Pachyonychia congenita: A rare genodermatosis

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ABSTRACT

Pachyonychia congenita (PC) is a rare genodermatosis with only 450 cases reported since 1906. It is of two types, type I due to mutation in genes 6a and 16, and 6b and 17 in type II with an autosomal dominant inheritance in both types. A 22 yr old female patient presented in our OPD with hypertrophy of finger and toe nails, palmoplantar keratoderma, oral punctuate leukokeratosis, hyperhidrosis in palms and soles with maceration and malodour since childhood. She had a positive family history with father and grandfather affected but less severely. Microscopy and culture of nail clippings and scrapping were done to rule out fungal infection. On biopsy acanthotic epidermis, parakeratosis, orthokeratosis were seen. No evidence of any associated malignancy was found after thorough workup. She was diagnosed as PC Type 1. She was put on topical steroids and orally on acetretin 25 mg OD. Paring of the nails was done too reduce the thickness of nails & to provide symptomatic relief. She was on a regular treatment for 3-4 months and showed some improvement in the form of reduced palmoplantar hyperkeratosis and reduced oral punctate keratosis but was later lost on followup. She showed no adverse effect to therapy during this period. This case is being reported because of its rarity.

Key words: Nail hypertrophy, oral leukoplakia, palmoplantar keratoderma

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INTRODUCTION

Pachyonychia congenital (PC) is a rare genodermatosis. Müller made one of the first documented[1] observations of pachyonychia congenita in 1904 followed by reports published in 1905 by Wilson and in 1906 by Jadassohn and Lewandowsky.[2] Only 450 cases have been reported since then.[3,4] Two main types of pachyonychia congenita are recognized: (1) pachyonychia congenita type - 1 (Jadassohn-Lewandowsky type) and, (2) pachyonychia congenita type - 2 (Jackson-Lawler type). PC type 1 is the more common subtype. PC type 2 is distinguished by the development of natal teeth, widespread steatocystomas, and occasionally pili torti. A third variant, pachyonychia congenita tarda has also been described and is characterized by a later onset that ranges from late childhood to middle age.[4]

CASE REPORT

The patient was a 22 yr female, born of a consanguineous marriage who came to our OPD with chief complaint of hypertrophic brittle nails since childhood. Her finger and toe nails both were affected and the nail beds were hypertrophied with [Figures 1 and 2] discoloration and longitudinal fissuring. She also had palmoplantar keratoderma [Figure 3] since childhood with thick plaques, hypertrophic keratosis, deep fissuring with oozing, crusting and bleeding points [Figures 4 and 5]. It was associated with pain and erythema. Hyperhidrosis of palms and soles was present and was confirmed by starch test. She also complained of oral leukokeratosis. Her father and grandfather had similar affection but to a lesser degree.

KOH microscopy and culture of nail clippings was done to rule out candidal or dermatophytic onychomycosis. On skin biopsy, acanthosis, parakeratosis, orthokeratosis were seen [Figure 6]. No evidence of any associated malignancy was found after thorough workup. She was diagnosed as pachyonychia congenita Type 1. She was managed with topical steroids and orally on acitretin 25 mg OD. Paring of nails was done to reduce the thickness of nails and to provide symptomatic relief. After one month of therapy, a reduction was seen in the thickness of hyperkeratotic lesions of palms and soles and

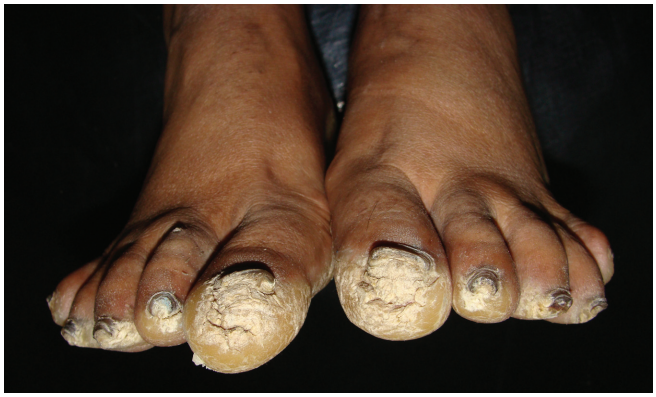

Figure 1: Brittle, hypertrophic nails, longitudinal fissuring, and hypertrophic nail beds

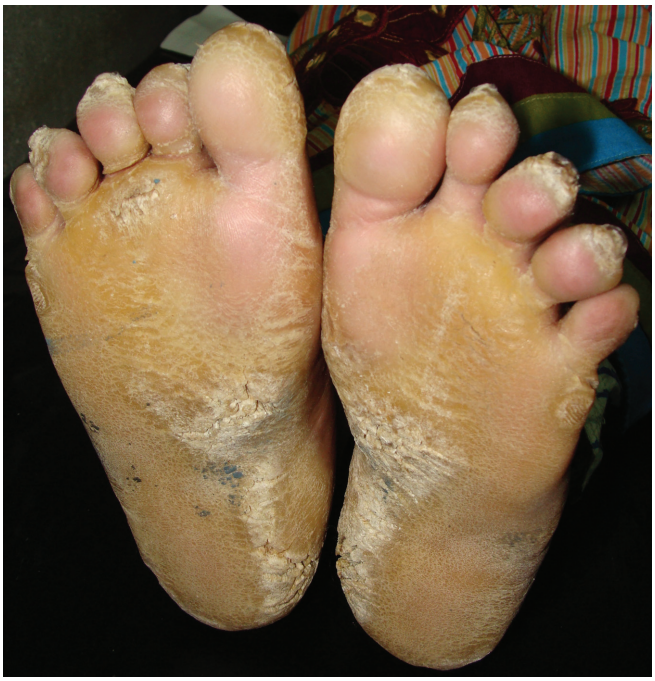

Figure 3: Hypertrophic keratinization over soles.

desquamation had started in these lesions. Same treatment was continued for two month but she was lost on follow up.

DISCUSSION

Pachyonychia congenita (PC) is a rare type of PPKD, which is characterized by subungual hyperkeratosis of the distal nails and focal palmoplantar hyperkeratosis. It is classified as pachyonychia congenita type 1 (Jadassohn–Lewandowsky) and pachyonychia congenital type 2(Jackson–Lawler) syndromes.[5] Common mode of inheritance is autosomal dominant but autosomal recessive forms are also reported.[6] Histopathology shows gross hyperkeratosis with alternating ortho- and parakeratosis. Acanthosis is present with patchy hypergranulosis, in which large keratohyalin granules are present without gross epidermolysis.[7] In PC-2, the cysts may be keratinous epidermoid cysts, eruptive vellus hair cysts or true

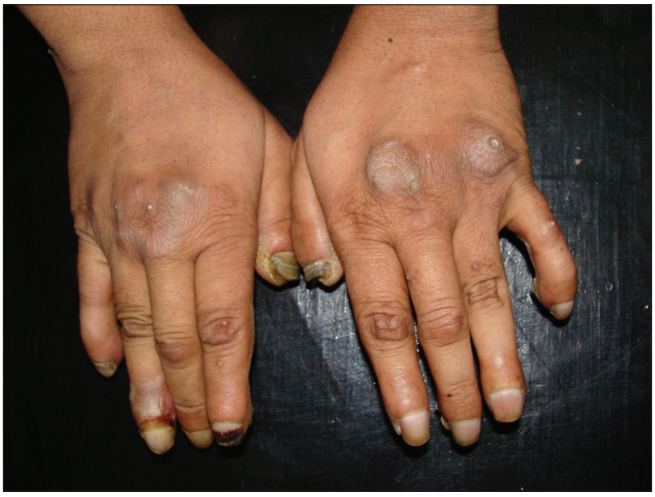

Figure 2: Brittle, hypertrophic nails, longitudinal fissuring, and hypertrophic nail beds

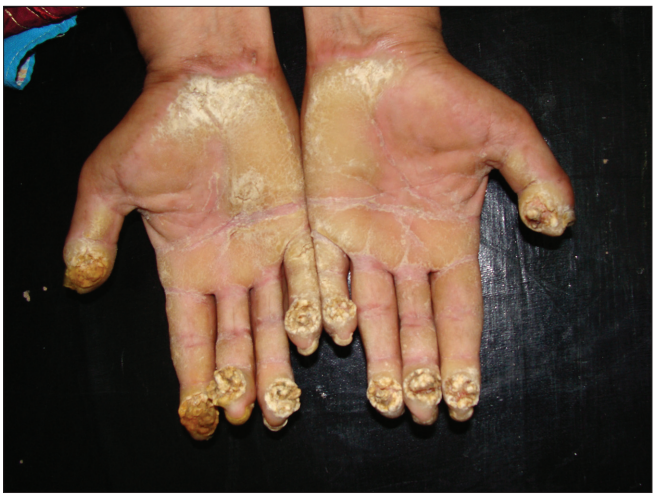

Figure 4: Painful hypertrophic keratinization at finger tips

steatocysts. Different histologies may be seen.[8]

PC type 1 is the more common variant. It is characterized by hypertrophic nail dystrophy (pachyonychia) which is a characteristic feature in 90-98% cases, present at birth or developing within the first few months of life. It may be accompanied by painful paronychia with difficulty in fine motor tasks. Other features include symmetric focal palmoplantar keratoderma, oral leukokeratosis (not premalignant), palmoplantar hyperhidrosis, follicular keratoses,[4] and laryngeal involvement. PC type 2 is characterized by almost all clinical features of PC type 1 but less severe keratodermas along with natal or prenatal teeth, numerous steatocystomas, although a variety of cysts, including epidermal inclusion cysts, pilosebaceous cysts, and vellus hair cysts, may be seen.[4]

In other clinical variants involvement of the nails alone has been reported. Further genetic studies are required to study possible variants and associations of PC.

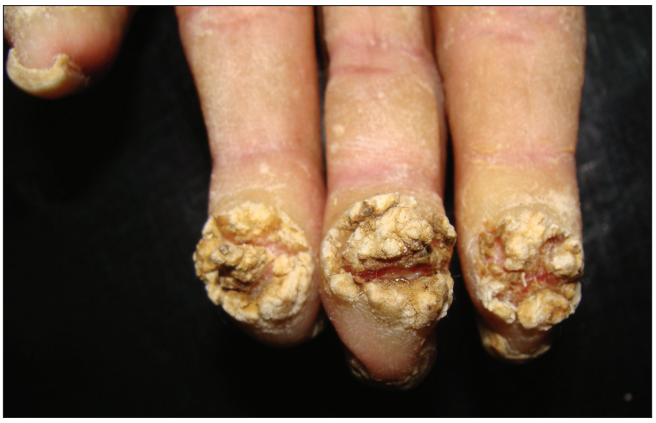

Figure 5: A closeup view of palmar keratoderma

Emollients and keratolytics (e.g. salicylic acid, corn plasters, benzoic acid, propylene glycol) may help mild keratodermas; a comfortable footwear may reduce blistering and callosities. Physical debridement of nails can also be done to reduce the thickness of nails. Mechanical reduction of hyperkeratosis and nails produces symptomatic benefit. Antifungal creams and systemic antifungal agents can be used to provide some relief but may need repeated intermittent courses.[9] Acitretin 25–35 mg/day may be effective but causes increased tenderness in the lesions.[7] A prolonged course of retinoids may produce a degree of flattening of the nails and other complications such as periosteal hyperostosis, increased sensitivity and fragility of the underlying epidermis, and this limits their usefulness.[9] Treatment of hyperhidrosis (aluminum chloride lotion, and iontophoresis) may reduce blistering and the use of botulinum toxin under regional analgesia may provide pain relief for several months. The mechanisms of manipulating gene expression by small molecules or gene therapy has become possible. Genetic therapies for such diseases must either suppress the production of the toxic proteins or correct the genetic defect in the chromosome. Utilizing the technological by-products of the human genome project, such as RNA interference (RNAi) and quantitative RT-PCR (qRT-PCR), physicians and scientists have collaborated to create a candidate siRNA therapeutic that selectively inhibits a mutant allele of KRT6A, the most commonly affected PC keratin. In vitro investigation of this siRNA demonstrates potent inhibition of the mutant allele and reversal of the cellular aggregation phenotype.[10]

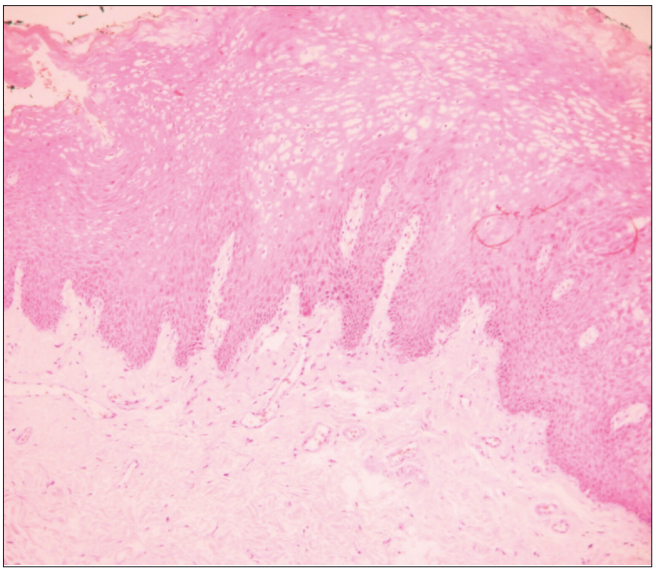

Figure 6: Acanthosis, parakeratosis, and ballooning of epithelial cells [H & E, 10x]

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