

Aquagenic Wrinkling of the Palms: Response to Topical Tacrolimus

Abstract

Aquagenic wrinkling of the palms (AWoP) is a rare dermatosis of significant psychosocial embarrassment and missed employment opportunities. It is characterized by development of translucent papules and wrinkling of the palms and rarely of soles shortly after immersion in water. Associated burning pain or pruritus of variable intensity is often distressing. The symptoms subside spontaneously 10–60 minutes after drying of hands only to recur following contact with water resulting in mild palmar hyperkeratosis over time. Although, cystic fibrosis remains the most described association, its cause is unknown in majority. The treatment is usually unsatisfactory and remains challenging. Response to antihistamines, iontophoresis, topical aluminum chloride 15-20% solution, and aluminum chloride hexahydrate 20% in anhydrous ethyl alcohol remains inconsistent. Keratolytic creams, petroleum jelly and/or use of gloves are not found useful at all. This paper describes a case of AWoP treated successfully with topical tacrolimus 0.1% ointment. We feel that topical tarolimus provides an effective and safe therapeutic option in AWoP.

Keywords: *Acquired aquagenic palmoplantar keratoderma, aquagenic syringal acrokeratoderma, calcineurin inhibitors, tacrolimus, transient reactive papulotranslucent acrokeratoderma*

Introduction

Aquagenic wrinkling of the palms (AWoP) is a rare disorder affecting females more often than males. Clinically, translucent papules, and wrinkling of the palms, uncommonly of soles, described as ‘hand in bucket’ sign appear shortly after immersion in water.^[1] The onset is hastened with more pronounced manifestations by hot water. There is usually associated burning pain or pruritus of varying intensity. The skin typically regains its texture and symptoms subside spontaneously 10–60 minutes after drying of hands. Slight palmar hyperkeratosis marked with dilated eccrine ducts ensues over a time. Histological features of compact orthohyperkeratosis and dilated eccrine ostia with or without acanthosis, and spongiosis around the eccrine ducts are not pathognomic and the diagnosis mostly remains clinical. Although an autosomal recessive mode of inheritance has been suggested, its etiopathogenesis remains obscure for paucity of cases. Its association with atopic dermatitis, Raynaud’s phenomenon, focal hyperhidrosis, and use of cyclooxygenase enzyme (COX)-2 inhibitors (aspirin,

rofecoxib) remains anecdotal.^[2–4] However, cystic fibrosis, an autosomal recessive disease caused by mutations in CFTR (cystic fibrosis transmembrane conductance regulator) gene, remains most described association. In nearly 80% cystic fibrosis cases, occurrence of this phenomenon after water immersion is considered a clinical sign of the disease; its elicitation is delayed in cystic fibrosis carriers.^[2,5] Its occurrence in patients with cystic fibrosis has been posited to increased water-binding capacity of keratins because of high salt concentrations, defective barrier function, weakness of the eccrine duct wall, eccrine duct ostia occlusion, and/or abnormal regulation of cell-membrane water channels, such as aquaporin 3, in the epidermis.^[6]

Although transient in nature, treatment is often sought for symptomatology which is often distressing, cause significant psychosocial embarrassment, and limit opportunities for gainful employments. However, its treatment is largely unsatisfactory as relapses are common after contact with water. Herein, we describe a case of this uncommon entity treated with previously unused topical tacrolimus.

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Case Report

A 23-year-old woman had a 6-8-month history of excessive wrinkling, swelling and burning pain of palms within few minutes of their coming in contact with water during hand washing or bathing for 5-20 minutes irrespective of the climatic conditions. The symptoms were more pronounced with warm water. She would become asymptomatic 30–40 minutes after drying her hands. She was born to healthy non-consanguineous parents after uneventful gestation and delivery. Her medical history was unremarkable and she was not taking any medications nor had palmoplantar hyperhidrosis. There was no personal or family history of atopy, cystic fibrosis or other significant illness and no other family member had similar problems. Repeated courses of oral antihistamines and topical cream containing 10% each of urea, lactic acid, propylene glycol and liquid paraffin did not benefit. She had been avoiding contact with water and socializing with friends and relatives. Mucocutaneous examination showed only slight desquamation over right thenar area. After immersing hands in water for 10 minutes, her palmar skin became pebbly, slightly edematous, and markedly wrinkled, associated with burning pain [Figure 1]. The skin became normal about half an hour after drying

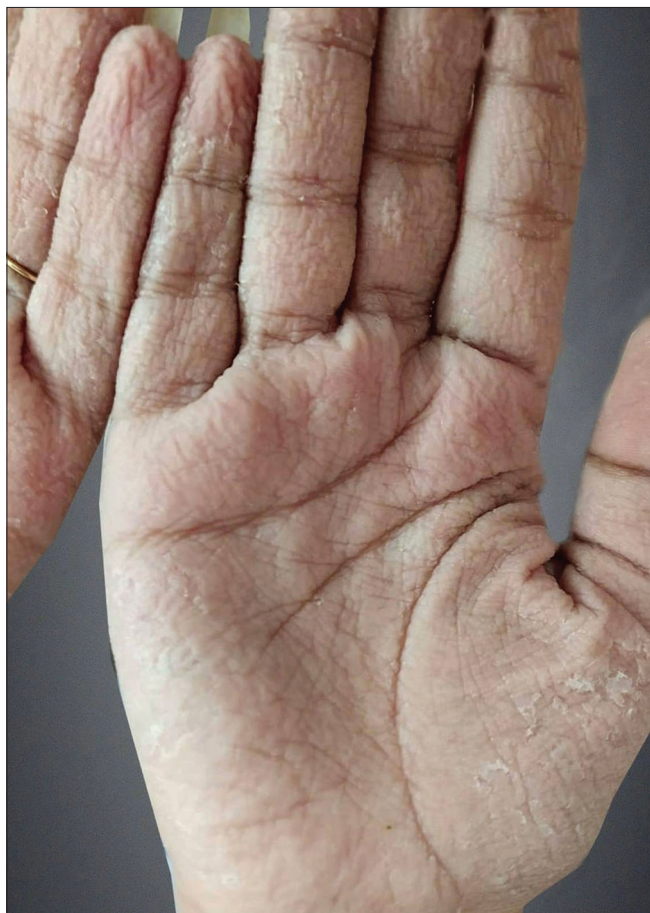


Figure 1: Palmar skin has become pebbly and slightly edematous with excessive wrinkling after immersion of hands in water for 10 minutes and shows slight desquamation over right thenar area

of hands. No other abnormality on mucocutaneous and systemic examination or lab investigations was detected. She did not consent for biopsy. With a clinical diagnosis of AWP, she was prescribed twice daily application of tacrolimus ointment (0.1%) with an advice to continue her daily routine including wet work and follow up every week. Her palm skin texture and symptoms improved substantially within first week [Figure 2]. The improvement continued and she regained normal skin texture in 3 weeks [Figure 3] when she stopped treatment on her own. Relapse of her problem 2 months later also responded to retreatment with tacrolimus given for 3 months and without recurrence for more than a year now [Figure 4].

Discussion

The most treatment strategies targeted to prevent water exposure, reduce any associated hyperkeratosis and alleviation of symptoms remain ineffective and frustrating in AWP. Antihistamines, iontophoresis, topical aluminum chloride 15-20% solution, aluminum chloride hexahydrate



Figure 2: Substantial improvement noted in skin texture and wrinkling of palmar skin 1 week after treatment with tacrolimus 0.1% ointment applied twice daily



Figure 3: Except for exaggerated palmar creases complete improvement of palmar skin after 3 weeks of treatment with tacrolimus 0.1% ointment applied twice daily

20% in anhydrous ethyl alcohol have been tried with variable results.^[7,8] Topical 20% aluminum chloride solution reportedly provided rapid improvement of symptoms but was highly irritant and caused intolerable dryness and pain.^[8] However, significant improvement was observed with topical aluminum chloride 15% in gel formulation which was less drying/irritating and better tolerated in a study.^[8] The experience with topical 12% ammonium lactate creams or petroleum jelly and/or the use of gloves mostly remained frustratingly poor as was also noted in our case. Repeated treatment with topical keratolytic cream containing urea and sodium lactate along with antihistamines in her case did not benefit and avoidance of contact with water in daily life was impracticable causing significant psychosocial problems. We observed complete resolution of skin changes and symptoms with topical tacrolimus 0.1% ointment in 3 weeks. Subsequent recurrence two months after stopping treatment also responded well without relapse signifies that the topical tacrolimus for about 3 weeks was perhaps remittive.

Tacrolimus, a calcineurin inhibitor approved by USFDA for treating atopic dermatitis, is used for several off label indications by virtue of its immunomodulatory properties

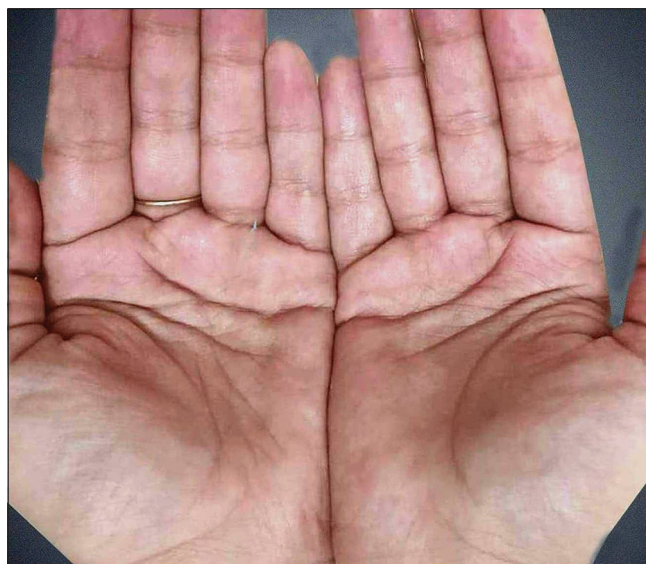


Figure 4: Palmar skin normalized completely after 3 months of treatment

and efficacy comparable to potent topical corticosteroids without their adverse effects. The exact mechanism of its therapeutic efficacy in AWoP, however, will be conjectural. It has been postulated that COX-2 inhibitor-induced AWoP involves an increase in the sodium retention via sodium re-absorption by COX-2 inhibition in epidermal cells akin to their effect on renal cells.^[3] The calcineurin inhibitors, cyclosporine and tacrolimus, have been shown to selectively modulate renal cyclooxygenase isoenzymes COX-1 and more selectively COX-2 and synthesis of COX-2 dependent prostanoids regulating cell homeostasis in keratinocytes in experimental animals and healthy human volunteers.^[9,10] In addition to its immunomodulatory effect, findings such as these may eventually explain efficacy of topical tacrolimus in AWoP. However, its efficacy and therapeutic potential needs validation by more comprehensive studies.

Interestingly, there seems no consensus in the published literature about nomenclature of this uncommon disorder. The palmar skin wrinkling occurs in early stage while development of mild keratoderma manifests subsequently because of frequent recurrences. The nomenclature; acquired aquagenic palmoplantar keratoderma, transient reactive papulotranslucent acrokeratoderma, aquagenic syringeal acrokeratoderma, or acquired aquagenic palmoplantar keratoderma, perhaps exemplify presentation of aquagenic wrinkling of the palms/soles representing various stages in the clinical course of a single disorder. We feel that nomenclature acquired aquagenic wrinkling of the palms/soles for cases not associated with cystic fibrosis is more apt to describe this unique entity for uniformity sake. Whereby, elicitation of this phenomenon in cystic fibrosis patients can be labeled as 'hand in bucket sign'. Nevertheless, our view points are open to debate as much needs to be learned especially at the molecular level to further our understanding of this rare entity.

Statement of ethics

Informed consent was obtained from patient for publication of material with the understanding that names and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975 as revised in 2013.

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The authors sincerely thank the patient for her consent.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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