

THE PACHYONYCHIA CONGENITA SYNDROME

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Abstract. This study presents two patients showing different clinical types of the Pachyonychia congenita Syndrome (PcS). For the first time there is a description of the histopathology of the blister and vesicle formation, as well as of the plantar keratosis. The essential resemblance in the histopathological changes of the different symptoms of the syndrome is discussed.

Key words: Pachyonychia congenita Syndrome; Clinical types; Histopathology; Bulla; Vesicula

Since Jadassohn & Lewandowsky (10) used the term pachyonychia congenita in 1906 more than 150 examined cases have been reported in the literature. Congenital pachyonychia, i.e. the symmetrical thickening of all nails, is the most striking and consistent symptom of this disorder but it is not the only one. Therefore we prefer Pachyonychia congenita Syndrome (PcS), since this name better reflects the scope of the different symptoms as well as the question of whether this syndrome is one nosologic entity or not.

From the clinical point of view it is practical to distinguish three types, for which we suggest the following names:

Type I, or Jadassohn-Lewandowsky Syndrome. This type is characterized by (A) symmetrical hard thickening of all finger and toenails, (B) keratosis palmo-plantaris, most frequently plantar callosities, confined to the sites of pressure, (C) follicular keratosis, varying from simple keratosis pilaris to larger horny papules on knees and elbows, (D) blister formation, especially under and around the callosities, (E) leukokeratosis of the oral mucosa and sometimes also of the laryngeal mucosa, (F) hoarseness, (G) hair abnormalities, and (H) palmar and plantar hyperhidrosis. Pachyonychia was absent in only three of 93 cases reviewed by Moldenhauer & Ernst (13). In frequency of occurrence the pachyonychia is followed by plantar keratoses (72%) and leukokeratosis oris (57%). This type I is by far the most frequently occurring, so much

so that Moldenhauer & Ernst considered the symptoms typical for types II and III as coincidental.

Type II, or Jackson-Sertoli Syndrome (9, 15). In addition to the symptoms of type I, natal teeth and multiple cysts are also observed. These cysts are localized mainly on the trunk, the axillae, the neck, the scalp and the face. Most authors consider these cysts steatocystoma multiplex (8, 9, 15). It may be noted that leukokeratosis of the oral mucosa has never been reported in type II.

Type III, or Schäfer-Brünauer Syndrome (4, 14). This extremely rare type consists of the symptoms of type I, associated with leukokeratosis of the cornea (dystrophy).

The syndrome appears to be transmitted by a simple autosomal dominant gene, probably with a high penetrance and a variable expression (8). The purpose of this report is to describe the clinical and histopathological findings in two patients with the Pachyonychia congenita Syndrome, one with type I and one with type II.

CASE REPORTS

Case 1

A woman, aged 25, belongs to the PcS type I. She shows the typical symmetrical, progressive thickening of all finger and toenails up to 8 mm. The soles, including the plantar side of the toes, demonstrate thick, yellow, partly circumscribed keratoses on the sites of pressure, sometimes with bulla formation under and just around them. On the non-weight-bearing parts of both soles, about ten scattered minute vesicles are found. The extremities show keratosis pilaris. The skin of the extensor sides of the lower legs is locally xerotic. The pattern of hair growth is normal. The oral cavity shows irregularly shaped white plaques, leukokeratosis oris. There was no hoarseness and the eyes were normal.

Lesions have been present as long as the patient can remember. The warmer the weather and the more she walks, the more she complains of callous formation, blistering and pain. Up to now, blisters on the feet have

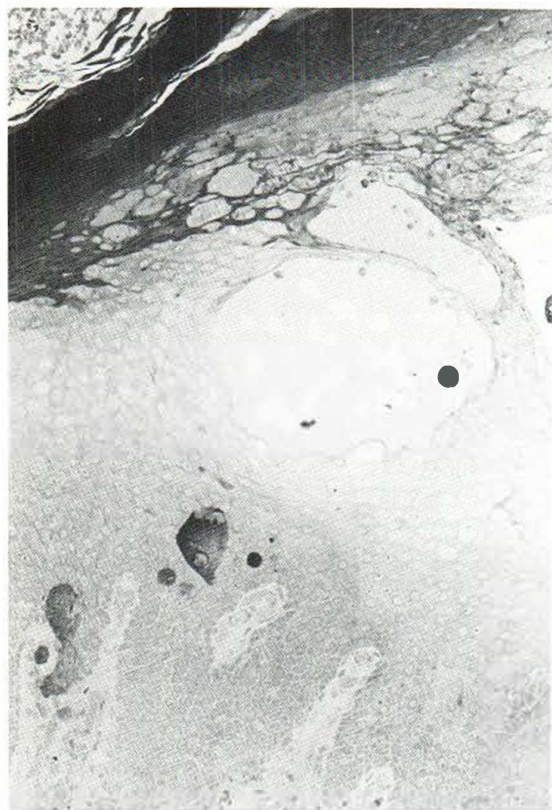


Fig. 1. A vesicle from the sole (toluidine blue, $\times 120$).

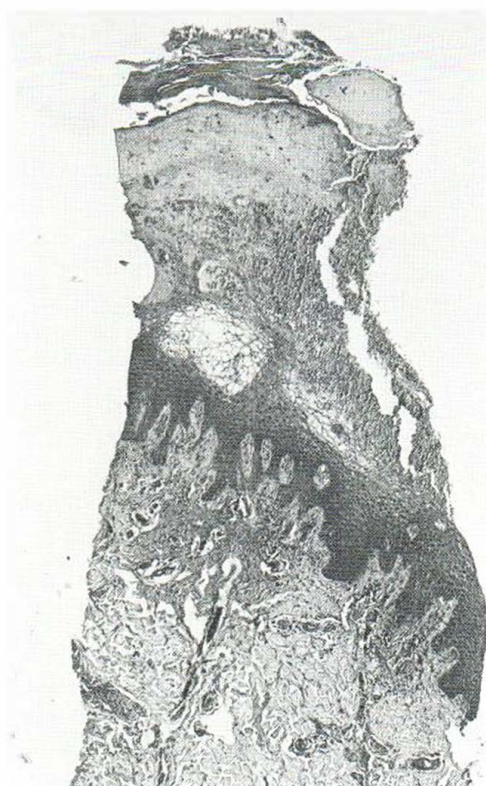


Fig. 2. Blister formation under a callus (H&E, $\times 50$).

developed every summer. The minute vesicles on the soles were seen only during two very hot summers. The walking distance before getting complaints is about 10 min in summer and about $1\frac{1}{2}$ hours in winter. The whitish patches in the mouth change rather quickly in shape and site, depending on the pressure exerted. The leukokeratosis of the alveolar process has faded away since she was fitted with a comfortably fitting dental prosthesis.

During the time that the patient was a secretary, there were large horny papules on her elbows. Her only son, aged six, shows also a PcS type I with pachyonychia of all nails, keratosis plantaris with blister formation and keratosis pilaris. Leukokeratosis has never been present up to now. The patient's deceased father would have been affected in the same way; in his second marriage he had a normal son. According to genealogical studies, no history of consanguinity could be elicited over the last five generations.

Case 2

A woman, aged 27. The fingernails are only slightly thickened; some are partly pale-yellow. The toes, on the contrary, show typical signs of pachyonychia, with a distal thickness of 5 to 7 mm. The soles demonstrate thick yellow keratoses without blister formation. The skin of

the legs below the knee is xerotic. There is no leukokeratosis oris and no hoarseness. Some 40 yellow cysts, up to 1 cm in diameter, are found on the neck, trunk and buttocks. The small ones have a somewhat bluish tinge. The hairs of the eyebrows stick straight out. The rest of the hair growth pattern does not deviate.

This patient was born with two natal teeth, incisors in the lower jaw. Blister formation on the soles commenced at the age of 18 and has returned every summer. She has never had keratosis pilaris, horny papules or leukokeratosis oris. Her only child was also born with two natal teeth in the lower jaw. The patient's father and her daughter—both examined by us—have the same deviant eyebrows. The family history yields 35 subjects in the four last generations with at least 12 subjects obviously affected, viz. 5 males and 7 females.

HISTOLOGICAL STUDIES

Case 1

Two biopsies, the first from a vesicle and the second from the margin of a thick plantar keratosis with bulla formation beneath it, revealed identical features (Figs. 1, 2).

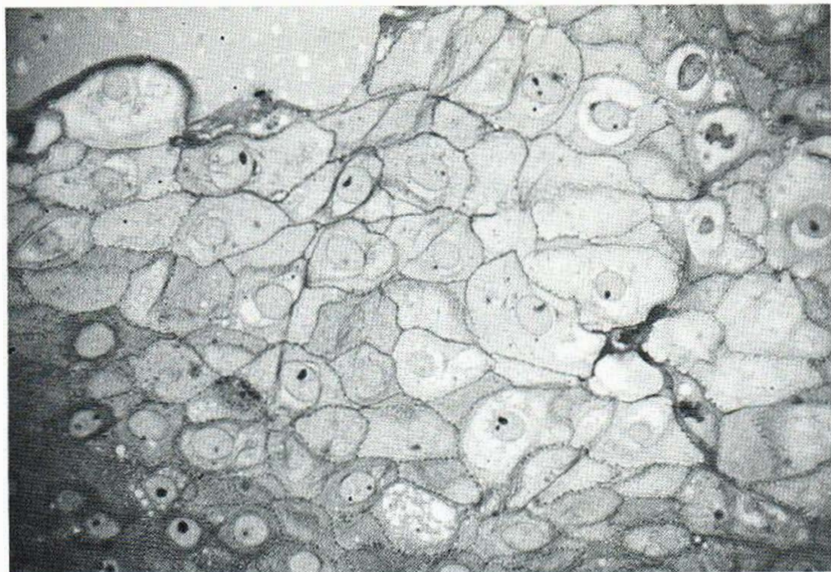


Fig. 3. Perinuclear vacuolization, detail from Fig. 1 ($\times 450$).

Locally in the epidermis, where vesicle formation develops, the cells in the upper layers of the stratum Malpighii show in their migration to the surface an increasing intracellular oedema, with an ever-increasing perinuclear vacuolization finally leading to vesicle formation (Fig. 3) and loss of keratohyalin granules. Alternating para- and slight orthokeratosis is seen in the horny layer. At places where it has not led to vesicle formation, hypergranulosis is observed, i.e. abundant and partly large, rather regularly shaped keratohyalin granules. The dermis shows a slight perivascular lymphocytic inflammatory infiltrate.

A third biopsy was taken from the leukokeratosis on the inferior alveolar process. The upper layers show intracellular vacuolization focally.

Case 2

A biopsy specimen obtained from the margin of a plantar keratosis of PcS type II yielded the following features (Fig. 4): in the acanthotic Malpighian layer, the prickle cells appear to maintain their volume by moving toward the surface, instead of flattening. Intracellular oedema and vacuolization is not seen. The granular layer varies in thickness: almost absent above the tips of the papillae, elsewhere six layers thick. In the granular layer and the subjacent layers of the stratum Malpighii there seems to be an increased number of partly extremely large, keratohyalin granules (Fig. 5). In the horny

layer, orthokeratosis and extensive areas of parakeratosis are present. In the superficial dermis no significant pathological changes are seen.

DISCUSSION

That the histopathology of blister formation and also of plantar keratosis of the Pachyonychia congenita Syndrome has not been described earlier in the literature is probably due to the difficulty of easily obtaining specimens from the feet. Yet the blister formation is present rather often and the histological picture with its increasing intracellular vacuolization appears to be specific. The histological differential diagnosis of the above-described bulla formation in PcS includes:

(1) Granular degeneration, or epidermolytic hyperkeratosis (1). This phenomenon is characterized by perinuclear vacuolization in the spinous and granular layers, hypergranulosis and hyperkeratosis. The architecture is irregular, due to the varying degree of vacuolization and indistinct cellular boundaries. This is not the case in PcS. Here the blister formation shows a regular architecture, as is revealed above. The keratohyalin granules in epidermolytic hyperkeratosis are irregular in size and form, whilst in PcS they are rather round. Moreover, there is marked parakeratosis in PcS instead of hyperkeratosis.

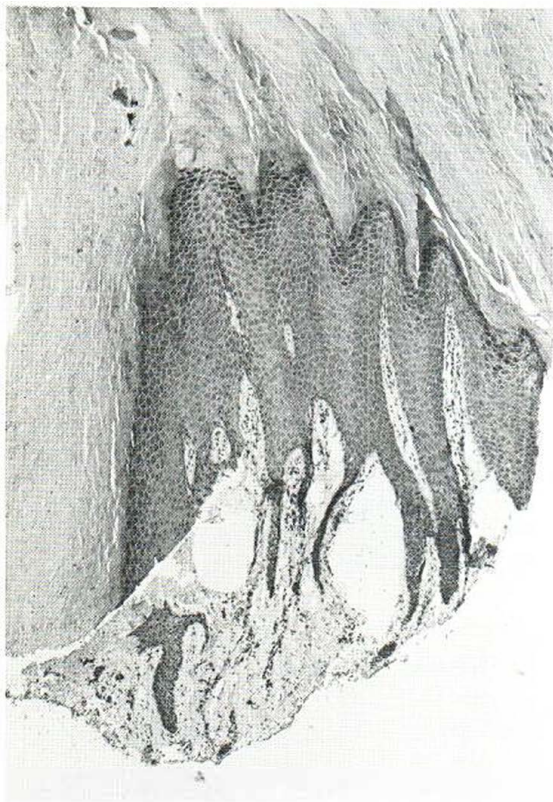


Fig. 4. Plantar keratosis (H&E, $\times 50$).

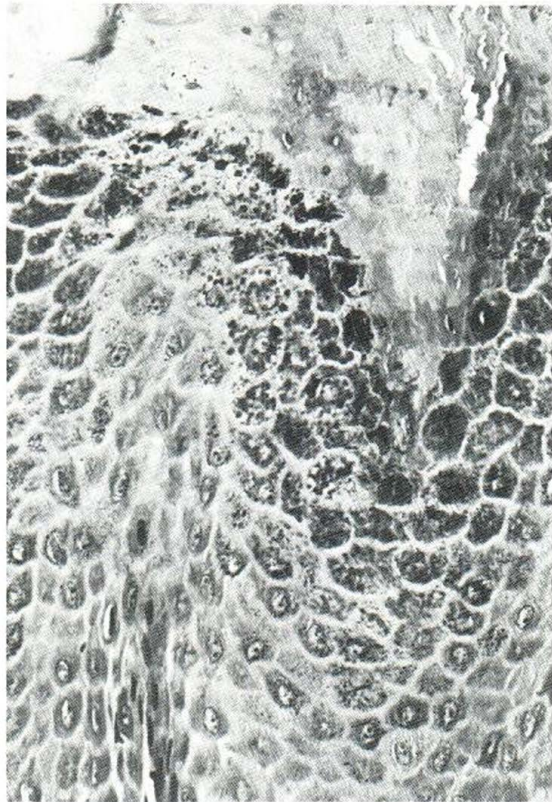


Fig. 5. Hypergranulosis, detail from Fig. 4 ($\times 300$).

(2) Epidermolysis bullosa of the hands and feet (Cockayne).

(3) The friction blister.

The histological picture of Epidermolysis bullosa of the hands and feet is exactly the same as that found in friction blisters, luxated in normal individuals (17). In the margins of these bullae, intracellular oedema can be seen, but at the site of mid-intra-epidermal bulla formation, separation has taken place because of necrotic and dyskeratotic degeneration of cells. The type of hypergranulosis as observed in PcS is absent.

The histopathological changes of the leukokeratosis of the alveolar process found in case I are identical with those from other sites on the oral mucosa, i.e. from the tongue, the buccal surface (7) and the polypean dental papilla (2), as well as with the laryngeal lesions (5). If the histological pictures of the different symptoms of types I, III and II are compared respectively, a fundamental resemblance in the pathological changes may be observed. The histopathological resemblance between the bulla

formation of the skin and leukokeratosis of the oral (7) and laryngeal mucosa (5) is the most obvious, due to their intracellular vacuolization. The horny papules or horny elements also show focally vacuolated cells in the upper stratum Malpighii and in the partially thickened or flattened granular layer (16, 18). The pathological features of the nails insofar as present and insofar not being an artefact, seem to fit into the same picture as well (7). The (leuko) keratosis of the cornea, the prime symptom of PcS type III, has likewise an increasing vacuolization of the epithelial cells (4, 14). In contrast, the plantar keratosis on the sole in PcS type II, as is described in our 2nd patient, exhibited no intracellular vacuolization. Nevertheless the main abnormalities found, viz. the irregular granular layer and the type of hypergranulosis, agree with findings in biopsies from the follicular keratotic elements of type I (16, 18). Recently the combination found in three patients of steatocystoma multiplex and natal teeth without other symptoms has been announced as a separate syndrome, also with autosomal dominant

inheritance (12). The authors' argument not to consider this as PcS was the absence of pachyonychia. In our opinion this argument is not conclusive, for of 93 cases analysed, 3 did not have pachyonychia (13). We prefer to regard this newly found combination as PcS type II A.

Hair anomalies in PcS are reported by Boxley (3) in a family with PcS, type II. He found hair with an irregular diameter of the shaft and with occasional twists. Our patient 2 and her father and daughter showed the same abnormal eyebrows. This hair anomaly probably belongs to type II. If the characteristic abnormal form of the nails is recognized, the diagnosis Pachyonychia congenita Syndrome can be readily established. But when blister formation is paramount and the nail abnormality is less prominent or absent as in our case 2, difficulties do arise. Several authors have had to revise their first diagnosis of Epidermolysis bullosa dystrophica into PcS (11, 13). As is shown above, a biopsy of the bulla formation can confirm or supply the diagnosis thanks to its specific picture.

Although four clinical types can be distinguished in PcS, a marked division into types does not seem justifiable because of the strong overlapping between types. The differences could be explained as a variable expression and the histopathological changes seem to take place within the same picture. Therefore for the present we would regard the clinical types as one nosologic entity: the Pachyonychia congenita Syndrome.

REFERENCES

1. Ackerman, A. B.: Histopathologic concept of epidermolytic hyperkeratosis. *Arch Dermatol* 102: 253, 1970.
2. Anneroth, G., Isacson, G., Lagerholm, B., Lindvall, A. M. & Thyresson, N.: Pachyonychia congenita. *Acta Dermatovener (Stockholm)* 55: 387, 1975.
3. Boxley, J. D. & Wilkinson, D. S.: Pachyonychia and multiple epidermal hamartomata. *Proc R Soc Med* 64: 298, 1971.

4. Brünauer, S. R.: Zur Symptomatologie und Histologie der kongenitalen Dyskeratosen. *Dermatol Zschr* 42: 6, 1925.
5. Cohn, A. M., McFarlane, J. R. & Knox, J.: Pachyonychia congenita with involvement of the larynx. *Arch Otolaryngol* 102: 233, 1976.
6. Forslind, B., Nylén, B., Swanbeck, G., Thyresson, M. & Thyresson, N.: Pachyonychia congenita. *Acta Dermatovener (Stockholm)* 53: 211, 1973.
7. Gorlin, R. J. & Chaudhry, A. P.: Oral lesions accompanying pachyonychia congenita. *Oral Surg* 11: 541, 1958.
8. Hodes, M. E. & Norins, A. L.: Pachyonychia congenita and steatocystoma multiplex. *Clin Genet* 11: 359, 1977.
9. Jackson, A. D. M. & Lawler, S. D.: Pachyonychia congenita, a report of six cases in one family. *Ann Eugenics* 16: 141, 1951.
10. Jadassohn, J. & Lewandowsky, F.: Pachyonychia congenita. In *Ikongraphia dermatologica* (ed. Neisser & Jacobi), Band I, 29 pp. Urban & Schwarzenberg, Berlin, 1910.
11. May, St B.: Epidermolysis bullosa with pachyonychia in three generations. *Arch Dermatol* 85: 662, 1962.
12. McDonald, R. M. & Reed, W. B.: Natal teeth and Steatocystoma multiplex complicated by Hydradenitis suppurativa. *Arch Dermatol* 112: 1132, 1976.
13. Moldenhauer, E. & Ernst, K.: Das Jadassohn-Lewandowsky Syndrom. *Hautarzt* 19: 441, 1968.
14. Schäfer, E.: Zur Lehre von der congenitalen Dyskeratosen. *Arch Dermatol Syph (Berlin)* 148: 425, 1925.
15. Sertoli, P.: Sopra una disonichia ereditaria familiare. *Dermo-sifilograf* 24: 268, 1949.
16. Siemens, W.: Über Keratosis follicularis. *Arch Dermatol Syph (Berlin)* 139: 62, 1922.
17. Sulzberger, M. B., Cortese, Th. A., Fishman, L. & Wiley, H. S.: Studies on blisters produced by frictions. *J Invest Dermatol* 47: 456, 1967.
18. Thormann, J. & Kobayasi, T.: Pachyonychia congenita Jadassohn-Lewandowsky. A disorder of keratinization. *Acta Dermatovener (Stockholm)* 57: 63, 1977.

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