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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 with cutaneous amyloidosis and hyperpigmentation—a distinct variant


Two kindreds manifesting an unusual form of pachyonychia congenita are described. Clinical involvement consists of nail dystrophy, which tends to improve with age, and moderate palmpoplantar hyperkeratosis. In addition, all affected members show a characteristic pattern of cutaneous hyperpigmentation, which resembles macular amyloidosis around the neck and waist, but which confers a dappled appearance to the axillae, popliteal fossae, thighs, buttocks, and lower aspect of the abdomen. With advancing age the pigmentation fades. Histologic and ultrastructural examination of the hyperpigmented skin has revealed pigmentary incontinence and deposition of amyloid within the papillary dermis. These features appear to constitute a distinct variant of pachyonychia congenita. (J Am Acad Dermatol 1987;16:935-40.)

Pachyonychia congenita is a rare genodermatosis in which combinations of ectodermal defects serve to distinguish two major forms of the condition. The Jadassohn-Lewandowsky type1 is characterized by pachyonychia, palmoplantar hyperkeratosis and hyperhidrosis, a predisposition to plantar friction blisters, follicular keratoses, and oral leukokeratosis. The less common Jackson-Lawler form2,3 is similar but lacks the oral mucous membrane changes and possesses the additional features of natal teeth and cutaneous cysts. Although pachyonychia congenita is usually inherited in an autosomal dominant fashion, a recessive pattern of inheritance has recently been described.4

A single case of pachyonychia congenita associated with a distinctive pattern of hyperpigmentation was described by Buckley and Cassuto in 1962.5 The subjects of the present report belong to two pedigrees manifesting the same unusual pigmentary anomaly, unequivocally inherited in an autosomal dominant manner (Fig. 1), thus establishing this association as another distinct variant of pachyonychia congenita. Furthermore, light and electron microscopic examination of the pigmented skin has revealed the deposition of amyloid within the dermis.

CASE REPORTS

Case 1. A 29-year-old white woman (III-4, pedigree 1; Fig. 1) had abnormal fingernails and toenails since childhood. A pronounced convex transverse curvature of the nails developed in infancy; the nails gradually became thickened and discolored over the first few years of life, sparing only the lateral two toenails on each foot. The nail plates had frequently been shed, often as a result of trauma, a tendency that continued into adult life, with regrowth occurring in a dystrophic fashion. The appearance of her nails, however, gradually improved on reaching adulthood. From an early age she suffered with a moderate degree of palmpoplantar hyperkeratosis, associated with dryness of the palms and soles, and mild thickening of the skin over the elbows and knees. The only other clinical feature of

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Accepted for publication Oct. 30, 1986.
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note has been the presence of asymptomatic macular hyperpigmentation, commencing in childhood and involving the neck, axillae, trunk, thighs, and popliteal fossae. The pigmented changes around the neck and waist have faded and virtually disappeared in recent years, leaving discrete areas of hyperpigmentation involving the axillae (Fig. 2), lower aspect of the abdomen, and legs.

Case 2. A 17-year-old young man (III-6, pedigree 1; Fig. 1), the brother of Patient 1, had a similar history to that of his sister. The nail dystrophy was identical, with involvement of all his nails (Fig. 3) except the lateral pair on each foot. In the axillae and popliteal fossae, the lower aspect of the abdomen, and on the buttocks and thighs the skin was dappled, like that of his sister, but around the neck and waist it was diffusely hyperpigmented and in areas had a rippled pattern (Fig. 4).

Case 3. A 59-year-old woman (II-3, pedigree 1; Fig. 1), the mother of Patients 1 and 2, had a history of nail dystrophy and hyperpigmentation similar to that affecting her children. However, by middle adult life the nail changes had become minimal and the skin discoloration had gradually faded. Examination revealed only mild thickening of the nail plates and slight hyperkeratosis of the soles, with no evidence of hyperpigmentation.

Case 4. A 3-year-old child (IV-7, pedigree 1; Fig. 1), the proband and the son of Patient 1, was following a similar clinical course to the other affected members of his family. Since the age of 2 his toenails had become mildly dystrophic, and he had, in his fourth year, developed dappling within his axillae and over the inner aspect of his thighs, together with diffusely hyperpigmented skin around his waist and neck, giving an unwashed appearance.

Case 5. A 25-year-old man (V-1, pedigree 2; Fig. 1), the proband of pedigree 2, had possessed, from the age of 2 years, thickened, wedge-shaped fingernails and toenails (Fig. 5). They had occasionally been shed, usually following trauma, but had always regrown in a similar dystrophic form. Since reaching adulthood, the appearance of the nails had gradually but markedly improved. He had also suffered with a moderate degree of palmar plantar keratoderma, a mild tendency during childhood to plantar blister formation, and dryness of the palms and soles. Asymptomatic, cutaneous hyperpigmentation, involving the neck, trunk, axillae, and thighs, developed at approximately 3 years of age, and, although on the neck it had virtually resolved, it persisted on the trunk.

Lab results (exclusive of data presented in Table 1) showed no abnormality.

In Patient 2, the globulin fraction of the serum protein was elevated.

Specific details regarding the cases (Cases 1 and 2) have been omitted.
Fig. 3. Case 2 (III-6, pedigree 1). Pachyonychia with pronounced transverse curvature. The palmar skin is dry and thickened.

Fig. 4. Case 2. Diffuse and rippled pigmentation around the neck.

sisted elsewhere. Around the neck it was rippled in appearance (Fig. 6), but in other body regions it consisted of discrete macules, up to 1 cm in diameter.

Laboratory investigations. Mycological examination of the nails in Patients 1, 2, and 5 was negative. In Patients 1 and 2, a full blood picture and immunoglobulin electrophoresis were normal, and Bence-Jones proteinuria was absent.

Specimens of hyperpigmented skin were obtained, with informed consent, from the axillae (Patients 1 and 2), the neck (Patients 2 and 5—in Patient 5, from material obtained at age 12 years), and the flank (Patient 5). Sections stained with hematoxylin and eosin revealed the presence of numerous melanophages (confirmed by a positive Masson-Fontana stain) within the papillary dermis. There was an exaggeration of the rete ridge pattern and foci of mildly expanded dermal papillae, which contained aggregates of an amorphous eosinophilic material. Special stains, including Congo red, methyl violet, periodic acid–Schiff, van Gieson, and thioflavine T, showed this material to have the staining characteristics of amyloid, including green
Fig. 5. Case 5 (V-1, pedigree 2). Wedge-shaped fingernails at the age of 12 years.

Fig. 6. Case 5. Rippled pigmentation around the neck at 12 years of age.

Fig. 7. Case 2. Light micrograph of a section of pigmented skin from the axilla, showing dermal melanophages and the scalloped appearance of the dermoepidermal junction resulting from the deposits of amyloid immediately beneath. (Hematoxylin-eosin stain; original magnification, ×100.)

skin from the axilla of Patient 1, the neck of Patient 2, and the flank of Patient 5 confirmed in each the presence of accumulations of material beneath the dermoepidermal junction (Fig. 8), consisting of a meshwork of interfacing, nonbranching fibrils, typical of amyloid. Amyloid deposition was not apparent around blood vessels or nerves but was frequently associated with the melanosome-engorged macrophages.

DISCUSSION

There appears little doubt that the type of pachyonychia congenita described by Buckley and Cassuto is a distinct entity. Affected individuals, who are otherwise healthy, possess normal nails at birth, which, during the early years of childhood, become thickened and discolored and are intermittently shed. An unusual feature of the nail dystrophy is the gradual resolution in early adulthood. Apart from palmoplantar keratoderma and
Patient 2, the presence of amyloid in the dermoepidermal shwark of the nail, and the blood vessels of the nail, all contribute to the coarseness of the skin over extensor surfaces, this variant appears to lack features associated with the other forms of pachyonychia congenita, such as a pronounced susceptibility to plantar friction blisters, hyperhidrosis, keratotic papules, hair abnormalities, natal teeth, and cutaneous cysts. Although the original description referred to oral leukoplakia and to corneal opacities, neither abnormality was evident in these five patients.

Cutaneous hyperpigmentation is an unusual occurrence in pachyonychia congenita. A patient reported by Schäfer had increased pigmentation involving the axillae, popliteal fossae, and buttocks, but also exhibited many of the features of the Jadassohn-Lewandowsky type. In the Buckley and Cassuto form, the pigimentary changes commence during childhood and involve principally the neck, axillae, trunk, buttocks, thighs, and popliteal fossae. Around the neck and waist the pigmentary changes tend to be diffuse or mildly rippled, reminiscent of macular amyloidosis, but elsewhere it is speckled. Between early adulthood and middle age the hyperpigmentation gradually fades and disappears. The pigmented areas are the result of pigimentary incontinence associated with the deposition of amyloid in the papillary dermis. It seems reasonable to presume, as the pachyonychia congenita syndrome represents a constellation of ectodermal developmental anomalies, that the amyloid material originates from the keratin of epidermal cells, as it probably does in macular and lichen amyloidosis.

The association of pachyonychia congenita with cutaneous amyloidosis has not been recorded previously, apart from a report concerning macular amyloidosis associated with a familial nail dystrophy, which would seem to describe this same unusual pachyonychia congenita phenotype.
PIBI(D)S syndrome—trichothiodystrophy with xeroderma pigmentosum (group D) mutation

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An autosomal recessive syndrome is described that associates extreme photosensitivity with a defect of the deoxyribonucleic acid (DNA) excision repair system, mild noncongenital ichthyosis, brittle cystine-deficient hair, impaired intelligence, neurologic disorders, and short stature. A curious very sociable behavior, cataract and retinal dystrophy, recurrent infections, and unusual face are additional features. Fertility may be decreased. This syndrome is related to xeroderma pigmentosum complementation group D but differs from it in the absence of skin tumors, at least in the first two decades of life. (J AM ACAD DERMATOL 1987;16:940-7.)

The term trichothiodystrophy has been used¹ to define a rare recessive symptom complex comprising brittle and sulfur-deficient hair, impaired intelligence, decreased fertility, and short stature; otherwise named BIDS syndrome.² Some of the patients with trichothiodystrophy who also exhibit congenital ichthyosis have been grouped under the acronym IBIDS³ and later tentatively assimilated to an early description of Tay.⁴

In 1983 we described briefly a patient with trichothiodystrophy who complained of extreme photosensitivity, and, on the basis of other cases...