

PACHYONYCHIA CONGENITA

A Clinical, Histological and Microradiographic Study with Special Reference to Oral Manifestations

Göran Anneroth, Göran Isacson, Björn Lagerholm, Ann-Marie Lindvall and Nils Thyresson

From the Departments of Oral Pathology and Medical Physics, Karolinska Institutet, the Department of Dermatology, Karolinska sjukhuset, and The Eastman Institute, Stockholm, Sweden

Abstract. This paper presents a clinical, histological and microradiographic study of three patients with pachyonychia congenita with special reference to oral manifestations. The patients, who are relatives, exhibited thickening of finger- and toe-nails, follicular keratosis, palmoplantar keratosis and hyperhidrosis, oral leukokeratosis, and natal teeth. It is stated in the discussion that natal teeth and oral leukokeratosis may constitute the earliest clinical manifestations of pachyonychia congenita and that they appear to occur earlier than nail lesions. When there is a hereditary disposition for pachyonychia congenita, it is important to inspect the oral cavity at an early stage.

Key words: Pachyonychia congenita; Histopathology; Microradiography; Natal 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 dystrophic lesions in the form of a symmetrical, hard thickening of finger- and toe-nails, skin changes in the form of palmoplantar hyperkeratosis and hyperhidrosis, follicular keratosis (especially on knees and elbows), callosities 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 natal teeth (11, 7, 16). Moldenhauer & Ernst (16) analysed 96 cases of pachyonychia congenita and found that 96.8% exhibited nail lesions, 72% palmoplantar keratoses, 58.5% follicular acneiform 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 syndrome would appear to be of more frequent occurrence 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 cases of white sponge naevus and hereditary benign intra-epithelial dyskeratosis (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 margin of the tongue. Herpetic lesions, as also hoarseness 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 & Gorlin (22), the following histological characteristics. The epithelium exhibits pronounced hyperparakeratosis and acanthosis with absence of stratum granulosum. In the superficial layer of the epithelium and in the stratum spinosum, intracellular vacuolization and oedema are observed, as also pycnotic cells. Exfoliative cytology reveals the presence of large epithelial cells with intracellular cytoplasmic vacuoles and a relatively small nucleus. The cytoplasm of some cells contains small, round, eosinophilically 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 Eastman Institute for dentitio connatalis 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 Dermatology, Karolinska sjukhuset, for nail and tongue lesions.

The pregnancies of the two mothers had run a normal

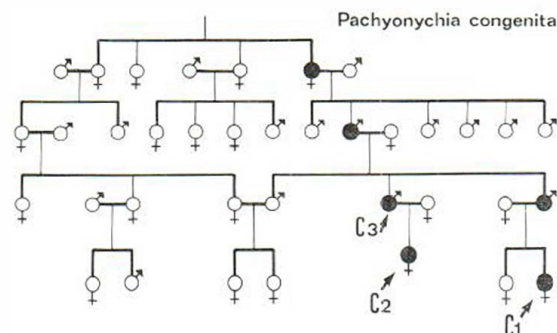


Fig. 1. The genealogical table of the family studied.

course; the deliveries were also normal and occurred at the proper time. The girl's great-grandmother and grandfather on the paternal side and their two fathers, who are brothers, have pachyonychia congenita (Fig. 1) and were said to have had natal teeth.

Case 1

The patient had at birth two dental formations in the frontal region of the mandible, located in polypean elevations with narrow adhesion to the mucosa.

Clinically the teeth appeared to be abnormal. They were soft and translucent and the mineralization was incomplete. On examination 5 days after birth the teeth were faintly rose-coloured cervically. As there appeared to be an imminent risk of spontaneous loosening, the teeth were extracted. During the first 2 months the nails were normal but later changed and rolled inwards at the edges. At 6 months of age all nails on fingers and toes were greatly thickened and

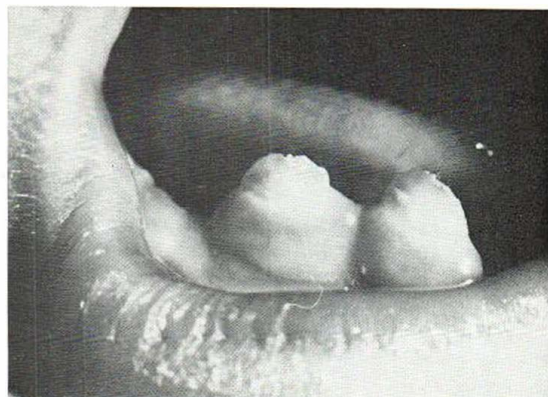


Fig. 3. 01- and -01 three days after birth. The tooth-like formations were very mobile and were seated on an elevated mucosal papilla.

yellowish in colour. The forefinger and thumb nails (Fig. 2) were especially affected. They were greatly thickened and distally compressed.

Hair changes were now also seen. The hair, which at birth had been dark, curly and lustrous, became fair and for the most part was replaced by thinner, less lustrous and less curly hair. On inspection at 3 years of age the teeth and the oral mucosa were normal. Pinhead-sized milia-like whitish papules were earlier in evidence over the whole body, but now remain only on the face and extremities. Since 2 years of age the patient has also been troubled by blisters on the feet, which makes it difficult for her to walk, especially in the summer. Moreover, the patient shows hyperhidrosis on palms and soles. Otherwise her general condition is satisfactory.

Case 2

Immediately after birth it was found that in the oral mucosa in region 01-01 the patient had two soft dental-sac-like elevations, in the incisal portions of which tooth-like hard tissue

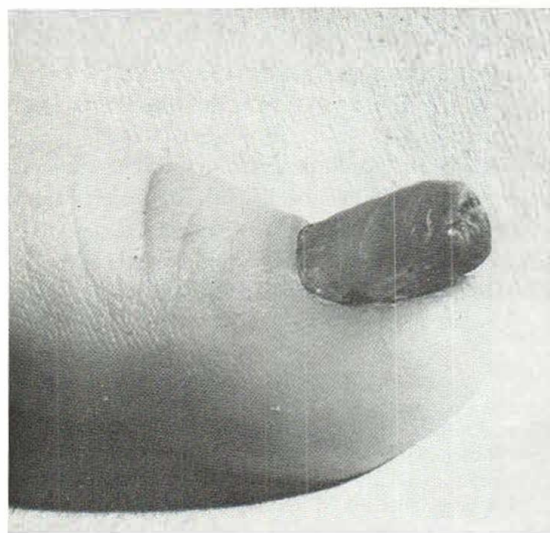


Fig. 2. Case 1 at 2.5 years of age. All nails on hands and feet were greatly thickened, laterally compressed, and yellowish in colour.

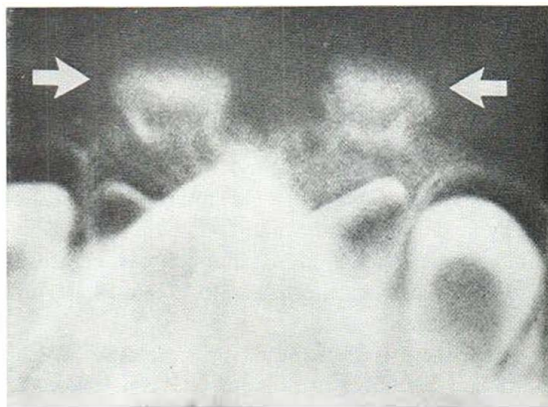


Fig. 4. X-ray of case 2 five months after birth. Two tooth-like formations (second primary dentition) appear as radiopaque areas (arrows).

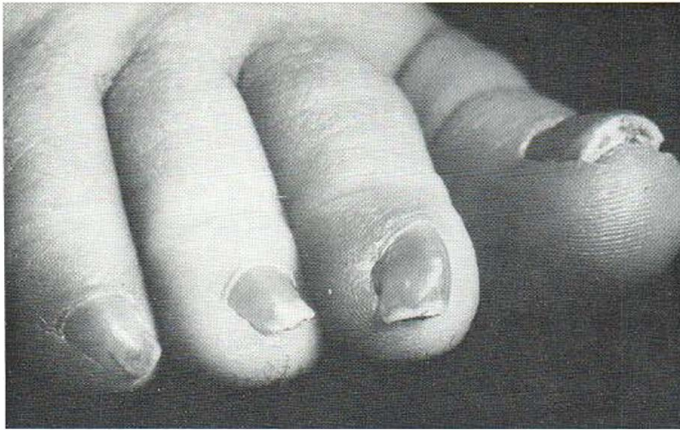


Fig. 5. Case 2 at 6 months of age. All nails on hands and feet were convex, markedly thickened, and yellowish in colour.

was observed. The two dental formations were mobile and grey-rose in colour. A hard-tissue-like portion in region -04 was found to be loosely seated in the mucosa and was removed. On clinical examination 3 days after birth, 01- and -01 were partially erupted (Fig. 3) very mobile, and attached to an elevated mucosal papilla. After 32 days these deciduous teeth formations were so loose that they were removed. The papilla-like elevations persisted one month after the extraction. At 5 months of age two new teeth, 01- and -01, erupted. Despite the fact that the time of eruption was prolonged the teeth appeared to be clinically and radiographically normal (Fig. 4). On the buccal crista distal to region 05- and -05, leukoplakia-like lesions were seen. At 22 days of age nail lesions started in the form of a slight contraction of the sides and of a yellowish hue. At 6 months of age all nails on fingers and toes were greatly thickened and yellowish in colour (Fig. 5). Pinhead-sized milia-like whitish papules were observed in the area around the alae. Her general condition was otherwise satisfactory.

Case 3

The patient, who is the father of case 2, had pronounced nail lesions. Both toe- and finger-nails were markedly convex, thickened, and drawn in at the sides. Striated leukoplakia-like lesions were seen on the lateral borders and tip

of the tongue (Fig. 6). The patient has no troublesome skin lesions.

METHODS

The teeth, in some cases with an adhering piece of soft tissue, were cut in two lengthwise pieces with a diamond wheel. One half of the tooth was decalcified in 5% nitric acid, embedded in paraffin and sectioned into 6 μ m thick sections, which were stained with Mayer's haemalum-eosin, Weigert's haematoxylin-van Gieson, Goldner, and Brown & Brenn (3).

Some of the sections were used for microradiography with ultrasoft X-rays according to the principles for contact microradiography reported by Engström & Lindström (4) and Lindström (14). The X-ray tube was designed by Engström & Lundberg (5). The voltage was 3.0 mV. The tissue section was placed at a distance of about 55 mm from focus, which was about 0.1 mm in diameter. Most of the emitted X-ray quanta had wavelengths of 8–12 Å. The contrasts on the developed microradiograph were caused by variations in the dry mass distribution of the various organic tissue components. For the histological production of the microradiographs the technique described by Engström et al. (6) and Bergendahl & Engfeldt (1) was used.

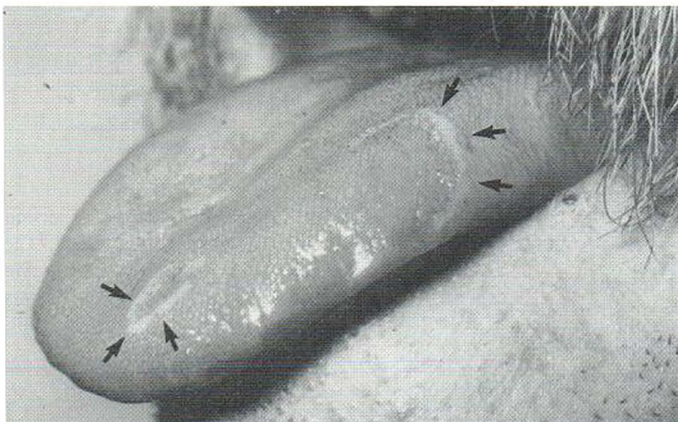


Fig. 6. Case 3, a 30-year-old man, exhibited striated leukoplakia-like lesions on the sides of the tongue (arrows).

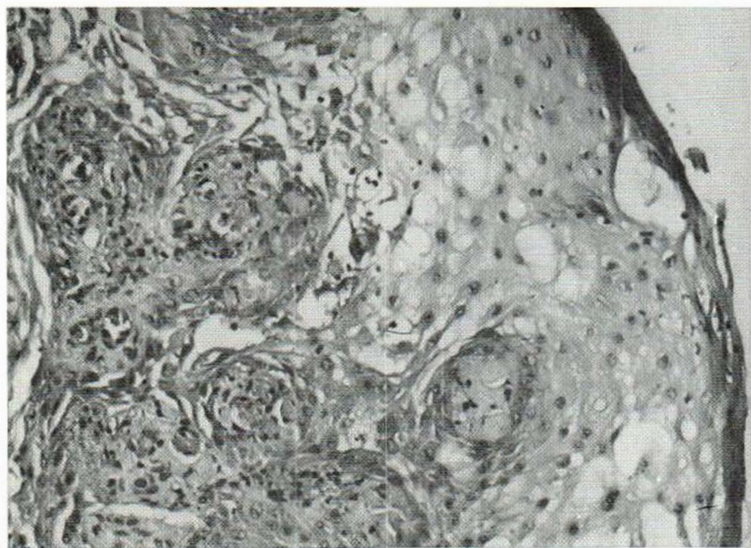


Fig. 7. Case 1. The mucosal papilla, to which the teeth were attached, showed an irregular proliferation of rete pegs. In the stratum corneum and stratum spinosum there is pronounced inter- and intracellular oedema. In the epithelium, cells with dyskeratotic changes are also seen. Haematoxylin-eosin. $\times 150$.

RESULTS

Case 1

The polypean dental papillae exhibit histologically some hyperplasia of the mucosa with irregular proliferation of rete pegs. 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 microradiographs 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 keratohyalin granules is noticeable. The superficial layer has the appearance chiefly of parakeratosis, but the light superficial zone on the microradiographs 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 trabeculae, 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 germ-like appearance (Fig. 10) and



Fig. 8. Microradiograph 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 increased keratinization. The vacuoles caused by the intracellular oedema appear as black, oval or circular cavities. $\times 160$.

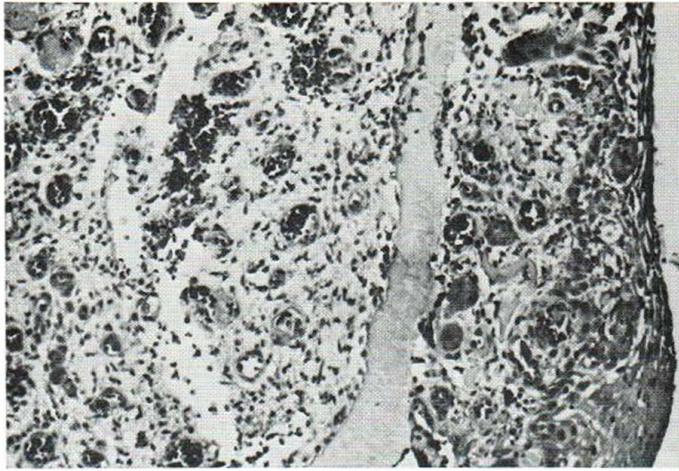


Fig. 9. Case 1. The dental papilla is fibroblastic and vascular. In the connective tissue an osteodentine-like hard tissue trabecula is seen, which is partially covered with osteoblast-like cells. Haematoxylin eosin. $\times 110$.

exhibits a high dry mass concentration on the micro-radiographs.

Case 2

The incisors exhibit at some points an irregular dentinal structure with disturbed mineralization (Fig. 11). No pulpal or papillary tissue is observable. Odontoblasts are lacking, as also is predentine. Residues of a fibrous connective tissue, instead, delimit the part of the tooth adjoining the connective tissue, and the predentine zone has been replaced by an osteodentine-like substance with cell inclusions (Fig. 12). The orally situated part of the tooth exhibits bacterial colonies and caries on the surface (Figs. 12 and 13). Bacteria are also in evidence in dentinal tubuli (Fig. 13). On the microradiographs a high dry mass concentration is seen in the superficial layer of the carious region. -04 exhibits pronounced dysplasia. In the orally situated portion there is a thin enamel matrix, below which dentinal tissue with sparse dentinal tubuli is observable (Fig. 14). A predentine-like zone delimits the dentine from a vascular pulpal tissue, which at some

points is loose and at others fibrous and which lacks a regular odontoblastema. In the peripheral parts the dentine becomes more irregular and osteodentine-like, and the underlying connective tissue is here fibrous, hyaline and deficient in cells (Fig. 15). A deep invagination exists at one point (Fig. 15).

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 hyperorthokeratosis. In the superficial layers of cells and in the stratum spinosum there is a widespread intracellular oedema. In the subepithelial connective tissue there are at some points indications of a bandlike confluent lympho- and plasmocytic cell infiltrate and an increased number of mast cells. No liquefaction degeneration of the cells in the stratum basale is noticeable, however, and the boundary between epithelium and connective tissue is sharply delineated. No manifest exocytosis. No evidence of malignancy exists.



Fig. 10. Case 1. In the connective tissue an osteodentine-like formation is seen. Mallory $\times 16$.



Fig. 11. Case 2. The incisors have at some points an irregular dentinal structure with disturbed mineralization. Haematoxylin-eosin. $\times 150$.

DISCUSSION

Lesions characteristic of pachyonychia congenita, in the form of thickening of finger- and toe-nails, palmo-plantar 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 accorded with that reported by Witkop & Gorlin (22). The oral leukokeratoses exhibit certain histo-

pathological characteristics in common with three other benign, hereditary oral mucosal hyperplasias, namely white sponge naevus, hereditary benign intra-epithelial dyskeratosis and Darier's disease (22). Pachyonychia congenita can be distinguished from the others by, among other means, the absence of intra-epithelial dyskeratosis and papillomatosis and villi-like proliferation of the basal epithelial cellular layer. Nor are grains or corps ronds found in pachyonychia congenita.

Natal teeth, i.e. teeth which are erupted at birth (15), have been reported only briefly in pachyonychia congenita by a few authors (17, 11, 16). Natal teeth also occur in infants in whom this syndrome is absent. The aetiology in such cases is unclear. Here, again, hereditary factors appear to be important (10, 2, 15).

The clinical picture of the teeth examined in this



Fig. 12. Case 2. -01. The predental zone is replaced by an osteodental (OD) with cell inclusions. Orally are seen bacterial colonies and caries (C). Haematoxylin-eosin. $\times 170$.

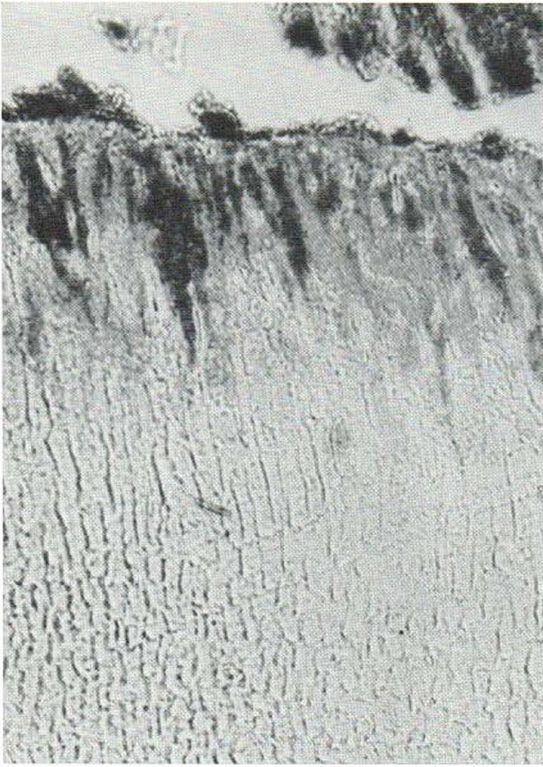


Fig. 13. Case 2. -01. In the peripheral part of the dentine, ampoules with bacteria in the dental channels are seen. Brown-Brenn. $\times 380$.

study accorded with that reported by Jackson & Lawler (11). No histological investigation of natal teeth in conjunction with pachyonychia congenita has previously been presented. On the other hand,

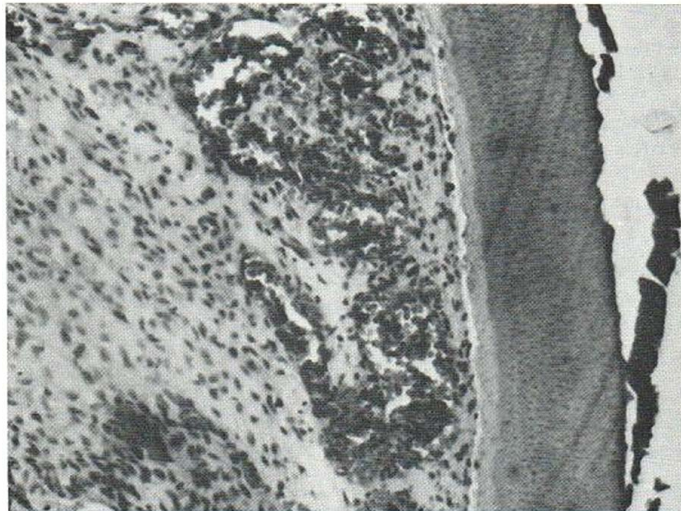


Fig. 14. Case 2. -04 exhibits pronounced dysplasia. In the orally situated portion there is a thin enamel matrix and thereunder a dentinal tissue with sparsely located dental channels. Haematoxylin-eosin. $\times 150$.

natal and neonatal teeth in infants unaffected by this syndrome have been examined histologically (10, 19, 20), microradiographically and by polarized light technique (24). Some of the dental lesions were common to all cases, such as the occurrence of interglobular dentine, irregular osteodentine-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. Bjuggren (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 on pressure. If they are very loose, they may be swallowed or aspirated. Natal teeth may also injure the mother's breast during breastfeeding and lacerate the infant's tongue.

Natal teeth and oral leukokeratoses would seem, from this investigation, to be the earliest clinical manifestations of pachyonychia congenita and generally appear prior to nail lesions. When there is

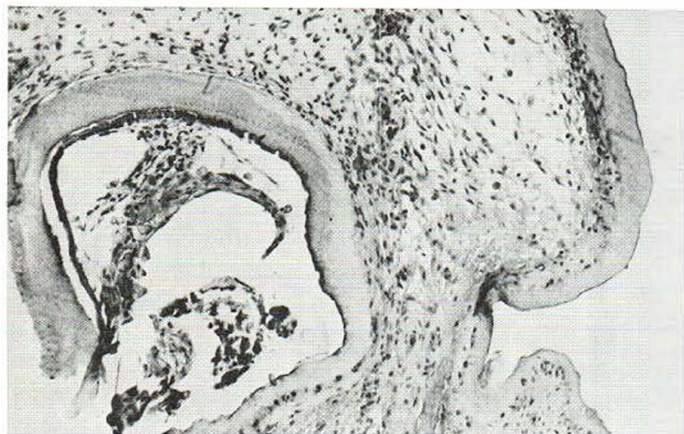


Fig. 15. Case 2. -04. In the cervically situated portions the dental tissue changes to an irregular osteodentine-like hard tissue. The underlying connective tissue here is hyaline and deficient in cells. A deep invagination is also seen. Haematoxylin-eosin. $\times 45$.

a hereditary predisposition to pachyonychia congenita, therefore, it is important that both dermatologists and dentists should inspect the oral cavity at an early stage. For the same reason the jaws should be X-rayed for the presence of supernumerary natal tooth germs.

REFERENCES

- Bergendahl, G. & Engfelt, B.: Preparing material for microradiography. *Acta Path Microbiol Scand* 49: 30, 1960.
- Bjuggren, G.: Premature eruption in the primary dentition—a clinical and radiological study. *Swed Dent J* 66: 343, 1973.
- Brown, J. H. & Brenn, L.: Method for differential staining of Gram-positive and Gram-negative bacteria in tissue sections. *Bull Johns Hopkins Hosp* 48: 69, 1931.
- Engström, A. & Lindström, B.: A method for the determination of the mass of extremely small biological objects. *Biochim Biophys Acta* 4: 351, 1950.
- Engström, A. & Lundberg, D.: A simple X-ray tube for high resolution microradiography. *Exp Cell Res* 12: 198, 1957.
- Engström, A., Lundberg, B. & Bergendahl, G.: Microradiography with ultrasoft X-rays. *J Ultrastruct Res* 1: 147, 1957.
- Gorlin, R. J.: Genetic disorders affecting mucous membranes. *Oral Surg* 28: 512, 1969.
- Gorlin, R. J. & Chaudhry, A. P.: Oral lesions accompanying pachyonychia congenita. *Oral Surg* 11: 541, 1958.
- Gorlin, R. J. & Pindborg, J. J.: *Syndromes of the Head and Neck*. Blakiston Div., McGraw-Hill Book Co. Inc, New York, 1964.
- Hals, E.: Natal and neonatal teeth. *Oral Surg* 10: 509, 1957.
- Jackson, A. D. M. & Lawler, S. D.: Pachyonychia congenita. A report of six cases in one family. *Ann Eugenics* 16: 141, 1949.
- Jadassohn, J. & Lewandowski, F.: Pachyonychia congenita. In *Ikongraphia Dermatologica*, p. 29. Urban & Schwarzenberg, Berlin, 1906.
- Kumer, L. & Loos, H. O.: Über pachyonychia congenita (Typus Riehl) *Wien Klin Wochenschr* 48: 174, 1935.
- Lindström, B.: Roentgen absorption spectrophotometry in quantitative cytochemistry. *Acta Radiol, Suppl.* 125, 1955.
- Massler, M. & Savara, B. S.: Natal and neonatal teeth. *J Pediatr* 36: 349, 1950.
- Moldenhauer, E. & Ernst, K.: Das Jadassohn-Lewandowsky-Syndrom. *Hautarzt* 19: 441, 1968.
- Murray, F. A.: Congenital anomalies of the nails. Four cases of hereditary hypertrophy of the nail-bed associated with a history of erupted teeth at birth. *Br J Dermatol* 33: 409, 1921.
- Riehl, G.: Eigenartige Keratosis palmaris et plantaris mit Nagelveränderungen. *Z Haut Geschlechtskr* 6: 335, 1923.
- Southam, J. C.: The structure of natal and neonatal teeth. *Dent Prac Dent Res* 18: 423, 1967.
- Sponge, J. D. & Feasby, W. H.: Erupted teeth in the newborn. *Oral Surg* 22: 198, 1966.
- Söderqvist, N. A. & Reed, W. B.: Pachyonychia congenita with epiderma cysts and other congenital dyskeratoses. *Arch Dermatol* 97: 31, 1968.
- Witkop, C. J. & Gorlin, R. J.: Four hereditary mucosal syndromes. *Arch Dermatol* 84: 762, 1961.
- Young, L. L. & Lenox, J. A.: Pachyonychia congenita. *Oral Surg* 36: 663, 1973.
- Zoony, N. N., Silberkweit, M. & Brown, C. H.: Polarized light and microradiographic study of natal teeth. *J Dent Child* 34: 433, 1967.

Received January 17, 1975

G. Anneroth, D.D.S.
Department of Oral Pathology
Institution of Pathology
Karolinska sjukhuset
S-104 01 Stockholm 60
Sweden