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CASE REPORT

Aquagenic Palmoplanta keratoderma: Response to Topical Pimecrolimus and Literature Review

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Abstract: Aquagenic palmoplantar keratoderma (APK) is a rare skin disease characterized by temporary papules and macerated plaques triggered by contact with water. Failure to receive timely and proper treatment may seriously damage the patient's daily life. The precise pathogenesis of APK (Aquagenic Palmoplantar Keratoderma) remains poorly understood, and safe and efficacious therapeutic options are currently lacking. The conventional therapy mainly involves topical application of aluminum chloride, followed by botulinum toxin injection, topical corticosteroids, topical salicylic acid, barrier agents, and oral antihistamines. This case report presents an APK patient who showed improvement after tw1o months of treatment with pimecrolimus cream, slight symptom recurrence following water exposure or sweating.

Keywords: aquagenic palmoplantar keratoderma, water contact test, pimecrolimus

Introduction

Aquagenic palmoplantar keratoderma (APK) is a rare skin disease, which is characterized by the rapid appearance of white papules, excessive wrinkling and swelling of the palm after brief contact with water. Under normal circumstances, wrinkles appear on the palms within an average of 12 minutes when soaked in water.[1,2] We described a female patient who was treated with pimecrolimus for affected hands and wrists.

Case Presentation

A 50-year-old woman presented to the outpatient dermatology department with an over 20-years history of rapid appearance of white papules, excessive wrinkling and swelling of the palm after brief exposure to warm water or sweating,but there were no symptoms of itching, burning, or pain. Upon water removal, the symptoms disappeared rapidly. She denies having a history of atopic dermatitis or hyperhidrosis, smoking, or a history of special medications, as well as denying engaging in long-term frequent hand washing work, and no other family members have experienced similar symptoms.

On examination, after soaking both hands in hot water or sweat, diffuse white spots were visible on the dorsal of the hands and wrists, with skin lines remaining. The palmar skin exhibited a pebbly appearance and slight edema, accompanied by excessive swelling (Figure 1A and B). Approximately half an hour after the sweat evaporated, the skin keratinization of the dorsal of the hands and wrists subsided, leaving behind a few white spots, and only a few erythematous spots were visible on the palms (Figure 1C and D). Due to the patient's clinical symptoms, a biopsy was not taken. Based on her history,the appearance of her hands and an otherwise normal physical examination, we diagnosed aquagenic palmoplanta keratoderma(APK). She applied topical Pimelomos ointment twice a day and was advised to continue her daily routine, including weekly moisturizing and follow-up. Her palm texture and symptoms improved within a week (Figure 2). When she stopped treatment and was exposed to sweat or hot water again after 2 months, the symptoms recurred but also responded to retreatment with pimecrolimus.

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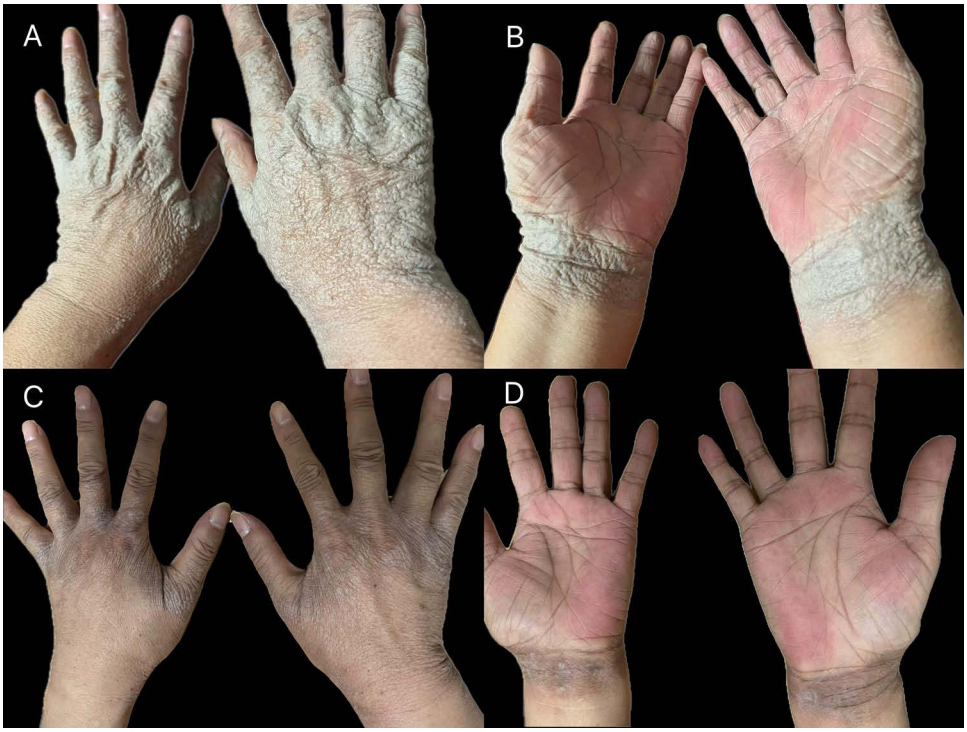

Figure 1 Clinical images of aquagenic plamoplantar keratoderma in a 50-year-old woman. (**A**) Diffuse white spots were visible on the dorsal aspects of the hands and wrists, with skin lines remaining. (**B**) Visible erythema on the palm, diffuse white spots were visible on the wrists. (**C**) Upon the removal of water, the skin keratinization on the dorsal aspects of the hands subsided, leaving behind a few white spots. (**D**) After the palm dries,only a few erythematous spots were visible on the palms.

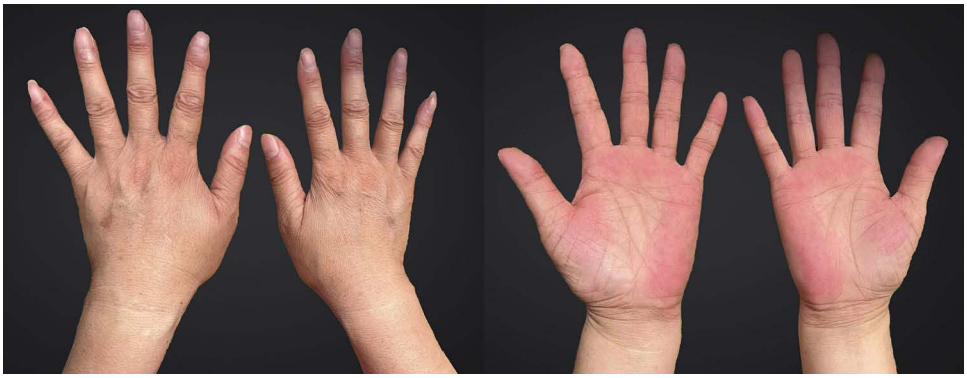

Figure 2 Substantial improvement noted in skin texture and wrinkling of hand skin 1 week after treatment with pimecrolimus ointment.

Discussion

APK is triggered on the palms and soles after brief immersion in water, and is characterized by the rapid appearance of translucent papules or macerated plaques.[1] The pathogenesis is still unclear; in atopic dermatitis, impaired barrier function leading to increased skin water absorption, and hyperhidrosis, cystic fibrosis, or drug-induced increase in sweat salt concentration may play a role.[1–6] While there has been a strong association between APK and cystic fibrosis(CF), APK has also been shown to be drug-induced independent of CF history. In this case, the patient has no history of medication,we plan to further investigate whether it is related to cystic fibrosis, as APK may be a skin manifestation of CF.

Most treatment strategies aimed at preventing water exposure, reducing any related hyperkeratosis, and alleviating symptoms have proven ineffective and disappointing results in APK.[7] The experience of using Vaseline and/or the use of gloves is still mostly frustrating, as pointed out in our case. In her case, repeated treatment with urea cream did not yield

any benefits, and avoiding contact with water in daily work and life was impractical and could cause serious psychological and social problems.[7] We observed that the patient's skin symptoms were relieved in one week of topical pimecrolimus. Mild recurrence occurred after stopping treatment for two months, and the therapeutic effect was good after retreatment that the topical pimecrolimus was perhaps remittive therapy.

As a clinically approved calcineurin inhibitor for atopic dermatitis, the immune mechanism of pimecrolimus is often used for off label therapy, and its efficacy is comparable to that of topical corticosteroids. It is speculated that COX-2 inhibitors induce APK by inhibiting sodium reabsorption in epidermal cells and increasing sodium retention, analogous to renal effects. In a randomized study, calcineurin inhibitors inhibited COX-2 activity, thereby suppressing sodium transport in epidermal cells.[8] In the experimental model, calcineurin inhibitors selectively regulate the renal cyclooxygenase subtype COX-1 and more selectively regulate COX-2 dependent prostaglandin synthesis, thereby regulating the homeostasis of keratinocytes.[9–11] These mechanisms extending beyond immunomodulation—may elucidate topical pimecrolimus efficacy in APK pathogenesis.

We searched PubMed for eligible articles related to APK from 2015 to 2025 using the following keywords: "Aquagenic palmoplanta keratoderma"; "treatment" and "case report". After screening, 10 articles meet the eligibility criteria and have been included.[9,12–20] Table 1 shows the characteristics of patients and data on treatment and response. Overall, four patients experienced recurrence symptoms or treatment failure. These patients showed slight improvement in symptoms after local application of urea cream, aluminum chloride, Vaseline and intradermal injections botulinum

Table 1 Treatment in Reported APK Cases

Study Number	First Author (Year of Publication)	Sex/Age	Disease Duration (Years)	Body part	Concomitant Diseases	Treatment Protocols of APK	Efficacy and Recurrence	Adverse Events
1	Mahajan VKi(2021)[9]	F/23y	6-8 month	Both palms	NA	Oral antihistamines and topical cream containing urea, lactic acid, propylene glycol and liquid paraffin; Topical tacrolimus BID	After using topical tacrolimus BID,Completely clear after 3 weeks and small recurrence after stopped treatment	NA
2	Kutlubay Z (2015)[12]	M/18y	NA	Hands, toes, and the junction between the sole and the heel of both feet	NA	Topical application of urea and aluminum chloride, intradermal injections botulinum toxin	Treatment failure	NA
3	Montoya C (2019)[13]	M/16y	1 year	Both palms	NA	NA	NA	NA
4	Y. Tai(2021)[14]	F/34Y	1 month	Both palms	NA	Moisturizer and Vaseline	Significant improvement in 2 months,and small recurrence at the 2-month follow-up consultation	NA
5	Vazquez T(2020)[15]	M/46y	20 years	Palms and soles	HIV	The urea cream	Consistent improvement in 12 months	NA
6	Dixit Nt(2018)[16]	M/36y	3 years	Dorsal aspect of hands, volar aspect of wrists and circumferentially around the ankles	NA	On oral oxybutynin chloride 2.5mg BID	Significant improvement in 3 weeks	NA
7	Torres-Laboy PM(2021)[17]	M/16y	10 years	Bilateral palms and interdigital	Asthma	Vitamins (ADEK) and mineral supplements; elexacaftor-tezacaftor-ivacaftor(100 mg/50 mg/ 75 mg)	Consistent improvement	NA

(*Continued*)

Table 1 (Continued).

Study Number	First Author (Year of Publication)	Sex/Age	Disease Duration (Years)	Body part	Concomitant Diseases	Treatment Protocols of APK	Efficacy and Recurrence	Adverse Events
8	Lindsay J(2024)[18]	M/24y	10 month	Both palms	NA	Moisturizer; aluminum chloride hexahydrate	Consistent improvement	NA
9	Polascik BW(2025)[19]	M/24y	NA	Both palms	Food allergy, asthma, atopic dermatitis	Topical aluminum chloride; botulinum toxin	Completely clear after 2 months and recurrence after one month	NA
10	Sezer E(2015)[20]	M/31y	NA	Both palms	Hyperhidrosis	Endoscopic thoracic sympathectomy	Significantly improvement	NA

Abbreviations: F, female; M, male; Y, year; NA, not applicable; APK, Aquagenic palmoplanta keratoderma; BID, twice daily;

toxin, but relapsed after discontinuation of the medication. Five patients showed improvement in symptoms after receiving urea, oral oxybutynin, and endoscopic thoracic sympathetic nerve examination, but no long-term treatment observation results were mentioned.

Although patients usually experience symptoms such as burning, pain, or itching after immersion in water, this patient did not have similar symptoms. As in our case, physical findings typically resolve promptly after water removal. Lesions on the dorsal fingers are rarer than palmar involvement.[4,5] Many APK cases may be overlooked clinically without a water contact test.[1]

In conclusion, we report a case of hand involvement in a healthy female APK patient treated with pimecrolimus. It is worth noting that clinicians use water contact testing as a screening test for suspected APK patients; furthermore skin biopsy and cystic fibrosis transmembrane conductance receptor mutation testing are recommended.

Ethical Statement and Informed Consent

This patient in this manuscript has given written informed consent to publication of her case details. The study was approved by The Second Affiliated Hospital of Zhejiang Chinese Medical University ethical and review board.

Consent Statement

In this study, this patient provided written informed consent for the publication of this case information and accompanying images.

Disclosure

All authors declare no conflicts of interest in this work.

References

1. Park L, Khani C, Tamburro J. Aquagenic wrinkling of the palms and the potential role for genetic testing. *Pediatr Dermatol*. 2012;29(3):237–242. doi:10.1111/j.1525-1470.2011.01609.x
2. Gild R, Clay CD, Morey S. Aquagenic wrinkling of the palms in cystic fibrosis and the cystic fibrosis carrier state: a case–control study. *Br J Dermatol*. 2010;163(5):1082–1084. doi:10.1111/j.1365-2133.2010.09914.x
3. Seitz CS, Gaigl Z, Bröcker EB, Trautmann A. Painful wrinkles in the bathtub: association with hyperhidrosis and cystic fibrosis. *Dermatology*. 2008;216(3):222–226. doi:10.1159/000112929
4. Angra D, Angra K, Rodney IJ. Aquagenic palmoplantar keratoderma with dorsal hand involvement in an adolescent female. *JAAD Case Rep*. 2016;2(3):239–240. doi:10.1016/j.jdcr.2016.05.016
5. Yoon TY, Kim KR, Lee JY, Kim MK. Aquagenic syringeal acrokeratoderma: unusual prominence on the dorsal aspect of fingers? *Br J Dermatol*. 2008;159(2):486–488. doi:10.1111/j.1365-2133.2008.08633.x
6. Rongioletti F, Tomasini C, Crovato F, Marchesi L. Aquagenic (pseudo) keratoderma: a clinical series with new pathological insights. *Br J Dermatol*. 2012;167(3):575–582. doi:10.1111/j.1365-2133.2012.11003.x
7. Syed Z, Wanner M, Ibrahimi OA. Aquagenic wrinkling of the palms: a case report and literature review. *Dermatology Online J*. 2010;16:7. doi:10.5070/D35D57W5ZZ
8. Øzbay LA, Stubbe J, Jespersen B, Jensen BL. The effects of calcineurin inhibitors on prostanoid synthesis: a randomized cross-over study in healthy humans. *Transpl Int*. 2013;26(2):131–137. PMID: 23190385. doi:10.1111/tri.12004

9. Mahajan VK, Negi R, Thakur P, Kukreja A. Aquagenic wrinkling of the palms: response to topical tacrolimus. *Indian Dermatol Online J*. 2022;13(3):380–383. doi:10.4103/idoj.idoj_657_21
10. 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. doi:10.1001/archderm.142.12.1661
11. Robida AM, Xu K, Ellington ML, Murphy TJ. Cyclosporin A selectively inhibits mitogen-induced cyclooxygenase-2 gene transcription in vascular smooth muscle cells. *Mol Pharmacol*. 2000;58(4):701–708. doi:10.1124/mol.58.4.701
12. Kutlubay Z, Engin B, Baglam S, Khatib R, Demirkesen C, Aydemir EH. Case report: treatment failure in a case of aquagenic syringeal acrokeratoderma. *J Cosmet Laser Ther*. 2015;17(4):224–226. doi:10.3109/14764172.2014.1003240
13. Montoya C, Arias LM, Salazar M, Restrepo R. Water-induced dermatosis: aquagenic keratoderma. A case report. *Biomedica*. 2019;39(2):247–251. English, Spanish. doi:10.7705/biomedica.v39i2.4524
14. Tai Y, Fukumoto T, Oka M, Nishigori C. Frequent handwashing and disinfection: a potential new trigger for aquagenic wrinkling of the palms caused by COVID-19 outbreak. *J Eur Acad Dermatol Venereol*. 2021;35(1):e9–e10. doi:10.1111/jdv.16906
15. Vazquez T, Zarei M, Herskovitz I, Price A, Villada G, Keri J. Atypical familial aquagenic syringeal acrokeratoderma. *J Cutan Pathol*. 2020;47(11):991–996. doi:10.1111/cup.13704
16. Dixit N, Sardana K, Tandon S, Singh Y. Atypical aquagenic keratoderma treated with oxybutynin chloride. *An Bras Dermatol*. 2018;93(2):308–309. doi:10.1590/abd1806-4841.20187262
17. Torres-Laboy PM, Melendez-Montañez JM, De Jesús-Rojas W. Aquagenic wrinkling of the palm: a rare diagnostic clue of cystic fibrosis and the response to CFTR-modulating therapy. *Cureus*. 2021;13(4):e14425. doi:10.7759/cureus.14425
18. Lindsay J, Incristi AR, Arnett B, Costa M, Chong C. A case of aquagenic syringeal acrokeratoderma in a male patient undergoing treatment with an angiotensin-converting enzyme inhibitor. *Cureus*. 2024;16(11):e74157. doi:10.7759/cureus.74157
19. Polascik BW, Karklins SP, Johnson MC, Hammert WC, McMichael AJ. Acquired aquagenic syringeal keratoderma following COVID-19 infection. *Hand*. 2025;20(1):NP12–NP19. doi:10.1177/15589447241233371
20. Sezer E, Durmaz EÖ, Çetin E, Şahin S. Permanent treatment of aquagenic syringeal acrokeratoderma with endoscopic thoracic sympathectomy. *Indian J Dermatol Venereol Leprol*. 2015;81(6):648–650. doi:10.4103/0378-6323.168331