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Case presentation

Aquagenic wrinkling of the palms: a case report and literature review

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Abstract

Aquagenic wrinkling of the palms (AWP) is an unusual and rare dermatological condition characterized by excessive palmar wrinkling, occurring within a few minutes of water exposure. Cystic fibrosis (CF) or CF carrier state associated forms, drug induced cases, and idiopathic forms have been described. We report the case of a 27-year-old woman with a 7-year history of transient excessive wrinkling of her palms after brief exposure to water. We present also a comprehensive review of the literature. We believe that AWP has been underdiagnosed thus far and we would like to encourage investigations such as sweat chloride test or genetic studies in these patients because of the association with CF or CF carrier state, particularly when AWP appears in younger ages.

Key words: Aquagenic wrinkling of the palms, cystic fibrosis, transient reactive and acquired papulotranslucent acrokeratoderma, aquagenic palmoplantar keratoderma, aquagenic syringal acrokeratoderma

Introduction

Aquagenic wrinkling of the palms (AWP) is an uncommon condition characterized by excessive wrinkling, palmar edema, and whitish papules possibly accompanied by pain, pruritus, or discomfort after brief exposure to water [1]. Etiology is unknown, but several studies indicate an association with cystic fibrosis (CF) or CF carrier state; some case reports also demonstrate various drugs as possible triggering factors [2-4]. In addition, idiopathic forms have been described [5]. We herein report a case of idiopathic AWP and perform a thorough review of the literature.

Case synopsis

A 27-year-old woman presented to our outpatient clinic with a 7-year history of transient excessive wrinkling of her palms after brief exposure to water during daily activities such as hand washing or showering. Other body sites were unaffected. The patient noted that tender swelling of the palms, followed after a few minutes by development of white papules, plaques, and wrinkling occurred shortly after water exposure. The lesions tended to resolve within 30-40 minutes after drying hands. Her medical history was unremarkable and she was taking no medications. Family history was negative for similar skin manifestations and the patient denied positive personal and family history of CF. Her palms were unremarkable on physical exam. After immersion of her hands in water for 3 minutes, numerous white translucent papules and plaques as well as marked wrinkling of both palms appeared. This “hand in bucket sign” (Figure 1) was consistent with the diagnosis of AWP.

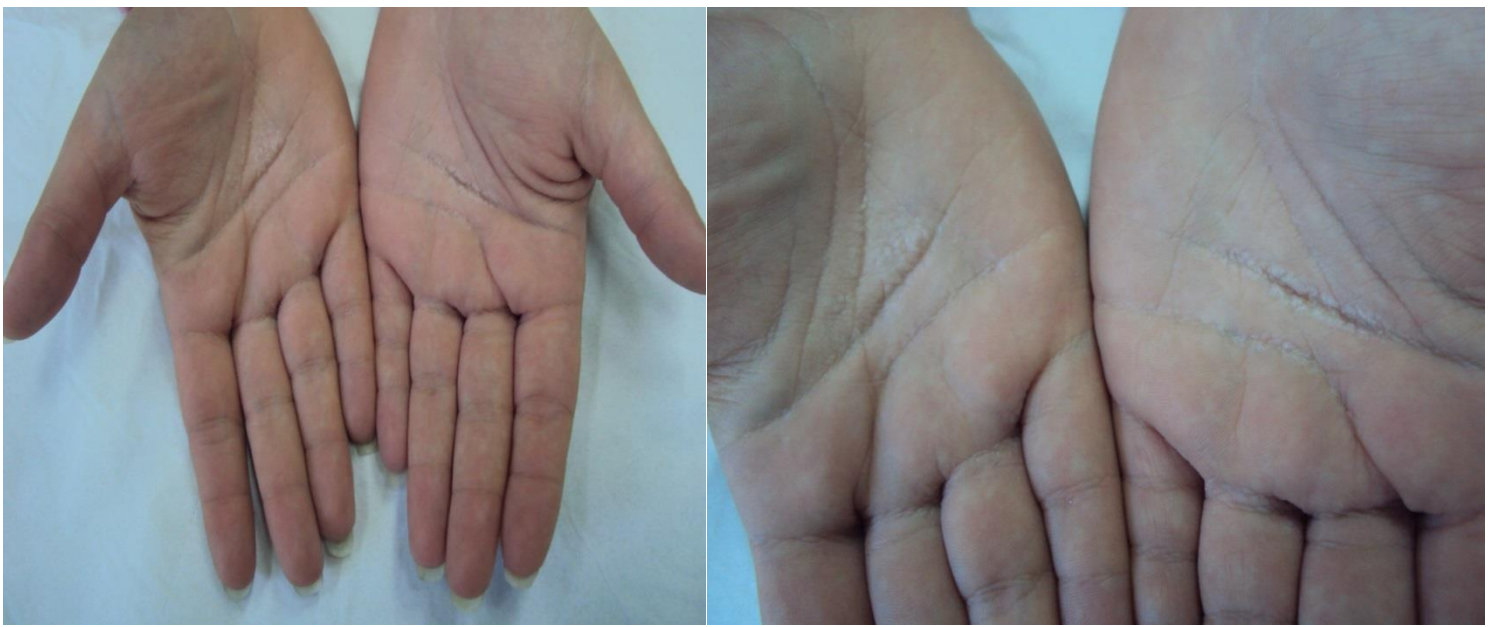


Figure 1. Appearance of translucent white papules and palmar wrinkling after hand immersion in water for 3 minutes.

Owing to the well-documented possible association of AWP with CF or a CF carrier state, a sweat chloride test and genetic studies for the most common cystic fibrosis transmembrane conductance regulator (CFTR) disease causing mutations were performed; both tests gave normal results. However, a limitation of the genetic test is its inability to detect rare CFTR mutations. Therefore, even though the patient did not present any CF related sign or symptoms and showed a CF negative family history, a CF carrier state could not be definitively excluded. The patient was put on daily treatment with topical mometasone furoate ointment 0.1% and urea 10% and was encouraged to avoid unnecessary exposure to water and humidity. Nevertheless, APW still persisted after 4 weeks. The patient refused other proposed treatments (botulinum toxin injection or iontophoresis) and the condition persisted with only little improvement regarding intensity and duration of the skin manifestations at 3 months follow-up.

Discussion

Wrinkling of the palms is a physiological response to prolonged water immersion, occurring an average of 11.5 minutes after exposure [6]. Conversely, AWP, also known as *transient reactive and acquired papulotranslucent acrokeratoderma*, *aquagenic palmoplantar keratoderma*, or *aquagenic syringeal acrokeratoderma*, is an unusual and rare dermatological condition characterized by an excessive and rapid palmar wrinkling, occurring within few minutes of water exposure. A macerated appearance of the palms appearing as white edematous translucent papules and plaques is the main feature of AWP; it may also be associated with discomfort and functional impairment [1]. Particularly, patients may complain of paraesthesia and burning or pruritic sensations with thickening and wrinkling of the palms shortly after immersion in water (2-5 minutes). The condition spontaneously resolves within several minutes to a few hours.

Idiopathic cases [5,7,8], drug induced forms [4,9], and cystic fibrosis (CF) [1,2,10-13] or CF carrier state-associated cases [3,13,14] have been described. Particularly, a detailed review of the literature showed a total of 227 cases of AWP described so far [1-5,7-53]. Most cases (154/227, 67.9%) were associated with CF, followed by idiopathic forms (57/227, 25.1%), CF carrier state related forms (10/227, 4.4%), and drug induced cases (6/227, 2.6%) (Table 1).

Table 1. AWP cases described in literature.

Patients	Mean age (years)	Sex (%)	AWP form (%)
227*	n/a*	n/a*	154 CF (67.9%) 10 CF carrier state (4.4%) 6 Drug-related (2.6%) 57 idiopathic (25.1%)
87**	22.4	36 M (41.4%) 51 F (58.6%)	20 CF 4 CF carrier state 6 drug-related 57 idiopathic

*Some studies are lacking of AWP patients' demographic data (age and sex).

**AWP patients with literature available demographic data (87/227).

AWP= aquagenic palmar wrinkling, CF= cystic fibrosis, n/a= not applicable.

However, it should be considered that genetic or sweat tests were not performed in all studies, particularly those describing idiopathic cases. Involved drugs were reported to be rofecoxib, aspirin, spironolactone, paracetamol, indometacin with sulfasalazine, ascorbic acid with clarithromycin, and the association of indomethacin, caffeine, and prochlorperazine dimaleate. Accurate data regarding age and sex were available only for 87/227 (38.3%) of the subjects, showing a higher prevalence of AWP in female patients (51/87, 58.6%) and mean age of onset of 22.4 years (range: 3-65).

The actual prevalence of AWP in the general population is unknown, but the condition is thought to be rare and its etiology and pathogenesis are still poor understood. Abnormality and weakness of sweat ducts as well as defective stratum corneum barrier function have been implied in AWP development [15,16]. It has been postulated that abnormal electrolyte fluxes resulting in sodium retention within epidermal keratinocytes and osmotically induced cell volume increase could be an explanation. Particularly, in CF and CF carrier related forms, it is believed that sweat hypertonicity induced by loss of function of CFTR through reduced electrolyte reabsorption in eccrine ducts, may lead to an increased rate of diffusion of water into palmar skin through eccrine glands ducts [18,54]. Moreover, CFTR impairment increases salt concentration in the epidermis and the water binding capacity of keratin [3]. However, dysregulation of aquaporin 3 and 5, proteins responsible for rapid water transport across cell membrane has also been proposed in AWP development, especially for CF-unrelated forms [55,56]. For example, nonsteroidal anti-inflammatory drugs use has been linked with AWP development [4,9,57] owing to the fact that these drugs are able to alter aquaporin expression and promote increased sodium reabsorption in epithelial cells through cyclooxygenase inhibition.

AWP diagnosis is easily made by the medical history. Clinical examination is generally inconclusive but the “hand in the bucket” test (water immersion) can be used to confirm AWP diagnosis. Rapid and excessive skin wrinkling is generally easily demonstrated [3]. Histopathological examination is rarely required; it generally discloses orthokeratotic hyperkeratosis, dilated eccrine ducts, and, rarely, hypergranulosis [18,49]. Because of the well-known possible association to CF or CF carrier state (44-88% and up to 25%, respectively) [12,21], patients with AWP should be promptly screened through sweat chloride and genetic testing for CFTR mutations [18]. Indeed, AWP diagnosis may be one of the main warning signs suggesting the need for further evaluations and referral to detect patients with mild forms of CF who might develop late-onset or slowly progressing disease [17].

Percentages of success in AWP management are very variable [23,24] and different treatments have been proposed: botulinum toxin injection [22,23], topical aluminum chloride [2,23,24], topical urea and salicylic acid combination [25], iontophoresis [15], 12% ammonium lactate [15], and topical corticosteroid [15,23].

This case has been here reported because of possible underreporting of AWP cases thus far. Greater awareness of AWP is needed since, given its frequent association with CF and CF carrier state, AWP diagnosis should guide dermatologists to conduct detailed medical history and physical examination in search of high-risk individuals, which require prompt further work up.

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