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PACHYONYCHIA CONGENITA

A Clinical, Histopathologic and Microangiographic Study with Special Reference to Oral Manifestations

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Abstract. This paper presents a clinical, histopathological and microangiographic study of three patients with pachyonychia congenita with special reference to oral manifestations. The patients, who are related, exhibited thickening of finger- and toe-nails, follicular keratoses, palmar/plantar keratoses and plantar hyperkeratosis, oral leukokeratosis, into total teeth. It is noted in the discussion that total teeth and oral leukokerati-
oses may constitute the earliest clinical manifestations of pachyonychia congenita and that they appear to occur earlier than nail lesions. When there is a hereditary dis-
position for pachyonychia congenita, it is important to inspect the oral cavity at an early stage.

Key words: Pachyonychia congenita; Histopathology; Microangiography; Nails; Teeth; Oral leukokeratosis

Jadassohn & Lewandowsky (12) described a type of congenital dysplasia of the nails and skin, which they called pachyonychia congenita. The dysplasia is characterized clinically by a syndrome with dys-
trophic lesions in the form of a symmetrical, hard thickening of finger- and toe-nails, skin changes in the form of palmar/plantar hyperkeratosis and hyper-
keratosis, follicular keratoses (especially on knees and palms), cuticularities and bullae on the palms of the hands and soles of the feet, oral leukokeratosis on the tongue and buccal mucosa, and abnormalities of the cornea (corneal dystrophy) and nasal teeth (11, 7, 16). Holldenhauser & Ernst (16) analysed 96 cases of pachyonychia congenita and found that 98.8% ex-
blished nail lesions, 72% palmar/plantar keratoses, 78% follicular seborrhoeform keratoses and 54.4% oral leukokeratoses.

The disease is transmitted by simple autosomal, dominant heredity with incomplete penetrance (7).

Men are more often affected than women. The syn-
drome would appear to be of more frequent occur-
dence among Jews (7).

Oral lesions are common in conjunction with pachyonychia congenita. In most cases they have been reported to be in evidence already at birth (8) and resemble those found in white speckle naevus and hereditary benign intra-epithelial dysker-
atosis (9, 22). The oral leukokeratoses manifest themselves clinically in the form of white or greyish opaque spots or striations. The lesions may be focal, in such cases usually on the lips and the buccal mucosa, posteriorly along the interdental line, or may cover the entire mucosa along the lateral mar-
gins of the tongue. Herpetiform lesions, as also round-
ness owing to thickening of the posterior commissure in the larynx (13), are other reported symptoms. The lesions of the oral mucosa have, according to Witkop & Gordin (22), the following histological characteristics. The epithelium exhibits pronounced, hyperkeratosis and acanthosis with absence of stratum granulosum. In the superficial layer of the epithelium and in the stratum spinosum, intraellular-
ly vacuolization and oedema are observed, as also perivascular cells. Exfoliative cytology reveals the pres-
ence of large epithelial cells with intracellular cyto-
plasmic vacuoles and a relatively small nucleus. The cyto-
plasm of some cells contains small, round, eosinophilic stainable bodies.

CASE REPORTS

Three patients with pachyonychia congenita are reported. Two of them, girls, 3 years (case 1) and 1.5 months old (case 2), are cousins and were referred to the Eastern Institute for dense corneas and to the Department of Dermatology, Karolinska sjukhuset, for nail and skin lesions. The younger girl's father (case 3) was referred to the Department of Den-
matology, Karolinska sjukhuset, for nail and mucus lesions. The pregnancies of the two mothers had run a normal

Fig. 1. The general outline of the family studied.

Fig. 2. Case 1. at 2.5 years of age. All nails on hands and feet were greatly thickened, laterally compressed, and yellowish in colour.

Fig. 3. X-ray of case 2 five months after birth. Two tooth-like formations (secondary primordia) appear in mesial 
and 
Fig. 4. Case 2 immediately after birth it was found that in the oral mucosa in region 43-44 the patient had two soft enamel-like elevations. In the facial portion of which tooth-like hair felt
was observed. The two dental formations were mobile and grey in colour. A buccal plaque-like portion in region 44 was found to be loosely seated in the mucosa and was re- moved. On clinical examination 3 days after birth, 41 and 44 were partially erupted (Fig. 3) very mobile, and attached to an elevated mucosal papilla. After 12 days these deciduous teeth were removed. The plaque-like elevations persisted one month after the eruption. At 3 months of age two new teeth, 51 and 52, erupted. Despite the fact that the time of eruption was pro- longed the tooth appeared to be clinically and radiographic- ally normal (Fig. 4). On the bucal crest distal to erupted 41 and 42, buccal plaque-like lesions were seen. At 22 days of age new lesions started in the form of a slight contracting of the sides and of a yellowish hue. At 6 months of age all teeth on fingers and toes were greatly thickened and yellowish in colour (Fig. 5). Plaque-like white plaque-like whitish papules were observed in the areas around the alve. Her general con- dition was otherwise satisfactory.

Four 3

The patient, who is the father of case 2, had pronounced oral lesions. Both thele- and thre-nails were markedly com- pacts, thickened, and drawn in to the sides. Similar leko- plaques were seen on the lateral borders and tip of the tongue (Fig. 6). The patient has no tricho-noma skin lesions.

METHODS

The teeth, in some cases with an adhering piece of soft tissue, were cut in two longitudinal pieces with a diamond wheel. One half of the tooth was decalcified in 5% nitric acid, em- bedded in paraffin and sectioned into 4 μm thick sections, which were stained with Mayer's haemalum-eosin, Weigert's haematoxylin-van Gieson, Gallocyanin, and Brown & Brenn (3).

Some of the sections were used for microtomography with ultrasonic X-rays according to the technique for contrast micro- radiography reported by Engström & Lindström (4) and Lindström (14). The X-ray tube was designed by Engström & Lindberg (5). The voltage was 3.0 mV. The issue section was placed at a distance of about 55 mm from focus, which was about 0.8 mm in diameter. Most of the emitted X-ray quanta had wavelengths of 8-12 Å. The contrasts on the developed microfilms were caused by variations in the dry mass distribution of the various organic tissue compo- nents. For the histologic production of the microfilms the technique developed by Engström et al. (6) was used.

Fig. 6. Case 3, a 25-years-old man, exhibited stained leko-plaques lesions on the sides of the tongue (arrow).

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Fig. 6. Case 3, a 25-years-old man, exhibited stained leko-plaque-like lesions on the sides of the tongue (arrow).
RESULTS

Case 1
The polyene dental papillae exhibit histologically some hyperplasia of the mucosa with irregular proliferation of rete paps. In the superficial cell layers and the stratum spinosum a widespread and heavily cytoplasmic vacuolization and intracellular oedema are visible (Fig. 7). The vacuoles appear on the microphotographs as circular or oval cavities (Fig. 8). Desmosomal structures appear to be mainly intact. Irregularly localized in the mucosa are single cells or small accumulations of cells with changes similar to those in dyskeratosis (Fig. 7). No differentiation of keratinocytes granules is noticeable. The superficial layer has the appearance chiefly of parakeratin, but the light superficial zone on the microphotographs indicates a high dry mass concentration, probably due to a certain degree of keratinization in the superficial layer (Fig. 8). The underlying connective tissue is rich in vessels and fibroblasts. Osteodentine-like hard tissue inclusions, partly covered with osteoblast-like cells, are seen in the connective tissue (Fig. 9). One of these trabeculae is larger than the others, has a horn-like appearance (Fig. 10) and

![Image](Image-6x529-to-481x1223)

Fig. 7. Case 1. The mucous papilla, to which the teeth were attached, showed an irregular proliferation of rete paps. In the stratum corneum and stratum spinosum there is pronounced inter- and intracellular oedema. In the stratum malpighii, cells with dyskeratotic changes are also present. Haematoxylin-eosin. ×150.

Fig. 8. Microphotograph of a section close to that shown in Fig. 7. The organic mass is markedly increased in the stratum corneum, which appears as a light band. Probably due to the increased keratinization. The vacuoles caused by the intracellular oedema appear as black, oval or circular foci. ×150.
The mucosal papillae are irregular and focal. In the stratum corneum there is a marked increase in the keratinisation, cells with keratohyaline granules are also seen (Fig. 10).

The microangiograms of the mucosa show a high dry mass concentration on the microangiograms.

Case 2

The incisors exhibit at some points an irregular osseous tissue structure with disturbed mineralisation (Fig. 11). No pulpal or papillary tissue is observable. Osseous lacunae are lacking, as also the predentine. Pieces of a fibrous connective tissue, instead, show the part of the tooth adjoining the connective tissue, and the predentine zone has been replaced by an odontodentine-like substance with cell lacunae (Fig. 12). The orally situated part of the tooth exhibits bacterial colonies and caries on the surface (Figs. 12 and 13). Bacteria are also observed in dentinal tubuli (Fig. 13). On the microangiograms the high dry mass concentration is seen in the super-

The histological examination of the excised tongue mucosa shows it to be hyperplastic. The epithelium exhibits acanthosis and parakeratosis and at some points moderate hyperkeratosis. In the superficial layers of cells and in the stratum spinosum there is a widespread intracellular edema. In the subepithelial connective tissue there are at some points indications of a band-like confluence lympho-

Fig. 9. Case 1. The dental papilla is fibro-

blastic and vascular. In the connective tissue an odontodentine-like hard tissue trabeculae is seen, which is partially covered with osse-

blastic-like cells. Haematoxylin eosin. × 110.

Case 3

The histological examination of the excised tongue mucosa shows it to be hyperplastic. The epithelium exhibits acanthosis and parakeratosis and at some points moderate hyperkeratosis. In the superficial layers of cells and in the stratum spinosum there is a widespread intracellular edema. In the subepithelial connective tissue there are at some points indications of a band-like confluence lympho-

Fig. 10. Case 1. In the connective tissue an odontodentine-like formation is seen. Mallory × 16.

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Fig. 11. Case 2. The incisors have at some points an irregular dentin structure with uncalcified mineralization. Masson-Trichrome. × 150.

DISCUSSION

Lesions characteristic of pachyonychia congenita, in the form of thickening of finger and toe-nails, palmarplantar hyperkeratosis, follicular keratosis, hyperhidrosis, and oral leukokeratosis, have been found in the present patients. Oral lesions in the form of leukokeratoses have been reported in 54.7% of pachyonychia congenita cases (16). Gorlin & Chaudry (8) have described these lesions as focal, often bilateral, located on the lips, the lateral margin of the tongue, and the buccal mucosa along the interdental line. The location on the gingiva, as documented in the present study (case 2), has only been reported two cases previously (18, 23).

The histological picture of the oral leukokeratoses according with that reported by Wijkop & Gorlin (22). The oral leukokeratoses exhibit certain histo-

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Fig. 12. Case 2. - 01. The predental zone is replaced by a uniform keratinized (OD) with cell inclusions. Orally are seen bacterial colonies and curd (C). Haematoxylin-eosin. × 170.
natal and neonatal teeth in infants unaffected by this syndrome have been examined, histologically (10, 19, 20), microscopically, and by polarized light technique (24). Some of the dental lesions were common to all cases, such as the occurrence of interglobular dentine, irregular osteodontine-like structures with cell inclusions, and caries. The premature eruption of natal teeth is probably caused by a hereditary superficial location of the tooth germ, which in turn predisposes to dysplastic lesions in the form of incomplete root development and mineralization disorders (2, 10, 15, 24).

The occurrence of two primary dentition as reported in case 2 is an extremely seldom phenomenon. Bjurman (2) examined a comprehensive material of 232 natal and neonatal teeth, which all belonged to the regular primary dentition. After the natal or neonatal teeth were lost, 8 of them were replaced by some kind of tooth formation with dwarfed roots, but no normal second primary dentition was found. The natal teeth in this study were extracted, though this is not necessary in all cases of natal and neonatal teeth.

However, natal teeth should be removed when, owing to their greater mobility, they cause pain or pressure. If they are very loose, they may be swallowed or aspirated. Natai teeth may also injure the mother’s breast during breastfeeding and impair the infant’s tongue.

Natal teeth and oral leukokarioses would gain, from this investigation, to be the earliest clinical manifestations of Pachyonychia congenita and generally appear prior to nail lesions. When there is...
REFERENCES


7. Gerlin, R. J.: Genital disorders affecting mucous mem-


8. Gerlin, R. J. & Chaufax, A. P.: Oral lesions accom-


11. Jackson, A. D. M. & Lawler, S. D.: Pachyonychia con-

Acta Dermato-venerologica Stockholms 53

12. Jafroid, J. & Lewandowski, F.: Pachyonychia con-
genita. In Heterochromatodermatologia, p. 29-Urban 


16. Mühlenhauer, E. & Ernst, K.: Das Jadaschus-Lewen-


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