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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: A Four Generation Pedigree

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Pachyonychia congenita is a rare genodermatosis characterized by symmetrical thickening and discoloration of the nails with a wedge-shaped, pinched-up, or claw-like appearance. Subungual hyperkeratosis results in a lifting up of the free edge of the nail. Nail changes may be seen alone or in combination with a variety of other cutaneous findings. The authors present a kindred with fifteen cases of pachyonychia congenita in four generations, in Lebanon County, Pennsylvania.

Pachyonychia congenita is an uncommon genodermatosis affecting the nails and other ectodermal tissues, first described by Jadasshon and Lewandowsky in 1906.1 This condition is characterized by symmetrical thickening of all nails with subungual hyperkeratosis and elevation of the distal nail plate. The nails may appear wedge-shaped, pinched-up, or claw-like, and generally display a yellow to brown discoloration. Often, paronychia and shedding of the nails are observed. Pachyonychia congenita is usually inherited as an autosomal dominant trait. In most forms of this disorder, nail changes are present at birth or appear within the first six months of life.2-4

Nail involvement affects the hands as well as the feet and may be seen alone or in combination with an assortment of other cutaneous findings. When associated with other symptoms, the term pachyonychia congenita syndrome best describes the scope of different symptoms.2 Associated findings may include hyperkeratosis and hyperhidrosis of the palms and soles, follicular keratoses affecting the knees or elbows, and painful bullous lesions proximate to hyperkeratotic areas. Leukokeratosis of oral, anal, and laryngeal mucoza may also be present with partial or complete alopecia or sparse, dry, kinky hair.2-4 Laryngeal obstruction, hoarseness, severe dental caries, joint hypermobility, early onset of large joint arthritis, and patent ductus arteriosus have also been reported in patients with the pachyonychia congenita syndrome.5-7 The most troublesome effects of this condition appear to be the deformed nails and bullae. The dystrophic nails are often unsightly, painful, and may interfere with manual dexterity.

A less frequent variant of pachyonychia congenita, the Jackson-Lawler form, was reported in 1951. In this form of the syndrome, erupted teeth at birth and epidermoid cysts are present without oral mucous membrane involvement.6-9 Other extremely rare forms of pachyonychia congenita are associated with leukokeratosis of the cornea and cutaneous amyloidosis with hyperpigmented patches.10

Several studies have identified the transmission of pachyonychia congenita as a simple autosomal Mendelian dominant trait.2,3,5,9 However, there have also been reports of an autosomal recessive mode of inheritance in children who were the product of consanguineous marriages.11,12

Nail changes are the most highly penetrant part of pachyonychia congenita syndrome and may represent the earliest manifestations of this disorder. Haber and Rose reported an unusual case in which there was a recessive mode of inheritance with late development of nail changes at approximately twelve years of age.12 Moldenhauer and Ernst, in their review of ninety-three cases, reported that nail changes were absent in only three patients. They found that 97 percent of the patients demonstrated nail involvement, 72 percent had plantar keratosis, 59 percent had follicular keratosis, and 57 percent demonstrated leukokeratosis of the oral mucosa.13

Patients with pachyonychia congenita may present with a variety of complaints ranging from mild cosmetic concerns to painful blisters and/or life-threatening respiratory distress.7 The diagnosis may need to be differentiated from epidermolysis bullosa, hereditary onychogryphosis, oral thrush, or other genetic hyperkeratotic syndromes. The completely expressed syndrome is rarely mistaken for anything else.

The basic pathogenetic process in pachyonychia congenita has not been elucidated. Thomsen and associates reported on biopsy specimens from the fingers of a thirty-seven-year-old woman with pachyonychia congenita. A specimen from the distal nail bed demonstrated hyperkeratosis, irregular acanthosis, papillomatosis, and focal areas of benign dyskeratosis. They found the proximal nail fold, matrix, and proximal portion of the nail bed to be normal on histologic examination. They did, however, report finding a granular layer in the distal portion of the nail bed, which consisted of keratoxyline granules of varying sizes and vacuolated keratinocytes.14 Normally the nail bed does not

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FIGURE 1. Top: Symmetrical dystrophic changes of the fingernails. The nails are yellow-gray and appear claw-like, pinched together at the distal portion with mild elevation of the free edge. Bottom: Symmetrical dystrophic changes of the toenails. The lesser toenails are yellow with longitudinal white striations. The hallux nail plates are thickened, green to brown, and striated.

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have a granular layer. Forslind and associates reported the pathologic process to be localized in the matrix of the nail bed (the ventral nail plate).\textsuperscript{15}

Treatment of the various components of pachyonychia congenita has been generally unrewarding. Nail involvement has been treated surgically with procedures ranging from simple avulsion of the nail plate, to avulsion of the nail plate and excision of the nail bed and matrix, to amputation of the distal phalanx of each finger.\textsuperscript{14,16} Mechanical reduction of the nails with a drill and burr is mentioned by Langford as effective for temporary relief of pain and deformity.\textsuperscript{17} Topical keratolytic agents, vitamins A and E, x-ray therapy, and isotretinoin have all been tried, with minimal success in changing the pattern of abnormal keratinization.\textsuperscript{18}

**Case Report**

In this report, we present a fifteen member, four generation pedigree of pachyonychia congenita based entirely on nail involvement. The propositus was a thirty-two-year-old white man who presented with a complaint of recurrent infected, acne-like cysts on his neck, which had been present in varying degrees of severity for approximately ten years. His neck lesions were described as small follicles showing comedo obstruction and cyst formation. These cystic lesions were consistent with those reported to be associated with pachyonychia congenita syndrome.\textsuperscript{2} He had no lesions of the oral
mucosa. An incidental finding was thickening of all nails on the hands and feet, which the patient reported as present since birth (Figure 1). The fingernails were symmetrically dystrophic, claw-like, and opaque with a yellow-grayish hue. They were pinched up in appearance, with subungual hyperkeratosis pushing up the free edge of the nail. All lesser toenails were dystrophic and yellow with longitudinal white striations. The great toenails were green to brown, striated, deviated laterally, and thickened to a greater degree.

He detailed a family history of deformed nails and tender plantar calluses affecting male and female members of four generations of his family. He traced the condition to his grandmother (AB) who was born in Germany. AB gave birth to seven children, four boys and three girls. Two of the boys (HB and MB) were reported to have pachyonychia congenita (Figures 2 and 3). HB had fifteen children, with six affected siblings: four boys and two girls. The propositus was a member of this family group. His uncle, MB, had three children, one boy and two girls, with only one brother affected (SB) (Figure 4).

SB and his two children were presented at dermatology grand rounds, where a more detailed family history was elaborated with the assistance of their mother. SB and both of his children were examined and found to have nail involvement. In addition, the boy was found to have sparse, thin hair.

The four generation pedigree for this family is intriguing due to its size, spanning four generations. Of all family members, fifteen were identified as having pachyonychia congenita. The family was not receptive to requests for additional information or examination, which might have revealed further findings associated with pachyonychia syndrome.

**Comments**

We have presented a kindred with fifteen cases of pachyonychia congenita in four generations. All members affected have thickened nails and some (by history) have plantar keratoses. The propositus presented with cystic lesions on his neck but denied any history of neonatal teeth. The propositus, his cousin SB, and his cousin’s children were the only family members we examined ourselves. All information on other family members was gathered by history, and appears to be less than complete. The ratio of affected to unaffected offspring from affected parents (14:36) is somewhat less than the 50:50 probability in an autosomal dominant inheritance pattern. There were not an equal number of affected male and female subjects (nine to six). This discrepancy is thought to be related to an insufficient family history. It is unfortunate that this kindred chose to be private and to limit its cooperation with us. They refused to allow us to interview other family members and to complete a questionnaire designed to identify the presence of signs and symptoms associated with pachyonychia congenita syndrome.

The primary concern of the patients in this report was
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FIGURE 4. Pachyonychia congenita affecting the propositus' cousin and his two children, a boy and girl.