

PACHYONYCHIA CONGENITA

A Histologic and Microradiographic Study

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Abstract. A biophysical study of a specimen from a patient, one of a family suffering from pachyonychia congenita associated with hyperhidrosis palmaris et plantaris, is described, and two case histories are given. The morphological and quantitative data reveal that the pathological changes are exclusively localised in the nail bed (the ventral nail plate) and possibly in the connective tissue supporting the ventral nail plate. The major anomaly is a pronounced increase in thickness and dry mass of the nail bed (the ventral nail plate). The hard nail plate proper shows no pathological changes.

Pachyonychia congenita is a rare genodermatosis mainly characterized by nail dystrophies. The condition is associated with hyperkeratosis and plantar hyperhidrosis and to a lesser degree with palmar hyperhidrosis. The hyperhidrosis in combination with hyperkeratosis leads to the formation of painful blisters and oozing, especially on the soles. Furthermore, bright red papules with central follicular plugs may be found on the extensor surface of elbows and knees. The condition is generally associated with keratosis pilaris on the outer aspects of the upper and lower extremities, sometimes on the back, on the buttocks and the lumbar region. A common trait is oral leukoplakia, usually associated with a *Candida albicans* infection. In addition, a thickened membrana tympani and corneal dyskeratosis may also be found. Partial diffuse alopecia has been reported. Reports on pachyonychia congenita have been given by several authors (1, 5, 6, 7, 12, 13, 14). The syndrome, as classified by Kummer & Loos (8) describes three types of the syndrome:

Type I: Symmetrical keratosis of hands and feet, and follicular keratosis of the body.

Type II: (Riehl) In addition to the symptoms of

type I, oral leukoplakia is observed. This is the most common type.

Type III: Includes the characteristics of types I and II and, in addition, corneal dyskeratosis.

Present investigation. The clinical part of the present investigation includes direct observations of two young sisters and their mother, all suffering from the disease as well as the history of the mothers family (Fig. 1). The biophysical investigation was performed on a nail biopsy obtained from the mother.

Scope of the investigation. The present biophysical study of a case of pachyonychia congenita takes advantage of the quantitative aspect of microradiography which allows mass determination at cellular levels to reveal the site of the pathological changes and to explain the remarkable hardness of the thickened nail. The investigation is thus an extension of previous biophysical studies which have offered an expla-

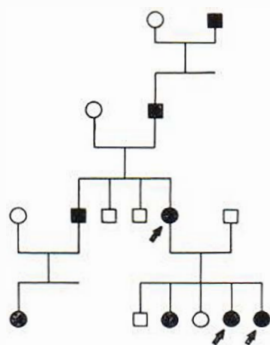


Fig. 1. Pedigree of the family studied. □, men; ○, women. Filled symbols indicate pachyonychia congenita cases. The patients studied in the present investigation are indicated by arrows.



Fig. 2. Nails of case 1.

nation for the strength of the normal human nail plate based on the structural arrangement at different levels of resolution (2, 3, 4).

CASE REPORTS

Case 1. An 8-year-old girl with persistent nail dystrophy and hyperhidrosis of the palms and soles since birth. The patient has developed a number of cutaneous manifestations on the soles, elbows and knees as well as on the mucous membranes of the mouth. All nails (hands and feet) are markedly thickened, opaque and show transverse ridges (Figs. 2 and 3). Areas of the soles which are subject to pressure, i.e. toes, heels etc. exhibit prominent hyperkeratosis, fissures and solitary vesicles. Elbows and knees show minute pale papules with central hyperkeratotic core. On the lateral margins of the tongue as well as on the buccal mucous membrane hyperkeratotic plaques (leukoplakia) are found as well as fungal colonies (*Candida albicans*). Fissures at the corners of the mouth are conspicuous. Subjectively the patient suffers no great discomfort from her nail condition. However, the hyperhidrosis of the soles (and palms to a lesser degree) constitutes a condition which, at least in summertime, greatly disables the patient. The suffering is obviously due to the combination of heat, friction

and humidity acting on the hyperkeratotic skin, leading to advancement of the hyperkeratotic changes and resulting in disabling painful fissures and vesiculation on the soles. The patient appears to be mentally normal for her age although she is reported to meet with difficulties in her school work.

Case 2. The younger sister of case 1, aged 1, who has dystrophy of the nails and hyperhidrosis of palms and soles since birth as well as a multifocal fungal infection (*Candida albicans*). All nails are markedly thickened, opaque and show transverse ridges. She has suffered from repeated paronychia of *Candida albicans* genesis and has oral and diaper dermatitis caused by the same organism. Her mental development appears to be normal when compared with that of her age group.

Case 3. A 37-year-old woman, the mother of cases 1 and 2, with persistent nail dystrophy since birth, hyperhidrosis and repeated oral candida infections and pachyonychia. All nails are markedly thickened and opaque.

These three patients, cases 1, 2 and 3, have several cases of diagnosed pachyonychia congenita in the mother's line of heredity. These cases are likewise associated with hyperhidrosis of the palms and soles. The mother and one uncle were subject to sympathectomy after puberty followed by a clinical regression of the hyperhidrosis symptoms. The symptoms of the disease are traceable to generations older than that of the mother (Fig. 1).



Fig. 3. Close-up view of the thickened nails. Case 1.

EXPERIMENTAL STUDY

Microradiography which allows quantitative mass determination at cellular levels utilizes lyophilized tissue material which is freeze-sectioned and freeze-dried (10, 11). Such sections are exposed to soft X-ray ($\lambda > 8 \text{ \AA}$) so as to obtain contact radiograms on a fine grain photographic emulsion. A section and a reference system with an elementary composition corresponding to organic material are exposed simultaneously (9). Densitometry of the section microradiogram and the reference system allows quantitation of the order of 5 picograms ($5 \times 10^{-12} \text{ g}$).

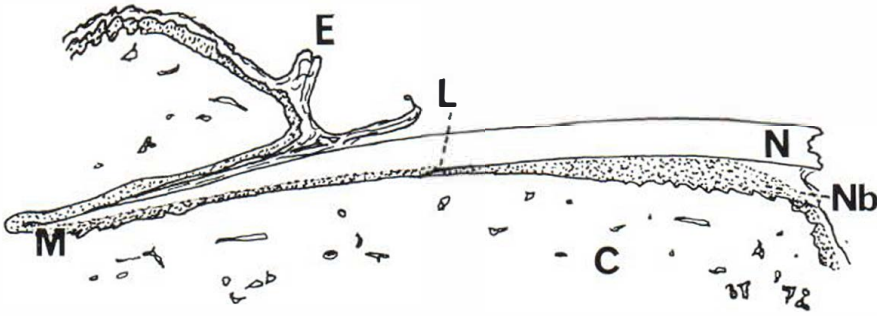


Fig. 4. Schematic representation of the normal nail. M, Matrix; L, lunula; N, nail plate; Nb, nail bed (also called the ventral nail plate); E, epidermis. For more

detailed information about the structural entities of the nail, cf. Forslind, B.: *Acta Dermatovener (Stockholm)* 50: 161, 1970.

MATERIAL AND METHODS

A 2 mm wide biopsy including the nail root, the hard nail plate and the nail bed was cut under local anaesthesia (15) from digit IV of the left hand of case 3. The specimen was transported from the operation theatre to the histological laboratory in an ice-cooled sterile glass jar and prepared for microradiography by freeze-sectioning within 5 mm of the incision. A few sections were stained with haematoxylin-eosin. The remaining sections were used in the microradiographic experiments designed to evaluate dry mass/unit area.

RESULTS

In the dorsal part of the nail fold (the roof of the proximal nail fold) the boundary between the epithelium and the dermis is a smooth, almost straight line in the section. The two parts of the matrix of the hard nail plate [the dorsal and the intermediate nail plates (2)] appear to be somewhat more irregular than in the normal one. Small epithelial papillae from this matrix

penetrate the dermis. The hard nail plate proper does not take up any stain as in the normal case. No nuclear remnants are visible in this part of the nail. The cuticula of the nail which emanates from the epidermis of the dorsal part of the nail fold, the matrix cells, and the cells in the process of keratinization of the hard nail plate proper appear normal in haematoxylin-eosin stained sections as well as in the microradiographs (Figs. 4, 5 and 7). The matrix of the nail bed [the ventral nail plate (2)] is much thicker than is normally the case. The cells above the matrix layers are extensively elongated, mainly in a volar-dorsal direction. The horny cells of the ventral nail plate show a staining reaction similar to that of normal stratum corneum with the haematoxylin-eosin stain. Some nuclear remnants can be seen even close to the intermediate nail plate (the volar part of the hard nail plate proper). The boundaries of these cells are not possible to outline with certainty. In the freeze-dried sections

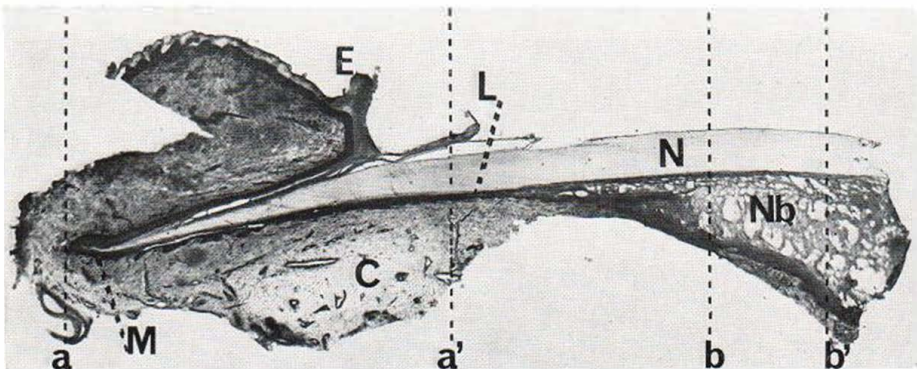


Fig. 5. Microphotograph of haematoxylin-eosin stained freeze-section of specimen from a case of pachyonychia congenita. (For legend see Fig. 4.) Areas studied by micro-

radiography in parallel unstained sections are indicated by vertical dash lines, i.e. a to a' represented in Fig. 7 and b to b' represented in Fig. 6 b.

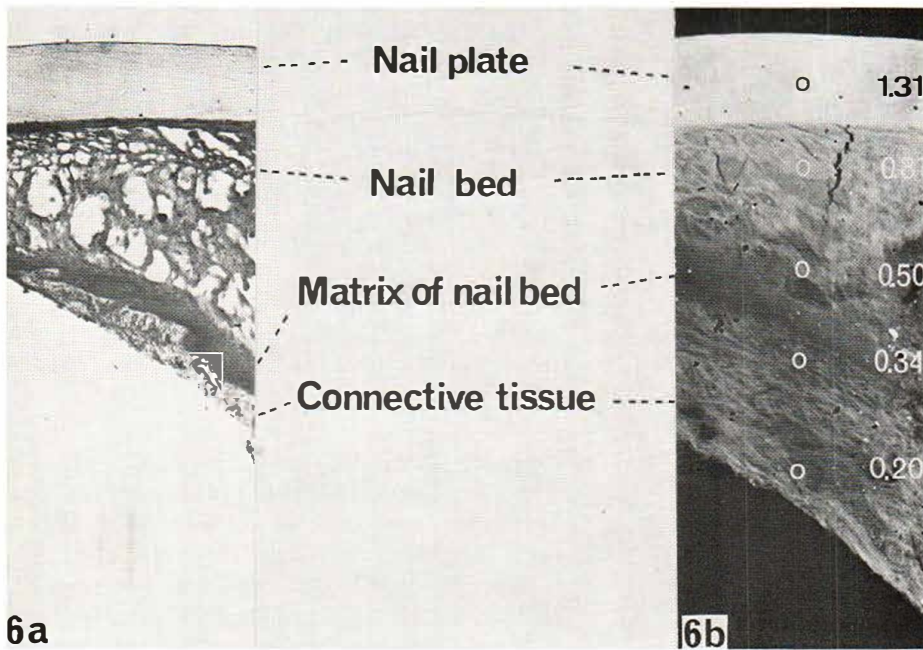


Fig. 6. (a) Enlarged area of Fig. 5 (b to b'). The haematoxylin-eosin staining of the freeze-sectioned nail has resulted in loss and/or condensation of material in the nail bed, thus explaining the great number of vacuoles seen in the section. (b) Microradiograph from section neighbour to that of Fig. 6a. Light areas indicate high

absorption of X-rays (high mass per unit area). The actual points of densitometry are indicated by circles and corresponding dry mass values (g/cm^2) are presented at the right hand margin of the micrograph. It is seen that a high density is recorded over a large part of the nail bed.

which were subsequently stained, large vacuoles are seen in this mass of cells but such phenomena are not present in the microradiographic sections. The connective tissue underlying the nail bed (ventral nail plate) is characterized by a pronounced development of fibroblasts. These cells are seen to be oriented perpendicular to the basal membrane of the epithelial cells. In contrast, the

connective tissue adherent to the matrix of the hard nail plate proper has a normal appearance. *Quantitative microradiography.* Evaluation of the dry mass per unit area from the microradiographs shows that the dry mass increase in the hard nail plate proper does not deviate from that of a normal nail. However, in the parakeratotic nail bed (ventral nail plate) higher values of the

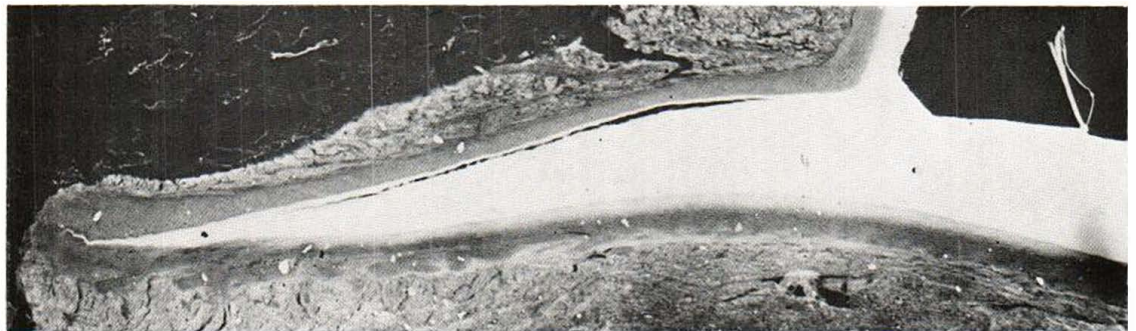


Fig. 7. Microradiograph of the same section as seen in Fig. 6b representing the area a to a' in Fig. 5. The density distribution over this part of the nail plate of the

pachyonychia congenita nail does not differ from that of a normal nail (cf. Forslind, B. et al.: *Acta Dermatovener (Stockholm)* 51: 89, 1971).

dry mass are observed than in the normal case, the highest value being roughly elevated by a factor 3. A typical distribution of dry mass values from the pachyonychia sections is shown in Fig. 6.

DISCUSSION

It is stressed that the present experimental reports concerns only a single biopsy (cut into several 10- to 30-micron sections) from one case of the disease, pachyonychia congenita. The conclusions drawn in the following discussion are consequently limited to the present case.

All present evidence from the investigation at light microscope resolution, including the microradiographic experiments, indicates that the pathological process is localized only in the matrix of the nail bed (the ventral nail plate). This finding confirms the suggestion previously proposed (7), but does not confirm the findings of a stratum granulosum in nail matrix proper (6). The fact that the histological stain produces large vacuoles in the nail bed indicates that some material was dissolved and/or redistributed during the staining process. Vacuoles of this type were also reported in a study previously referred to (7). The relative inconsistency of details in the histological picture of pachyonychia congenita cannot as yet be explained exclusively in terms of preparational differences. Possible differences in the expression of the disease must be taken in account.

The microradiographic investigation gives evidence of at least a threefold increase of dry mass per unit area within the nail bed (the ventral nail plate). In a normal case the increase is of the order of 0.5. In the pachyonychia sections the mass per unit area of the topmost cells of the nail bed (the ventral nail plate) and the apparently normal cells of the intermediate nail plate make a quotient of 0.6 or more whereas this quotient in the normal case is of the order of 0.2-0.3. This increase of mass in the pachyonychia nail bed (ventral nail plate) offers, at least in part, an explanation for the hardness of this part of the nail evidenced at clinical examination. An electron microscopic study of the structural arrangements of the keratin filaments in these cells could provide further understanding of the hardness of the nail bed.

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