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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.
Autosomal Recessive Pachyonychia Congenita

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We report the second and third cases of pachyonychia congenita inherited as an autosomal recessive disorder. Our cases were unusual, with the fingernails showing yellowish-brown color and appearing clinically as Terry's nails. These patients were originally diagnosed as having epidermolysis bullosa simplex because of a history of a lifelong blistering disorder. The clinical features and surface of pachyonychia congenita, as well as the factors for the long delay in diagnosis of our cases, are discussed.

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Pachyonychia congenita (PC) has typically been reported to be an autosomal dominantly inherited condition. We have recently seen two brothers with pachyonychia congenita who were inherited in an autosomal recessive manner.

REPORT OF CASES

Case 1—A 23-year-old man presented with a diagnosis of epidermolysis bullosa simplex that had been made in infancy. At the age of 3 months, he developed blisters, usually on his hands and feet but also occasionally on other parts of his body, which healed without scarring. The shedding of his hands and feet was worse in the summer. The blistering problem was much worse during childhood but has gradually improved over the years, and at the present time, blisters are extremely infrequent. Hair has never occurred in the patient's mouth. He has been treated over the years by several dermatologists who were involved in the diagnosis. Therapy with oral vitamin E was of no benefit.

At the age of 3 months, the patient was noted to have a thickening of the tongue and also of the buccal mucosa. These whitish areas varied in severity but never completely cleared. A chronic angular cheilitis has been a problem, and treatment with topical betamethasone 17-valerate cream has been helpful. Discrete yellowish thickenings appeared on the patient's palms when he was 9 years old. A more diffuse yellowish thickening has occurred on both soles. The patient's fingernails have been noted to have a whitish appearance since he was 12 years old and have not changed significantly with time. His teeth have always been normal, and there is no history of ocular problems.

The patient has one brother who is also affected in the same manner. Two sisters and a third brother have no similar problems, and both parents are normal. There is a strong history of consanguinity between the parents, which is discussed below in detail under "Genetics."

Physical examination revealed one intact bulla on the plantar surface of the fifth toe of the left foot. The fingernails were remarkable for a proximal area of leukonychia with obliteration of the lunulae and 3 to 4 mm of normal pink distal nail bed, giving the fingernails an appearance of Terry's nails (Fig 1). In a few fingernails, more of the distal nailbed appeared normal, and these nails resembled half-and-half nails. No onycholysis was seen in the fingernails. The toenails showed mild onycho-

lysis, with slight elevation of the nail plates by a small amount of yellowish subungual debris. There were macer-
ated areas in the webbed spaces of the toes. A punctate keratoderma with 2- to 3-mm yellowish firm papules was seen on the palms bilaterally, while the soles displayed a diffuse yellowish keratoderma. Hyperkeratotic papules were seen on the dorsa of the toes and fingers. The patient's tongue had a thick well-demarcated whitish coating on the dorsum (Fig 2), with whitish areas on both buccal mucosal surfaces. Angular cheilitis was evident bilaterally. The patient's teeth appeared normal, and no cysts were seen on his skin. He has been assessed by an orthodontologist and has no evidence of any normal abnormality.

The constellation of features, with leukokeratosis of the tongue and buccal mucosa, keratoderma of the palms and soles, keratotic papules on the tongues and fingers, bunion, and uncorrected nail changes, was felt to be compatible with a diagnosis of PC rather than epidermolysis bullosa simplex.

Laboratory studies revealed a normal complete blood cell count and normal hepatic and renal functions. A swab
from the mouth yielded a few yeast cells on culture. Fungal scraping from the right first and fourth toenails yielded Trichophyton mentagrophytes. Both T. mentagrophytes and Corynebacterium minutissimum were isolated from the cultures of the webbed spaces of the toes. No fungus grew on cultures of the fingernails.

Case 2.—The 25-year-old brother of patient 1 has had similar clinical features and was believed to have epidermolysis bullosa simplex. At the age of 3 months, he was noted to have a whitish coating on his tongue. Blistering on his hands and feet developed around the age of 3 years, but are very infrequent at the present time. The yellowish thickenings of his palms and soles were noted at the age of 10 years. The patient has also had white nails for as long as he can remember, but the exact age of onset is uncertain.

Physical examination revealed no intact blisters but one erosion on the dorsum of the right big toe. All fingernails showed an almost total leukonychia, except for the distal 2 to 3 mm, which appeared pink, giving the nails the appearance of Terry's nails. There was mild onycholysis, with a small amount of subungual debris of the fingernails. The toenails appeared yellowish, with some distal onycholysis and subungual hyperkeratosis (Fig 3). A punctate keratoderma of the palms was evident, with a diffuse yellowish keratoderma of the soles. Many hyperkeratotic papules were present on the dorsum of the toes and fingers, with several follicular hyperkeratotic papules present on the left knee (Fig 4). An extensive whitish plaque covered the dorsum of the patient's tongue. His teeth were within normal limits. The clinical diagnosis was PC.

PATHOLOGY

A skin biopsy specimen was obtained from the dorsum of one foot of patients 1 and 2 after preheating the skin in water at 40°C and then rubbing the area for five minutes with a cotton swab, to rule out the possibility of epidermolysis bullosa coexisting with PC. Both skin biopsy specimens were examined under the electron microscope. The specimen from patient 1 showed no evidence of bulla formation and no pathologic change. The specimen from patient 2 showed a separation in the mid epidermis associated with some degenerative changes of the adjacent keratinocytes and was believed to be compatible with a friction blister.
more diffuse. The granular layer of the epidermis was absent below the parakeratotic area (Fig 5). No actual perforation into the dermis was seen.

GENETICS

There is a strong history of consanguinity in this family. The parents of the two affected children are first cousins once removed on one side and second cousins on the other side. The parents’ families originate from the same small town in southern Italy. There is no family history of PC. Both parents were examined and were found to have no clinical features of this condition. The family’s pedigree is shown in Fig 6. The parents’ coefficient of kinship was determined to be 3/64.

COMMENT

Pachyonychia congenita is a rare genodermatosis that was first described by Jadassohn and Lewandowsky in 1906. They described a patient with hypertrichosis, palmoplantar keratosis, hyperhidrosis, blistering of the feet during the summer, and leukokeratosis of the tongue.

In 1936, Kumar and Loos attempted to classify cases of PC into three types: Type I consists of the typical nail changes as well as symmetrical keratosis of the hands and feet and follicular keratosis of the scalp. Type II (Riehl type) is like type I, but, in addition, oral leukokeratosis is seen. Type III includes the features of type I, as well as corneal keratopathy.

Recently Schöndorf divided the PC syndrome into three types. Type I (Jadassohn-Lewandowsky syndrome) consists of the following: (1) symmetrical hard thickening of all finger and toenails; (2) keratosis palmaris et plantaris; (3) palmar and plantar hyperhidrosis; (4) follicular keratosis, especially on knees and elbows; (5) blister formation, especially
under and around calliologies: (6) leukokeratosis of the oral mucosa and occasionally of the laryngeal mucosa, which can produce hoarseness; and (7) hair abnormalities. Type II Jackson-Stellmack syndrome has the same clinical features as type 1, but in addition, nodal teeth and multiple cysts (ectodysplasia) multiply on the upper palate. Leukokeratosis of the oral mucosa does not occur. Type 3 (Scheiffer-Brinanner syndrome) has the same features as type 1, with the addition of associated leukokeratosis of the cornea.

Pachyonychia congenita is transmitted as a simple mendelian dominant disorder with variable expressivity. There are many family studies in the literature to support a dominant inheritance pattern, and it appears to be due to two types of PC as autosomal dominants. To our knowledge, there is only one report of PC with autosomal recessive inheritance in the literature. This was a 4-year-old Malay girl with type 1 (Jadassohn-Lewandowsky syndrome) PC. The child was the product of a marriage between two first cousins, and, because of this, the PC was believed to be inherited as a recessive trait. However, the authors acknowledge the possibility that a spontaneous mutation could have occurred.

To our knowledge, our patients represent the second report and the second and third cases of PC inherited in an autosomal recessive manner. The history of consanguinity, as well as the occurrence of two affected brothers in a family of five children with normal parents, makes autosomal recessive inheritance extremely likely. Identical spontaneous mutations in brothers are very unlikely. A germ-cell mutation in one of the mother’s autosomes or X chromosomes is a possible explanation for two affected siblings. However, this is an extremely rare occurrence and, in view of the history of consanguinity, autosomal recessive inheritance is probable.

There are several other aspects of our cases that are noteworthy. Our patients had most of the usual features of Schüle-Schüle type 1 PC, except for the typical nail abnormalities. Clinically in PC, the nail bed becomes hyperkeratotic and elevates the nail plate. The nail plate appears yellow or brown and assumes a grooved or longitudinal pattern. The nail bed and nail matrix are usually normal. In our cases, the nail abnormalities were very mild. The nail plate was yellowish-white, and slight longitudinal grooves were present. The nail bed and nail matrix were normal. The presence of X-ray studies in our cases could have been helpful in our evaluation. The nail abnormalities were not as severe as those reported in the literature.

The presence of T. mentagrophytes in two nails of the right foot in case 1 is interpreted as a secondary dermatophyte infection in an already present normal nail. A tongue swab from the patient also yielded a few yeast cells. An associated Candida albicans infective superinfection on the leukokeratosis of the tongue and oral mucosa in PC has been previously described.

Several cases of PC have been previously reported as presenting as epidermolysis bullosa. The reason for this is not understood, but one possible explanation is that the skin, nails, and hair abnormalities in PC are not specific to this disease.

It should be remembered that, although abnormal nails are characteristic for PC, they are not necessary for the diagnosis of this syndrome. Moldenhauer and Ernst reviewed 90 cases of PC and found that the nails were absent in three cases. In PC, the nails are usually normal at birth but become progressively discolored and thinned within the first year of life. The nails in our autosomal recessively inherited patients were remarkable because of the unusual clinical appearance and the late age of development of abnormal nails around 12 years of age. The leukokeratosis of the fingernails, with its appearance resembling Terry’s nails, has not to our knowledge been previously reported in PC.

Whether these unusual nail changes are a specific feature of autosomal recessive PC or merely represent a variation of the feature seen in other cases is unknown. Future case reports of autosomal recessively inherited cases are needed to answer this question. In the only other reported case of autosomal recessive PC, the nails were described as markedly hyperkeratotic, deformed, and dystrophic, an appearance similar to that of dominantly inherited cases.

It appears that a spectrum of nail changes can occur in PC, ranging from obvious clinical abnormality, as demonstrated in the study of Moldenhauer and Ernst, to a spectrum of nail changes where patients may be described as having a delay in appreciation of a nail abnormality being present, in view of the subnails of the nail changes.

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lar portion of a hair follicle. Previous reports of the pathology of these papules have shown hyperkeratosis without parakeratosis, a thick stratum granulosum, and acanthosis. There is a previous report of a keratotic papule in a patient with PC showing a cornoid lamella. Also, one report described the simultaneous occurrence of PC and Kyrie's disease in the same patient, because the pathology revealed large orthokeratotic and parakeratotic plugs penetrating the epidermis to the point of breaking into the dermis. We believe these two reports represent a phenomenon similar to the parakeratotic plug shown on the biopsy specimen of our patient 2 and is simply a manifestation of the widespread abnormality of keratinization that occurs in PC.

References


