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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.
THE SYNDROME PAGE

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What Syndrome Is This?

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Figure 1. Left hand. Onychogryphosis.

Figure 2. Forearm. Follicular-based keratotic papules.

Figure 3. Left foot. Hyperkeratotic plaques with bullae and erythema.

CASE REPORT

A 17-year-old white boy had onychogryphosis and subungual debris of all 20 nails which had developed in infancy. Subsequent palmoplantar hyperkeratoses with painful bullae have made it difficult for him to participate in sports. Physical examination further reveals follicular hyperkeratoses on the extensor aspects of the extremities and the buttocks, as well as coarse, wiry body hair with eyebrows that project perpendicularly from the skin. There is no evidence of oral or ocular lesions, cutaneous cysts, hyperhidrosis, or hoarseness. It is not known whether natal or neonatal teeth were present, and because the patient was adopted no family history is known.
PACHYONYCHIA CONGENITA

Pachyonychia congenita (PC) is an uncommon genodermatosis of abnormal keratinization characterized by dystrophic nails and hyperkeratosis of the palms, soles, oral mucosa, and hair follicles. Descriptions of the disorder date back to 1716 when the Danish physician Museus described a young girl with "unguibus monstrositii," or monstrous nails, horny plaques over the elbows and knees, hyperhidrosis, and painful plantar calluses (1). The syndrome was later reported by Muller (1904) and Wilson (1905), and then more extensively described by Jadassohn and Lewandowsky (1906), who are credited with naming the syndrome pachyonychia congenita (2-4). Since 1904, approximately 250 cases have been reported (1).

The four major features of the syndrome are onychogryphosis, palmoplantar keratoderma, follicular hyperkeratosis, and oral leukokeratosis. Several classification systems have been proposed based on the prevalence of associated findings (5-7). In 1935 Kumer and Loos (8) proposed three separate groups: type I with onychogryphosis, palmoplantar keratoderma, and follicular keratosis, type II with these findings plus oral leukokeratosis, and type III with all former findings plus corneal dyskeratosis. In 1980 Schonfeld (5) extended the classification to include, in addition to the four major features of PC, the findings of bullae, hoarseness, palmar hyperhidrosis, and hair abnormalities under type I (also called Jadassohn-Lewandowski syndrome), the additional findings of natal teeth and multiple cysts as part of type II (Jackson-Sertoli syndrome), and the addition of corneal dyskeratosis under type III (Schaefer-Brunauer syndrome). Finally, in 1988, Feinstein et al. (6) incorporated the features of steatocystoma multiplex, cataracts, angular cheilosis, mental retardation, and laryngeal lesions into another system of classification, which is detailed in Table 1.

<table>
<thead>
<tr>
<th>TABLE 1. Classification (6) of Pachyonychia Congenita</th>
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<tbody>
<tr>
<td>Type I</td>
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<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Onychogryphosis</td>
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<tr>
<td>Palmoplantar keratoderma</td>
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<tr>
<td>Follicular keratosis</td>
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<tr>
<td>Oral leukokeratosis</td>
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<tr>
<td>Corneal dyskeratosis</td>
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<td>Bullae</td>
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<td>Hoarseness</td>
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<td>Palmoplantar hyperhidrosis</td>
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<td>Hair abnormalities</td>
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<td>Natais teeth</td>
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<tr>
<td>Steatocystoma multiplex</td>
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<td>Cataracts</td>
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<td>Angular cheilosis</td>
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<td>Mental retardation</td>
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<td>Laryngeal lesions</td>
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Onychogryphosis in pachyonychia congenita is characterized by yellow-brown thickening of the distal two-thirds of the nails with subungual debris resulting in elevation and exaggerated curvature. Whereas these nail findings are usually seen in infancy, onset in the teenage years or later has been described and is referred to as pachyonychia congenita tarda (9-11). In addition, onychogryphosis may be the only abnormality in some families (12,13). Trauma may induce chronic paronychia. The second major feature of PC is keratotic papules and plaques on the palms and soles. Painful bullae and fissures at friction sites may occur within these lesions. The third feature is follicular hyperkeratosis that occurs on the buttocks and extensor aspects of the extremities. This resembles keratosis pilaris, but may coalesce into thick, verrucous plaques. Oral leukokeratosis, particularly of the tongue, is the fourth major finding and has been variably reported as being almost always present or as having an approximate incidence of 34% (14,15). The oral lesions have no inherent malignant potential.

Associated clinical features in decreasing order of frequency are palmoplantar hyperhidrosis, natal or neonatal teeth, angular cheilosis, pili torti, bushy eyebrows, corneal dyskeratosis, laryngeal keratosis which may result in hoarseness, cataracts, mental retardation, and diffuse alopecia (6). Epidermal inclusion cysts and steatocystoma multiplex have also been described.

Histologic findings include parakeratosis, acanthosis, and elongated rete pegs, particularly around hair follicles, which may be obstructed by horny material (6). Hypergranulosis and basal layer hypertrophy may be present. There is a dermal perivascular infiltrate of lymphocytes, plasma cells, and mast cells. Bullous lesions demonstrate intracellular edema with intraepidermal vesicle formation and loss of keratohyalin granules (5).

Pachyonychia congenita is a genetic disorder of autosomal dominant inheritance with variable expression and a high degree of penetrance (5,16,17). There are three cases reported of recessive inheritance (18). Recently the two major subtypes of PC (Jadassohn-Lewandowski/type I and Jackson-Sertoli/type II) were found by genetic linkage analysis to be caused by mutations in keratins 16 and 17, respectively. A point mutations on chromosome 17q, which carries the gene for keratin 16, was demonstrated in PC type I, and a point mutation on chromosome 12q, which carries the gene for keratin 17, was demonstrated in PC type II (16,19). In addition, a keratin 6 deletion mutation has been reported in a Slovenian family with PC type I (20). As a consequence of these mutations, the keratin protein structure is disrupted, preventing normal filament aggregation. The nail, hair follicle, tongue, palm, and sole are the main sites of constitutive expression of keratins 6, 16, and 17,
which corresponds to the distribution of lesions seen in pachyonychia congenita.

Oral retinoids have been effective for skin lesions in some cases of pachyonychia congenita. Blisters and fissures on the soles can prohibit walking, thus protective footwear may be helpful. Variable success has been reported with topical corticosteroids, keratolytics, oral vitamins A, B, and E, sodium levothryoxine, and X-ray and ultraviolet radiation. Onychogryphosis is not responsive to topical or systemic therapy and extensive surgical removal of nail plate, bed, and matrix must be undertaken with subsequent skin grafting. Symptomatic laryngeal lesions can be evaluated by laryngoscopy and removed, although they tend to recur. Natal or neonatal teeth can be removed to prevent aspiration. The teeth may also be painful, which can discourage an infant from eating (6,7,14).

REFERENCES


CALL FOR PAPERS

The editors of The Syndrome Page welcome submission of your manuscripts for consideration. Please submit them in triplicate to Susan B. Mallory, M.D., Department of Dermatology, St. Louis Children’s Hospital, 400 S. Kingshighway, St. Louis, MO 63110.