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Unilateral aquagenic keratoderma treated with botulinum toxin A

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Abstract

Background: Aquagenic keratoderma is a rare transient disease that occurs after water immersion and disappears shortly after drying. Most cases involve the palms and fingers bilaterally but it can also affect the soles. Few cases have been associated with drugs but its pathogenesis remains unclear.

Main observation: We report a 60-year-old man with a 30-year-history of aquagenic keratoderma of the right palm without associated hyperhidrosis or history of drug intake. After unsuccessful treatment with 15% aluminium chloride hexahydrate gel, botulinum toxin A injections led to significant improvement within 2 weeks.

Conclusions: To our knowledge, this case is the first report of idiopathic unilateral aquagenic keratoderma in the medical literature. It is the third report of successful treatment with botulinum toxin A which is in favor of a role of sweat glands in the pathogenesis of aquagenic keratoderma.

Introduction

Aquagenic keratoderma (AK) is a rare condition characterized by acquired, recurrent and transient keratoderma after 2 to 10 minutes of water immersion, which disappears minutes to an hour after drying. It was first documented by English and McCollough[1] in 1996 and was termed "transient reactive papulotranslucent acrokeratoderma" at that time. Afterwards this relatively new entity was coined by "aquagenic palmoplantar keratoderma", "aquagenic syringeal keratoderma", "aquagenic keratoderma", "aquagenic wrinkling of the palms", and "aquagenic acrokeratoderma". AK is predominant in young females and usually occurs sporadically.[2] So far, 55 cases have been reported in the medical literature. We present a patient with unusual unilateral palmar AK who responded to treatment with botulinum toxin A.

Case report

A 60-year-old man presented with a 30-year-history of episodes of wrinkling and desquamation of his right palm following hand immersion in water, especially when warm or hot. Physical examination showed hyperkeratosis of the right palm prior to water immersion, and whitish wrinkled thickening of the palm following the immersion (Fig. 1). There was no associated hyperhidrosis, dysesthesia or history of drug intake. The history and clinical observation led to the diagnosis of AK.

Treatment with 15% aluminium chloride hexahydrate gel for 3 months was unsuccessful. Thus injections of 50 units of botulinum toxin A reconstituted in 5 mL of isotonic sodium chloride solution (concentration: 1 unit of botulinum toxin per 0.1 mL) were performed in the right palm, preceded by lidocaine injections (2% lidocaine) through a pressurized device (Med-Jet MBX).[3] Each lidocaine injection done with this device creates a whitish anesthetized wheal and should be separated by 1.5 cm from the other. Then one subdermal injection of 2 units of botulinum toxin using a 33-G needle is done inside each anesthetized wheal.

Botulinum toxin treatment led to significant improvement in our patient within 2 weeks (Fig. 2). AK recurred after 6 months necessitating another treatment with botulinum toxin injections.

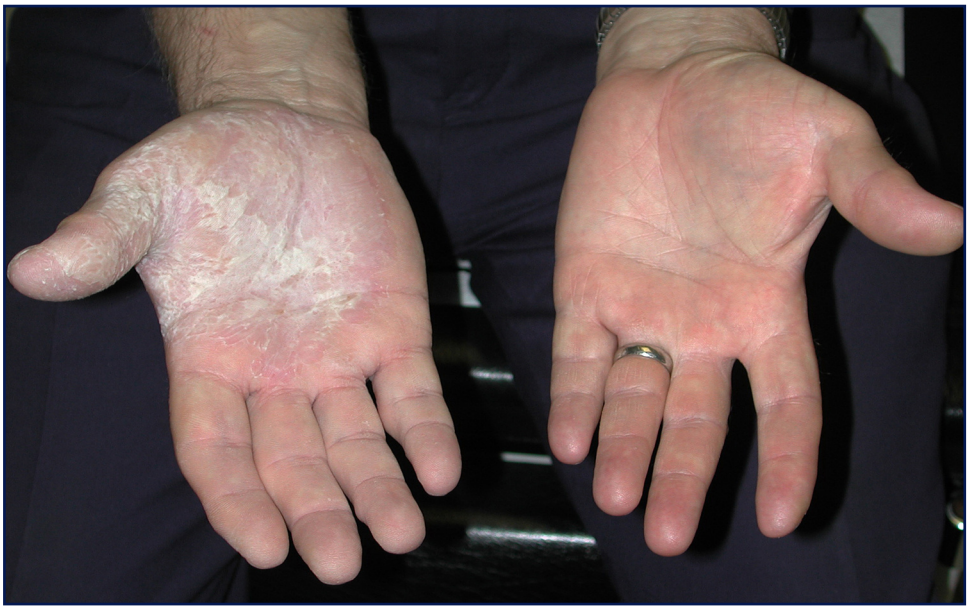

Figure 1

Confluent whitish papules on the right palm after 5 minutes of immersion of the hands in tap water.

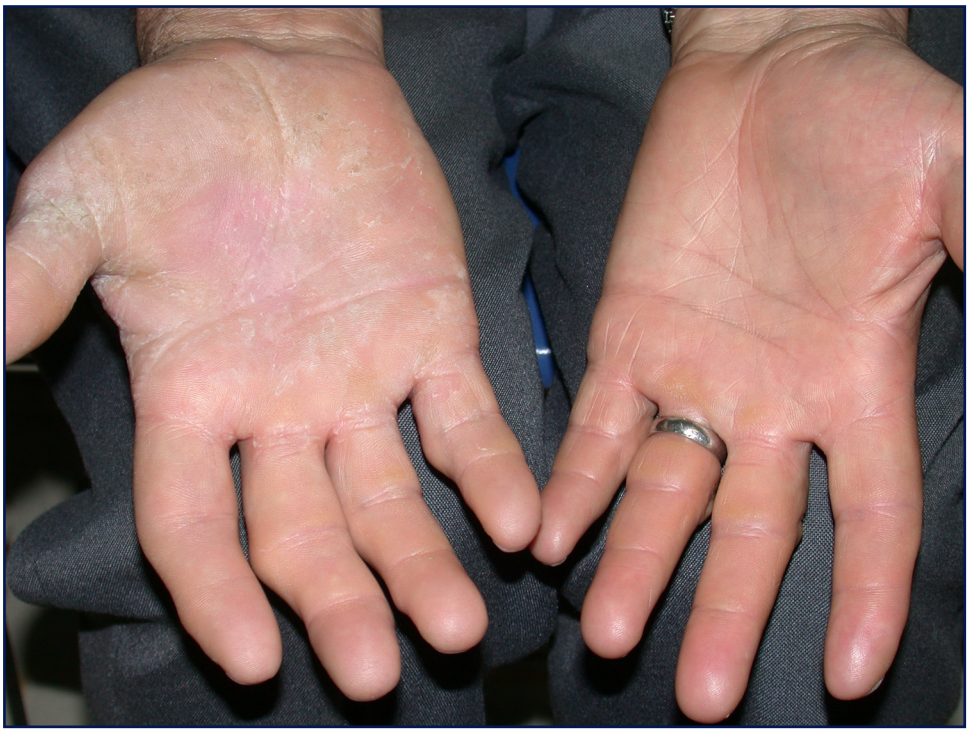

Figure 2

Significant improvement of the right palm after immersion of the hands in tap water after 2 weeks of treatment with botulinum toxin injections.

Discussion

AK presents as translucent whitish and pebbly thickening of the palms and soles after immersion in water.[4] Most cases involve the palms and fingers bilaterally and few cases affect the soles.[2] To our knowledge, there was only one previous case of unilateral palmar AK in the medical literature.[5] That case was associated with aspirin intake while our case occurred without any history of drug intake. Warm water provokes the lesions of AK more rapidly than cold water, as in our patient.[2] The "hand-in-the bucket" sign, when patients submerge their hands in water to demonstrate the lesions, constitutes a clue to diagnosis.[3] Patients may report tightness, pruritus, mild pain, burning sensation and hyperhidrosis.[2,4,6] Histopathology is nonspecific and may show orthokeratotic hyperkeratosis and dilated eccrine ducts.[2,6]

The pathogenesis of AK remains unclear. MacCormack *et al*[7] suggested that the clinical manifestations of AK could be due to dilatation of eccrine ostia in order to release sweat to compensate for mild hyperkeratosis. Another theory proposed that AK is a disorder of the integrity of the stratum corneum, resulting in increased water absorption.[8] Our patient had a hyperkeratosis of the right palm developing progressively over the years which suggests that his hyperkeratosis is rather a secondary phenomenon induced by repeated exposure to water. Moreover he did not have associated hyperhidrosis. These findings do not

Table 1. Cases of aquagenic keratoderma reported in the medical literature, their treatment and response to treatment.

Cases of Aquagenic keratoderma	Treatment	Treatment result
	Aluminum-based	
Yan *et al* (3 cases)[4]	Aluminum hydroxide	Improvement
Bellotch *et al* (1 case)[13]		Improvement
Katz *et al* (2 cases)[14]		Improvement
Neri *et al* (1 case)[15]		Improvement
Suchak *et al* (1 case)[16]		Improvement
Kocatürk *et al* (1 case)[17]		Improvement
Seitz *et al* (1 case)[9]		Improvement
Katz *et al* (1 case)[14]		No response
Baldwin *et al* (1 case)[18]		No response
Flann *et al* (1 case)[19]	Aluminum chloride hexahydrate	Improvement
Kabashina *et al* (1 case)[20]		No response
Diba *et al* (1 case)[11]		No response
Bagazgoita *et al* (1 case)[6]		No response
Our case		No response
The last 3 cases responded to botulinum toxin injections		
Falcón *et al* (1 case)[21]	Aluminum chloride 20%	No response
Pastor *et al* (3 cases)[22]	Aluminum chloride hexahydrate 20% + urea cream 20%	Improvement
Pardo *et al* (1 case)[23]	Aluminum chloride + silicone-based protection cream	Improvement
Badazzi *et al* (1 case)[12]	Aluminum chloride	Improvement
Sais *et al* (1 case)[24]	Aluminum chlorohydrate 18%	No response
Conde-Salazar (2 cases)[25]		Improvement
Luo *et al* (2 cases)[26]	3% potassium aluminum sulfate solution	Improvement
	Salicylic-acid based	
Saray *et al* (2 cases)[27]	20% salicylic based in vaseline	Complete resolution
	20% salicylic based in vaseline + 10% urea cream	Complete resolution
Polat *et al* (2 cases)[28]	5% salicylic acid in ointment	Improvement but recurrence
Yalcin *et al* (1 case)[29]		Improvement
Adişen *et al* (1 case)[30]		Improvement
Itin *et al* (1 case)[8]	Oral anntihistamines	Improvement
Suchak *et al* (1 case: the same case improved with aluminium hydroxide)[16]		No response
Luo *et al* (1 case: the same case improved with formalin 3%)[26]	Oral antihistamines combined with topical steroids	No response
Luo *et al* (2 cases)[26]	Formalin 3% in alcohol	Improvement
Luo *et al* (1 case)[2]		Improvement
Lowes *et al* (1 case)[31]	Iontophoresis (combined with aluminium hydroxide)	Improvement
Diba *et al* (1 case)[11]	Botulinum toxin injections	Improvement
Bagazgoitia *et al* (1 case)[6]		Improvement
Our case		Improvement
Drug-related: Carder *et al* (1 case: rofecoxib)[10] Vildósola (1 case: celecoxib)[32] Khuu *et al* (1 case: aspirin)[5] Ludgate *et al* (1 case: tobramycin)[33]	Withdrawal	Complete resolution in all cases
Lim *et al* (1 case)[34]	No treatment	Spontaneous resolution
MacCormack *et al* (2 cases)[7]		
Itin *et al* (1 case)[8]		
English *et al* (2 cases)[1]	Not mentioned or no treatment	Not mentioned or no treatment
Schmults *et al* (1 case)[35]		
Davis *et al* (1 case)[36]		
Gild *et al* (1 case)[37]		
Tan *et al* (1 case)[38]		
Yoon *et al* (1 case)[39]		
Xia *et al* (1 case)[40]		
Garçon *et al* (1 case)[41]		

support the hypothesis that AK is due to a defect in the palmar stratum corneum. A third theory, based on association of AK with cystic fibrosis[9] and intake of aspirin[5] or cyclo-oxygenase-2 inhibitors,[10] suggests that AK could be due to increased sweat salt concentration in the stratum corneum.[2,9]

Spontaneous resolution has been reported in 4 cases and some cases clear after a few years.[8,11,12] Table 1 shows a list of all the cases of AK reported in the medical literature and their response to treatment. Modalities of treatment usually used for hyperhidrosis, such as aluminium chloride hexahydrate and iontophoresis, have been efficacious in treating several patients with AK.[2,4,6] Moreover, there were 2 previous reports of successful treatment of AK with botulinum toxin.[6,11] The first case was associated with hyperhidrosis. The absence of hyperhidrosis in the second case as well as in our case is in favor of involvement of the sweat glands in the pathogenesis of AK. The first case treated with botulinum toxin recurred after 5 months of treatment while it was not mentioned whether there was a recurrence or not in the second case.[6,11] Our patient's AK recurred after 6 months of treatment. Thus, repeated injections of botulinum toxin might be necessary at intervals of 5 to 6 months in AK patients.

Conclusions

This case is unusual by its unilateral idiopathic palmar involvement and by its long history. Moreover, it is the third reported case to respond favorably to botulinum toxin A. The successful treatment of AK with hyperhidrosis treatments points to the involvement of the sweat glands in the pathogenesis of this entity. AK is probably more prevalent than reported in the literature because of its transient nature; its recognition may provide a better understanding of the pathogenesis and appropriate modalities of treatment of this condition.

References

1. English JC 3rd, McCollough ML. Transient reactive papulotranslucent acrokeratoderma. *J Am Acad Dermatol*. 1996; 34: 686-687.
2. Luo DQ, Li Y, Huang YB, Wu LC, He DY. Aquagenic syringeal acrokeratoderma in an adult man: case report and review of the literature. *Clin Exp Dermatol*. 2009; 34: e907-909.
3. Benohanian A. Palmar hyperhidrosis. Needle-free anesthesia as an alternative to Bier's block and peripheral nerve blockade for botulinum toxin therapy. *Dermatol Online J*. 2006; 12: 26.
4. Yan AC, Aasi SZ, Alms WJ, James WD, Heymann WR, et al. Aquagenic palmoplantar keratoderma. *J Am Acad Dermatol*. 2001; 44: 696-699.
5. Khuu PT, Duncan KO, Kwan A, Hoyme HE, Bruckner AL. Unilateral aquagenic wrinkling of the palms associated with aspirin intake. *Arch Dermatol*. 2006; 142: 1661-1662.
6. Bagazgoitia L, Pérez-Carmona L, Salgüero I, Harto A, Jaen P. Aquagenic keratoderma: successful treatment with botulinum toxin. *Dermatol Surg*. 2010; 36: 434-435.
7. MacCormack MA, Wiss K, Malhotra R. Aquagenic syringeal acrokeratoderma: report of two teenage cases. *J Am Acad Dermatol*. 2001; 45: 124-126.
8. Itin PH, Lautenschlager S. Aquagenic syringeal acrokeratoderma (transient reactive papulotranslucent acrokeratoderma). *Dermatology*. 2002; 204: 8-11.
9. Seitz CS, Gaigl Z, Bröcker EB, Trautmann A. Painful wrinkles in the bathtub: association with hyperhidrosis and cystic fibrosis. *Dermatology*. 2008; 216: 222-226.
10. Carder KR, Weston WL. Rofecoxib-induced instant aquagenic wrinkling of the palms. *Pediatr Dermatol*. 2002; 19: 353-355.
11. Diba VC, Cormack GC, Burrows NP. Botulinum toxin is helpful in aquagenic palmoplantar keratoderma. *Br J Dermatol*. 2005; 152: 394-395.
12. Bardazzi F, Savoia F, Dika E, Tabanelli M, Giacomini F. Acquired aquagenic keratoderma. *Ped Dermatol*. 2007; 24: 197-198.
13. Bellotch I, Vergara G, Albares MP, Pascual JC, Silvestre JF, et al. Aquagenic keratoderma. *J Eur Acad Dermatol Venereol*. 2003; 17: 306-307.
14. Katz KA, Yan AC, Turner MI. Aquagenic wrinkling of the palms in patients with cystic fibrosis homozygous for the delta F508 CFTR mutation. *Arch Dermatol*. 2005; 141: 621-624.
15. Neri I, Bianchi F, Patrizi A. Transient aquagenic palmar hyperwrinkling: the first instance reported in a young boy. *Ped Dermatol*. 2006; 23: 39-42.
16. Suchak R, Lawlor F. Water-induced palmar tingling and swelling. *Clin Exp Dermatol*. 2006; 32: 119-120.
17. Kocatürk E, Kavala M, Büyükbabani N, Türkoğlu Z. Whitish papules on the palm. *Int J Dermatol*. 2007; 46: 736-737.
18. Baldwin BT, Prakash A, Frenske NA, Messina JL. Aquagenic syringeal acrokeratoderma: report of a case with histologic findings. *J Am Acad Dermatol*. 2006; 54: 899-902.
19. Flann S, Pembroke A. A localized form of aquagenic syringeal acrokeratoderma. *Clin Exp Dermatol*. 2009; Oct 23 [Epub ahead of print].
20. Kabashina K, Shimauchi T, Kobayashi M, Fukamachi S, Kawakami C, et al. Aberrant aquaporin 5 expression in the sweat gland in aquagenic wrinkling of the palms. *J Am Acad Dermatol*. 2008; 59: (2 Suppl 1): S28-32.
21. Falcón CS, Ortega SS. Aquagenic syringeal acrokeratoderma. *J Am Acad Dermatol*. 2008; 59 (5 Suppl): S112-113.
22. Pastor MA, González L, Kilmurray L, Bautista P, López A, et al. Aquagenic keratoderma: 3 new cases and a review of the literature. *Actas Dermosifiliogr*. 2008; 99: 399-406.
23. Pardo J, Sánchez-Motilla JM, Latasa JM. Atypical aquagenic keratoderma. *Actas Dermosifiliogr*. 2005; 96: 540-542.
24. Sais G, Bigatà X, Admella C. Aquagenic syringeal acrokeratoderma. *Actas Dermosifiliogr*. 2007; 98: 69-70.
25. Conde-Salazar L, Angulo J, González-Guerra E, Requena L, Casado I, *et al*. Aquagenic syringeal acrokeratoderma. presentation of two cases. *Actas Dermosifiliogr*. 2006; 97: 275-277.
26. Luo DQ, Zhao YK, Zhang WJ, Wu LC. Aquagenic acrokeratoderma. *Int J Dermatol*. 2009; Dec 11 [Epub ahead of print].
27. Saray Y, Seçkin D. Familial aquagenic acrokeratoderma: case reports and review of the literature. *Int J Dermatol*. 2005; 44: 906-909.

28. Polat M, Gür G, Pelitli A, Yalçin B, Tamer E, et al. Acquired aquagenic papulotranslucent acrokeratoderma: report of two cases. *Am J Clin Dermatol.* 2008; 9: 263-265.

29. Yalcin B, Artuz F, Toy GG, Lenk N, Alli N. Aquired aquagenic papulotranslucent acrokeratoderma. *J Eur Acad Dermatol Venereol.* 2005; 19: 654-656.

30. Adişen E, Karaca F, Gürer MA. Transient reactive papulotranslucent acrokeratoderma in a 50-year-old woman: case report and review of the literature. *Am J Clin Dermatol.* 2008; 9: 404-409.

31. Lowes MA, Khaira GS, Holt D. Transient reactive papulotranslucent acrokeratoderma associated wiht cystic fibrosis. *Australas J Dermatol.* 2000; 41: 172-174.

32. Vildósola S, Ugalde A. Celecoxib-induced aquagenic keratoderma. *Actas Dermosifiliogr.* 2005; 96: 537-539.

33. Ludgate MW, Patel N, Lamb S. Tobramycin-induced aquagenic wrinkling of the palms in a patient with cystic fibrosis. *Clin Exp Dermatol.* 2009; 34: e75-77.

34. Lim KS, Ng SK. Aquagenic wrinkling of the palms in a boy with a congenital cardiac anomaly. *J Eur Acad Dermatol Venereol.* 2007; 21: 985-986.

35. Schmults C, Sidhu G, Urbanek RW. Aquagenic syringeal acrokeratoderma. *Dermatol Online J.* 2003; 9: 27.

36. Davis LS, Woody CM. Idiopathic aquagenic wrinkling of the palms. *Pediatr Dermatol.* 2004; 21: 180.

37. Gild R, Clay D. Aquagenic wrinkling of the palms in a cystic fibrosis carrier. *Australas J Dermatol.* 2008; 49: 19-20.

38. Tan C, Zhu WY, Min ZS. Aquagenic acrokeratoderma. *J Clin Dermatol.* 2008: 37: 275-276.

39. Yoon TY, Kim KR, Lee JY, Kim MK. Aquagenic syringeal acrokeratoderma: unusual prominence on the dorsal aspect of fingers? *Br J Dermatol.* 2008; 159: 486-488.

40. Xia Y, Gunning ST, Schulz-Butulis BA. What is your diagnosis? Aquagenic syringeal acrokeratoderma (ASA). *Cutis.* 2006; 78: 304, 317-319.

41. Garçon N, Roguedas AM, Misery L, Audrezet MP, Ferec C. Aquagenic wrinkling of the palms in a patient with cystic fibrosis heterozygous for the Delta F 508 mutation. *Ann Dermatol Venereol.* 2008; 135: 232-234.