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Revue française d'allergologie xxx (2019) xxx–xxx

State of the art

A rare case of localized aquagenic urticaria in a preschool child, including a literature review[☆]

Rare cas d'urticaire aquagénique localisée chez un enfant d'âge préscolaire avec la revue de littérature

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Received 4 March 2019; accepted 14 May 2019

Abstract

Aquagenic urticaria (AU) is a rare physical urticaria induced by contact with water. It may have distinctive clinical features, namely 1–2 mm folliculopapular urticaria, a pattern also characteristic of cholinergic urticaria. AU has a truncal and upper extremity distribution within 20–30 minutes after contact with water, regardless of its temperature or source. AU is usually symptomatic, with mild to severe pruritus and burning sensation. To date, some 60 cases have been reported in the literature, with an extremely low number of preschool children affected. Herein we describe a preschool-age boy diagnosed with localized AU and we compare the findings with those of the other AU subgroups reported in the literature. © 2019 Elsevier Masson SAS. All rights reserved.

Keywords: Aquagenic urticaria; Physical urticarial

Résumé

L'urticaire aquagénique (UA) est une urticaire physique rare, induit par le contact avec de l'eau. Elle peut être distincte sur le plan clinique, comme par exemple dans l'urticaire folliculopapulaire de 1 à 2 mm, caractéristique également caractéristique de l'urticaire cholinergique. L'UA a une distribution des troncs et des membres supérieurs dans les 20 à 30 minutes suivant le contact avec de l'eau, quelle que soit sa température ou sa source. AU est habituellement symptomatique avec prurit léger à sévère et sensation de brûlure. À l'heure actuelle, jusqu'à 60 cas ont été signalés dans la littérature, dont un nombre extrêmement rare chez les enfants d'âge préscolaire. Nous présentons un garçon d'âge préscolaire diagnostiqué avec une UA localisée et comparons ses découvertes avec les autres sous-groupes d'AU rapportés dans la littérature. © 2019 Elsevier Masson SAS. Tous droits réservés.

Mots clés : Urticaire aquagénique ; Urticaire physique

1. Introduction

Aquagenic urticaria (AU) is a form of physical urticarial which can be induced by cutaneous exposure to water. AU, is a very rare disease and may cause severe morbidity [1]. Till

now about 60 cases have been reported in the literature [2–4]. Wheals occur when a patients' skin makes contact with any type of water, regardless of its temperature within 30 min of exposure, and can last for 30 min to 2 h after cessation of exposure. It was first described in 1964 by Shelly and Rawnsley in a 15-year-old girl who had 1–3 mm folliculopapular wheals and surrounding erythema after contact to water [3]. Its prevalence is higher in females with an onset of disease usually occurring during or post puberty [1]. In the diagnosis of the patient, history is utmost important and is usually achieved after excluding all other causes of physical urticaria, confirmed by a water

[☆] This manuscript has not been published or submitted to elsewhere for publication except "Revue Française d'Allergologie".

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challenge test (WCT). Herein, we present a preschool boy diagnosed with localized AU, and a brief review of the literature with other subgroups of AU.

2. Case report

A 5-year-old male patient scheduled for adenoid vegetation surgery was referred to our paediatric allergy outpatient clinic for high total IgE and peripheral eosinophilia. It was learned that over the previous year, after washing his face with tap water the patient presented small wheals, pruritus and erythema on the facial skin that resolved spontaneously within 30–40 minutes. This sign was limited to the patient's face and appeared immediately after contact with all tap water, regardless of temperature. The wheals were not induced by seawater or spring water and were not accompanied by any additional symptoms. The condition had been present for one year. No significant features were noted in the patient's background or family history. Physical examination revealed no pathological findings. Laboratory tests including acute phase reactants, liver function tests, electrolytes, renal function tests, complement (C3, C4), thyroid hormones (TSH, ST4), autoantibodies (antinuclear antibody, anti-thyroid peroxidase), viral markers (cytomegalovirus [CMV], Epstein-Barr virus [EBV], respiratory multiplex polymerase chain reaction [multiplex PCR], parvovirus, hepatitis and human immunodeficiency virus [HIV]), stool microscopy and urinary analysis were within the normal limits. No pathological features were found in chest X-rays or on abdominopelvic ultrasonography. Skin prick testing was negative.

Our initial diagnosis was AU and an ice-cube test was performed to exclude cold urticaria. No lesions appeared on the forearm after cold stimulation. Pressure tests and exercise tests were also performed to differentiate the diagnosis of AU from other physical urticarias. The results were negative. To confirm the diagnosis of aquagenic urticaria, cotton soaked with tap water at room temperature was applied to the patient's face, upper anterior body, back and forearm for 30 minutes. On all the areas of application, urticarial plaques formed only on the lower facial area. The test was considered positive. The same tests were repeated with alcohol, but no reaction occurred. All these findings confirmed the diagnosis of localized AU. Oral cetirizine treatment was given for four weeks, after which all symptoms had disappeared, with no recurrence of the urticarial rash.

3. Conclusion

Aquagenic urticaria is more common in girls at puberty and during the postpubertal period [4,5]. Our case concerns the youngest patient reported in Turkey to date. Although many cases are sporadic, familial cases have also been reported [4,6,7], but our patient had no familial history. With AU, itchy follicular papular urticaria occurs in areas coming into contact with water. Small pruritic wheals (1–3 mm in diameter) similar to cholinergic urticaria occur on the erythematous surface within 1–30 minutes of contact with water and are generally limited to the neck, arms and upper body. These urticarial rashes disappear



Fig. 1. Patient's face after a water challenge test.

spontaneously within 30–60 minutes. Although it is known that the formation of urticarial rash is not affected by the temperature or source of water, in recent years there have been reported cases of aquagenic urticaria due to the salt concentration or osmolarity of water [8]. This type of urticaria is called salt-dependent AU. However, based on our patient's history, diagnostic tests were performed, and urticarial rashes occurred only with tap water. In the case of AU, no urticarial plaque forms after contact with alcohol or other organic solvents [9], and no reaction to the alcohol test occurred in our patient. Systemic symptoms such as dizziness, wheezing or shortness of breath are very rare [10,11]. When our patient underwent a WCT, localized urticarial lesions appeared on the face minutes after contact with tap water without any other symptoms. Contrary to the reported cases, urticarial rashes occurred on our patient's lower face. In the literature, this feature was noted mostly in patients with localized salt-dependent AU [8,12,13]. We would thus suggest that localized forms of the AU subgroups may more frequently involve the lower facial area of patients.

The diagnosis of AU is based on clinical history and a water challenge test. In the standard WCT for AU, a water-soaked cotton compress at 35 °C is applied to the upper body for 30 minutes [5,14]. This test may be performed with tap water, distilled water or physiological saline (0.9% NaCl). While AU may be triggered by water at any temperature, water-soaked cotton should be kept at room temperature to avoid any mix-up of cold urticaria and local urticaria. We applied cotton soaked with tap water at room temperature to our patient's upper body for 30 minutes, following which urticarial rash developed solely on his face. This supported the diagnosis of local AU (Fig. 1). Dermographism, cholinergic urticaria and cold urticaria may be associated with AU [10,15]. The elevated patches in cholinergic urticaria and AU are similar; trigger factors should thus be investigated to rule out cholinergic urticaria. None of our patient's urticarial

Table 1
Characteristics of aquagenic urticaria and its subgroups according to published data.

	Aquagenic urticaria	Salt-dependent aquagenic urticaria	Familial aquagenic urticaria
<i>Symptoms often start at</i>			
Puberty [21]	Childhood (uncommon) [11]		
Post puberty [8]		Childhood [22] (uncommon)	
Early age [4,6]			After birth [23] (uncommon)
<i>Gender</i>	Female predominance [21]	Female predominance [8]	Female predominance [4,6]
<i>Generalized/localized</i>	Generalized [21] > Localized	Localized [21] > Generalized	Generalized
<i>Commonly involved body areas</i>	Trunk, upper arms [21]	Lower facial area and neck, back	Trunk, upper arms, thighs, abdomen and feet [4]
	The affected area is generally refractory to repeated stimulation for several hours [21]		Palms and soles remain free of lesions [4]
<i>Triggering factors</i>	Tap water, snow, sweat, saliva, tears [8]	Seawater, swimming pool water, also sweat sporadically [8]	Baths, showers, rain, swimming pool, seawater, sweating [4]
	But not triggered by seawater or water ingestion [8]	But not triggered by tap water or water ingestion [8]	But not triggered by tears or water ingestion [4]
			Wheals nevertheless appeared more intense with seawater vs. tap water, and with hot water vs. warm and cold water
<i>Other conditions</i>	HIV and hepatitis C [5] Lung cancer Papillary thyroid carcinoma [24]		Bernard-Soulier syndrome [6] Familial lactose intolerance [4], atopy [4], polymorphous light eruptions [26]
	Migraine, atopic dermatitis and asthma [10] Cholinergic [16] Cold urticaria [25]	Allergic rhinitis, food allergy [8]	
<i>Water challenge test [8,27]</i>	Room temperature	Room temperature	Room temperature
Tap water	+	-	+
NaCl 0.9%	+	-	+
NaCl 3.5%	-	+	+
Glucose 20%	-	±	?
NaHCO ₃ 5.3%	-	±	?
Distilled water	+	-	+
<i>Prognosis</i>	Normally resolution [2,14,17,18]	Resolves in children but adults remain refractory to antihistamines [8,12,27]	Worsening in adults [8]

rash after contact with tap water was affected by triggering factors (hot bath, excitement, stress, exercise, etc.) and a negative ice-cube test ruled out cold urticaria. Our patient's total IgE level and peripheral eosinophilia differed from values reported in the literature, but no allergic disease was detected. This feature is most often seen in salt-dependent AU [8]. Table 1 summarises the characteristics of cases in AU subgroups reported to date.

Although the pathogenesis of AU is unknown, many mechanisms have been proposed. Shelly and Rawnsley [2] initially concluded that water produces a substance that reacts with sebum to induce histamine release by perifollicular mast cells. Sibbald et al. [16] suggested a relationship between urticarial rashes and penetration of water into the components of the skin. Czarnetzki et al. [7] suggested penetration by residual antigens of water in the epidermal layer into deeper layers of the skin, triggering histamine release from sensitized mast cells in the dermis. Acetylcholine and methacholine are thought to be the causative mediators in the pathogenesis, but the result of

mechanisms triggered by these mediators is contradictory [7,11,16,17]. Serum histamine levels also vary among patients [9].

We suggest that multiple pathophysiological mechanisms play a role in the development of AU. Antihistamines are used in the first-line treatment of AU, but the therapeutic effect and prognosis are variable [9]. In some cases, the symptoms are completely controlled by antihistamines, whereas in others the latter may be ineffective [11,18]. Our patient recovered completely after one month of oral treatment with cetirizine 5 mg, and no recurrence of urticarial lesions was seen at 6 months of follow-up.

In refractory cases, UV radiation (psoralen plus UVA therapy and UVB) may be used, either alone or in combination with antihistamines. UV therapy is based on the hypothesis that water penetrates and interferes with dendritic cells, leading to decreased immunosuppression or mast cell degranulation through mediation of epidermal thickening [9,19]. Barrier creams (water-oil emulsion creams) applied on the skin are

effective in protecting against water [20]. Barrier creams have been used in the literature and have been shown to be useful in salt-dependent aquagenic urticaria [8,13]. However, some rare case reports also show their efficacy in patients with localized AU [20]. Aquagenic urticaria in HIV responds to stanozolol [5]. On evaluating patient response to current treatment options, we suggest that the best approach involves tailoring the patient's treatment based on age, concomitant diseases or symptoms, and AU subgroup.

Although a few preschool cases of local aquagenic urticaria have been reported, it is important to make a differential diagnosis based on the causes of physical urticaria. Clinicians should also consider localized AU during differential diagnosis of chronic urticaria in preschool age children.

Funding

No financial support was provided for this trial.

Contribution of authors

I confirm that all people listed as authors of the manuscript have contributed substantially to study planning, data collection or interpretation of results and have written or critically revised the manuscript and approved its final submitted version.

NE, SO and IB designed the study and wrote the manuscript. NE, SO and IB contributed to data collection. All authors of the original manuscript have read, approved and in full agreement with the manuscript.

Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgements

We have no acknowledgement to be declared.

References

- [1] Hamie L, Abou-Rahal J. Water-related dermatoses. *Int J Dermatol* 2019;58:515–29, <http://dx.doi.org/10.1111/ijd.14316> [Epub ahead of print. Review].
- [2] Shelly WB, Rawnsley HM. Aquagenic urticaria. Contact sensitivity reaction to water. *JAMA* 1964;189:895–8.
- [3] Kontou-Fili K, Borici-Mazi R, Kapp A, et al. Physical urticaria: classification and diagnostic guidelines An EAACI position paper. *Allergy* 1997;52:504.
- [4] Treudler R, Tebbe B, Steinhoff M, Orfanos CE. Familial aquagenic urticaria associated with familial lactose intolerance. *J Am Acad Dermatol* 2002;47:611–3.
- [5] Fearfield LA, Gazzard B, Bunker CB. Aquagenic urticaria and human immunodeficiency virus infection: treatment with stanozolol. *Br J Dermatol* 1997;137:620–2.
- [6] Pitarch G, Torrijos A, Martínez-Menchón T, Sánchez-Carazo JL, Fortea JM. Familial aquagenic urticaria and Bernard-Soulier syndrome. *Dermatology* 2006;212:96–7.
- [7] Czarnetzki BM, Bretholt KH, Traupe H. Evidence that water acts as a carrier for an epidermal antigen in aquagenic urticaria. *J Am Acad Dermatol* 1986;15:623–7.
- [8] Gallo R, Gonçalves M, Cinotti E, Cecchi F, Parodi A. Localized salt-dependent aquagenic urticaria: a subtype of aquagenic urticaria? *Clin Exp Dermatol* 2013;38(7):754–7.
- [9] Dice JP. Physical urticaria. *Immunol Allergy Clin North Am* 2004;24:225–46.
- [10] Baptist AP, Baldwin JL. Aquagenic urticaria with extracutaneous manifestations. *Allergy Asthma Proc* 2005;26:217–20.
- [11] Luong KV, Nguyen LT. Aquagenic urticaria: report of a case and review of literature. *Ann Allergy Asthma Immunol* 1998;80:483–5.
- [12] Margerin F, Wetttlé C, Merklen-Djafri C, Cribier B. Localized salt-dependent aquagenic urticaria: a case report. *Ann Dermatol Venereol* 2015;142(12):771–5.
- [13] Vieira M, Rosmaninho I, Lopes I, Guilherme A, Moreira da Silva JP. Localized salt-dependent aquagenic urticaria, a rare subtype of urticaria: a case report. *Eur Ann Allergy Clin Immunol* 2018;50(3):141–4.
- [14] Panconesi E, Lotti T. Aquagenic urticaria. *Clin Dermatol* 1987;5:49–51.
- [15] Magerl M, Borzova E, Giménez-Arnau A, Grattan CE, Lawlor F, Mathelier-Fusade P, et al. The definition and diagnostic testing of physical and colinergic urticarias – EAACI/GA2LEN/EDF/UNEV consensus panel recommendations. *Allergy* 2009;64:1715–21.
- [16] Sibbald RG, Black AK, Eady RA, James M, Greaves MW. Aquagenic urticaria: evidence of colinergic and histaminergic basis. *Br J Dermatol* 1981;105:297–302.
- [17] Chalamidas SL, Charles CR. Aquagenic urticaria. *Arch Dermatol* 1971;104:541–6.
- [18] Medeiros M. Aquagenic urticaria. *J Investig Allergol Clin Immunol* 1996;6:63–4.
- [19] Martínez-Escribano JA, Quecedo E, De la Cuadra J, Frias J, Sánchez-Pedreño P, Aliaga A. Treatment of aquagenic urticaria with PUVA and asetemizole. *J Am Acad Dermatol* 1997;36:118–9.
- [20] Bayley P, Gadroy A, Messer L, Bazex J. Localized aquagenic urticaria: efficacy of barrier cream. *Contact Dermatitis* 2003;49:160–1.
- [21] Rothbaum R, McGee JS. Aquagenic urticaria: diagnostic and management challenges. *J Asthma Allergy* 2016;9:209–13 [eCollection Review].
- [22] Napolitano M, Gallo R, Donnarumma M, Patruno C. Salt-dependent aquagenic urticaria in children: report of two cases. *Pediatr Allergy Immunol* 2018;29:324–6.
- [23] Seize MB, Ianhez M, de Souza PK, Rotta O, Cestari Sda C. Familial aquagenic urticaria: report of two cases and literature review. *An Bras Dermatol* 2009;84(5):530–3 [Review. Portuguese].
- [24] 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):1461–2.
- [25] Mathelier-Fusade P, Aissaoui M, Chabane MH, Mounedji N, Leynadier F. Association of cold urticaria and aquagenic urticaria. *Allergy* 1997;52(6):678–9.
- [26] Juhlin L, Malmros-Enander I. Familial polymorphous light eruption with aquagenic urticaria: successful treatment with PUVA. *Photodermatol* 1986;3(6):346–9.
- [27] Gallo R, Cacciapuoti M, Cozzani E, Guarrera M. Localized aquagenic urticaria dependent on saline concentration. *Contact Dermat* 2001;44(2):110–1.