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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.
A Case of Pachyonychia Congenita with Oral Leukoplakia and Steatocystoma Multiplex

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Abstract

Pachyonychia congenita (PC) is an uncommon autosomal dominant genodermatosis affecting the nails and other ectodermal tissues. The most striking features are symmetrically thickened dysmorphic nails and hyperkeratotic skin lesions.

We report a case of pachyonychia congenita in a 30-year-old male patient who had thickening and gray-brown discoloration of all nails and many nodules on his back and neck. He also had hyperkeratotic skin lesions on both feet. His tongue had irregularly-shaped, whitish plaques. Histology of these nodules revealed the characteristic features of steatocystoma multiplex. After treatment with oral retinoic acid, his hyperkeratotic skin lesions improved.

Key words: Pachyonychia congenita; steatocystoma multiplex

Introduction

Pachyonychia congenita is an uncommon genodermatosis of abnormal keratinization initially described by Jadassohn and Lewandowsky. Characteristic yellow-brown nails, marked distal subungual hyperkeratosis, and elevation of the nail plate are the primary diagnostic findings of this syndrome. Other minor diagnostic criteria include palmoplantar keratoderma, leukokeratosis oris, follicular keratosis, bullae on the palms and soles, and laryngeal leukokeratosis. Sometimes this syndrome is associated with epidermal cysts, acniform lesions, and steatocystoma multiplex.

Herein, we report a case of pachyonychia congenita associated with steatocystoma multiplex.

Fig. 1. Symmetrically thickened and elevated fingernails and toenails

Case Report

A 30-year-old male patient visited our department for the evaluation of thick nails, hyperkeratotic skin lesions on both feet, and asymptomatic multiple nodules in his back. Thickening of the nails has been present as long as the patient could remember. Since the age of seven years, he has complained of hyperkeratotic skin lesions on both hands and feet, with pain on walking. He also had suffered from painful blistering on his soles, especially during summer.
Asymptomatic cystic lesions on back were observed in his late twenties. Family history was non-contributory. A physical examination revealed typical symmetrical thickening of all fingernails and toenails (Fig. 1). Yellowish plaques with fissures on both soles were also observed (Fig. 2). His tongue showed irregularly-shaped, white plaques (Fig. 5). On his back and neck, there were numerous, skin-colored to yellowish nodules of variable size (Fig. 4). There was no evidence of ocular lesions. It was not known whether natal or neonatal teeth were present.

The following studies were normal or negative: complete blood cell count, urine analysis, liver function test, blood urea nitrogen, creatinine, lipid profile, chest PA, KOH and cultures for fungus from nails and whitish plaques on the tongue.
Skin biopsies were taken from the hyperkeratotic plaque on his sole and a skin-colored nodule on his back. The former showed marked hyperkeratosis and acanthosis (Fig. 5). The latter revealed a cystic lesion lined by stratified squamous epithelium and sebaceous glands, which was consistent with steatocystoma multiplex (Fig. 6).

He was given oral acitretin (30 mg/day), and the hyperkeratotic skin lesions on both soles improved. In addition, we also intralesionally injected steroid to improve the nail lesions, but this had no effect.

Discussion

Pachyonychia congenita is a genetically determined ectodermal dysplasia of autosomal dominant inheritance with variable expression and a high degree of penetrance, in which the main phenotypic characteristic is hypertrophic nail dystrophy (1, 2). An autosomal recessive inheritance has also been suggested in some cases (3, 4). It was first described by Jadassohn and Lewandowsky in 1906 association with palmoplantar keratoderma and ectodermal defects (5). Since then, more than 150 examined cases have been reported in the literature.

The most striking features are symmetrically hard thickening of all fingernails and toenails, which appears at birth or soon after. Steiglitz and Centerwall (6) found that approximately 97% of cases reviewed have dystrophic nails with all fingernails and toenails affected. Other cutaneous manifestations include keratosis palmoplantaris, follicular keratosis, blister formation, and leukokeratosis of the oral mucosa, hair abnormalities, and palmar and plantar hyperhidrosis.

Schönfeld (1) has divided pachyonychia congenita into three types, the above described one being most common and designated Type I (Jadassohn-Lewandowsky type). Type II (Jackson-Lawler type) has the same features as Type I, but has the distinctive features of natal teeth and steatocystoma multiplex. Oral leukokeratoses are not generally observed. Type III (Schafer-Brunauer type) has the clinical findings of Type I plus leukokeratosis of the corneas. However a marked division into types does not seem justifiable because of their strong overlapping. The differences could be explained as variable expressions. Interestingly, our patient shows both oral leukoplakia and steatocystoma multiplex. The former can be seen in PC-1, but is not present in PC-2, and the latter is a distinctive feature of PC-2, but not of PC-1. This interesting combination might be based on a novel molecular mechanism.

The nail changes may appear at birth or soon after. The nails are thick, distally pigmented, and dystrophic. The distal portion may produce a subungual keratinous mass, which pushes the nail plate upward; when severe, fine movements of the fingers may be impaired (7, 8). In some cases, these nail changes may be the only abnormality (9, 10). Our patient had typical nail changes from birth.

In the skin, symmetric hyperkeratosis of the palms and soles is manifested as localized or diffuse keratoderma. Painful friction blisters may develop on the plantar aspects of the toes or heels or along the edges of the feet; these are aggravated by warm weather, trauma, and badly fitting shoes. Our patient
also had yellowish plaques with fissures on both soles, and painful blisters often developed.

On the extensor surfaces of the extremities and buttocks, there are follicular, keratotic, grayish black papules which have horny cones in their centers that fit into corresponding craterlike depressions. The oral lesions take the form of white opaque thickenings, which are focal, involving only a portion of the buccal mucosa or tongue, or generalized, covering the entire mucosal surface of the tongue, lip, and cheek. This is often mistaken for oral candidiasis, but treatment with antifungals is fruitless. Angular cheilosis is also commonly present. Oral lesions have been variably reported as being almost always present or as having an approximate incidence of 34% (8). They have no tendency to develop into malignant neoplasms. Premature eruption of teeth and hoarseness with thickening of the posterior commissure may be found in association with skin lesions. Our patient showed irregularly-shaped whitish plaques on his tongue. KOH and culture for fungus on this lesion were negative. Hair abnormalities such as diffuse alopecia and hair shaft abnormalities may occur in some patients, and, although hypotrichosis of the scalp is present in 10% of patients (11), it has not been completely characterized histologically. Stephen et al. (12) reported that transverse section histologic features in PC-associated alopecia include diminished hair follicular density with preservation of follicular units, prominent miniaturization of follicles, dyskeratosis of outer root sheath keratinocytes, and moderate parakeratotic and orthokeratotic follicular hyperkeratosis. Even though our patient didn’t show alopecia, slightly helicoidal hair was present.

Ectodermal dyskeratosis may affect the eyes, ears, and nose. Epidermal cysts, acneiform lesions, and steatocystoma multiplex may occur on the face, neck, or trunk. Our patient shows all the manifestations of the combined syndrome except neonatal teeth.

The phenotypes of PC suggest that these diseases are caused by keratin mutations (14-17). The mutations in keratin K16 or its expression partner K6a cause the Jadassohn-Lewandowsky form (PC-1) and mutations in K17 alone, an unpaired accessory keratin, result in the Jackson-Lawler form (PC-2). Like the epidermal keratins (K1, K2e, K5, K9, K10 and K14), in which mutations result in epidermal fragility with or without hyperkeratosis, mutations in K16 and K17 lead to keratinocyte damage and hyperproliferation in specific ectodermal structures. This appears as a variety of abnormal phenotypic features. The association with steatocystoma multiplex was also noted (13). Recently, Smith et al. (14) reported PC-2 kindred in whom the causative mutation resides in the K6b, revealing genetic heterogeneity in PC-2 and suggesting that this K6b is the expression partner of K17. They also confirmed the co-expression of these genes by in situ hybridization and immunohistochemical staining.

Histopathologic findings include marked hyperkeratosis, acanthosis, and elongated rete ridges, particularly around hair follicles, which may be obstructed by horny material (7). Hypergranulosis and focal parakeratosis may occasionally be present (8). There is a slight infiltration of lymphocytes into the upper dermis. Melanophages and epidermoid cysts sometimes are also seen within the dermis. Blister formation is often present, and the histological picture with its increasing intracellular vacuolization appears to be specific. Electron-microscopic studies of PC have revealed an increase in the tonofibrils of the basal cells (18). This increase in tonofibril density was more evident in the stratum spinosum, while intracellular edema was present in both the stratum spinosum and the granular layer. The histology of the cystic lesions in our patient is distinct and diagnostic, and the distribution of sebaceous glands seen in our patient fulfills the criterion for diagnosis.

Treatment is essentially symptomatic, with the major emphasis placed on ameliorating
the discomfort of the hyperkeratotic skin and nail lesions. Systemic retinoid treatment has been effective in some patients. Treatment of the dystrophic nails is still far from satisfactory. It is difficult to keep the nails well trimmed with the use of clippers. Radical excision of the nail, nail matrix and nail bed followed by vigorous curettage and electrodesiccation of nail matrix and nail bed, and skin implantation at the site of nail removal can improve function and appearance (8). In symptomatic laryngeal lesions, surgical excision of a focal, hyperplastic epithelial mass resulted in improvement of hoarseness. Natal or neonatal teeth can be removed to prevent aspiration.

References