

Aquagenic Urticaria-Chronic Spontaneous Urticaria with Diagnostic Challenges

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ABSTRACT

Aquagenicurticaria is a form of physical urticaria characterized by a development of wheals and pruritus to exposure of water, regardless of its temperature or content [1]. It is a chronic spontaneous urticaria where patients demonstrate a spontaneous episodic appearance of self-limiting wheal of about 0.2 cm-5.0 cm for longer than 6 weeks in response to exposure of water [1,2]. The pathogenesis of this condition is unclear, given its infrequent presentation, but is believed to be both histamine-mediated and histamine-independent pathway [1,2]. In addition, there have been associations with other forms of physical urticaria. Patients with this condition may have a family history [1]. It is a self-limiting condition and thus diagnosis is based on history and water challenge test. It is treated with antihistamine agents for symptomatic relief. The patient denies any other systemic symptoms such as allergies, eczema and wheezing. Although the presentation is mostly on her torso and extremities, it also appears on her face and other parts of the body. Patient symptoms have been related to all water sources and symptoms do not appear on mucosal surfaces and are not related to oral intake of water, demonstrating its physical character. The prescribed non-sedating anti H1 antihistamines (levocetirizine) and asked to follow up 1 month and the patient reported significant relief in symptoms within 1 week of starting levocetirizine.

CASE REPORT

We have a 24-year-old female patient with no past medical history or previous allergies presenting with a history of developing a self-limiting urticarial lesion mostly on her back and extremities following exposure to water. She began experiencing these symptoms several years ago, after puberty. It is associated with pruritus, stinging and the urticaria presents within 20 minutes of exposure to any form of water and lasting about 3-6 hours. She denies any other systemic symptoms such as allergies, eczema and wheezing. Although the presentation is mostly on her torso and extremities, it also appears on her face and other parts of the body. Her symptoms have been related to all water sources. Therefore, excluding of any external factors such as water impurities and contaminants. She does have a family history of aquagenicurticaria in her father which started around puberty and resolved after a few years.

These symptoms do not appear on mucosal surfaces and are not related to oral intake of water, demonstrating its physical character. The rash was described as an erythematous pruritic maculopapular plaques of 0.2 cm-5.0 cm size, that appeared more commonly on her back and face (around nose) and spared her palms and soles. As

per her history, she tried to change the temperature of water and the symptoms persisted despite using cold or warm water. Sweating and salt-water exposures such as with beach water also induced this condition, although the urticaria under these circumstances were more pronounced with larger size and more edema.

We diagnosed her with Aquagenic Urticaria after we performed a water challenge test. We obtained informed consent and performed this test in a controlled environment with epinephrine and code cart. The water challenge test was conducted within 1-2 days of patient reporting the symptoms. This test was performed on the patient's back with purified water of room temperature. We applied water-soaked towels on the patient's back. Both ice cold and hot water were used along with water at room temperature. The patient was observed for 40 minutes following the water challenge test. Simultaneously, we also performed tests for other forms of common physical urticaria including dermographism and thermal urticaria. Dermographism was tested with a pen stroke. Thermal urticaria (hot and cold urticaria) was tested with hot/warm compress and an ice pack respectively. At 40 mins, she manifested pruritic urticarial lesions of size 3mm in areas exposed to water. The pruritis preceded the lesions. Patient did not report any systemic symptoms such as wheezing. The patient did not have

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Received: April 24, 2020; Accepted: May 19, 2020; Published: July 26, 2020

Citation: Pete Prashamsa S, Bilori, David RM (2020) Aquagenic Urticaria-Chronic Spontaneous Urticaria with Diagnostic Challenges. J Clin Exp Pharmacol. 10:268. doi: 10.35248/2161-1459.20.10.268

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any reaction to hot and cold packs. She demonstrated some degree of dermographism that was self-limiting and lasted < 20 mins of onset.

We prescribed her non-sedating anti H1 antihistamines (levocetirizine) and asked to follow up 1 month. She reported significant relief in symptoms within 1 week of starting levocetirizine. Our study was limited, since the patient had already received 1- 2 doses of Levocetirizine before the water challenge test was performed. Despite this, the patient manifested an urticarial rash.

DISCUSSION

Aquagenic Urticaria was first described in 1964. Shelley and Rawnsley were the first people who reported this condition [3]. Since then, about 50 cases have been reported worldwide. Given the benign nature of this condition, the incidence may be underestimated. Although there seems to be a female predominance, males are also affected. But patients with this condition mostly seek medical care not for cosmetic reasons, but because of the associated pruritus and stinging, which is of great discomfort and may affect routine activities.

There have been many theories explaining the pathogenesis of this condition. Shelley and Rawnsley hypothesized that water reacts with sebaceous glands in the skin, generating toxic metabolites that actively stimulate mast cell degranulation causing histamine release and urticarial [3]. Another group Tkach, in 1981 hypothesized that a sudden osmotic change in the hair follicles lead to passive diffusion of water [4]. This may hold well with a theory of why this condition may have a genetic predisposition. Yet another hypothesis states that this could be secondary to a reaction of water-soluble antigen in the epidermis with exposed water, leading to histamine release [5]. Although, the histamine release theory has been the mainstay in most of the above-mentioned hypotheses, there has been a non-histamine related explanation to this condition [1]. This theory explains why there has not been a documentation of increase in serum histamine level in these patients.

Aquagenicurticaria is a clinical diagnosis. The best way to diagnose this condition is with a water challenge test. It is easily inducible and self-resolving [1,6]. A water challenge test is positive if there is development of urticaria or pruritus at the end of 20-40 minutes. Most of the patients complain of stinging and pruritus a few minutes prior to appearance of urticarial [1,6]. A significant limitation to this test is when a patient has received antihistamine or any form of steroids which interferes with this test and must be avoided prior to water challenge test. Water challenge test may be combined with testing for other physical urticarias. A patient with chronic spontaneous urticaria may have different physical urticarias and therefore ruling out these other conditions is important to ensure appropriate diagnosis [2]. Although we have discussed about measurement of serum histamine levels to understand the mechanism of this condition, this testing is not required in routine clinical practice and is expensive [2]. Also, routine investigation with a biopsy is unnecessary, unless there is a strong suspicion for a coexisting vasculitis. Following a positive water challenge test, patients may be simply treated with Antihistamines. Urticaria Activity Scoring over 7 days (UAS7) may be used to evaluate the severity of this urticarial [2,7]. It is a simple once or twice daily, diary-based 7-day reporting of urticaria by patients, which is then scored with values ranging between 0-50 [7]. A consistent UAS7 reporting may be used over time to assess

the severity of the urticaria at the time of diagnosis and then for follow up of treatment efficacy [7].

The rationale for treatment of these patients is to decrease the associated pruritus and stinging and improve the functionality. Hence patients may be treated with non-sedating antihistamines (Anti H1, second generation) and followed up in 2-4 weeks for symptomatic relief and UAS-7 scoring. First generation antihistamines are avoided for their sedative side effects. In cases of coexisting physical urticaria of other form, a combination therapy may be tried [1]. For poorly controlled patients, there is evidence of use of omalizumab, an IgE blocker which has demonstrated successful remission of aquagenicurticarial [8].

Aquagenicurticaria does not manifest with any systemic symptoms. If there are no systemic life-threatening conditions, such as angioedema, the use of antihistamines and mast cell stabilizers should suffice in the treatment of this condition. Systemic involvement such as Angioedema or Anaphylaxis is not known of in Aquagenicurticaria, and their occurrence in association with an idiopathic chronic spontaneousurticaria may require work up for an alternate diagnosis. Alternate diagnosis may involve disorders such as Bradykinin mediated angioedema, Anaphylaxis, Cryopyrin-associated periodic syndrome (CAPS), Schnitzler's syndrome, Well's syndrome, Gleich's syndrome [2]. Steroids are not necessary for this condition and their use may result in consequences of steroid dependence and suppression of HPO (Hypothalamus-Pituitary-Ovarian) axis. Topical use of petroleum jelly prior to exposure to water, especially saltwater, may be of some relief [1]. Since, water-based activities such as bathing are unavoidable and avoidance may result in poor hygiene, it may be essential to treat and minimize the associated discomfort. It continues to remain unclear if this condition remits or persists and thus further documentation and reporting remains invaluable.

CONCLUSION

Aquagenicurticaria is a chronic spontaneous urticarial response to exposure to water without any systemic involvement such as angioedema. The etiopathogenesis of this condition is very unclear. However, most of the patients presenting with this condition complain of rash and itching that may interfere with normal daily activities. Therefore, requires to be assessed for severity with a UAS7 scoring and work up for appropriate diagnosis with a water challenge test and testing for other forms of chronic spontaneous physical urticaria. These tests are simple, inexpensive and the diagnosis is clinical without the need for any invasive work up. Following the diagnosis, patients may be treated with second generation antihistamine and followed up for the UAS-7 scoring to ensure remission.

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