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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

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Pachyonychia congenita is a rare hereditary disorder characterized mainly by nail hypertrophy and dyskeratoses of skin and mucous membranes. A thorough literature survey since its first description in 1904 up to 1985 revealed 168 cases of pachyonychia congenita. There were no indications of any sex or ethnic group predilection. Based on this survey the following classification is suggested: type I (56.2% of cases), hyperkeratosis of nails, palmo-planter keratosis, follicular keratosis, and oral leukokeratosis; type II (24.9% of cases), clinical findings of type I plus bullae of palms and soles, palm and plantar hyperhidrosis, natal or neonatal teeth, and steatocystoma multipplex; type III (11.7% of cases), clinical findings of types I and II plus angular cheilosis, corneal dyskeratosis, and cataracts; and type IV (7.2% of cases), clinical findings of types I, II, and III plus laryngeal lesions, hoarseness, mental retardation, hair anomalies, and alopecia. (J AM ACAD DERMATOL 1988;19:705-11.)

Pachyonychia congenita is a rare hereditary disorder characterized by nail dystrophy, palmar and plantar hyperkeratosis, leukokeratosis of the mucous membranes, follicular keratosis, and occasionally hyperhidrosis of palms and soles.

The first cases of pachyonychia congenita were described by Muller in 1904 and by Wilson in 1905. One year later the same condition was described in two siblings by Jadassohn and Lewandowsky. Different names were given to the disorder, such as keratosis disseminata circumscripta, tylomata, and leukokeratosis linguæ, pachyonychia ichthyosiformis, congenital dyskeratosis, and keratosis multififormis idiopathica.

To establish the diagnosis of pachyonychia congenita one must encounter hypertrophy of all nails and dyskeratotic skin lesions. Two conditions should be differentiated from pachyonychia congenita: (1) thickening of nails because of trauma (this condition does not usually involve all nails), and (2) congenital onychogryphosis (differs from pachyonychia congenita in that it does not include dyskeratotic skin lesions; it usually does not involve all the nails, and the toe nails are twisted inward).

In 1943 the clinical symptoms of pachyonychia congenita were summarized by Ormsby and Montgomery and included dystrophic nail changes, hyperkeratosis of hands and feet, hair anomalies, leukokeratosis of mucous membranes (especially tongue and oral mucosa), follicular keratosis (especially on elbows and knees), corneal dyskeratosis, and bullae found usually on the soles but sometimes on the buttocks and ankles.

The above description should be completed by natal and neonatal teeth, cataracts, plantar and occasionally palmar hyperkeratosis, congenital white sponge nevus, diffuse alopecia (which can also be congenital), angular cheilosis, constant or transient hoarseness, laryngeal lesions that may cause acute respiratory distress syndrome and therefore require surgery, and mental retardation. The relationship of mental retardation to pachyonychia congenita is not clear. It has been sug-
suggested that the fetal ectodermal lesions that affect the skin may also affect the central nervous system.¹⁴

GENETICS

Pachyonychia congenita is considered to be a genetic disease of an autosomal dominant inheritance with a high degree of penetration.¹⁵ An additional possibility is that the disease is a product of two adjacent genes.¹⁶ The last assumption is based on its coexistence with rare disorders such as steatocystoma multiplex.¹⁷

The disease affects both sexes equally. Jewish¹⁸ and Yugoslavian¹⁹ patients were reported to be affected more frequently than other ethnic groups.

HISTOLOGY

The condition is characterized by changes in the nail bed.¹⁹ There is a longitudinal lesion in the keratinized substance located between the nail and the nail bed. This longitudinal lesion is filled with granular tissue.²⁰ Other authors suggest that the matrix and not the nail bed is the site of the main pathology.²¹

In the dyskeratotic skin, especially around hair follicles, acenthosis, parakeratosis, and elongation of rete pegs can be found. The openings of hair follicles are blocked by horny material. The basal cell layer is hypertrrophic and occasionally there is a thickening of the granular layer.¹¹ In the dermis there is a perivasculare infiltrate composed mainly of lymphocytes, mast cells, and plasma cells. No obvious changes are observed in the connective tissue.²²

With electron microscopy one can find a few keratotic layers covering the epidermal cells. Their intercellular spaces are filled with a homogeneous shiny material, which probably represents a remnant of keratinosomes and desmosomes that were tightly arranged. The granular cells form three to four layers and contain thick masses of tonofilaments, scattered masses of keratohyalin, and a small number of keratosomes. Thick masses of tonofilaments are found at the periphery of the cytoplasm of the basal and malpighian cells. Ribosomes and mitochondria can be seen around the nucleus. The intercellular spaces of the cells are enlarged. The walls of the sweat glands contain a normal cell layer surrounded by multiple layers of horny cells. The cells of the granular layer contain keratohyaline and keratosomal masses with an unclear internal structure. The sweat glands are not completely plugged by the horny material.¹¹,²³

ASSOCIATED FINDINGS

A thorough literature survey of pachyonychia congenita since its first description in 1904 up to 1985 disclosed 168 cases of pachyonychia congenita. The prevalence of the disorder among the sexes is almost equal. The matter of a predominance for a certain ethnic group in the disease was not mentioned in most of the case reports. In 3% of the cases the patients' parents were blood relatives and 64.1% of the patients had relatives who suffered from the disease.

The main pathologic signs found in patients with pachyonychia congenita included hypertrophy and distortion of nails (in all cases), hyperkeratosis of palms and soles (62.0%), leukokeratosis (60.2%), follicular keratosis (36.9%), bullae on palms and soles (36.1%), plantar hyperhidrosis (19.8%), natal or neonatal teeth (15.6%), and angular cheilosis (10.7%). Less common were hair anomalies (9.6%), corneal dyskeratosis (7.8%), hoarseness (6.6%), cataracts (6%), mental retardation (4.2%), and alopecia (2.4%).

Among concomitant diseases the most common was steatocystoma multiplex (5.4%). As mentioned above, the defect might be in two closely located genes. Another disease accompanying pachyonychia congenita was chronic oral candidiasis, which might appear in abnormal mucous membranes found in pachyonychia congenita.¹² Four cases were reported to have multifocal candidiasis.¹⁰,¹⁹

Other coexisting diseases that were described only once included vitiligo, depression, schizophrrenia, systemic infection with herpes simplex, migraine headaches, diabetes mellitus, epilepsy, polydactyly, microcephaly, Lesch-Nyhan syndrome,¹⁴ and Kyrie's disease.¹⁰⁴

Additional clinical findings included enlarged thymus, electroencephalographic abnormalities, hypogonadism, and failure to thrive with

respiratory distress syndrome.\textsuperscript{14} In two cases\textsuperscript{9,10} quinine had been given to the patient's mother while she was pregnant.

Abnormal laboratory findings included eosinophilia with low IgD and high IgM levels,\textsuperscript{17} hypergammaglobulinemia,\textsuperscript{14} positive antinuclear factor and Latex test results,\textsuperscript{16} and traces of arsenic in blood and urine.\textsuperscript{15}

**CLASSIFICATION**

Numerous subdivisions of pachyonychia congenita have been suggested. According to Kumer and Loos\textsuperscript{34} pachyonychia congenita included the following:

Type A: Nail hypertrophy with palmoplantar hyperkeratosis and follicular keratosis of the body.

Type B: Findings of type A with oral leukokeratosis (Riehl type).

Type C: Findings on types A and B with corneal dyskeratosis.

According to this classification type B was the most common, whereas type C was very rare. Another classification was offered by Schönfeld\textsuperscript{15}.

Type A: Symmetric hypertrophy of nails, palmoplantar hyperkeratosis, follicular keratosis, blister formation, oral leukokeratosis, hoarseness, hair changes and hyperhidrosis of palms and soles (Jadassohn-Lewandowsky syndrome).

Type B: Findings of type A with neonatal teeth and steatocystoma multiplex (Jackson-Sertoli syndrome). Leukokeratosis of the oral mucosa has never been reported in this type.

Type C: Findings of type A with corneal dyskeratosis (Schaffer and Brunauer syndrome).

A third subtyping was suggested by Sivasundram et al.\textsuperscript{114}.

Type A: Jadassohn-Lewandowsky syndrome (see classification suggested by Schönfeld type A).

Type B: Hypertrophied nails and oral leukokeratosis with palmoplantar hyperkeratosis: The keratosis in this type is less severe.

Type C: Neonatal teeth, moderate nail hypertrophy, and mild hyperkeratosis of palms and soles.

Type D: Macular pigmentation of neck and axillae. Mild hyperkeratosis of nails and palmoplantar hyperkeratosis.

The following classification is offered based on the present survey of 168 cases of pachyonychia congenita. Prevalence figures have been calculated according to this classification (Table I).

Type I: Hypertrophy of nails, palmoplantar hyperkeratosis, follicular keratosis, and oral leukokeratosis (56.2%).

Type II: Clinical findings of type I plus bullae of palms and soles, hyperhidrosis of palms and soles, natal or neonatal teeth, and steatocystoma multiplex (24.9%).

Type III: Clinical findings of types I and II plus angular cheilosis, corneal dyskeratosis, and cataracts (11.7%).

Type IV: Clinical findings of types I, II, and III plus laryngeal lesions, hoarseness, mental retardation, hair anomalies, and alopecia (7.2%).

**PROPHYLAXIS AND TREATMENT**

The following is a summary of various treatment approaches.

**Nail lesions**

Local treatment with various ointments and administration of vitamins A, B, C, and E have been tried with no obvious improvement. The only effective treatment has been surgical. A simple nail removal is not enough, as the newly formed nail is also hypertrophied and distorted. Several surgical treatments have been suggested, including radical excision of the nail, nail bed, and nail matrix with skin implantation at the site of the removed nail.\textsuperscript{38,72,73,105} Such surgical treatment must be followed by vigorous curettage and electrofulguration of matrices and nail beds. The functional and aesthetic results are excellent.\textsuperscript{21} In severe cases, removal of the distal phalanx has also been suggested. In these cases everyday functioning is improved markedly.

**Skin lesions**

The literature offers many modalities of treatment of the various skin lesions, some of which have proved successful. Sodium lothyrroxine was tried to treat follicular keratosis with good results.\textsuperscript{29} X-ray and radium irradiation was tried without impressive results.\textsuperscript{44} Ultraviolet radiation was also used with some success.\textsuperscript{32} Gentian violet application was found to be effective.\textsuperscript{30} Ammoniated mercury was also tried, with no indication as to the success of treatment.\textsuperscript{42} Local steroid
Table I. Proposed classification for pachyonychia congenita

<table>
<thead>
<tr>
<th>Type</th>
<th>Basic clinical findings</th>
<th>Additional clinical findings</th>
<th>Relative prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Hypertrophy of nails, palmoplantar keratosis, follicular keratosis, oral leukokeratosis</td>
<td>Bullae of palms and soles, hyperhidrosis of palms and soles, natal or neonatal teeth, steatocystoma multiplex</td>
<td>56.2%</td>
</tr>
<tr>
<td>II</td>
<td>Clinical findings of type I</td>
<td></td>
<td>24.9%</td>
</tr>
<tr>
<td>III</td>
<td>Clinical findings of type II</td>
<td>Angular cheilosis, corneal dyskeratosis, cataracts</td>
<td>11.7%</td>
</tr>
<tr>
<td>IV</td>
<td>Clinical findings of type III</td>
<td>Laryngeal lesions, hoarseness, mental retardation, hair anomalies, alopecia</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

Creams have been tried both successfully and unsuccessfully. Vitamin B was given with some success and vitamin E was also reported to be effective. Plasma vitamin A levels were found to be low in patients with underdevelopment or organs of ectodermal origin. Although pachyonychia congenita is a disease in which plasma levels of vitamin A are known to be normal, vitamin A administration was found to be effective on the skin lesions in some cases. The nails received no benefit from vitamin A.*

Lesions on the soles were found to pose a problem, as some of the patients could not walk. The main treatments included saline solution dressings and adjustment of the soles. In one patient the bullae on the heels prevented him from walking normally. While at home he had to use crutches. This patient was treated with local steroid cream, x-ray irradiation, and vitamin A with only slight improvement. When all these treatments failed, treatment with hypnosis was initiated and after a few months he was able to carry on a normal life, wear normal shoes, and walk without any assistance.

In a few reports vitamin A acid derivatives were tried. In one case isotretinoin was administered. The histologic work-up showed marked improvement, but clinically improvement was only moderate. In another report aromatic retinoids caused a dramatic healing effect on the skin lesions.

Hyperhidrosis was treated by sympathectomy with limited results.

Oral lesions

In laryngeal and vocal cord lesions with no signs of hoarseness or respiratory problems, the lesions can be left untreated. Sometimes the lesions are composed of white plaques, mimicking candidiasis, but antifungal treatment is of no help. In other cases the lesions are those of white spongy nevus and are benign with no malignant potential. These should be left untreated.

If there are symptoms of hoarseness or respiratory problems, laryngoscopy will detect the lesions that must be removed. In this case improvement is always instant. This procedure must sometimes be repeated because hoarseness can return. Spontaneous remission of hoarseness has also been reported.

Teeth

Natal teeth (congenital teeth) appear at an incidence of 1:10,000 births and there is a familial trend to its appearance. These teeth are usually not normal in structure. They are motile and fall out within 1 year. They can be inhaled, cause pain, and discourage the infant from eating. They can also cause pain to the mother during breast feeding. It is therefore advisable to pull them out.

Neonatal teeth are teeth that appear a short time after birth. In contrast to congenital teeth, neonatal teeth are normal in structure and fall out at about 5 years of age. They may have to be removed for the same reasons mentioned above.

Neither natal nor neonatal teeth have an effect on the development of the normal teeth that appear later.

REFERENCES