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CASE REPORT

Aquagenic Keratodermia: 3 New Cases and a Review of the Literature

M. A. Pastor,[a] L. González,[b] L. Kilmurray,[b] P. Bautista,[a] A. López,[b] and A. M. Puig[b]

[a]Servicio de Dermatología and [b]Servicio de Anatomía Patológica, Hospital Santa Bárbara, Puertollano, Ciudad Real, Spain

Abstract. Aquagenic keratoderma is a rare type of transient acquired keratoderma that is triggered or exacerbated by immersion of the palms or soles in water. It is characterized by whitish or translucent papules with central punctate depressions that coalesce in macerated edematous plaques. It appears within a few minutes of exposure to water and subsides soon after drying.

We describe 3 new cases of aquagenic keratoderma in a 28-year-old man with a history of Behçet disease, an 18-year-old woman, and a 20-year-old man. We discuss the clinical and histopathologic features, treatment options, and course of the lesions in the cases described in the literature.

Key words: aquagenic keratoderma, keratoderma.

QUERATODERMIA ACUAGÉNICA: TRES NUEVOS CASOS Y REVISIÓN DE LA LITERATURA

Resumen. La queratodermia acuagénica es una rara variante de queratodermia adquirida y transitoria, que se desencadena o intensifica con la inmersión en el agua de las palmas o las plantas. Se caracteriza por pápulas blanquecinas o translúcidas, con una depresión puntiforme central, confluentes en placas edematosas, de aspecto macerado. Aparece a los pocos minutos de la exposición al agua y remite al poco tiempo del secado.

Se presentan tres nuevos casos de queratodermia acuagénica que afectan a un varón de 28 años con antecedentes de enfermedad de Behçet, una mujer de 18 años y un varón de 20 años. Se discuten la clínica, la histopatología, el tratamiento y la evolución de las lesiones de los casos descritos en la literatura.

Palabras clave: queratodermia acuagénica, queratodermia.

Introduction

English and McCullough[1] described the first cases of aquagenic keratoderma in 1997. Since then, 25 cases have been reported in 18 publications[1-18] (Table 1).

We report 3 new cases and review the literature in order to describe the clinical characteristics, histopathologic findings, etiology, treatment, and prognosis of this disease.

Correspondence:
María Antonia Pastor Nieto
Servicio de Dermatología
Hospital Santa Bárbara
Ctra. Malagón s/n
13500 Puertollano, Ciudad Real, Spain
tonales@terra.es

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Case Descriptions

Case 1

A 28-year-old man with Behçet disease who was undergoing treatment with prednisone, azathioprine, mycophenolate mofetil, colchicine, and acenocoumarin visited our clinic due to hyperkeratotic macerated plaques on the palms that had appeared a year earlier. The plaques appeared a few minutes after submerging the hands in water and subsided 1 hour after drying. The surface of the plaques revealed numerous punctuate depressions (Figure 1). Higher water temperatures and longer exposure times increased the severity of the lesions. Only mild to moderate palmar hyperhidrosis was observable during periods when the disease was inactive. The patient stated that he had no history of atopy or disorders of the nails or hair. A skin biopsy was performed 5 minutes after immersing the hands in water. The histopathologic study revealed hyperplasia of the eccrine

Table 1. Review of Published Cases of Aquagenic Acrokeratoderma

Author/Year/Name Suggested by Author	*Sex/Age, y/ Time Since Onset*	*FH*	*Distribution*	*Symptoms*	*Hyperhidrosis*
English and McCollough1/1996/transient reactive papulotranslucent acrokeratoderma	F/20/3-4 y	Yes/AR	Palms, fingers (sides)	Tightening sensation	Yes
	F/18/6 mo	Yes/AR	Palms	NS	NS
Lowes et al[2]/2000/transient reactive papulotranslucent acrokeratoderma	F/20/5 y	No	Edge of the hands	No	Yes
Yan et al[3]/2001/aquagenic palmoplantar keratoderma	F/10/1 y	No	Palms	Burning sensation, pain	Yes
	F/22/1 y	No	Palms, fingers (sides), soles	Pain, tingling sensation	No
	F/14/2 months	No	Palms, fingers (palmar surface)	Pain, burning sensation	No
Mac Cormack et al[4]/2001/aquagenic syringeal acrokeratoderma	F/15/7 mo	No	Palms	Itching, pain	No
	F/19/6 mo	No	Palms	Tightness, burning sensation	No
Itin and Lautenschlager[5]/2002/aquagenic syringeal acrokeratoderma (transient reactive papulotranslucent acrokeratoderma)	F/25/3 mo	No	Palms	Burning sensation	Yes
	F/33/9 mo	No	Palms	Pain	Yes
Carder and Weston[6]/2002/instant aquagenic wrinkling of the palms	F/18/ 3 wk	No	Palms	Mild pain	No
Betlloch et al[7]/2003/aquagenic keratoderma	F/14/1 y	No	Palms	Itching, pain	Yes
Schmults et al[8]/2003/aquagenic syringeal acrokeratoderma	F/32/3 mo	No	Palms	Tightness, tingling sensation, itching, mild pain	No
Davis and Woody[9]/2004/idiopathic aquagenic wrinkling of the palms	F/14/y	No	Palms, fingers (sides), creases between the fingers	No	No
Yalcin et al[10]/2005/acquired aquagenic papulotranslucent acrokeratoderma	M/42/1 y	No	Palms, edge of hands	No	No
Saray and Seçkin11/2005/familial aquagenic acrokeratoderma	M/45/1 y	Yes/AD	Palms, fingers (palmar surface), edge of hands	No	No
	M/6/3 mo	Yes/AD	Palms, fingertips	No	No
Diba et al[12]/2005/aquagenic palmoplantar keratoderma	F/35/2 y	No	Palms, soles	Mild pain	Yes

Disease History	*Histopathology findings*	*Treatment*	*Course*
No	Dilation of excretory orifices, mild hyperkeratosis	No	Periods of remission and exacerbation
NS	No biopsied	NS	NS
Cystic fibrosis, urticaria	Hyperkeratosis, dilation of excretory orifices	Iontophoresis	NS
Asthma	Not biopsied	Aluminum chloride hexahydrate, 20%	Improvement in 2 weeks, recurrence on suspension of treatment
Allergic rhinitis	Not biopsied	Aluminum chloride hexahydrate, 20%	√Treatment abandoned Improvement
Osteomyelitis of the hands	Not biopsied	Aluminum chloride hexahydrate, 20%	Improvement in 2 weeks
No	Dilation of excretory orifices, orthokeratotic hyperkeratosis, acanthosis, focal spongiosis around the eccrine ducts	Ammonium lactate cream, 12%	Treatment ineffective Gradual spontaneous improvement in 2 y
No	Orthokeratotic hyperkeratosis, dilation of eccrine ducts	Silicone cream	Spontaneous remission in 1-2 y
No	Not biopsied	Antihistamines	Spontaneous remission after 2 y
Malignant melanoma	Not biopsied	NS	Fluctuating intensity
MCTD, Raynaud, rofecoxib therapy	Not biopsied	Suspension of rofecoxib	Improvement after 3 weeks
No	Normal epidermis	Aluminum chloride hexahydrate	Improvement after 2 y
No	Orthokeratotic hyperkeratosis, dilated acrosyringium	Ammonium chloride solution	NS
Mild acne	Not biopsied	NS	NS
No	Orthokeratotic hyperkeratosis, acanthosis, prominent eccrine ducts with peripheral spongiosis	Salicylic acid, 5%	Good response Recurrences
No	Hyperkeratosis, hypergranulosis	Salicylic petrolatum, 20% and urea cream, 10%	Resolution in 1 mo
No	Not biopsied	Salicylic petrolatum, 20%	Resolution in 3 wk
No	Normal skin biopsy	Aluminum chloride hexahydrate Botulinum toxin	Aluminum chloride ineffective Improvement with botulinum toxin Recurrence after 5 mo

(Continues)

Table 1. Review of Published Cases of Aquagenic Acrokeratoderma

Author/Year/Name Suggested by Author	*Sex/Age, y/ Time Since Onset*	*FH*	*Distribution*	*Symptoms*	*Hyperhidrosis*
Vildósola and Ugalde13/2005/aquagenic keratoderma	F/31/NS	No	Palms, fingers (sides)	Pruritus	Yes
Pardo et al14/2005/aquagenic keratoderma	M/21/2 y	No	Backs of hands and fingers, creases between fingers, wrist (palmar surface), edge of hands	No	No
Neri et al15/2006/transient aquagenic palmar hyperwrinkling	M/8/1 y	No	Palms	Mild pain	Yes
Baldwin et al16/2006/aquagenic syringeal acrokeratoderma	M/24/3 y	No	Palms, fingers (palmar surface)	Pain	Yes
Conde-Salazar et al17/2006/aquagenic syringeal acrokeratoderma	F/20/8 mo	No	Palms	No	No
	F/21/5 y	No	Palms	No	No
Sais et al18/2007/aquagenic syringeal acrokeratoderma	F/28/years	No	Palms	Stinging sensation, tightness	No
Cases reported in this study/2007/ aquagenic keratoderma	M/28/1 y	No	Palms, fingers (palmar surface)	No	Yes
	F/18/1 mo	No	Palms, creases between fingers	No	Yes
	M/20/6 mo	No	Palms, creases between fingers	No	No

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; F, female; FH, family history; HCV, hepatitis C virus; M, male; MCTD, mixed connective tissue disease; NS, not specified (by authors).

sweat glands, with slight dilation, stratification, and serrated morphology of the lumen (Figure 2).

Case 2

An 18-year-old woman with a history of asthma and nail psoriasis visited our clinic due to mild hyperhidrosis and asymptomatic lesions on the hands that had appeared a month earlier. The lesions consisted of whitish plaques on the palms of the hand and the creases between the fingers. The plaques were exacerbated by sweating and after a few minutes of exposure to water, whereon they acquired a macerated appearance with attenuation of the palmar creases. The surface of the plaques revealed numerous millimeter-sized pores (Figure 3). The lesions subsided shortly after drying the hands, leaving minimal hyperkeratosis in the center of the palms. The soles of the feet were unaffected.

Case 3

A 20-year-old man presented with asymptomatic whitish velvety plaques on the palms of the hands and

Disease History	*Histopathology findings*	*Treatment*	*Course*
HCV, hemolytic anemia, rheumatoid arthritis, celecoxib therapy	Orthokeratotic hyperkeratosis, dilation of eccrine ducts, focal serosal metaplasia of eccrine coils	Zinc sulphate baths, 1/1000 and topical erythromycin solution	Considerable improvement without suspending celecoxib
No	Not biopsied	Towels impregnated with aluminum chloride hexahydrate and silicone-based protective cream for several months	Improvement
Hemangioma	Mild orthokeratotic hyperkeratosis, dilation of eccrine ducts	Aluminum hydroxide	Rapid improvement
No	Hyperplasia of eccrine glandular epithelium, focal stratification	Aluminum chloride	Treatment abandoned due to lack of effectiveness and intolerance
Allergic rhinoconjunctivitis in response to graminaceous plants	Orthokeratotic hyperkeratosis, acanthosis, mild dilation of acrosyringium, perivascular lymphocyte infiltration in the papillary dermis	Aluminum chlorohydrate, 18% (2-3 applications/wk)	Improvement
No	Mild dilation of acrosyringium	Aluminum chlorohydrate, 18% (2-3 applications/wk)	Improvement
No	Mild hyperkeratosis Mild dilation of acrosyringium	Aluminum chlorohydrate, 18%	No improvement
Behçet disease	Hyperplasia of eccrine sweat glands. Mild dilation, stratification and serrated lumen	Aluminum chloride hexahydrate, 20% and urea cream, 20%	Improvement
Nail psoriasis, asthma	Not biopsied	Aluminum chloride hexahydrate, 20%, and urea cream, 20%	Improvement
None	Not biopsied	Aluminum chloride hexahydrate, 20%, and urea cream, 20%	Improvement

the creases between the fingers. The plaques had appeared 6 months earlier; they were triggered a few minutes after immersing the hands in water and disappeared 15 minutes after drying (Figure 4). The patient had no history of atopy or disorders of the nails or hair. He used a pot scrubber to clean his hands. No lesions appeared on the soles at any time during the course of the disease.

In all 3 cases, treatment was initiated with a solution of 20% aluminum chloride hexahydrate in alcohol and a 20% urea cream; the lesions remitted completely within a few weeks.

Discussion

Various names have been suggested for the entity described here, including papulotranslucent acrokeratoderma,[1,2] aquagenic palmoplantar keratoderma,[3,12] aquagenic syringeal acrokeratoderma,[4,5,8,16-18] instant aquagenic wrinkling of the palms,[6] acquired aquagenic papulotranslucent acrokeratoderma,[10] aquagenic acrokeratoderma,[11,13,14] and transient aquagenic palmar hyperwrinkling.[15]

While most cases are acquired, 2 articles report familial aggregation. English and McCullough[1] described 2 sisters, aged 20 and 18 years, with disease affecting the palms, thus

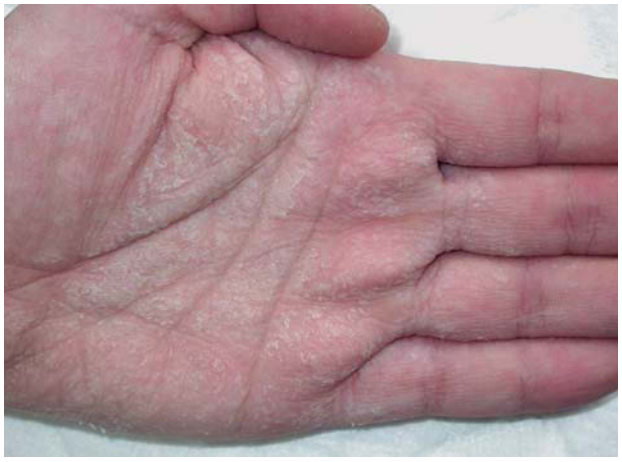

Figure 1. Case 1 Whitish, velvety plaques with birdshot appearance on the palm and fingers. The surface of the plaques has numerous punctate depressions.

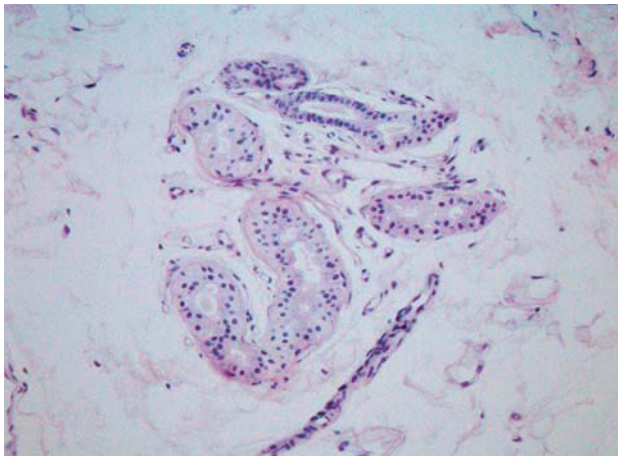

Figure 2. Case 1 Histopathologic study showing hyperplasia of the eccrine sweat glands, with mild dilation and serrated morphology of the lumen. Hematoxylin–eosin, ×20.

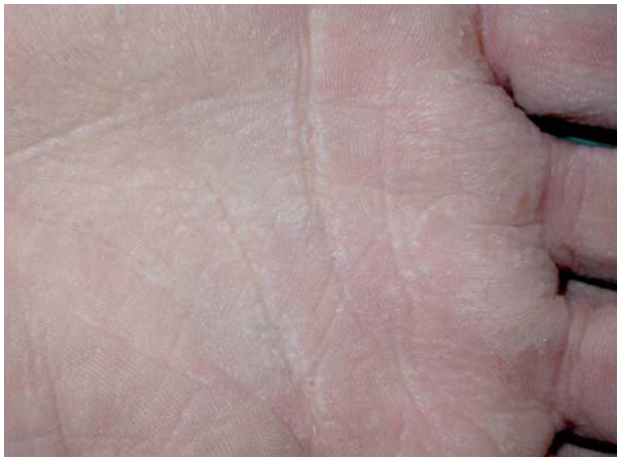

Figure 3. Case 2 Whitish hyperkeratosis on the palm with accentuation of the skin folds. The surface shows millimeter-sized pores.

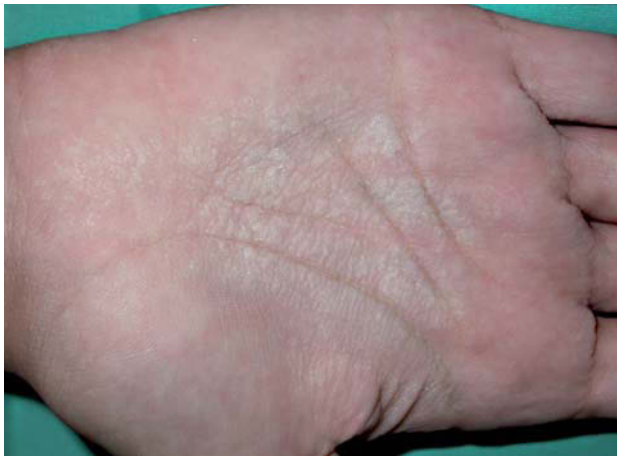

Figure 4. Case 3 Hyperkeratotic plaque with macerated appearance, punctate depressions, and accentuated folds in the center of the palm.

suggesting a pattern of autosomal recessive inheritance. Saray and Seckin[11] reported the cases of a 44-year-old man and his 6-year-old son, suggesting a possible autosomal dominant pattern of inheritance.

Aquagenic keratoderma more commonly affects women. Reported cases include 20 women (71.4%) and 8 men (28.5%). The mean age of patients is 22.1 years (range, 6-45 years). The mean time between appearance of the lesions and diagnosis is 31 months (range, 3 weeks to 5 years) for the 25 cases where the time is specified. The lesions appear a few minutes after exposure to water, though, in some cases, edema has been reported to occur immediately or after only a few seconds.[2,7,9] The "hands in the bucket" sign, which refers to patients who cause the lesions to occur by placing their hands in a bucket of water immediately before entering the doctor's surgery, is considered to be pathognomonic.[3] The lesions last from 10 minutes to 1 hour or, more rarely, 2 hours.[6] Symptoms occur in 57.1% of patients in the form of tightness of the skin,[1,18] burning sensation, pain,[5] tingling, or itching.[8] Some cases present a fluctuating course with exacerbations in autumn and winter and remissions in spring and summer.[5]

The lesions are distributed as follows: *a)* palms in 26 cases (92.8%), *b)* edges of the hands in 4 cases (14.2%), *c)* sides of the fingers in 4 cases (14.2%), *d)* creases between the fingers in 4 cases (14.2%), *e)* palmar surface of the fingers in 4 cases (14.2%), *f)* soles in 2 cases (7.1%), *g)* dorsal surface of the hands in 1 case (3.5%), *h)* fingertips in 1 case (3.5%), *i)* backs of the hands in 1 case (3.5%), and *j)* palmar surface of the wrist in 1 case (3.5%).

Associated hyperhidrosis was present in 42.8% of cases and occasionally led to the appearance of the lesions.[14,16]

Table 2. Differential Diagnosis Between Aquagenic Keratoderma and Hereditary Papulotranslucent Acrokeratoderma

	Aquagenic Keratoderma	*Hereditary Papulotranslucent Acrokeratoderma*
Age at onset	Young people	Adolescents
Distribution	Palms and soles	Edges of hands and feet
Trauma implicated	No	Yes
History of atopy	No	Yes
Abnormal hair	No	Sparse, fine hair
Inheritance	Sporadic in most cases	Autosomal dominant inheritance
Course	Transient	Permanent

In some cases, abnormalities are described in periods when the condition is inactive. These include mild hyperkeratosis in the center of the palms[1,17] and multiple translucent, nondesquamative papules in the center of the palms and the edges of the hands.[4,10]

Most of the cases are idiopathic, though 2 cases linked to cyclooxygenase-2 (COX-2) inhibitors have been reported: a patient with mixed connective tissue disease and Raynaud phenomenon who was undergoing treatment with rofecoxib[6] and a patient with rheumatoid arthritis who was being treated with celecoxib.[13] The medical histories of the other published cases include other diseases, such as asthma,[3] allergic rhinitis,[3,17] urticaria,[2] cystic fibrosis,[2] hepatitis C,[13] osteomyelitis,[3] melanoma,[5] acne,[9] hemangioma,[15] Behçet disease, and nail psoriasis. The relationship of these diseases with aquagenic keratoderma is unknown.

In the 16 cases (57.1%) in which a skin biopsy was performed, the histologic findings were the following: *a) dilation of the* acrosyringium in 11 cases (68.7%), *b)* orthokeratotic hyperkeratosis in 11 cases (68.7%), *c)* focal spongiosis around the eccrine ducts in 3 cases (18.7%), *d)* acanthosis in 2 cases (12.5%), *e)* glandular hyperplasia, focal stratification, and serrated lumen (glandular cells of increased size and abundant granular cytoplasm) in 2 cases (12.5%), *f)* absence of pathologic findings in 2 cases (12.5%), *g)* focal serosal metaplasia of the eccrine coils in 1 case (6.2%); *h)* hypergranulosis in 1 case (6.2%), and *i)* discrete perivascular lymphocytic infiltrate in the papillary dermis in 1 case (6.2%).

The pathogenesis of the disease is unknown. Some authors consider it to be a variant of hereditary papulotranslucent acrokeratoderma[1] (Table 2). Various hypotheses have been suggested to explain the etiology and pathogenesis of the disease, including an increase in water absorption capacity due to a defect in the barrier function of the stratum corneum,[5] a transitory structural or functional abnormality of the stratum corneum (proteins, lipids, moisturizing substances),[7] a defect in the sweat duct due to friction or occlusion,[4] or an increase in the ability of the keratin to bind water due to the increased salt content in the skin associated with cystic fibrosis or COX-2 inhibitors.[6]

There is a tendency for the disease to remit in most cases. Aluminum salts generally produce rapid improvement. In 2 cases, 20% salicylate in petrolatum caused the lesions to remit in 3-4 weeks.[11]

Ammonium lactate, 12%, was used with poor results in 1 case, which subsequently improved spontaneously.[4] Protective creams containing silicone have been suggested as adjuvant treatment to aluminum salts.[14] In the rofecoxib-induced case, the lesions improved 3 weeks after suspending treatment.[6] In the celecoxib-related case, however, the condition improved on treatment with zinc sulphate (1/1000) and erythromycin, without having to suspend treatment with celecoxib.[13] One article refers to the use of iontophoresis in a patient with cystic fibrosis but does not describe the course of the condition in this case.[2] Botulinum toxin was used successfully in a case that was refractory to aluminum chloride.[12]

Conflicts of Interest

The authors declare no conflict of interest.

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