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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.
Dear Editor,

Pachyonychia congenita (PC) consists of a group of rare autosomal-dominant ectodermal disorders characterized predominantly by nail dystrophy. There are two main clinical subtypes of PC: PC-1 is caused by mutations in keratin 6a (K6a) gene or keratin 16 (K16) gene, accompanied by nail dystrophy, severe palmoplantar keratoderma and oral leukokeratosis; and PC-2 is linked to mutations in the keratin 6b (K6b) gene or keratin 17 (K17) gene, associated with nail dystrophy, focal palmoplantar keratoderma and multiple steatocysts.1

A 9-year-old Chinese female was affected by thickened fingernails and toenails at 6 years of age. Physical examination showed hyperkeratotic fingernails and toenails (Fig. 1a,b). Steatocystoma multiplex, palmoplantar keratoderma and natal teeth were not found in this patient. Repeated fungal examination under a microscope and culture excluded onychomycosis. There were no other family members affected by this disease.

Following written informed consent, genomic DNA of the proband, her parents, and 100 unrelated and unaffected people was extracted from peripheral blood. Direct sequencing of DNA from the patient revealed a heterozygous 1495G→A mutation in the V2 domain of keratin 6b (K6b) gene (Fig. 1c,d). A heterozygous missense mutation 1495G→A (arrow), which predicts the amino acid change glycine to serine at codon 499 (G499S) was found.

Figure 1. (a,b) Photograph of the thickened fingernails. (c) Direct sequencing of the k6b gene. A heterozygous missense mutation 1495G→A (arrow), which predicts the amino acid change glycine to serine at codon 499 (G499S) was found. (d) Sequence in normal subjects.

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mutation in exon 9 of the K6b gene, in the tail domain, leading to the substitution of glycine 499 by serine (G499S; Fig. 1c). No mutations were found in K17, K16, K6a or K6c. No such mutation was found in her parents and the 100 unrelated controls (Fig. 1d).

Three mutations have been reported in K6b, but this is the first mutation to be reported in the tail domain of PC-2. Another known similar mutation was an insertion mutation located in the tail domain of K6a in PC-1.2 Unlike epidermolysis bullosa simplex, the correlation between severity of disease and the location of the mutation within the keratin molecule of PC is not clear. Connors et al.3 detected a case of late-onset PC association with a mutation K354N in the central 2B domain of K16. Our group has reported a mutation N109D in the second half of the 1A domain of K17 with delayed onset PC-2.4 Terrinoni et al.5 reported a postzygotic mutation in the V1 domain of K16 with unilateral palmoplantar nevus and delayed onset PC-1. In this report, we found a mutation in the V2 domain of K6b associated with late onset and milder thickened nails. The patients listed above had delayed-onset PC, the milder phenotypes, and their mutation located at the less critical site of the keratins which is consistent with Connors et al. and Xiao et al.’s speculation.3,4

In conclusion, we reported a Chinese female affected with delayed-onset PC-2 caused by a novel mutation in the K6b V2 domain. The more PC patients that are reported, the more clinical data is accumulated. It will help expand the understanding of relationship between genotype and phenotype in PC and may give some clues to the cause of the phenotypic variability.

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