Pachyonychia Congenita Project

15 March 2005

Use of Articles in the Pachyonychia Congenita Bibliography

The articles in the PC Bibliography may be restricted by copyright laws. These have been made available to you by PC Project for the exclusive use in teaching, scholarship or research regarding Pachyonychia Congenita.

To the best of our understanding, in supplying this material to you we have followed the guidelines of Sec 107 regarding fair use of copyright materials. That section reads as follows:

> Sec. 107. - Limitations on exclusive rights: Fair use
> Notwithstanding the provisions of sections 106 and 106A, the fair use of a copyrighted work, including such use by reproduction in copies or phonorecords or by any other means specified by that section, for purposes such as criticism, comment, news reporting, **teaching (including multiple copies for classroom use), scholarship, or research**, is not an infringement of copyright. In determining whether the use made of a work in any particular case is a fair use the factors to be considered shall include - (1) the purpose and character of the use, including whether such use is of a commercial nature or is for nonprofit educational purposes; (2) the nature of the copyrighted work; (3) the amount and substantiality of the portion used in relation to the copyrighted work as a whole; and (4) the effect of the use upon the potential market for or value of the copyrighted work. The fact that a work is unpublished shall not itself bar a finding of fair use if such finding is made upon consideration of all the above factors.

We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.

2386 East Heritage Way, Suite B, Salt Lake City, Utah 84109 USA
Phone +1-877-628-7300 • Email—Info@pachyonychia.org
www.pachyonychia.org

Case report

Acro-osteolysis: A complication of Jadassohn–Lewandowsky syndrome

S. B. Murugesh, MD, Suga Reddy, DVD, DNB, S. Ragunatha, MBBS, M. M. Mohammed Faizal, MBBS, and P. Shashikala, MD

From the Department of Dermatology and Venereology, and Department of Pathology, J.J.M. Medical College, Davangere, Karnataka, India

Correspondence
S. B. Murugesh
Professor and Head
Department of Dermatology and Venereology
J.J.M. Medical College
Davangere –577 004
Karnataka
India
E-mail: sbmurugesh@hotmail.com

Introduction

Pachyonychia congenita (PC) is a group of inherited ectodermal dysplasias whose most prominent feature is hypertrophic nail dystrophy.[1] Muller, in 1904, and Wilson, in 1905, described the first cases of PC. One year later the same condition was described in two siblings by Jadassohn and Lewandowsky.[2] It usually develops in early infancy and the onset of nail changes beyond the first few years after infancy is rare. There are two major types of PC: Jadassohn–Lewandowsky syndrome (PC1) and Jackson–Lawler syndrome (PC2). Acro-osteolysis is a crippling deformity usually seen in a wide variety of neurological and vascular disorders.[3] Very rarely the association of PC with acro-osteolysis has been reported in the literature.[4,5] The significance of this association is not known.[5] A case of acro-osteolysis as a complication of PC is presented with a review of relevant literature.

Case Report

A 45-year-old male patient born of a nonconsanguinous marriage presented with marked subungual hyperkeratosis, elevation of all finger and toe nails, and focal palmoplantar hyperkeratosis, mainly involving pressure-bearing areas (Fig. 1). Soles were severely affected, causing pain on walking. There was associated hyperhidrosis. There were no blisters on the palms and soles. Hyperkeratotic papules and plaques were also present over the extensor surface of the left elbow and dorsa of both hands (Fig. 2). White plaques were observed on buccal mucosa, labial mucosa, tongue and palate along with angular cheilitis (Fig. 3). There was no history of natal teeth. All these lesions had started in early childhood. The patient gave a history of similar skin lesions in his father, brother and son. Hoarseness, multiple epidermal cysts, steatocystomas, corneal dystrophy and hair abnormalities were absent. Systemic examination revealed no abnormality except secondary depression with a normal IQ.

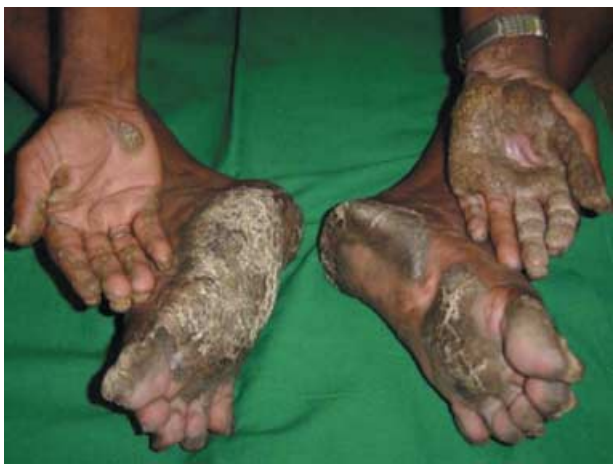

Figure 1 Finger and toe nails showing subungual hyperkeratosis and elevation of the nail plate. Palms and soles showing keratoderma mainly covering pressure-bearing areas

International Journal of Dermatology 2007, **46**, 202–205

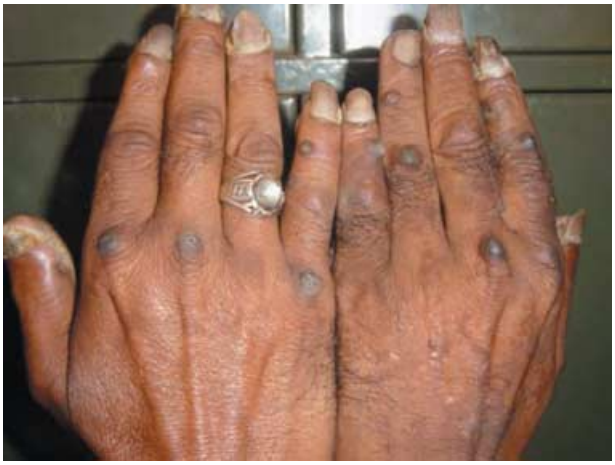

Figure 2 Hyperkeratotic papules over dorsa of the fingers and hands

Figure 3 Angular cheilitis and leukokeratosis of the tongue

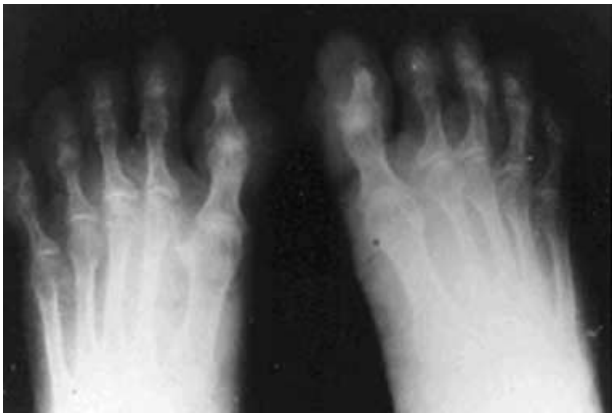

Figure 4 Acro-osteolytic bone changes of the feet and soft tissue shadow resulting from palmoplantar keratoderma

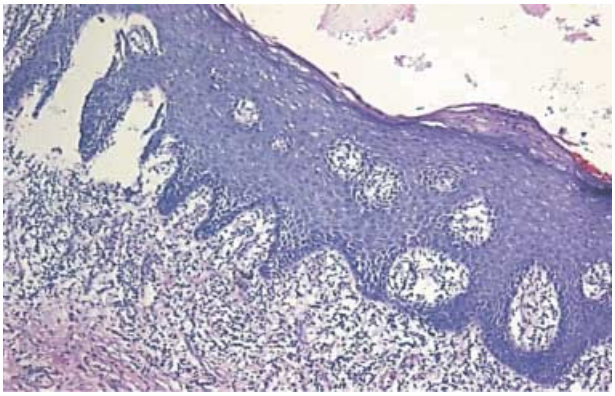

Figure 5 Histopathology of the oral mucosa showing hyperkeratosis, parakeratosis, acanthosis and chronic inflammatory infiltration (H&E ×10)

Investigations including complete hemogram, urine analysis, liver function tests, renal function tests and fasting blood sugar were within normal limits. Potassium hydroxide examination of nail clippings and fungal culture of nails revealed no fungal growth. X-ray of hands and feet showed acro-osteolysis, which was more severe in the feet (Fig. 4). Histopathological examination of oral lesions showed hyperkeratosis, parakeratosis, acanthosis and chronic inflammatory infiltrate suggestive of benign leucoplakia (Fig. 5).

Discussion

Pachyonychia congenita is a rare autosomal dominant form of ectodermal dysplasia associated with mutations in keratin genes 16, 17 and 6 (6a, 6b), which are expressed abundantly in the nail bed. The keratin 17 gene is also expressed in the nail matrix and in the hair follicle matrix of eyebrows and other facial hair.[6] The nails show wedge-shaped subungual hyperkeratosis, leading to elevation of the nail plate, which is darkened, thickened and friable, assuming an omega shape. In infancy, erythema of the nail bed may be the only visible sign. The keratoderma is focal, nonepidermolytic, typically found on friction, pressure and weight-bearing areas of palms and soles with associated hyperhidrosis.[7] The nail changes are evident at birth but commonly develop within the first few months of life, whereas the onset of keratoderma may be delayed upto 7 years of age.[8]

Numerous subdivisions and classifications of PC have been proposed by Kumer and Loos, Schonfeld, Sivasundram *et al.* and Feinstein *et al.*,[2] but two major clinical variants are generally recognized. The Jadassohn–Lewandowsky syndrome is associated with mutations in keratin 16 (K16) or keratin 6a genes (K6a). It is characterized by severe focal palmoplantar keratoderma (PPK), mainly involving plantar surface, the palms being involved in manual workers. Blistering may occur on

walking.[8] Jackson–Lawler syndrome is associated with mutations in keratin 17 (K 17) or keratin 6b genes (K 6b). It is characterized by mild PPK and multiple steatocystomas over the trunk, which appears at puberty, distinguishing it from PC1. Pili torti and natal teeth may also be observed in PC2.[1] Multiple epidermal cysts, such as eruptive vellus hair cysts, milia, scrotal and vulvar cysts, and hidradenitis suppurativa may also be present.[9] Features such as angular cheilosis, follicular keratoses, hoarseness and oral leukokeratoses may occur in both types.[1]

Apart from PC1 and PC2, other types of PC exist, but are not well characterized. Type III PC has been described as a combination of features of PC1 and PC2 with angular cheilitis, corneal dyskeratosis and cataracts. Type IV PC includes features through type I to type III PC with laryngeal lesions, hoarseness, mental retardation, hair abnormalities and alopecia.[2] Other variants such as PC with only nail changes without other abnormalities,[10] and PC with onset of the disease in teenage years (PC tarda)[5] have been described.

Our patient presented with characteristic features of Jadassohn–Lewandowsky syndrome. Absence of hoarseness or hair abnormalities in our patient can be explained by the incomplete penetrance of these phenotypes.[1] Histopathology of oral lesions in the present case was suggestive of benign leukoplakia. In PC, oral lesions do not undergo malignant change but squamous cell carcinoma has been reported in chronic plantar ulceration of PC. Laryngeal leukokeratosis, leading to severe respiratory distress has also been reported.[6]

Acro-osteolysis refers to the occurrence of destructive changes in the distal phalangeal bone.[3] It can be idiopathic or congenital or secondary to a wide variety of disorders. These include all types of arthritis, hyperparathyroidism, collagen vascular disorders, vascular and traumatic phenomena, neuropathic, neuroplastic and infectious factors.[3,11] The dermatological causes of acro-osteolysis are epidermolysis bullosa, ichthyosiform erythroderma, pachydermoperiostosis, porphyria, progeria, sezary syndrome, leprosy, tabes dorsalis and occupational exposure to vinyl chloride.[3] It is also observed in psoriatic arthritis, and following repeated trauma in psoriasis.[12] Acro-osteolysis in association with marked diffuse keratoderma, painless ulcers of the feet, and polyneuropathies of the lower legs is observed in Bureau Barriere syndrome.[13] A peculiar acro-osteolysis with a claw-like volar surface of distal phalanges is observed in a syndrome of keratosis palmoplantaris congenita, pes planus, onychogryphosis, periodontosis and arachnodactyly.[14]

To date there are only two reports in the literature describing the association of PC with acro-osteolysis.[4,5] The first case concerned a patient after 6 years of etretinate therapy. Other bone changes noted were demineralization, thinning, premature closure of the epiphyses, and increased curvature of long bones with osteopenia.[4] Similar bone changes have been reported during long-term etretinate therapy in a child with PC,[15] and in adults with disorders of keratinization,[16] but none of them showed acro-osteolysis. The second case was in a patient with PC tarda,[5] but without etretinate therapy, which is similar to our case.

The intimate relationship between the nail and the underlying bone is responsible for the common occurrence of bone alterations in nail disorders, and vice versa.[17] Absence of the terminal phalanx is often associated with a corresponding omission of the associated nail, suggesting that formation of the nail unit is dependent on the underlying bone.[18] Acquired acro-osteolysis can also lead to nail changes such as subungual hyperkeratosis, onycholysis, and increased curvature of the nail.[11] However, in pachyonychia congenita, the nails are primarily affected and acro-osteolysis is a secondary change. The exact pathogenesis of acro-osteolysis is not known. From a wide variety of etiological factors, it is evident that different noxious events can induce acro-osteolysis. However, vascular occlusion as the common pathogenic event for all varieties of acro-osteolysis is the widely accepted hypothesis.[3] Absence of etretinate therapy and other causes of acro-osteolysis in the present case, and the interrelation between the nail and the underlying bone, therefore suggest that the subungual hyperkeratosis may cause vascular occlusion leading to impaired perfusion of distal phalanges and acro-osteolysis. Treatment with etretinate may act as a contributing factor.

In conclusion, acro-osteolysis can occur as a complication of pachyonychia congenita. The management strategy should include an X-ray of the area and treatment to prevent the complication, especially in Jadassohn–Lewandowsky syndrome, where the nail changes are severe.

References

1 Irvine AD, McLean WHI. Human keratin diseases: The increasing spectrum of disease and subtlety of the phenotype-genotype correlation. *Br J Dermatol* 1999; **140**: 815–828.
2 Feinstein A, Friedman J, Schewach-Millet M. Pachyonychia congenita. *J Am Acad Dermatol* 1988; **19**: 705–711.
3 Baran R, Drawber RPR. The nails in dermatological diseases. In: Baran R, Drawber RPR, eds. *Diseases of the Nail and their Management*, 2nd edn. Oxford: Blackwell Science Publications, 1994: 135–174.
4 Cuny JF, Schmutz JL, Terver MN, *et al.* Rhematologic effects of etretinate. *Ann Dermatol Venereol* 1989; **116**: 95–102.
5 Paller AS, Moore JA, Scher R. Pachyonychia congenita tarda: a late onset form of pachyonychia congenita. *Arch Dermatol* 1991; **127**: 701–703.
6 Elston DM. The diagnosis: Pachyonychia congenita. *Cutis* 2003; **72**: 143–144.
7 Karol AL. Keratodermas. In: Bolognia JL, Jorizzo JL, Rapini RP, *et al.* eds, *Dermatology*, 1st edn. London: Mosby, 2003: 809–822.

8 Stevens HP, Kelselh DP, Leigh IM. The inherited keratodermas of palms and soles. In: Freedberg IM, Eisen AZ, Wolff K, *et al.* eds, *Fitzpatrick's Dermatology in Internal Medicine*, 6th edn. New York: McGraw-Hill, 2003: 505–514.
9 Covello SP, Smith FJ, Silleves Smith JH, *et al.* Keratin 17 mutations cause either steatocystoma multiplex or pachyonychia congenita type 2. *Br J Dermatol* 1998; **139**: 475–480.
10 Chang A, Lucker GPH, Peter CM, *et al.* Pachyonychia congenita in the absence of other syndrome abnormalities. *J Am Acad Dermatol* 1994; **30**: 1017–1018.
11 Scher RK. Acro-osteolysis and the nail unit. *Br J Dermatol* 1986; **115**: 638–639.
12 Gladman DD, Rahman P. Psoriatic arthritis. In: Ruddy S, Harris JR, Sledge CB, eds. *Kelly's Textbook of Rheumatology*, 6th edn. Philadelphia: W.B. Saunders Company, 2001: 1071–1079.
13 Griffiths WAD, Judge MR, Leigh IM. Disorders of keratinization. In: Champion RH, Burton JL, Burns DA, *et al.*, eds. *Rook/Wilkinson/Ebling Textbook of Dermatology*, 6th edn. Oxford: Blackwell Science, 1998: 1483–1588.
14 Puliyel JM, Iyer KSS. A syndrome of keratosis palmoplantaris congenita, pes planus, onychogryphosis, periodontosis, arachnodactyly and a peculiar acro-osteolysis. *Br J Dermatol* 1986; **115**: 243–248.
15 Cointin M, Sommelet-Olive D, Cuny JF, *et al.* Bone complications from chronic etretinate intoxication in children. *Ann pediatr (Paris)* 1990; **37**: 458–460.
16 Halkier- Sorensen L, Andresen J. A retrospective study of bone changes in adults treated with etretinate. *J Am Acad Dermatol* 1989; **20**: 83–87.
17 Tosti A, Piraccini BM. Biology of nails. In: Freedberg IM, Eisen AZ, Wolff K *et al.*, eds. *Fitzpatrick's Dermatology in Internal Medicine*, 6th edn. New York: McGraw-Hill, 2003: 159–163.
18 Baran R, Juhlin L. Bone dependent nail formation. *Br J Dermatol* 1986; **114**: 371–375.

