



Aquagenic urticaria: a case report and literature review

Urticária aquagênica: relato de caso e revisão de literatura

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ABSTRACT

Aquagenic urticaria is a rare form of chronic inducible urticaria (CIIndU) triggered by a specific stimulus. Pathogenesis is not fully understood, but symptoms appear minutes after cutaneous exposure to water, regardless of temperature, and wheals have a folliculocentric pattern. The diagnosis of CIIndU is confirmed by provocation testing using established protocols, and first-line treatment is second-generation antihistamines. In this article, we report a case of aquagenic urticaria and provide a brief review of the relevant literature.

Keywords: Chronic urticaria, pruritus, histamine H1 antagonists.

RESUMO

A urticária aquagênica é uma forma rara de urticária crônica induzida (UCInd) desencadeada por um estímulo específico. A patogênese não é totalmente compreendida, mas os sintomas se iniciam minutos após a exposição cutânea à água, independentemente de sua temperatura, e as urticacas têm o padrão foliculocêntricas. O diagnóstico é confirmado através do teste de provocação, e o tratamento de primeira linha são os anti-histamínicos de segunda geração. Neste artigo, relatamos um caso de urticária aquagênica e fazemos uma breve revisão da literatura sobre o tema.

Descritores: Urticária crônica, prurido, antagonistas dos receptores histamínicos H1.

Introduction

Shelley and Rawnsley¹ first described aquagenic urticaria in 1964, with the hypothesis of focal histamine release by perifollicular mast cells. It is a rare disease, characterized by the formation of perifollicular wheals with 1 to 3 mm in size, appearing after contact with water, regardless of temperature. Lesions tend to be located preferentially on the trunk and upper limbs and can last from 10 to 60 minutes.²⁻⁴

Aquagenic urticaria is considered a form of induced chronic urticaria, and is triggered by a specific stimulus. The induced urticaria (UCInd) affect about 0.5% of the population and can often coexist with chronic spontaneous urticaria (CSU).⁵

The diagnosis is based on the clinical history and confirmed by provocation tests, and the treatment comprises the management of the occurrence of symptoms and complete control of the disease, for as long as necessary for spontaneous remission to occur.⁵

Case report

Female patient, 24 years old, medical student, presents wheals mainly in the trunk and back region after exposure to water since the age of 8. Symptoms start approximately 20-30 minutes after exposure to bathing or contact with sea or swimming pool water,

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with total regression of wheals within 30 minutes at the end of exposure (Figure 1). Refers to worsening of crises closer to the menstrual period, when it presents greater intensity and distribution of wheals and pruritus.

The diagnosis was confirmed by the provocation test, with direct exposure to gauze moistened with water at room temperature on the back for 20 minutes, the maximum time for the onset of symptoms reported by the patient. A few minutes after the start of the test, she presented hives and itching in the exposed skin area (Figure 2), with total remission of symptoms within 30 minutes after exposure.

Laboratory tests revealed elevated antithyroglobulin and antithyropoxidase antibodies, however TSH

and free T4 were within the normal range. Still, it showed positivity in the antinuclear factor, which was a homogeneous nuclear pattern with titers of 1/160. Further investigation was performed with the autologous serum test (Figure 3) and the frick test, and both were negative.

The patient, even after diagnostic confirmation, chose not to adhere to treatment with a second-generation antihistamine. As a result, she had progression of wheals in previously unaffected sites, worsening of pruritus and quality of life, so treatment with a second-generation antihistamine at the usual dose was again proposed. Since then, the patient has been using the second-generation antihistamine intermittently.



Figure 1
Hives after exposure to bath

Discussion

Urticaria is a condition in which hives, angioedema, or both occur. Its classification is based on the duration of symptoms, being considered chronic when it occurs for more than six consecutive weeks. Chronic urticaria can be subdivided into spontaneous chronic urticaria (CIU) or induced chronic urticaria (IndUC). The UCInd are those in which the wheals and/or angioedema arise after a specific stimulus, which can be physical (symptomatic dermatographism, delayed pressure urticaria, heat or cold urticaria, vibrating urticaria, and solar urticaria) or non-physical (aquagenic urticaria, contact urticaria, and cholinergic).⁶⁻⁷

The estimated prevalence of NDICU is 0.5% in the general population.⁷ Aquagenic urticaria is a rare type of UCInd, predominantly affects females and often has its onset during puberty or post-puberty.⁸⁻¹⁰ However, reports of childhood onset and other cases of familial disease have been described.^{9,11} There is also an association of aquagenic urticaria with other types of physical urticaria, such as cholinergic urticaria, cold urticaria, or symptomatic dermatographism.^{1,2} To date, only about 100 cases have been reported in the literature.^{8,9}

For most individuals, aquagenic urticaria occurs without associated systemic repercussions, however some patients have reported symptoms such as headache, dizziness, difficulty breathing and palpitations, but these symptoms are rare.¹²⁻¹⁴

The exact pathology of UCInd has not yet been fully elucidated, but the activation of tissue-resident mast cells and the subsequent release of inflammatory



Figure 2

Provocation test with direct exposure to gauze moistened with water at room temperature on the patient's back

mediators such as histamine play important roles.¹⁵ Shelley and Rawnsley,¹ in 1964, suggested that the interaction of water with sebum or sebaceous glands could originate a toxic substance that caused mast cell degranulation and, consequently, histamine release and wheal formation.^{1,8} In 1981, Tkach¹⁶ formulated the hypothesis that the mechanism of aquagenic urticaria (UA) would be associated with sudden changes in osmotic pressure around the hair follicles, leading to an increase in the passive diffusion of water. Finally, in 1998 Luong and Nguyen¹⁷ suggested a mechanism that may be completely independent of histamine release; since patients with UA had their serum amine levels unchanged after exposure to water.^{3,8,9,13,17}

More recently, Maurer et al.¹⁵ proposed that type I autoimmunity or autoallergy would be a potential

pathophysiological mechanism, and, in this situation, the production of neoautoantigens would activate skin mast cells through recognition by IgE molecules coupled to their high-affinity receptors. These neoautoantigens would be produced through a specific (induced) physical stimulus, such as friction, cold and others. However, the exact pathogenesis is not fully understood and appears to be mediated both in a histamine-dependent and independent manner.⁹

The diagnosis of AU is based on anamnesis and confirmed by a water challenge test.¹⁴ The test can be administered in several ways; however, the standard method is a compress or towel soaked in water at room temperature (35-37 °C) or saline, and this should be placed on the patient's skin for 20 to 30 minutes, preferably choosing the upper part of the body, especially the back, as the lower extremities are



Figure 3
Negative autologous serum test

less commonly involved in this type of urticaria.^{3,9,18} Another possibility, if this test is negative, is to ask the patient to take a bath or shower or to immerse the affected parts of the body in water.⁸

There are also some unusual clinical presentations of UA related to reactions depending on the salinity of the water, for example, patients who report symptoms only after exposure to seawater (SDAU), and for these patients, the provocation test should be performed with a 3.5% sodium chloride solution.^{13,19}

PerLastly, differential diagnoses should always be evaluated, as it is difficult to differentiate UA from other types of induced urticaria (eg, cholinergic urticaria, heat urticaria, cold urticaria, pressure urticaria, and exercise-induced urticaria).^{9,13,20} In our patient, the clinical history clearly suggested the subtype of physical, aquagenic urticaria, and the appearance of wheals after the challenge test with water at room temperature and the patient at rest, together with the appearance of punctate wheals and an erythematous halo, removed the possibility of other forms of UCInd.

The treatment of aquagenic urticaria remains a challenge, however, second-generation antihistamines are used as a first line in standardized or even

quadrupled doses.^{7,8} In some cases, however, there is a failure to control symptoms with the use of antihistamines.¹¹

There are some reports that these refractory cases were treated with ultraviolet (UV) radiation (both psoralens plus UVA and UVB therapy), alone or in combination with antihistamines, and that the effect of this therapy would be to thicken the epidermis, which may prevent water penetration and interaction with dendritic cells or a decrease in mast cell response.¹¹

Another treatment possibility was described by Chicharro et al.,²¹ in which omalizumab was prescribed at a dose of 300 mg every 4 weeks, and the patient had complete resolution of symptoms after 2 months of treatment, without any adverse effects from the use of this medication.

Bearing in mind that this medication is an anti-IgE monoclonal antibody, widely used for the treatment of CSU, and that, to date, this medication is not licensed for the treatment of UCInds.¹⁵ Therefore, further studies are needed so that we can actually evaluate the results of this treatment in patients with aquagenic urticaria.

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