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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.
PACHYONYCHIA CONGENITA (MIM: 167200, 167210)
Includes Jadassohn-Lewandowsky; Jackson-Lawler; Onychogryposis

Samman and Fenton (1986) proposed four types of pachyonychia congenita: classic type I (Jadassohn-Lewandowsky type); type II, (Riehl), which is similar to type I but more mild and with chronic oral leukoplakia; type III (Jackson-Lawler), which is characterized by natal teeth, multiple epidermal inclusion cysts, with or without other abnormalities; and type IV, in which affected individuals have widespread macular pigmentation in the neck and axillae with moderate nail and skin changes. Other classifications distinguish a type III in which all the classic features are present and in addition there is corneal dystrophy (Schafer-Brunauer syndrome). Yet another scheme was suggested by Feinstein et al. (1988) in which the type IV form of pachyonychia congenita was characterized by mental retardation, laryngeal involvement, and alopecia. More recently with discovery of specific mutations, Jadassohn-Lewandowsky is referred to as PC-1; Jackson-Lawler as PC-2.

Among the many classification schemes, the major similarities appear to be in the diagnostic significance of (1) corneal dystrophy, (2) presence of natal teeth and multiple cysts (either steatocystoma multiplex or epidermal inclusion cysts), and (3) absence of oral leukoplakia.

I agree with Schonfeld's (1980) position that not all these distinctions may be warranted, overlap within families does occur, and one cannot accurately predict in many families whether an individual at risk for pachyonychia congenita will be spared a specific finding. I am also convinced that any inherited disorder with thickened nails in association with a second dermatologic feature has been labeled as pachyonychia congenita in case reports, further muddying the diagnostic waters.

**DERMATOLOGIC FEATURES**

**MAJOR.** The fingernails and toenails are thickened, friable, and darkened. Distal involvement may be greater than proximal involvement. Nail changes can be seen at birth and usually present within the first year of life. Although involvement is often symmetric, not all nails are necessarily involved. The toenails and fingernails of

Figure 3.43. (A–C) Varying nail changes in individuals with pachyonychia congenita. (C, courtesy of Dr. P. Fleckman, Seattle, Washington.)
the thumbs and index fingers tend to be more severely involved. The distal nail bed, as well as the nail plate, is also thickened. Nails may be shed; new nails are also dystrophic.

Hyperkeratosis and hyperhidrosis of the palms and soles are common.

Follicular hyperkeratosis, primarily of the elbows and knees, develops. More widespread distribution of these skin lesions can also occur.

Minor. There are occasional reports of blistering of the soles.

Epidermal inclusion cysts, sebaceous cysts, and cylindromas have been reported. There is some confusion about the histopathology of these lesions in pachyonychia congenita, and there may be overlap. These skin changes occur later in childhood and adult life and are typical of Jackson-Lawler (PC-2).

Alopecia, which may be congenital or occur later, and/or thinning and loss of sheen of the hair are described in some patients, typically in those with Jackson-Lawler (PC-2). Coarseness of eyebrows and body hair, with pilo torti of the hair shafts, has been described as well in this group.

Recurrent hyperpigmentation of the neck and axillae can occur and may represent a distinct subtype.

Hidradenitis suppurativa was described in one family.

ASSOCIATED ABNORMALITIES

Oral leukoplakia of the mucosa of the mouth and on the tongue is histologically similar to white sponge nevus. Malignant degeneration has not been reported. This feature is primarily seen in the Jadassohn-Lewandowsky form (PC-1) and is absent in the Jackson-Lawler variant (PC-2).

Natal teeth are occasionally present, as are malformed teeth, primarily in the Jackson-Lawler variant (PC-2).

The evidence for association with mental retardation in the literature is not compelling, and I suspect that this is not a true feature of pachyonychia congenita.

HISTOPATHOLOGY

Light. The nail plate and proximal nail matrix are normal. The nail bed shows marked hyperkeratosis. The distal nail matrix is hypertrophic. There is some disagreement about microscopic features.

Oral mucosa: Acanthosis, parakeratosis, and intracellular vacuolization are seen.

Hyperkeratosis: Hyperkeratosis, parakeratosis, acanthosis, and a moderate increase in
Figure 3.45. Nail changes and focal hyperkeratosis of palm and thumb. (Courtesy of Dr. P. Fleckman, Seattle, Washington.)

Figure 3.46. Hyperkeratosis of the sole. (Courtesy of Dr. P. Fleckman, Seattle, Washington.)

Figure 3.47. Epidermal inclusion cysts.

EM. Dense aggregation of tonofilaments at the periphery of the basal keratinocytes and abnormal keratohyalin have been described. These changes are not specific.

BASIC DEFECT

A mutation in K17 has been demonstrated in one family with Jackson-Lawler (PC-2). Heterozygosity for a nonsense mutation in K16 has been found in one pedigree with Jadassohn-Lewandowsky (PC-1); heterozygosity for a deletion in K6a in another.

TREATMENT

Treatment is primarily symptomatic. Emollients and keratolytics (e.g., Lac-Hydrin, glycolic acid, salicylic acid) can be used for the hyperkeratoses. Routine grinding of the nail plates can keep their interference with function at a minimum, but the nails remain cosmetically dystrophic. If limitation of hand function becomes unacceptable, ablation of the nail matrix is the only permanent effective therapy for the dystrophic nails. There has been mixed success with treatment with oral retinoids.

MODE OF INHERITANCE

Autosomal dominant. Both Jackson-Lawler (PC-2) and Jadassohn-Lewandowsky (PC-1)
Disorders of Epidermal Appendages

types have been mapped to the type I keratin cluster on 17q. KRT6 resides on 12q.

PRENATAL DIAGNOSIS

Possible in some instances by mutation or linkage analysis.

DIFFERENTIAL DIAGNOSIS

The involvement of the nails in pachyonychia congenita can often be distal and may be clinically indistinguishable from fungal infection on the basis of nail changes alone. KOH and fungal cultures are always appropriate.

The nail changes of dyskeratosis congenita (MIM:305000) are quite different from those of pachyonychia congenita, more similar to those of lichen planus, with hypoplasia and pterygia of the nails rather than thickening.

Onychogryphosis, the development of claw or talon nails, is usually acquired. One family with claw-like nail changes and plantar hyperkeratoses is described by McKusick (MIM: 164680). One individual had dry, coarse hair. Although five generations were involved, no male-to-male transmission occurred.

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SELECTED BIBLIOGRAPHY


Feinstein et al. (1988), Schonfeld (1980), and Sivasundaram et al. (1985) are three reports and reviews of pachyonychia congenita with distinct classification schemes. Everyone agrees on type I, but it is a free-for-all from there.


Authors describe the mucosal changes associated with the disorder as hyperkeratotic, in contrast to the dyskeratosis of true leukoplakia.


A report of a family with natal teeth, blistering of the soles, multiple skin cysts, follicular hyperkeratoses, and pachyonychia congenita. This family did not have leukoplakia.


Presents mutation data and correlates clinical differences between the forms of pachyonychia congenita with specific mutations. K16 and K17 are acidic keratins that are expressed to different degrees in different tissues. K16 alterations might affect oral mucosa more (where it is expressed in greater amounts), whereas K17 alterations might be more likely to lead to epidermal cyst formation, as its expression predominates in the infundibulum of sweat glands.


In this report there was reevaluation of three of the members of the Jackson-Lawler family.