Pachyonychia congenita

Summary

Pachyonychia congenita (PC) is a rare genodermatosis predominantly featuring painful palmoplantar keratoderma, thickened nails, cysts and whitish oral mucosa.

The prevalence is not known but approximately 1000 patients have been registered to date worldwide.

PC presents clinically as a spectrum of conditions. PC onset is variable with most cases manifesting soon after birth, others becoming clinically apparent only in late childhood and rarely in adulthood. The first signs of the disease usually are thickened nails or neonatal teeth. At least 3 phenotypes of hypertrophic nail dystrophy of feet and hands can be observed: nail grows to full length but a distal prominent hyperkeratosis causes an upward slant with an accentuated curvature of the nail; nail plate terminates prematurely leaving a distal region of hyperkeratosis and an exposed finger tip; or nail plate is thin with little or no hyperkeratosis. When children start walking, typically in the first years of life, a focal or diffuse palmoplantar keratoderma develops, with underlying blistering causing severe pain. In some cases, the onset of keratoderma is not seen until later childhood. By about 12 years of age the majority of patients have painful plantar keratoderma. Oral leukokeratosis occurs early, may possibly cause feeding difficulties and should be distinguished from oral candidiasis in infants. A follicular keratosis on the trunk and extremities may be seen at friction points such as waist, elbows and knees. Excessive sweating of palms and soles due to palmoplantar hyperhidrosis, widespread steatocystomas appearing during or after puberty, axillary and inguinal cysts, hoarseness in young children are other findings observed in some PC patients.

Although historically two subtypes have been described, PC-1 and PC2, it is today recommended to classify PC patients into four subgroups based the underlying molecular etiology: PC-K6a, PC-K6b, PC-K16 and PC-K17, as PC is caused by dominant negative mutations in at least 4 genes [KRT6A, KRT6B (12q13.13), KRT16, KRT17 (17q21.2)] encoding keratins preferentially expressed in basal and suprabasal layers of palmoplantar skin, epidermal appendages and oral mucosa.

Diagnosis is based on clinical examination and is confirmed by molecular genetic testing.
Differential diagnosis includes variants of PC (steatocystoma multiplex, which develops at puberty with little or no nail dystrophy, and focal non-epidermolytic palmoplantar keratoderma; see these terms) and disorders manifesting with dystrophic nails such as epidermolysis bullosa, Clouston syndrome (distinguished by the presence of alopecia), and acquired disorders such as psoriasis and lichen planus (see these terms).

Antenatal molecular diagnosis is feasible provided the causative mutation is known.

Recent data suggesting the possibility that the disease may rarely be inherited in a semi-dominant fashion emphasizes the importance of accurate molecular diagnosis for proper genetic counseling.

There is no curative treatment for PC yet. Treatment of manifestations will focus primarily on grooming of nails and management of pain due to palmoplantar keratoderma: it includes the use of emollients to reduce hyperkeratosis and strategies to limit frictions and trauma of the feet. Novel treatment modalities under investigation include small interfering RNA (siRNA) strategies, the use of systemic and topical rapamycin, and injection of botulinum toxin. Clinical studies based on library screening of existing drugs are ongoing.

Complications may include secondary infection that is usually well controlled by antibiotics therapy.

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Suggest an update

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