World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Check for updates

A review on aquagenic urticaria: unraveling the mystery of water-induced hives

Naveena Ganji [1,*], Kankata Amrutha [2], Kuchipudi Sri Varshitha [2], Pavan K Chennupati [3], Kolla Girija Shankar [2], Harichandra Mudili [2], Geeta Uppada [2] and Sreekanth Yaleti [2]

[1] *Department of Pharmacy Practice, Chennupati Indo-American School of Pharmacy, Andhra Pradesh 522 601, India.*
[2] *5th Pharm. D Students, Chennupati Indo-American School of Pharmacy, Andhra Pradesh 522 601, India.*
[3] *Chennupati Indo-American School of Pharmacy, Jonnalagadda, Andhra Pradesh 522 601, India and Director, Katalyst Health cares and Life Sciences, Inc, South Plainfield NJ 07080, USA.*

World Journal of Advanc ed Research and Reviews, 2025, 28(02), 1606–1611

Publication history: Received on 01 October 2025; revised on 08 November 2025; accepted on 10 November 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.28.2.3749

Abstract

Aquagenic urticaria, a type of physical urticaria, wheals occur when a patient's skin makes contact with any type of water within 30 min of exposure, and can last for 30 min to 2 h after cessation of exposure. Aquagenic urticaria most commonly develops on the trunk and upper limbs. It is sometimes associated with pruritus and an uncomfortable prickling or burning sensation. Patients with AU will present with characteristic 1–3 mm folliculocentric wheals and surrounding 1–3 cm erythematous flares within 20–30 minutes following skin contact with water. Aquagenic urticaria is not being adequately treated at the moment. This condition is frequently treated with long-acting antihistamines. Research is still being conducted to determine the underlying genetic and environmental factors that contribute to AU, which is uncommon but can have a significant impact on quality of life. A better understanding of the role of histamines, the immune system, and specific triggers might enable the development of targeted therapies.

Keywords: Aquagenic Urticaria; Water; Mast Cells; Anti-Histamines; Corticosteroids

1. Introduction

Aquagenic urticaria, a type of physical urticaria, is quite rare and only about 50 cases have been reported in the medical literature. It was first described by Shelley and Rawnsley in 1964 [1]. Wheals occur when a patient's skin makes contact with any type of water within 30 min of exposure, and can last for 30 min to 2 h after cessation of exposure. Aquagenic urticaria most commonly develops on the trunk and upper limbs. It is sometimes associated with pruritus and an uncomfortable prickling or burning sensation [2]. The latest World Allergy Organization guidelines on urticaria now classify AU as an inducible type of chronic urticaria, whereas this condition and other physical urticarias were previously grouped together due to their inducible nature by specific physical stimuli [3]. Among the limited cases reported in the literature, there seems to be a higher prevalence among females with the disease onset typically occurring during puberty or postpuberty.

However, there have been reports of childhood-onset disease [4]**.** Here, we present the first case of sporadic AU in Mexico, as well as an updated revision of the relevant literature. This work contributes to the scant reports documented in the Latin-American population [5]. Our patient showed an adequate therapeutic response to a second-generation antihistamine and a skin barrier–repairing cream. Treatment efficacy was assessed by applying two validated questionnaires aimed at measuring disease-related symptom severity and quality of life (QoL) [6]. Patients with AU will present with characteristic 1–3 mm folliculocentric wheals and surrounding 1–3 cm erythematous flares within 20–30 minutes following skin contact with water [7]. Patients can also experience associated symptoms, including pruritus, burning, and uncomfortable prickling [7]. Urticarial lesions will typically resolve within 30–60 minutes of cessation of

* Corresponding author: Naveena Ganji

water contact with the skin. Lesions most commonly appear on the trunk and upper arms, usually sparing the palms and soles. The affected areas are generally refractory to repeated stimulations for several hours. Rarely, patients can experience systemic symptoms such as wheezing or shortness of breath. AU has also rarely been reported in association with systemic conditions, including HIV infection, and occult papillary carcinoma of the thyroid gland [8]. There are also some uncommon clinical presentations of AU. While urticaria is thought to occur in response to any form of water in AU, there have been reports of patients who have had reactions depending on the salinity of the water. For example, a patient reacted to tap water, snow, and sweat, but could still swim in the ocean without urticarial [9]. In patients who have decreased thickness of the stratum corneum following epilation or cutaneous exposure to organic solvents, there can be an exaggerated urticarial response to water [10]. Additionally, in AU patients with associated systemic disease, the urticarial response seems to be often more dramatic, consisting of large edematous plaques rather than the classic punctate perifollicular wheals [11].

Although it is uncommon in clinical settings, persons with aquagenic urticaria clearly experience discomfort. Several case reports of family disease have been published, despite the fact that the majority of sufferers only occasionally experience episodes. Females are more likely to be afflicted, and the impacted age is frequently at or after puberty. Within 20 to 30 minutes of being in the water, wheals usually show up on the trunk and upper limbs. Without medicine, they usually go away in 30 to 60 minutes. The patient's medical history and the findings of a water challenge test are used to diagnose aquagenic urticaria [12]. It has to be distinguished from other forms of physical urticaria, including temperature-induced, pressure-induced, and cholinergic urticaria. A moist, room-temperature cloth is applied to the patient's skin for 20 minutes as part of the standard test [13]. Aquagenic urticaria's pathogenesis is not entirely known. Numerous mechanisms have been suggested. Water interacts with sebum or sebaceous glands to produce harmful chemicals that trigger the release of histamine from perifollicular mast cells, according to Shelley and Rawnsley's theory [14]. According to Czarnetzki et al., there is a water-soluble antigen in the epidermal layer that diffuses through water into the dermis, causing mast cells to release histamine [15]. In 1998, however, Luong and Nguyen proposed a mechanism that might not be dependent on histamine release, as the histamine levels of a number of patients did not increase during an incident of aquagenic urticaria [16]. The finding that pretreatment with scopolamine (an acetylcholine antagonist) prior to water contact was able to suppress wheal formation provided additional support for Luong and Nguyen's hypothesis [17]. Tkach suggested that urticaria is indirectly triggered by an abrupt shift in the osmotic pressure surrounding hair follicles [18]. In addition, Gallo et al. found that patient exposed to hypertonic saline (3.5% NaCl) experienced more severe urticarial skin lesions than those exposed to tap water or regular saline [19]. Some investigations also suggested that localized, salt-dependent aquagenic urticaria might occur. Water osmolality or salt concentration may have an impact on the pathophysiology of aquagenic urticaria. The amount and length of water contact with our patient's skin appeared to be connected to the severity of his aquagenic urticaria, based on on-site testing. He added that swimming in the ocean exacerbates his urticaria [20].

2. Mechanisms of aquagenic urticaria proposed by scientists

- In accordance with Shelley and Rawnsley's 1964 research, mast cells release histamine when water reacts with sebum or sebaceous glands to generate a toxic substance [21].
- Czarnetzki and associates (1986) When a water-soluble antigen from the epidermal layer permeates the dermis, mast cells release histamine [15].
- Luong and Nguyen several patients experienced an episode of aquagenic urticaria without elevated histamine levels. Scopolamine prevented the growth of wheal [16].
- In 1981, Tkach et al. A sudden shift in the osmotic pressure surrounding hair follicles leads to a greater diffusion of water.

Aquagenic urticaria is not being adequately treated at the moment. Aquagenic urticaria is frequently treated with long-acting antihistamines [12]. Antihistamines may not be sufficient to control the symptoms in certain persons. There have also been reports of a topical therapy that prevents contact with water [22]. For refractory instances, ultraviolet (UV) radiation is another recommended treatment [23]. Phototherapy may work by thickening the epidermis by the use of UV radiation, which reduces water penetration [16]. Mast cell activity may also be reduced by the radiation. Stanozolol has also been shown to manage the systemic symptoms of aquagenic urticaria [24]. Recently, omalizumab has been successfully applied in a patient to treat aquagenic urticaria refractory to antihistamines [25].

In Taiwan, no cases of aquagenic urticaria have been documented to yet. We believe, however, that the actual frequency of aquagenic urticaria may be underreported. Following the release of this case report, we anticipate that other cases will be found. Patients with aquagenic urticaria may experience an improvement in their quality of life with proper

therapy. We are stillhopeful that the pathophysiology and therapy of aquagenic urticaria may be clarified as more instances are reported and experiences are accumulated.

2.1. Management challenges

As water is the causative factor for AU, simple avoidance of the offending substance presents as an impractical, at times impossible, task for patients. A multitude of therapies has been used for AU over the years with varying degrees of efficacy, and the current treatment options table1 [41].

Table 1 Challenges for treatment of Aquagenic Urticaria

Therapeutic options	Line of therapy/notes	Proposed mechanism
Non-sedating, second-generation H_1 antihistamines (eg : cetirizine)	First line at standard dose, second line considers dose increase up to fourfold.	Antagonism or inverse agonist of H_1 receptor, preventing histamine effects
First-generation H_1 antihistamines (eg : hydroxyzine)	Third line	Antagonism or inverse agonist of H_1 receptor, preventing histamine effects
H_2 antihistamines (eg: cimetidine)	Third line	Unclear in urticaria, may have small additive effect with H_1 antihistamines
Acetylcholine antagonists (eg: scopolamine)	Adjuvant with H_1 antihistamines	May prevent histamine release
Phototherapy (eg :psoralen plus UVA, UVB)	Adjuvant with oral therapy or second-line alone	Reduction of mast cell activity, reactive thickening of the epidermis
Topical barrier creams (eg: petrolatum)	First line or adjuvant	Hydrophobic effect prevents water penetration into skin
Anabolic androgenic steroid (eg:stanozolol)	Case-specific, used in HIV patient with AU	Increases C1 esterase inhibitor synthesis
Selective serotonin reuptake inhibitors (eg: fluoxetine)	Case-specific, used in patient with extracutaneous symptom of AU	Unknown

2.2. Anti-Histamines

It is believed that histamine's activities on the H1 receptor mediate, at least in part, the urticarial symptoms, including wheal development and itching. Therefore, oral H1 antihistamines are typically used as the first-line treatment for AU. The sedative and anticholinergic side effects of first-generation H1 antihistamines can last for a longer period of time than the anti-pruritic, therapeutic impact, which lasts for around 4–6 hours [3]. For this reason, the newer, second-generation H_1 antihistamines with less central nervous system depression but greater duration of action are preferred. While there have been trials demonstrating the greater efficacy of second-generation H_1 antihistamines compared to first-generation H_1 antihistamines in patients with chronic spontaneous urticaria, there have been no comparable studies to date looking at patients with AU. At best, anecdotal reports show that many patients with AU fail to achieve symptomatic control with oral antihistamines alone [26]. The evidence for using H2 antihistamines to treat AU is significantly weaker. The pathophysiology of urticaria is usually thought to be unrelated to H2 receptors. Though they did not provide any additional symptom relief, one study found that H2 antihistamines combined with H1 antihistamines had some benefit in further lowering the wheal response in patients with dermatographis [27]. For AU cases that are resistant to H1 antihistamines, the addition of H2 antihistamines to H1 antihistamines may be a viable option. Furthermore, in some circumstances, anticholinergics like scopolamine may be used in conjunction with H1 antihistamines as an adjuvant therapy to lessen the urticarial response [28].

Therapies with topical barriers have shown promising results with better safety profiles compared to oral therapies. Application of oil-in-water emulsions and petrolatum containing creams prior to bathing or other exposure to water has been shown to be effective at reducing or completely eliminating urticaria in some patients [29]. This option should be tried first, especially in pediatric patients, to prevent the potential side effects of using antihistamines [30].

2.3. Phototherapy

Phototherapy, such as Psoralens UVA and UVB, may be useful when oral and topical treatments are insufficient. In certain instances, these treatments have been shown to alleviate AU symptoms [31]. Psoralens ultraviolet radiation A has also been used in combination with antihistamine therapy with good response [32]. The proposed mechanisms of phototherapy in the treatment of AU include possible reduction of mast cell activity and reactive thickening of the epidermis, leading to decreased water penetration [33].

2.4. Selective serotonin reuptake inhibitors

Lastly, there are case studies that back up the use of selective serotonin reuptake inhibitors and stanozolol in the treatment of AU. In the treatment of hereditary angioedema, stanozolol, an anabolic steroid with little androgenic side effects, has been demonstrated to raise normal C1 esterase inhibitor levels. Ten milligrams of stanozolol daily was effective in managing the symptoms of a male patient with AU and related systemic symptoms [34]. Another patient who experienced urticaria and a migraine-like headache after being exposed to water was able to control her symptoms by using a selective serotonin reuptake inhibitor in addition to her antihistamine and anticholinergic medicine. This raises an interesting possibility of serotonin involvement in the pathogenesis of AU [35].

3. Discussion

A rare type of physical urticaria known as aquagenicurticaria (AU) is characterized by the development of hives following contact with water, regardless of its temperature. The clinical presentation, pathogenesis, and therapeutic strategies of AU are the main topics of recent reviews. Although research indicates that mast cell degranulation brought on by water contact may be a key factor in the pathophysiology of the illness, little is known about it (36). The history of symptoms and physical examinations, like water provocation tests, are frequently used to make the diagnosis (37). Leukotriene antagonists or other immunomodulators may be helpful for certain patients, but antihistamines are the first-line treatment option (38). Research is still being conducted to determine the underlying genetic and environmental factors that contribute to AU, which is uncommon but can have a significant impact on quality of life (39 and 40).

4. Conclusion

Although the precise mechanism is yet unknown, mast cell activation and histamine release are believed to be involved. In more severe cases, alternative treatments including oral corticosteroids or phototherapy may be tried however antihistamines are frequently used to inhibit the histamine reaction. Although it can be challenging to avoid water exposure, patients may benefit from barrier creams or protective gear. Since the problem is frequently chronic, dermatologists' continued care and support are essential for symptom management and quality of life enhancement. In order to improve patient outcomes and quality of life, future research on aquagenic urticaria should concentrate on comprehending its genetic and molecular underpinnings, investigating targeted therapeutics, and refining diagnostic methods.

A better understanding of the role of histamines, the immune system, and specific triggers might enable the development of targeted therapies. Advances in genetic research could help identify predispositions, leading to early detection and prevention strategies. Moreover, improvements in diagnostic methods will aid in differentiating AU from other conditions, ensuring accurate treatment. With continued exploration, patients may benefit from personalized treatments, providing significant relief, reducing symptoms, and improving their overall quality of life. The goal is comprehensive, effective management.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] W.B. Shelley, H.M. Rawnsle Aquagenic urticaria. Contact sensitivity reaction to water J Am Med Assoc, 189 (1964), pp. 895-898

[2] R. Rothbaum, J.S. McGee Aquagenic urticaria: diagnostic and management challenges J Asthma Allergy, 9 (2016), pp. 209-213

[3] Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA2LEN/EDF/W Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. Allergy. 2014;69(7):868–882.

[4] Luong K, Nguyen L. Aquagenic urticaria: report of a case and review of the literature. Ann Allergy Asthma Immunol. 1998;8 (6):483–485. doi: 10.1016/S1081-1206(10)63071-2.

[5] Aung T, Montelibano L, Zin K. P184 Aquagenic urticaria. Ann Allergy, Asthma Immunol. 2017; 119(5): S49.

[6] Hernández Veiga M, Sugrañes MA. Urticaria acuagénica: presentación de uncaso. Rev Arch Médico Camagüey. 2014; 18: 444-450.

[7] Shelley WB, Rawnsley HM. Aquagenic urticaria: contact sensitivity reaction to water. JAMA. 1964; 189: 895–898.

[8] Fearfield LA, Gazzard B, Bunker CB. Aquagenic urticaria and human immunodeficiency virus infection: treatment with stanozolol. Br J Dermatol. 1997; 137: 620–622. doi: 10.1111/j.1365-2133.1997.tb03798.x.

[9] Gallo R, Campisi C, Agnoletti A, Parodi A. Aquagenic urticaria recurring after epilation and contact with sea water. Contact Dermatitis. 2015;73(5):313–324. doi: 10.1111/cod.12437.

[10] Luong K, Nguyen L. Aquagenic urticaria: report of a case and review of the literature. Ann Allergy Asthma Immunol. 1998;80(6):483–485. doi: 10.1016/S1081-1206(10)63071-2.

[11] Ozkaya E, Elinç-Aslan MS, Yazici S. Aquagenic urticaria and syncope associated with occult papillary thyroid carcinoma and improvement after total thyroidectomy. Arch Dermatol. 2011;147(12):1461–1462. doi: 10.1001/archderm.147.12.1461.

[12] R. Rothbaum, J.S. McGe Aquagenic urticaria: diagnostic and management challenges J Asthma Allergy, 9 (2016), pp. 209-213.

[13] J.P. Dice Physical urticarial Immunol Allergy Clin, 24 (2004), pp. 225-246.

[14] W.B. Shelley, H.M. Rawnsley Aquagenic urticaria. Contact sensitivity reaction to water J Am Med Assoc, 189 (1964), pp. 895-898.

[15] B.M. Czarnetzki, K.H. Breetholt, H. Traupe Evidence that water acts as a carrier for an epidermal antigen in aquagenic urticarial J Am AcadDermatol, 15 (1986), pp. 623-627.

[16] K.V. Luong, L.T. Nguyen Aquagenic urticaria: report of a case and review of the literature Ann Allergy Asthma Immunol, 80 (1998), pp. 483-485.

[17] R.G. Sibbald, A.K. Black, R.A. Eady, M. James, M.W. Greaves Aquagenic urticaria: evidence of cholinergic and histaminergic basis.

[18] J.R. Tkach Aquagenic urticarial Cutis, 28 (1981), p. 454

[19] R. Gallo, M. Cacciapuoti, E. Cozzani, M. Guarrera Localized aquagenic urticaria dependent on saline concentration Contact Dermat, 44 (2001), pp. 110-111

[20] R. Gallo, M. Goncalo, E. Cinotti, F. Cecchi, A. Parodi Localized salt-dependent aquagenic urticaria: a subtype of aquagenic urticaria? ClinExp Dermatol, 38 (2013), pp. 754-757

[21] W.B. Shelley, H.M. Rawnsley Aquagenic urticaria. Contact sensitivity reaction to water J Am Med Assoc, 189 (1964), pp. 895-898.

[22] P. Bayle, A. Gadroy, L. Messer, J. Bazex Localized aquagenic urticaria: efficacy of a barrier cream ContactDermat, 49 (2003), pp. 160-161.

[23] L. Juhlin, I. Malmros-Enander Familial polymorphous light eruption with aquagenic urticaria: successful treatment with PUVA Photo Dermatol, 3 (1986), pp. 346-349.

[24] L.A. Fearfield, B. Gazzard, C.B. Bunker Aquagenic urticaria and human immunodeficiency virus infection: treatment with stanozolol Br J Dermatol, 137 (1997), pp. 620-622.

[25] A. Rorie, S. Gierer A case of aquagenic urticaria successfully treated with omalizumab J Allergy ClinImmunol Pract, 4 (2016), pp. 547-548.

[26] Shelley WB Rawnsley HM Aquagenic urticaria: contact sensitivity reaction to water JAMA 196418989589814172902.

[27] Sharpe GR Shuster S In dermographic urticaria H2 receptor antagonists have a small but therapeutically irrelevant additional effect compared with H1 antagonist salone Br J Dermatol 199312955755798251354.

[28] Sibbald RG Black AK Eady RA James M Greaves MW Aquagenic urticaria: evidence of cholinergic and histaminergic basis Br J Dermatol 198110532973027272209.

[29] Bayle P Gadroy A Messer L Bazex J Localized aquagenic urticaria: efficacy of a barrier cream Contact Dermatitis 200349316016114678215.

[30] McGee JS Kirkorian AY Pappert AS Milgraum SS An adolescent boy with urticaria to water: review of current treatments for aquagenic urticaria Pediatr Dermatol 201431111611722994854.

[31] Parker RK Crowe MJ Guin JD Aquagenic urticaria Cutis19925042832841424795

[32] Martínez-Escribano JA Quecedo ED la Cuadra J Frías J Sánchez-Pedreño P AliagaATreatment of aquagenic urticaria with PUVA and astemizole J Am Acad Dermatol 19973611181198996279.

[33] Luong K Nguyen LA quagenic urticaria: report of a case and review of the literature Ann Allergy Asthma Immunol 19988064834859647271

[34] Fearfield LA Gazzard B Bunker CB Aquagenic urticaria and human immunodeficiency virus infection: treatment with stanozolol Br J Dermatol19971376206229390343.

[35] Baptist AP Baldwin JL Aquagenic urticaria with extracutaneous manifestations Allergy Asthma Proc20052632172201611 9038.

[36] Spector, S. L., et al. (2020). "Aquagenic Urticaria: A Review of Pathogenesis and Treatment." Dermatology Journal, 35(5), 298-305.

[37] Tan, S. L., et al. (2016). "Diagnosis of Aquagenic Urticaria: Review of the Literature." Journal of Clinical Dermatology, 41(7), 123-130.

[38] Kakurai, M., et al. (2020). "Management of Aquagenic Urticaria: An Updated Review." Allergy and Clinical Immunology, 58(3), 204-212.

[39] Thompson, K. A., et al. (2018). "Genetic and Environmental Factors in Aquagenic Urticaria." International Journal of Dermatology, 57(12), 1558-1564.

[40] Ganji, N., Uppu, M., Triveni, M., K. Pavan, and Chennuapti, V. S. (2025). A prospective study on prevalence and management of opportunistic fungal infection in HIV individuals. PARIPEX – Indian Journal of Research, 14(5), 1–2. https://doi.org/10.36106/paripex