challenge test, the diagnosis of aquagenic urticaria was confirmed. There was clinical improvement with the institution of ebastine 30 minutes before the contact with water and recurrence of symptoms when this H1 antihistamine was not administered prophylactically. The second case was a 12-year-old boy. He is the brother of the patient described hereinabove. He visited our department due to a similar skin reaction related to water

exposure that started two years before. He reported erythematous maculopapular skin lesions often with intense pruritus, especially on his back, when he took a shower or swam in the ocean or a pool. The lesions appeared within about 10 minutes after the water contact and resolved spontaneously within 30 minutes. He said that the lesions also appeared after sweating, even without physical exercise. There were no systemic associated symptoms. He had a personal history of atopic dermatitis. He had no personal history of allergies to drugs or food. Following a detailed inquiry about the children's relatives with similar skin reactions, it was noticed that the paternal grandfather had erythema of the face with associated pruritus when he took a shower, but it was never investigated. Given the known history of aquagenic urticaria of the sister, he was also submitted to a challenge test with water, which was positive (Fig. 2). The test of dermatographism over the forearm was also positive. He was never treated before and desloratadine was prescribed for symptom relief.



Figure 1. The Fric test was positive over the forearm.

Discussion

While water may be a seemingly innocuous substance to most of us, for some patients, water is a source of great discomfort. In aquagenic urticaria, hives appear rapidly (20-30 minutes) after direct contact with various sources of water, regardless of temperature,² and clear up within 30-60 minutes. Sweat, saliva, and even tears can also precipitate a reaction. The lesions are characteristically small (1-3 mm), erythematous, perifollicular, pruritic wheals usually located on the trunk and upper limbs. Systemic symptoms are rare but have been reported.^{2,4,6} Aquagenic urticaria is occasionally associated with other forms of inducible urticaria,^{2,6} such as dermatographism, cholinergic urticaria, or cold urticaria.

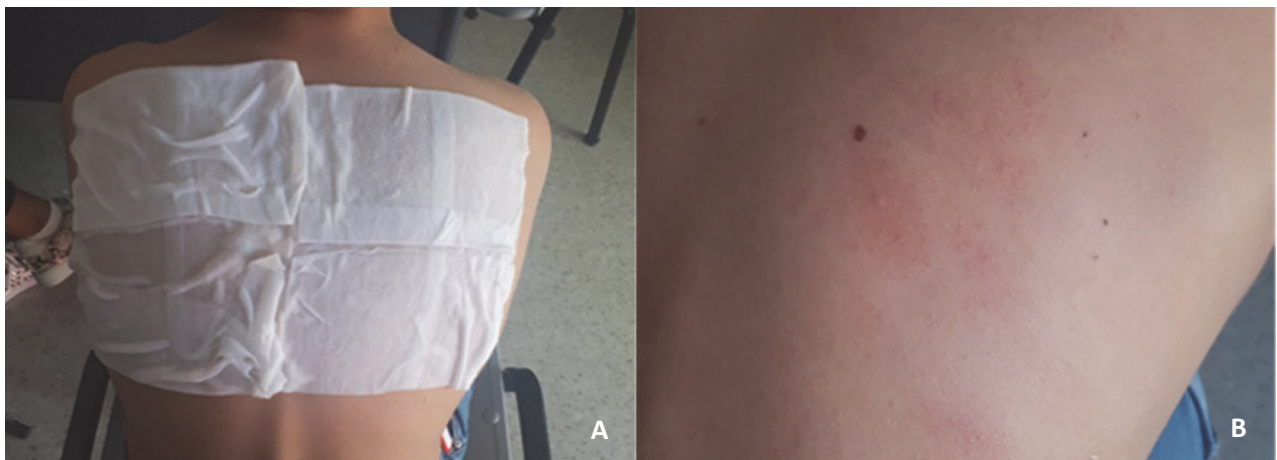


Figure 2. The site of compress application (A) and pinhead sized wheals surrounded by erythema on the patient's back (B).

A water challenge test performed at body temperature (35°C-37°C) for 30 minutes is recommended for the diagnosis of aquagenic urticaria.^{1-4,6} The upper body is chosen as the preferred site.² Differential diagnosis includes aquagenic pruritus, cholinergic urticaria, pressure urticaria, cold urticaria, and local heat urticaria. Although water of any temperature can provoke aquagenic urticaria, using ambient-temperature water avoids any possible confusion with cold-induced or local heat urticaria.²

The treatment consists of avoiding the precipitating physical factor when possible and a prophylactically administration of second-generation H1 antihistamines, up to four times the standard single daily dose. In refractory cases, ultraviolet (UV) radiation has been used with some efficacy. Other therapeutic options include topical barrier creams and propranolol at doses of 10/40 mg daily,² and a case of aquagenic urticaria successfully treated with omalizumab has been described in a patient with a refractory condition.¹⁰

Although almost all the cases of aquagenic urticaria are sporadic, there are a small number of familial cases in the medical literature.^{2,4-6} The first familial aquagenic urticaria case was reported in 1964: a 17-year-old girl and her father.⁷ The girl described herself as having been allergic to water for the past four years. Contact with water in the bath or showering, regardless of its temperature, produced small punctate hives on a bright red erythematous base on her shoulders, upper arms, face, and chest. Persisting for about 30 minutes, they fade without a trace. Her father had a similar intolerance of water contact in that his face becomes erythematous after each washing. In 1967, a case of familial aquagenic urticaria was reported in two siblings: a 27-year-old woman and her brother.¹¹ She had, since the age of 9, a history of the development of small white papules surrounded by bright red rings whenever the skin remained in contact with water for more than 5 minutes. The lesions developed regardless of the temperature of the water and occurred after bathing, showering, or swimming. They were not associated with the heating of the body, exercise, or emotional upset. The lesions had occurred mainly on the trunk. Her brother had a similar hypersensitivity response, but he was not available for examination. Other authors also reported two cases of aquagenic urticaria in the same family (a 30-year-old woman and her paternal aunt) with the same eruption due to water.¹² They responded well to antihistamine treatment. The first case of familial aquagenic urticaria in Brazil¹³ was in a mother (28 years) and her daughter (19 months). Both patients presented wheals following contact with water, especially when

showering, regardless of its temperature. The mother reported the onset of urticaria four years before and the daughter presented wheals since birth. Hydroxyzine treatment was proposed, but it was refused. The most recently reported case of familial aquagenic urticaria was of 18-year-old monozygotic twins,¹⁴ who presented with a three-year history of aquagenic urticaria. They were both avid triathletes and were, therefore, frequently exposed to water. Swimming or showering induced a prodrome of skin pruritus followed by the development of wheals over the trunk approximately 15 minutes after. The wheals were induced by both hot and cold water and resolved spontaneously after about one hour, leaving no residual mark. Neither brother had ever experienced any associated angioedema. Exercise such as running would only induce itching. The symptoms were controlled by taking prophylactic cetirizine 10 mg, once per day. Some of these familial cases have been reported in association with other conditions. For example, an association of familial aquagenic urticaria with familial lactose intolerance has been reported over three generations.¹⁵ The authors described a 19-year-old male patient with aquagenic urticaria whose grandmother, mother, aunt, and cousin were all affected. The patient, mother, and grandmother were also affected by familial lactose intolerance. In their patients, no prolonged therapeutic effect was achieved by either antihistamines or by UV B radiation. Other authors report the case of three affected female siblings (aged 30, 26, and 24 years) all with co-existent Bernard-Soulier syndrome, a rare autosomal recessive disorder causing a prolonged bleeding time. They postulated that, although the association could be a coincidence, it might constitute an association of genetic *loci*.

To the best of our knowledge, there has been no reported case of familial aquagenic urticaria in Portugal. With these two-related cases, the authors want to emphasize that, although this is a type of inducible urticaria that is rare in children, it should be recognized because it can cause systemic, potentially fatal reactions, and adequate treatment can enable a better quality of life. It is possible that the true prevalence of aquagenic urticaria is underestimated, and further studies are needed to understand its pathogenesis and treatment.

WHAT THIS CASE REPORT ADDS

- Aquagenic urticaria is a rare form of inducible urticaria.
- A water challenge test performed at body temperature for 30 minutes is recommended for diagnosis.
- It should be recognized because it can cause systemic, potentially fatal reactions and adequate treatment can enable a better quality of life.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

Funding Sources

There were no external funding sources for the realization of this paper.

Provenance and peer review

Not commissioned; externally peer reviewed

Consent for publication

Consent for publication was obtained.

Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Urticária Aquagénica Familiar

Resumo

A urticária aquagénica é uma forma rara de urticária induzível, precipitada pelo contacto da água com a pele, independentemente da sua temperatura e natureza. A sua fisiopatologia não está completamente esclarecida. Existem menos de 50 casos reportados. A maioria dos casos são esporádicos. No entanto, estão descritos alguns casos de incidência familiar. Descrevemos os casos clínicos de uma urticária aquagénica familiar em dois irmãos. De acordo com o nosso conhecimento, este é o primeiro

caso de urticária aquagénica familiar descrito em Portugal. Com estes dois casos os autores pretendem salientar que, embora este tipo de urticária seja raro, particularmente em idade pediátrica, deverá ser reconhecida devido ao risco de poder originar reações sistémicas potencialmente fatais e que um tratamento adequado pode permitir uma melhoria da qualidade de vida.

Palavras-chave: Adolescente; Água/efeitos adversos; Irmãos; Portugal; Urticária/diagnóstico; Urticária/etiologia