GENETICS AND GENODERMATOSES

PACHYONYCHIA CONGENITA - CAN A SPECIFIC PHENOTYPE BE A CLUE TO A GENETIC DEFECT?

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Background: Pachyonychia congenita (PC) is a rare genodermatosis transmitted as an autosomal dominant trait, caused by heterozygous mutations in any of the genes encoding the differentiation-specific keratins KRT6A, KRT6B, KRT6C, KRT16, or KRT17. PC affects different ectodermal structures to variable extent and characterized by hypertrophic nail dystrophy, painful palmoplantar blisters cysts, follicular hyperkeratosis and oral leukokeratosis.

Observation: We present a 6-year-old girl with hypertrophic nail dystrophy, follicular hyperkeratosis, circumscribed plantar keratoderma and oral leukokeratosis. Due to a mild hoarseness, indirect laryngoscopy showed no signs of laryngeal involvement. Histopathology of the plantar keratoderma showed massive hyperkeratosis with discrete focal parakeratosis, thickening of the granular layer with large keratohyalin granules. Histopathology of the hyperkeratotic papules on the trunk showed mild acanthosis and lamellar hyperkeratosis. The patient has been registered in the International Pachyonychia Congenita Research Registry (IPCRR) and a detailed genetic testing showed a mutation in the keratin gene KRT6A which causes PC type PC-K6a.

Key message: Although the condition has previously been subdivided into PC-1 (Jadassohn-Lewandowsky) and PC-2 (Jackson-Lawler) subtypes, the phenotypic characterization of over 700 mutation-verified PC patients enrolled in the IPCRR, shows that there is a considerable overlap between these subtypes. Patients with KRT17 mutations are more likely to have natal teeth and develop steatocystomas, while patients with KRT6A mutations more commonly manifest oral leukokeratosis, as is the case with our patient.
The IPCRR has contributed to publication of numerous papers which emphasized the importance of the mutation type affecting various clinical presentations of PC. Based on recent data, a new classification system has been developed for PC, and it is gradually replacing the earlier classifications. It is based almost exclusively on the mutated genes. In this report we have raised the hypothesis that distinctive clinical features may be highly

suggestive of a specific keratin mutation.