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Pachyonychia congenita tarda

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Summary

Pachyonychia congenita is a distinct hereditary disorder of keratinization, in which dystrophy of all nails is associated with palmoplantar keratoderma and other hyperkeratoses. Recently a late-onset type has been reported. We report a second family with late-onset pachyonychia congenita, showing a remarkable clinical heterogeneity. Furthermore, one patient demonstrated a number of associated hyperkeratoses not previously recognized. Acitretin proved useful in the treatment of this late-onset form of pachyonychia congenita.

Pachyonychia congenita was described by Muller in 1904¹ and Wilson in 1905.² Jadassohn and Lewandowski reported in 1906 on the association with palmoplantar keratoderma and other ectodermal defects.³ Since then, the presence of associated features has been considered essential for the diagnosis. Based on the prevalence of the associated symptoms, several classifications have been proposed.^{4–7} We recently described a monosymptomatic form of the disease, lacking the associated anomalies of the syndrome.⁸ Both autosomal dominant and autosomal recessive⁹ modes of inheritance have been described, reflecting genetic heterogeneity. Dystrophy of all nails is the main feature of the syndrome and usually presents within the first months of life.

Recently five patients were reported with the onset of the characteristic nail changes during the second and third decades of life.¹⁰ The term pachyonychia congenita tarda was proposed to describe this subset of pachyonychia congenita, characterized by palmoplantar keratoderma, hyperhidrosis and oral leucokeratosis associated with the nail lesions. No other hyperkeratoses were found to be associated.

We have observed a second family with the late-onset type of pachyonychia congenita, exhibiting remarkable phenotypic heterogeneity. Combined topical keratolytic

and oral retinoid treatment was started in one family member with a number of associated hyperkeratoses.

Case report

A 45-year-old man presented with a hyperkeratotic skin disorder localized to the nails, palms, soles, knees, lower legs, face and scalp. The dermatosis had started at the age of 44 and had progressed rapidly. Painful plantar keratoderma prevented him from walking.

On examination, all nails were dystrophic (Fig. 1). The free edges were raised by thick subungual hyperkeratosis with angulation of the lateral borders towards the centre. All nails appeared to be affected equally. In addition, a diffuse, thick, warty palmoplantar keratoderma was present (Figs 2 and 3). Nummular hyperkeratoses were observed at the knees, and similar lesions were noticed at the forehead and the scalp. The lower legs were covered by large brown scales, mimicking lamellar ichthyosis.

Family history revealed that his brother and father had similar, although less pronounced nail changes, (Fig. 4), which had started in, respectively, the third and fourth decades of age, neither had additional hyperkeratoses.

Histopathological examination of a biopsy taken from the palmar skin revealed hyperkeratosis and acanthosis, consistent with palmoplantar keratoderma. Mycological culture and microscopic examination of the subungual hyperkeratosis proved negative.

To remove the hyperkeratoses, topical treatment was given with salicylic acid 20% in petrolatum, resulting in a significant improvement within 3 weeks. Subsequently, oral retinoid treatment was started with acitretin 35 mg daily, to prevent new hyperkeratoses from developing. After 2.5 weeks of therapy, a further reduction of hyperkeratoses was observed (Fig. 5) and the daily dosage of acitretin was reduced to 20 mg for the next 6 weeks, with continued improvement. Because of elevated liver enzymes, the daily dosage was further reduced to 10 mg for 4 weeks and eventually stopped, resulting in a relapse of the hyperkeratoses. The nail changes, however, responded poorly to the retinoid therapy.

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Figure 1. Characteristic dystrophic changes, affecting all nails symmetrically. At the dorsum of the right hand, two verrucous hyperkeratotic plaques are visible, extending from the palmar skin to the dorsal surfaces.



Figure 2. The plantar skin is diffusely covered by a thick, warty hyperkeratosis, causing painful fissures.



Figure 3. Verrucous hyperkeratotic plaques at the palmar surfaces.



Figure 4. Nail changes observed in the patient's father, less pronounced though similar to those presented in Figure 1.

Discussion

The present communication reports a second family with pachyonychia congenita tarda. The characteristic nail changes, which had started in the third and fourth decades of life, were observed in all three affected family members. The patient described exhibited, in addition, a diffuse, incapacitating palmoplantar keratoderma, ichthyosiform scaling on both legs and nummular hyperkeratoses at the knees, face and scalp, which appeared simultaneously with the nail dystrophy. Associated dyskeratoses were absent in his two affected family members. In classical pachyonychia congenita, however, hyperkeratotic skin lesions, such as palmoplantar keratoderma, follicular keratosis, verrucosities over knees, elbows, buttocks and popliteal area, and oral leucokeratosis,¹¹ have been well documented to be variably associated. The range of associated hyperkeratoses and the variable expression we observed in our cases with the late-onset variant of pachyonychia congenita, therefore, similar to pachyonychia congenita. Nevertheless, some additional hyperkeratoses we observed, including nummular hyperkeratoses on the face and scalp, as well as the ichthyosiform scaling on both legs, have not been described previously and are therefore new to the syndrome. The inheritance pattern of our pedigree is highly suggestive of an autosomal dominant mode of inheritance, and therefore consistent with the other family with pachyonychia congenita tarda described.¹⁰ There are no reports available at the moment on the therapy of pachyonychia congenita tarda. In classical pachyonychia congenita, retinoids have been reported to be effective in alleviating the palmoplantar keratoderma, the subungual hyperkeratosis,¹² the keratotic patches on the knees and the leucokeratotic lesions in the mouth.¹³ One of our cases demonstrated acitretin to be effective in



Figure 5. Palmar skin after 3 weeks of local keratolytic and 2.5 weeks of acitretin treatment.

preventing new hyperkeratoses from developing in the late-onset type. Simple local keratolytic measures proved useful in reducing the hyperkeratoses.

We conclude that both the classical and late-onset variant of pachyonychia congenita are characterized by heterogeneity in expression of a number of associated hyperkeratoses. It seems rational to distinguish pachyonychia congenita tarda from pachyonychia congenita by the differences in age of onset. Retinoids constitute a promising approach to the treatment of the hyperkeratoses in both variants.

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