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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 JADASSOHN

A VARIETY OF ICHTHYOSIS (PACHYONYCHIA ICHTHYOSIFORMIS)
INVOLVING CHIEFLY THE NAILS

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Under the caption "Congenital Dyskeratosis," Erich Schäfer described a syndrome based on observations gathered from one case of his own and from thirteen others reported in the literature. The condition is characterized by: pachyonychia; acnciform, follicular keratosis, especially about the knees and elbows; symmetrical and circumscribed plantar and palmar keratosis; hyperhidrosis of the palms and soles; leukoplakia of the oral mucosa, and anomalies of the hair. All the fourteen cases showed pachyonychial changes as a constant finding, while the remaining clinical features were variants.

In Schäfer's case a boy, 12 years old, had had the characteristic ungual manifestations from birth. Brettauer's report dealt with a boy 9 years old. The finger-nails were thickened, opaque, lusterless, partially loosened and in places swollen and lap-rolled in the longitudinal axis of the finger. According to Heller, Jadassohn and Lewandowsky's case of pachyonychia congenita belongs in this group. Siemens likewise reported an example of congenital dyskeratosis under the title "Keratosis Follicularis." Babicke recorded an instance of plantar and palmar keratosis which was neither inherited nor familial. Andrews and Strumwasser's patient, began to show pachyonychial changes two weeks after birth. Fox's patient also presented thickening of the nails and other suggestive features of this disorder.

From the Department of Dermatology and Syphilology, Columbus Hospital.
2. Brettauer, cited by Heller.


Associated defects have been described. In the patients seen by
Bettmann,\textsuperscript{8} Jadassohn and Lewandowsky,\textsuperscript{9} Strandberg\textsuperscript{10} and Schäfer\textsuperscript{4}
bullae appeared from time to time on the thickest parts of the soles.
Andrews and Strumwasser's\textsuperscript{6} patient had herpetic lesions on the oral
mucosa at intervals. In the majority of cases keratosis of the mucous
membranes of the mouth (leukoplakia) has been noted. In Burns'\textsuperscript{10}
patient, a boy, the nasal mucosa was similarly affected while the tympanic
membranes were so thickened and retracted that the boy was totally deaf.

Opacities and partial blindness due to dyskeratosis of the cornea
have been reported by Brettauuer,\textsuperscript{2} Brunauer\textsuperscript{11} and Burns.\textsuperscript{10} Riehl's
patient,\textsuperscript{12} a Bulgarian, had abnormally long bones, excessive motility of
the joints and the striped or linear form of palmar keratosis. The boy
seen by Schäfer\textsuperscript{1} had bilateral cataract and twinning of the incisor teeth.

Mental deficiency was noted by Brunauer.\textsuperscript{11}

Pachyonychia congenita of Jadassohn affects chiefly males and appears
to be most prevalent among Slavs and Jews of Slavonic origin.
It is rarely represented in the sibships of twins, the notable exception
being the boy seen by Mendes da Costa and van der Valk,\textsuperscript{13} who was
one of triplets.

**REPORT OF A CASE**

The patient was a school boy, 9 years old. Notwithstanding his Italian parent-
age he had light blue eyes, a fair complexion and light brown hair. He resembled
very much the male parent, who had been treated for syphilis about twenty
years previously. Several years before he married, the Wassermann reaction of
the blood had been reported negative. The mother's blood had given a negative
Wassermann reaction before her only child was born. There was no con-
sanguinity of the parents, nor had any abnormality similar to that displayed by
the patient been reported in the grandparents, ascendants or collaterals. The
patient had been normal at birth. His infancy and childhood were uneventful
except for an attack of measles, which was associated with respiratory com-
plications.

Four years before I saw the patient the perimarginal tissues of the middle finger
of the left hand became red and boggy. A physician removed the nail plate. Six
months later the patient injured the great toe of his left foot. Subsequently all
the nails of the left foot became red and boggy. Another physician extracted the
diseased nails. Within a few weeks the toe-nails of the right foot became involved,
for which roentgen treatments were given, with aggravation of the condition. The
mother then proceeded to take the matter in her hands and pulled out all the
loosened nails.

\textsuperscript{8} Bettmann, in Schwalbe, Ernst: Die Morphologie der Missbildungen des
Menschen und der Tiere, Jena, Gustav Fischer, 1909, p. 735.

\textsuperscript{9} Strandberg, cited by Cockayne, E. A.: Inherited Abnormalities of the

\textsuperscript{10} Burns, cited by Cockayne.\textsuperscript{9}

\textsuperscript{11} Brunauer: Dermat. Ztschr. \textbf{42}:6, 1924.


Other important features in the history were: (1) hyperhidrosis confined to the palms and soles, of several years' duration; (2) dry, itchy skin and marked pityriasis scaling of the scalp since the age of 2 years; (3) epiphora (right eye) for two years; (4) hemangiomata at the tip of the tongue, first noticed soon after birth (the mother stated that the vascular tumor would from time to time enlarge and simulate a strawberry), and (5) slight deafness.

The patient was examined in a clinic for cutaneous diseases. On the tentative diagnosis of syphilitic onychia, he received a course of eleven intramuscular injections of a bismuth compound and eight intravenous injections of neoarsphenamine, without clinical improvement. Three Wassermann tests of the blood were negative, and repeated mycologic examinations of the nails were uniformly negative. There was also no response to local fungistatic therapy.

My examination revealed the boy to be neither mentally deficient nor physically inadequate. There was no evidence of hypogenitalism; however, the testicles were only partially descended. The skin was xerotic throughout. A fine pityriasis Scaling was noted on the scalp, face and trunk. On the cheeks, ears and margins of both eyelids the skin was so thin that the underlying vascular network was visible (telangiectatic), and over the extensor surfaces of the extremities it was studded by many keratotic follicles (lichen pilaris).

The hair of the scalp was dry and lusterless. There were no corneal opacities or cataracts present. The conjunctivae were clear. The lacrimal ducts of the right eye were not patent, for the ophthalmologist was unable to pass a probe in spite of repeated attempts. The obstruction of the ducts, accounting for the unilateral epiphora, was probably due to the same ichthyotic process noted elsewhere. The tympanic membranes were slightly thickened and retracted. There were no dental defects, such as twinning of the upper incisors. The anterior two thirds of the tongue was splashed by irregular patches of a smooth, white infiltration (leukoplakia, fig. 1). There was neither smooth atrophy of the tongue nor interstitial glossitis. On the tip of the tongue a reddish, smooth, rounded, nut-sized nodule, which could be partially dehematized, was visible. There was no abnormality of the thyroid gland.

On the elbows were patches composed of grouped pinkish, pea-sized papules which were capped by fine, adherent scales. Similar patches were noted over both knees, except that on the left kneecap the papules were discrete and distributed in an irregular fashion. Many discrete pinkish papules, intermingled with typical lesions of lichen pilaris, were scattered over the extensor surfaces of all the extremities.

The skin of the palms was glazed, moist and slightly thickened, but was not as keratotic as in keratoderma palmatis; the surface of the soles was likewise hyperhidrotic and somewhat cornified. The skin over the terminal phalanges was dry, erythematous and thinned, while the tips of the fingers and toes suggested "clubbing" (fig. 2).

The finger-nails presented a bizarre picture. Some were thickened, yellowish white, loosened laterally (over the distal third of the nail bed) and lap-rolled to describe the letter O when viewed anteriorly. Other nails were absent, so that the concave nail bed was covered by a dark, horny pellicle. The remainder were deformed (gryphotic), opaque and longitudinally furrowed, and displayed the stair-step-like exfoliation. The nails of the great toes were dark, unevenly thickened (due to subungual keratosis and heaping up of the nail plate) and shortened anteroposteriorly. The remaining toe-nails were thin (excessive exfoliation?), tapered in an upward direction and lacked the lunula, which was also absent on the finger-nails.
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While the patient was under observation it was noticed that the subungual keratosis would lift up the free margin of the nail which was about to be shed. The free margin would become thicker, darker and more opaque, while the nail plate loosened laterally. Eventually the plate would be shed, leaving a dark pellicle (fig. 2).

Routine laboratory investigations gave negative results. A biopsy specimen taken from the patch over the right knee was examined by Dr. D. L. Satenstein.

Fig. 3.—A section showing the increased horny cell layer with lamellation. The granular cell layer is thickened. The rete cells are small and show premature keratinization.

The most conspicuous features of the sections examined were (fig. 3): (1) a marked thickening of the horny layer, which was composed of loose, horny lamellae; (2) a relative thickening of the prickle cell layer, in which the cells were decreased in volume owing to premature keratinization; (3) a sparse cellular infiltration about the vessels in the upper cutis; (4) large size of the lumen of the sweat glands and small size of the sebaceous glands; (5) hypertrophy of the collagen bundles and no disappearance of the elastic tissue or fat; (6) cornification of the follicular openings, but not of the sweat pores, and (7) presence of the...
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granular layer throughout, though less marked in some areas than in others, and
lack of nuclei in the horn cells.

A section of one of the nails revealed a swelling of the horn cells making up
the nail plate. The horn cells retained their globular outline and presented evi-
dence of degeneration (fig. 4).

The patient was given small doses of thyroid extract. The skin was anointed
daily with a bland cream, and a weak sulphur ointment was suggested for the
nails. The results have not been satisfactory.

Fig. 4.—Photomicrograph showing swollen horn cells and degenerative cells.

COMMENT

The formation of keratin is a specific function of the epithelial cells.
Dyskeratosis is an underlying disturbance of this specific function, i.e.,
there is an interference with the aging process of epithelial cells. The
abnormal cornification may be characterized by (1) faulty development
or (2) abnormal behavior. The change is most marked in the horny
layer. The dyskeratotic process (i.e., the disturbance in the evolution
of epithelial cells with special reference to cornification) may; according to Satenstein's classification, be accelerated, resulting in a premature senility of epithelial cells, or it may be retarded, causing delayed juvenility of these cells. In the former, one finds the dry, and in the latter, the wet, type of dyskeratosis. In both types, the basal cell layer may be normal.

The disturbed keratinization may affect isolated cells or groups of cells, sections, layers, or even the entire epidermis. Moreover, it may or may not be accompanied by inflammatory manifestations in the cutis, epidermis or both. Finally, the dyskeratotic process may be the pre-dominating change or simply a secondary feature.

Ichthyosis is an example of the dry type of dyskeratosis, for it is characterized by premature keratinization owing to premature aging of the prickle cells. This faulty or improper aging of the epithelial cells results in (1) a horny layer which may be normal or increased to a varying extent, depending on the rapidity of keratinization, producing loose, horny lamellae; (2) a granular layer which may be normal or increased owing to premature keratinization; (3) a thinned or thickened prickle cell layer showing keratinization as well as shrinking of the affected cells; (4) an increased number of mitoses in the basal cell zone, and (5) a papillomatous configuration of the epidermis without a verrucous surface. The horny layer progresses down the follicles and sweat pores. The follicular cornification is most marked on the extensor surfaces.

Gassmann's histologic investigations of ichthyosis and the ichthyotic-like diseases are in agreement with the foregoing summary of the pathologic process in ichthyosis.

While ichthyosis has sites of predilection, the integument as a whole may be involved to a varying extent. The hyperkeratosis is commonly of varying degree and intensity. The involvement is usually unequal; thus, in the average case, the lesions on the extensor surfaces and on the lower extremities are more severe. On the other hand, the brunt of the dyskeratosis may sometimes be borne principally by structures such as the nails, which are infrequently involved. It then happens that the unusual variant is overlooked either because the changes occur in parts which are ordinarily not involved or because they are not well known.


This fa controversy existence of a condition with no recognizable feature, by a number of physicians. Ichthyosis is the nosologic category that is obscured.

An instance of Jadassoh's condition is a typical case of ichthyosis and was reported by him. Since then, the diagnosis has improved, and the more diagnostic criteria have been established. Ichthyosis is a disease of the skin, and the skin is a complex organ. Moreover, there are varieties of ichthyosis.

According to pachyonychia congenita, the skin will have a double dom family history.

19. Finlen: Geschlechtskr. New York, Ox
This failure to recognize aberrant types in the past has resulted in controversies (Unna, Kaposi, Neisser and others) as to the existence of localized or circumscribed forms of ichthyosis in connection with mal de Meleda, keratoderma palmaris et plantaris, etc. Moreover, by naming differently the varied combinations of this disorder (ichthyosis) clinical entities, supposedly new, have been described while the nosologic status of the numerous variants has apparently been obscured.

An instance of this inaccurate classification is pachyonychia congenita of Jadassohn, of which my patient's condition is a typical example. The condition has been reported under various titles. It is characterized by the typical changes in the nails and the associated lesions of the skin and mucous membranes already alluded to. The histopathologic changes are those of the dry or accelerated type of dyskeratosis, which is featured by premature keratinization.

Since the dry type of dyskeratosis is the essential change in ichthyosis, and since the clinical features of pachyonychia congenita (Jadassohn) are typical of ichthyosis with the addition of the ungual changes, I believe that Jadassohn's pachyonychia is a rare variety of ichthyosis in which the nails show the most marked and most constant features.

The fact that pathologic nails are not frequently observed in ichthyosis, even in the recorded severe types, does not warrant the exclusion of pachyonychia congenita from the ichthyosis group of dermatoses. Moreover, the line of demarcation between ichthyosis and the several varieties of keratoderma cannot be drawn, for in both premature keratinization is manifested by premature aging of the prickle cells.

According to Cockayne, when sufficient data have been collected, pachyonychia congenita together with several other abnormalities of the skin will probably be found to be the result of an inheritance of a double dominant, in which (1) direct descent is rare in comparison with familial and sporadic incidence and (2) seldom continues for more than...
two generations. These apparently explain the fact that in my patient the ectodermal defect appeared to arise \textit{de novo}.

Since the term "congenital dyskeratosis" does not convey an exact impression as to what the outstanding clinical features of this disorder are and while Jadassohn's caption does not suggest the pathologic aspects, I propose the title "pachyonychia ichthyosiformis," which I believe meets all the requirements.

**SUMMARY**

1. A typical case of pachyonychia congenita Jadassohn in an Italian boy is recorded.

2. A survey of the literature and a study of the patient force the conclusion that Jadassohn's pachyonychia is a variant of ichthyosis affecting chiefly the nails.

3. The designation "pachyonychia ichthyosiformis" is suggested for the condition.

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**CASE I.**—A family history years when, in arms and hands this seemed to alter the onset her head, and edematous and the edema fades and the hands.

Examination signs of recent face, neck, shou regions. The n hard, stringy, at Movements were and elbows press. The skeletal\textit{mu} temperature was the pulse rate. Blood cell counts, taken from biops.