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 The fact that a work is unpublished shall not itself bar a finding of fair use if such finding is made upon consideration of all the above factors.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.
Jadassohn Lewandowsky Syndrome: A Rare Entity

Anupama Manohar Prasad, Yugandar Inakanti, and Shiva Kumar

From the Department of DVL, P.E.S. Institute of Medical Sciences and Research, Kuppam, Andra Pradesh, India

Address for correspondence: Dr. Yugandar Inakanti, Department of DVL, P.E.S. Institute of Medical Sciences and Research, Kuppam - 517 425, Chittoor District, Andhra Pradesh, India. E-mail: dryugandar@gmail.com

Received 2014 Nov; Accepted 2015 Jan.

Copyright © Indian Journal of Dermatology

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Abstract

Pachyonychia congenita (PC) is a rare autosomal dominant genodermatosis characterized by hyperkeratosis affecting the nails and palmoplantar areas, oral leucokeratosis, and cystic lesions. It is classically subdivided into two major variants, PC-1 (Jadassohn–Lewandowski syndrome) and PC-2 (Jackson-Lawler syndrome), according to the localization of the mutations in the KRT6A/KRT16 or KRT6B/KRT17 genes, respectively. We report a 9-year-old male patient with a history of thickened, discolored nails, raised spiny skin lesions all over the body since birth with focal plantar keratoderma and absence of natal teeth.

Keywords: Jadassohn–Lewandowski syndrome, keratins, nails, pachyonychia congenita, palmoplantar keratoderma

What was known?

Jadassohn–Lewandowski syndrome is an autosomal dominant skin disorders characterized predominantly by thickened nails, palmoplantar hyperkeratosis, keratosis pilaris, hyperkeratotic follicular papules on the sites of friction, hair abnormalities and hyperhidrosis of the palms and soles. These disorders have been suggested to be due to mutations in paired keratins.

Introduction

Pachyonychia congenita (PC) describes a group of rare autosomal dominant skin disorders characterized predominantly by dystrophic, thickened nails and painful and highly debilitating palmoplantar hyperkeratosis.[1,2] Müller made one of the first documented observations of PC in 1904.[3] The next reports were published in 1905 by Wilson[4] and in 1906 by Jadassohn and Lewandowsky.[5] With a base on phenotypes, PC is classified in four types: PC I to III and PC tarda.[6,7]

The objective of this case report is to describe the clinical features of PC-I. Although with inherent limitations of a single case, this report may contribute to better understanding about this rare condition.

Case Report

A 9-year-old male born at term to non consanguineous parents was referred to our outpatient clinic for evaluation of thickened nails starting at the age of 6 months.
He presented with history of pinhead-sized yellowish spiny skin lesions all over body noted at birth that had slowly grown during the first year of age and abnormalities nails. No history of natal or neonatal teeth was there. The patient intelligence was normal. No similar complaints in family.

Physical examination showed:

- Skin: Multiple follicular discrete papules present over the face, upper chest, buttock, elbow, knees and flexures [Figures 1 and 2]
- All 20 nails were thickened, yellowish discoloration with increased curvature and subungual hyperkeratosis [Figures 3–5]
- Focal plantar keratoderma [Figure 6]
- Oral mucosa: Mucosal leucokeratosis [Figure 7]
- There were no abnormalities in examination of palms, otolarynx and ophthalmology.

All laboratory investigations were within normal limits. KOH mounts of toe and finger nails were negative for fungal elements. Histopathology examination of Follicular keratotic papule showed follicular plugging, hyperkeratosis and acanthosis. A skin biopsy of sole showed marked hyperkeratosis, acanthosis, moderate hypergranulosis and minimal dermal inflammatory infiltration. Based on characteristic clinical findings and histopathology features, diagnosis of PC type 1 or Jadassohn–Lewandowski syndrome was confirmed.

**Discussion**

PC is a rare, autosomal dominant disorder characterized by triad of subungual hyperkeratosis with accumulation of hard keratious material beneath the distal portion of the nails, lifting the nails from the nail bed, keratosis palmaris et plantaris with thick callosities, especially on the soles and thick white areas on the oral mucosa.[8] Other associated features which may occur include keratosis pilaris, hyperkeratotic follicular papules on the sites of friction, hair abnormalities and hyperhidrosis of the palms and soles. These disorders have been suggested to be due to mutations in paired keratins, K6a/K16 (in PC1) and K6b/K17 (in PC2). According to these mutations, various clinical variants have been described:

PC-I or Jadassohn–Lewandowski syndrome (MIM #167200) is a common entity characterized by onychogryposis on all the digits (100%), hyperkeratosis of the palmo plantar (50-90%) and of extensor areas, follicular keratosis (37%), oral (50-75%) or laryngeal (6-15%) leukokeratosis, acral hyperhidrosis (20-75%) and blisters (36%).[5,6,7,8,9,10,11,12]

In patients with PC-II or Jackson–Lawler syndrome (MIM #167210), main changes are natal or neonatal teeth (15-50%), cutaneous cystic lesions (25%), disorders in scalp and eyebrow hairs (9-25%), in addition to corneal dystrophy (8%); moreover, the nail hyperkeratosis is less accentuated in PC-II than in PC-I.[6,9,10,11,12]

PC-III (Schafer-Brunauer syndrome) shows combined features of type 1 and 2 with angular cheilosis, cataract and corneal dyskeratosis.[7] Despite recent advances in genetic analysis, misdiagnosis can occur because same mutations may show diverse features.

A fourth variant, PC tarda, has also been described and is characterized by a later onset that ranges from late childhood to middle ages. Other rare variants include PC with only nail involvement.

**Pathogenesis** Keratins are structural proteins that promote the integrity of epithelial cells. As a result, mutations in the genes encoding keratins lead to cell fragility.[1] The skin expresses the largest number of keratin genes of any organ in body. PC is caused by mutations in five keratin genes KRT6a, KRT6b, KRT6c, KRT16 and KRT17 which are expressed only in palmo plantar skin, the nail bed, pilosebaceous unit and oral mucosa, leading to selective involvement of these sites in PC.[1]

**Genetic Diagnosis** PC is an autosomal dominant disorder. More than 45% of cases appear spontaneously without any family history of PC. Given the overlapping clinical presentation with other genetic disorders, only genetic testing can confirm the PC diagnosis.

With nearly 100 distinct PC mutations now identified, correlating the signs of PC with specific mutations...
and genes has led to a new classification system of PC, now classified into five subgroups corresponding to the underlying genetic defect: PC-K6a, PC-K6b, PC-K6c, PC-K16 and PC-K17.

**Histological Findings**  
Histological examination of plantar hyperkeratosis plaques reveals an acanthotic epidermis with parakeratosis and orthokeratosis compatible with rapid keratinocyte proliferation and differentiation. Cytologic atypical is not seen.

Complications like respiratory distress due to laryngeal leucokeratosis and acroosteolysis, malignant changes in palmoplantar lesions can occur in PC.

**Treatment**  
Treatment options for PC fall into four broad categories:

- Non-invasive (mechanical) e.g. abrasion with some hand tool
- Invasive (surgical) e.g. electrofulguration, excision
- Chemical methods using urea, propylene glycol, alpha hydroxy acid
- Pharmacological (vitamin A, retinoid), all basically targeted at reducing the hyperkeratosis involving different sites.

When the familial mutation is known, genetic counseling can be done and if required, prenatal diagnosis can be done at early stage of pregnancy by chorionic villi biopsy. In our case, we advised keratolytics and oral isotretinoin.

**Conclusion**

PC is a rare genetic disorder for which there are very few therapeutic options available. Free genetic testing is provided to each patient through the International Pachyonychia Congenita Research Registry (IPCRR) sponsored by the PC Project ([www.pachyonychia.org](http://www.pachyonychia.org)) which is a non-profit USA public charity, supports clinical and research activities related to the treatment of pachyonychia congenital. In India, we don’t have such projects working on PC. With this case, we intend to draw attention to this condition and the role of the dermatologist in the diagnosis.

**What is new?**

Pachyonychia congenita is a rare genodermatosis due to mutations in one of four keratin genes. To the best of our knowledge this represents the first report of isolated PC with healthy other siblings and parents.

**Acknowledgement**

We gratefully acknowledge the help of the Principal, PESIMSR, Kuppam and the professor and head of the Department of DVL, PESIMSR, Kuppam.

**Footnotes**

**Source of support:** Nil  
**Conflict of Interest:** Nil.

**References**


Figures and Tables
Figure 1

Follicular keratotic papules over the face and shoulders
Figure 2

Follicular papules over both shoulders and back upper chest
Figure 3

Thickened, discolored and increased curvature of fingernails
Sparing of palmar surface of both hands
Figure 5

Thickened, discolored and increased curvature of toe nails
Figure 6

Focal plantar keratoderma
Oral leucokeratosis over tongue