

# **PACHYONYCHIA CONGENITA TARDA IN ASSOCIATION WITH INSULIN DEPENDENT DIABETES MELLITUS SUCCESSFULLY TREATED WITH VITAMIN A AND E**

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## **ABSTRACT**

Pachyonychia congenita (PC) is a rare, autosomal dominant disorder characterized by discoloration and thickening of the nails, usually beginning within the first few months of life. An 11-year-old girl presented with subungual hyperkeratosis and nail plate thickening with increased transverse curvature, distal elevation and yellow-brown discoloration, and mild thickening of the nails since 2 years. The changes, which affected all 20 nails, had developed at the age of 9 years. The patient's clinical presentation and history were compatible with a diagnosis of pachyonychia congenita, a rare heritable disease that affects the nails, skin, oral and laryngeal mucosae, teeth, and hair. Dominant-negative mutations in four keratin genes (K6a, K6b, K16, and K17) lead to keratinocyte fragility and the resultant pachyonychia congenita phenotype. Successful targeted therapies are currently lacking for this disabling disorder. In this patient there was association of pachyonychia congenita with diabetes mellitus. Reports of the onset of nail changes beyond the first few years of life are rare. The patient was successfully treated with vitamin A and E along with topical applications of urea–lactic acid moisturizing ointment twice weekly.

**KEY WORDS :** Pachyonychia congenita ,nails,hyperkeratosis,diabetes mellitus,curvature.

## **INTRODUCTION**

Pachyonychia congenita was originally described by Wilson<sup>1</sup> in 1905, although the association of the disorder with palmoplantar keratoderma and other ectodermal defects was first reported by Jadassohn- Lewandowsky.<sup>2</sup> PC has been subdivided into four groups, based on the clinical features associated with nail changes.<sup>3</sup> Common to almost all patients who have been described, regardless of the form of inheritance or subclassification of the disorder, is the onset of pachyonychia in infancy. Very few cases have been reported so far with late onset. Pachyonychia congenita (PC) is a rare, autosomal dominant disorder characterized by discoloration and thickening of the nails, usually beginning within the first few months of life. Reports of the onset of nail changes beyond the first few years of life are rare.

The term pachyonychia congenita tarda (PCT) has been suggested by Paller et al for the late onset form of PC.<sup>4</sup> We herein report one such case. Dominant-negative mutations in four keratin genes (K6a, K6b, K16, and K17) lead to keratinocyte fragility and the resultant pachyonychia congenita phenotype. Successful targeted therapies are currently lacking for this oftentimes disabling disorder. In this patient there was association of pachyonychia congenital with diabetes mellitus.

## **CASE REPORT**

A 11 year old girl presented to the department of Dermatology for the evaluation of asymptomatic nail changes that had developed at the age of 9 years of age. The patient had chief complaints of thickening and wedge shaped nails since last 2 years. History dated back to 2 years when patient started developing thickening and discoloration of left thumb nails within 2 weeks, both nails of hands were involved (Fig 1). After 2 weeks of discoloration, involvement of big toe nail was seen, which later involved other toe nails (Fig 2) .The nails thickened progressively with a beak like longitudinal hypercurvature. The nails were extremely hard, greatly thickened, opaque, brown, lusterless, laterally curved and distally elevated. The free edge of the nail was raised by a thick horny mass of subungual keratosis.

Physical examination revealed all 20 nails demonstrated subungual hyperkeratosis that was associated with distal elevation and increased transverse curvature of the nail plate, which leads to an omega appearance. The nail plates also were thick and yellowish green in color. No palmoplantar keratoderma, follicular keratoses, or cutaneous cysts were evident. The hair and teeth were normal, and there were no other oral mucosal lesions. There was marked thickening of the fingernails and toenails, with subungual hyperkeratosis but a smooth surface. Some of the nails had a "pinched" appearance at the distal aspect, and the nail tip was angulated upward.

There was no history of natal or neonatal teeth, loss of primary teeth, acral blisters, plantar pain, or hoarseness. The patient had no known medical problem, and

her growth and development have been normal. No other family member was affected. No palmoplantar keratoderma, follicular keratoses, or cutaneous cysts were evident. The hair and teeth were normal, and there were no oral mucosal lesions. Results of KOH examinations were negative. Fungus cultures from the nails yielded no organisms. X-rays of hands/feet did not reveal any abnormality. The biopsy of the patient could not be performed as the patient refused biopsy.

Since then the disease is non progressive. The patient is a diabetic and is on injectable insulin since last 3 years. The family history of diabetes mellitus is strongly positive with both mother, father, maternal and paternal grandfather being diabetic. Though acitretin is the drug of choice, yet the patient was not put on acitretin to avoid serious side effects, especially early closure of the epiphysis. The patient was put on vitamin A 100000 units and vitamin E 800 units alongwith topical applications of urea – lactic acid moisturizing ointment daily. Both vitamins were given intermittently for three weeks followed by rest period of one week. Fundus examination was done every three months. The patient achieved remission over a period of one year. There were no side effects and no recurrence during the follow up period upto two years. The patient is on regular follow up every three months.

## **DISCUSSION**

Pachyonychia congenita (PC) represents a group of rare, autosomal dominant keratin disorders with characteristic nail findings and with the additional abnormalities of the palmoplantar skin, pilosebaceous apparatus, oral and laryngeal mucosae, teeth, and hair.<sup>5</sup> Dominant-negative mutations producing aberrant keratin proteins that interfere with keratin filament assembly and lead to keratinocyte fragility are central to the pathogenesis of PC. The molecular bases of the two major clinical types of PC, PC-1 (Jadassohn-Lewandowski type) and PC-2 (Jackson-Lawler type), were elucidated in the 1990's. Defects in the genes encoding keratins 6a and 16 were found to underlie PC-1, whereas defects in keratins 6b and 17 were shown to underlie PC-2. To date, more than 80 mutations in these four keratin genes have been identified in PC families, the vast majority of which occur within the helix boundary motifs that flank the central helical rod domain. Variants of PC-1 and PC-2 with delayed onset (PC tarda) represent exceptions that result from mutations elsewhere in the genes that encode keratins 16 and 17, respectively.<sup>6</sup>

The hallmark of PC is hyperkeratosis of the nail bed, which leads to elevation, which is most pronounced distally, and increased transverse curvature of the nail plate. This abnormality results in an omega or pincer nail. The nail plates are also discolored, thick, and friable, and they sometimes fail to reach the distal fingertip. All 20 nails are involved, although the findings are often most severe on thumbs, index fingers, and toes<sup>7</sup>.

Additional features of PC, in order of decreasing prevalence, include: focal palmoplantar keratoderma (plantar, 90 %; palmar, 50 %); palmoplantar hyperhidrosis (75 %); oral leukokeratosis (50 %, more prominent in PC-1); follicular keratoses in sites of friction, such as the elbows, knees, and waistline (50 %); natal or neonatal teeth (PC-2, 50 %; PC-1, 0 %); cutaneous cysts (25 %, more common in PC-2); coarse or twisted hair (25 %, more common in PC-2); hoarseness due to laryngeal involvement (15 %); and corneal abnormalities (<5 %). A history of natal or neonatal teeth is highly suggestive of PC-2. Whereas epidermal inclusion cysts can be observed in both types of PC, the presence of steatocystomas or vellus hair cysts points to a diagnosis of PC-2. However, the typical post-pubertal onset limits this feature's utility as an early discriminating factor. Although the presence of pili torti also favors a diagnosis of PC-2, brittle, coarse hair has been observed in both types. The development of painful oral and nipple lesions during breastfeeding and copious production of ear wax were recently described as additional clinical manifestations of PC<sup>8</sup>.

Nail thickening due to orthokeratotic hyperkeratosis of the nail bed is the main feature of pachyonychia congenita. It is often seen in association with several other diseases. Because of the protean expressions of the syndrome, several classifications have been proposed. Feinstein et al<sup>9</sup> based on a study of 168 patients have classified it into 4 types : Type I consists of thickening of nails, palmoplantar keratosis, follicular

keratosis and oral leukokeratosis with a relevant prevalence of 56.2%. Type II in which in addition to type I changes, palmoplantar bullae, hyperhidrosis, natal or neonatal teeth and steatocystoma multiplex are seen. It has a relative prevalence of 24.9%. Type III has a relative prevalence of 11.7% and clinical findings of type II with angular cheilosis, corneal dyskeratosis and cataracts in addition. Type IV has laryngeal lesions, hoarseness, mental retardation, hair anomalies and alopecia in addition to findings of the type III syndrome. The relative prevalence of this type is 7.2%.

The case is reported because of its rarity and also because of its association with insulin dependent diabetes mellitus.

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