Pachyonychia Congenita Project

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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.

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PACHYONYCHIA CONGENITA TYPE I PRESENTING WITH SUBTLE NAIL CHANGES

Abstract: **Pachyonychia congenita type I is an autosomal dominant disorder where nail abnormalities are a constant feature and develop during childhood. We report here a family with pachyonychia congenita type I and very mild nail changes to underline that this diagnosis should be considered even in the absence of severe nail thickening.**

Pachyonychia congenita type I (OMIM-167200) is an autosomal dominant disorder also called Jadassohn-Lewandowsky Syndrome. It can be caused by a mutation in the keratin-16 gene (*KRT16*) on chromosome 17 or in the *KRT6*a gene on chromosome 12 (gene map locus 17q12-q21, 12q13). These genes encode for structural proteins expressed by epithelial cells (1).

Clinically it is characterized by nail abnormalities, hyperkeratosis of the palms, soles, knees and elbows, tiny cutaneous horns in many areas, and leukokeratosis of the oral mucous membranes. Hyperhidrosis of the hands and feet is usually present (2).

Nail abnormalities are a constant feature and develop during childhood. In typical cases the 20 nails are thickened, very difficult to trim, darkened and with an increased transverse curvature. Nail thickening is a consequence of nail bed hyperkeratosis and is more evident on the distal half of the nails, which have an upward angling. The thumb and index finger are more severely affected. Development of nail thickening may be preceded by nail bed erythema (2).

Recent evidence indicates that pachyonychia congenita (PC) may also present with very subtle nail changes and that there is not a strict correlation between mutations detected at molecular level and clinical phenotype that may vary in severity even within members of the same family (3).

CASE REPORT

A family has recently consulted us because their 6-month-old boy presented with mild subungual hyperkeratosis and distal onycholysis of the fingernails and toenails since birth (Fig. 1). The skin, mucosa, and hair were normal.

The 35-year-old mother had onycholysis and splinter hemorrhages of the fingernails and very mild thickening of the toenails (Fig. 2). The 78-year-old grandmother only had mild onycholysis of some fingernails (Fig. 3), and hyperkeratosis limited to the pressure areas of the soles.

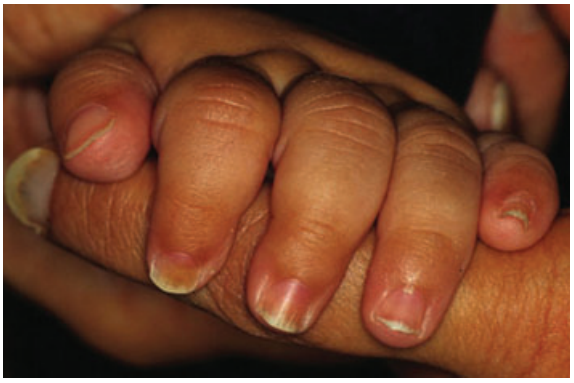

Figure 1. The 6-month-old boy presenting with mild distal nail thickening, mild onycholysis, and nail bed hyperkeratosis.

Figure 2. The 35-year-old mother presenting with onycholysis and splinter hemorrhages of the fingernails.

Mutation analysis performed on two members of the family (35-year old and the 78-year-old women) showed that they were heterozygous carriers of a dominant missense mutation in the *KRT6*a gene. The mutation is designated as p.Arg164Pro and it results in the substitution of Arginine (R) by Proline (P) at codon 164 located in the 1A domain of keratin 6a protein.

The 6-month-old boy (proband) did not perform the mutation analysis because of his young age. No treatment was prescribed except for mild emollients. The follow-up of the child at 1 year of age showed worsening of the fingernail abnormalities with nail thickening and proximal progression of the onycholysis associated with yellow–red discoloration and splinter hemorrhages (Fig. 4).

Figure 3. The 78-year-old grandmother presenting with mild onycholysis of some fingernails.

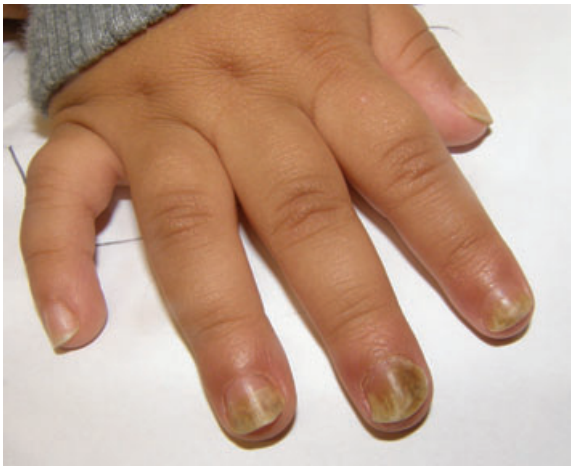

Figure 4. The boy at 1 year of age showing proximal progression of the onycholysis associated with yellow–red discoloration and splinter hemorrhages. Nail thickening is worsened but still very mild (see first fingernail).

DISCUSSION

Pachyonychia congenita is a disorder with few clear cut clinical or histopathological pathognomonic changes. There are only strongly suggestive features. The advent of gene and other molecular studies has greatly helped in the diagnosis of this disorder.

A mutation in KRT6A, p.Arg164Pro, was identified in this family presenting with only mild features of pachyonychia congenita. The nail changes observed were very minor and, unlike the majority of cases of pachyonychia congenita with known mutations in KRT6A, the affected members of this family had very little/no painful plantar hyperkeratosis. This mutation was previously reported (3) in a family with a more severe phenotype. Variation in clinical severity both within and between families with the same mutation in KRT6A has been reported previously. It is probable that other factors including environmental, and genetic modifiers may also be involved in determining the clinical severity.

With this report we would like to underline the importance of a careful examination of the nail apparatus and, even if the nail alterations were very mild, think about a congenital disorder, especially if other family members are affected by similar changes.

ACKNOWLEDGMENTS

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PRIMARY CUTANEOUS ASPERGILLOSIS IN AN IMMUNOCOMPETENT PATIENT: SUCCESSFUL TREATMENT WITH ORAL VORICONAZOLE

Abstract: **We report a case of primary cutaneous aspergillosis in an immunocompetent child that responded rapidly to oral voriconazole therapy. Voriconazole may be considered as a treatment option for pediatric patients with primary cutaneous aspergillosis.**