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Pachyonychia congenita and steatocystoma multiplex

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Pachyonychia congenita and steatocystoma multiplex are each rare conditions. It is still not widely appreciated that they are both manifestations of the same autosomal gene. Extensive clinical, X-ray and laboratory investigations on two affected members of a family, in which three generations are known to be affected, failed to reveal any specific abnormality other than the skin and nail lesions.

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Both steatocystoma multiplex and pachyonychia congenita have been reported as individual and combined entities. Each condition is relatively rare, and it is not often appreciated that they are probably manifestations of the same gene. The first report of the association of the conditions was by Vineyard & Scott (1961), although earlier authors (Jadassohn & Lewandowski 1906, Andrews & Strumwasser 1929) noted that skin lesions often occur in association with pachyonychia. Conversely, steatocystoma also occurs alone, and the only mention prior to 1961 of dystrophy of the nails occurring with steatocystoma is the report of koilonychia in one of three cases reported by Contreras & Costello (1957). Some earlier cases of pachyonychia congenita, such as those of Jackson & Lawler (1951–52) were associated with sebaceous cysts and probably represent steatocystoma (Shrank 1966), whereas the cases of Soderqvist & Reed (1968) probably suffered from a form of dyskeratosis. In an excellent review of pachyonychia congenita, Moldenhauer & Ernst (1968) considered 96 cases. They did not mention steatocystoma, but by 1973, Moldenhauer & Seidel were aware of the relationship between that condition and pachyonychia.

The reports in which steatocystoma multiplex (often confirmed by histological findings) is associated with pachyonychia congenita are: Vineyard & Scott (1961), Shrank (1966), De Groot (1966), Ionescu et al. (1968), Valasquez & Bustamente (1972) and Moldenhauer & Seidel (1973). (The family reported by Shrank (1966) had been reported earlier by Jackson & Lawler (1951–52).)

In this report we present the results of an extensive study on a father and his daughter, and review briefly the literature on the condition.

Case Reports

Patient 1. H.S., Jr. (Proband), is a 26-year-old white male who at birth was covered with milia and had two supernumerary

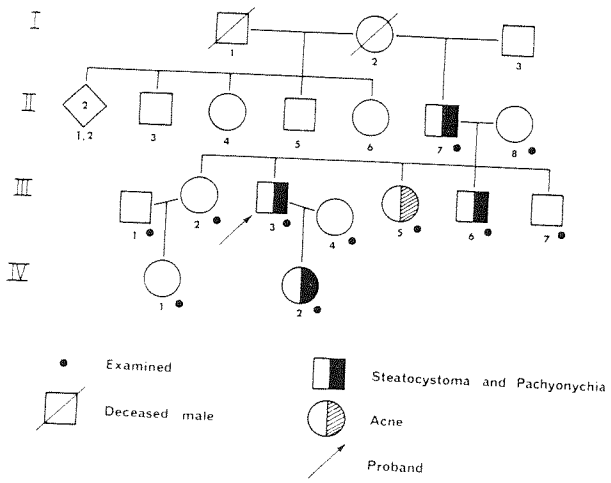

Fig. 1. Pedigree of family described in this paper.

teeth. Between 1 and 2 years of age, the milia opened leaving enlarged pores. At 4 or 5 years of age he developed cysts on his buttocks. These became painful, enlarged and infected, and discharged pus. He has been on antibiotic therapy for about the last 5 years. He has hyperhidrosis which is worse in the summer. Bullae develop on his feet and are superseded by keratoses which make walking painful. Occasionally "bumps" develop on his tongue and sores at the corners of his mouth, but he denies leukoplakia or hoarseness. He has always had deformed nails. The family pedigree is shown in Figure 1. Similar involvement of the skin and nails was noted in his father (II–7), one brother (III–6) and the patient's daughter (Case 2; IV–2). One sister (III–5) has acneiform lesions on the face. It is impossible to trace the pedigree beyond the patient's grandparents.

Physical examination was unremarkable except for thickness of the distal two-thirds of the nails of the hands and feet with multiple subungual hemorrhages (Fig. 2A and 2C), calluses on the plantar surface of the balls of the feet and around the toes (Fig. 2A and 2B), and numerous cysts (Fig. 2D) and scars over the body. The hair is fine. There was a 1 cm nodule, thought to be of no significance, in an otherwise small thyroid gland. Consultants in endocrinology, orthopedics, ophthalmology, hematology, oral-facial genetics and cardiology could find no abnormalities other than those mentioned. Normal laboratory findings included complete blood count (16 % eosinophils), platelet examination, urinalysis, hematocrit, karyotype, serum electrolytes, calcium, and phosphorous, blood creatinine, urea nitrogen and uric acid, sedimentation rate, sweat chlorides (44 mEq/1), serum IgA, IgG, C13, C14, T4. A fluorescent antibody test for LE and an LE preparation were negative, as was urine submitted for genetic screening. A slide test for rheumatoid arthritis was negative. The serum IgM was elevated (160 mg/dl; normal 80 ± 29) and the IgD depressed (1.6 mg/dl; normal 10 ± 4). An electrocardiogram was normal. X-ray examination, including PA and lateral of the chest and a skeletal survey, showed only mild scoliosis of the thoracic spine with some very minimal symmetrical wedge deformity of the mid thoracic vertebrae, the result of a stabilized Scheuermann's disorder. X-rays of the hands were negative. A biopsy of one of the cystic lesions was obtained. Microscopic examination revealed steatocystoma multiplex (Fig. 3). Panorex views of the mouth and bite wings revealed no abnormalities, although the enamel was thought to be thin.

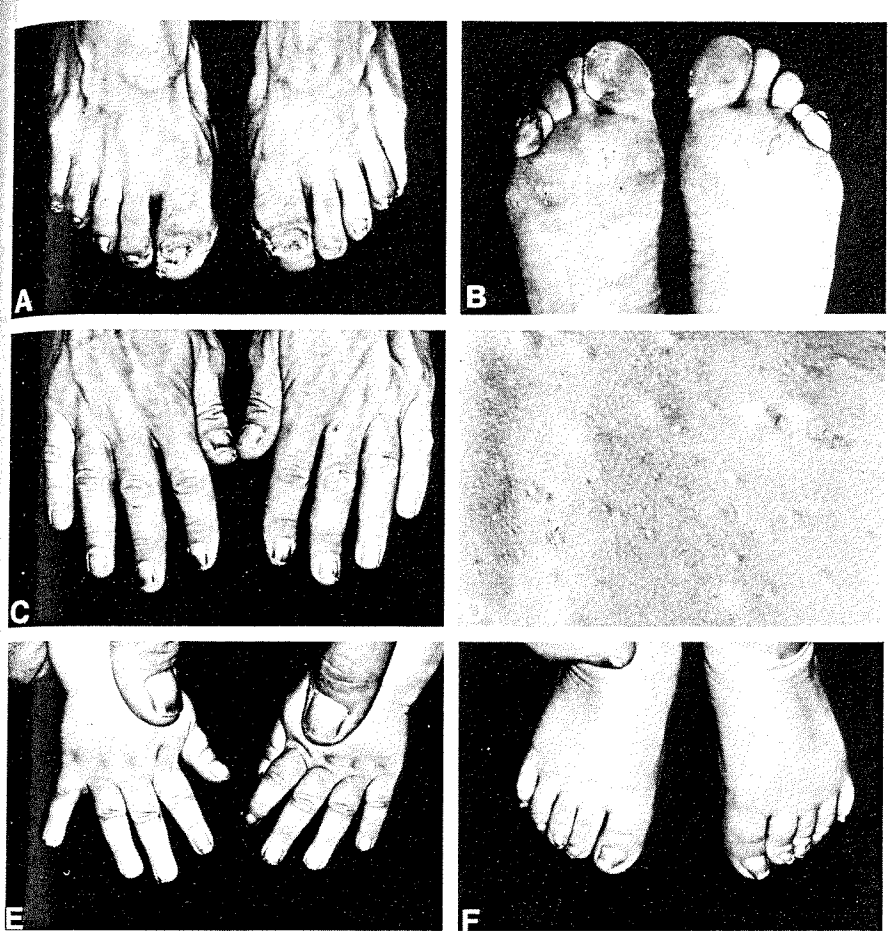

Fig. 2. Patient 1: (A) Feet showing distorted nails and calluses. (B) Calluses and peeling areas on soles of feet. (C) Hands showing distorted nails and subungual hemorrhages. (D) Steatocystoma. Patient 2: (E) Hands and (F) feet showing distortion of nails. Note father's nails in (E).

Patient 2. J.S. is the 16-month-old daughter of H.S., Jr. She was the 2.9 kg product of a normal pregnancy and delivery. The neonatal period was unremarkable except for some jaundice. She walked at 12 months and can now say a few words. At birth, two

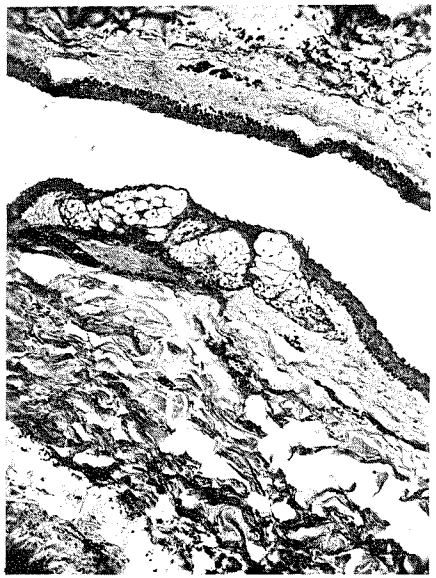

Fig. 3. Photomicrograph of cyst removed from Patient 1 at operation. Low power view illustrating sebaceous glands next to cyst wall.

teeth were noted. She also had 10–20 widely scattered milia, and thickened fingernails. Physical examination showed a well developed and nourished, friendly white female. Physical examination was entirely negative except for yellowish distorted nails on the hands (Fig 2E) and feet (Fig. 2F) and multiple white 0.5–1 mm papules scattered on the face and trunk. She too has fine hair. She was examined by orthopedic, pediatric, ophthalmologic and oral-facial consultants who found nothing other than the described lesions. Normal laboratory examinations included sweat chlorides (18 mEq/1), complete blood count (3 % eosinophils), hematocrit, karyotype and serum calcium and phosphorous. Urine for genetic screening showed reducing substances which were probably ribose or arabinose. EKG revealed only sinus tachycardia. A skeletal survey was within normal limits.

Discussion

The clinical picture of pachyonychia congenita, as presented by Jadassohn & Lewandowski (1906), includes nail lesions, palmar and plantar keratoses, hyperhidrosis, bullae, follicular keratosis and oral lesions (Butterworth & Strean 1962). The oral pathology includes leukoplakia, angular cheilosis (Gorlin & Chaudry 1958) and hoarseness (Kumer & Loos 1935). Neonatal teeth are common (Murray 1921). Different authors describe a variety of skin lesions which range in distribution from scattered to almost confluent, as in the present case, and include ichthyosis and acne conglobata as well as the keratoses etc. listed above. The association with steatocystoma multiplex was noted by Vineyard & Scott (1961). The patients under consideration in our report show all the manifestations of the combined syndrome, with the exception of leukoplakia, although the father gives a history of some type of oral lesions. The nail thickening is not as marked as in some published cases, but the steatocystomata are more numerous than in others.

There are a number of pedigrees in the literature. These are consistent with an autosomal dominant mode of inheritance, and Berendes (1972, 1974) analyzed the genetic information on a number of cases of steatocystoma multiplex, including those with pachyonychia congenita. He reached the conclusion that the evidence favored autosomal dominant transmission. Our pedigree, which shows male-to-male transmission and includes three generations, is consistent with this conclusion.

The nature of the cysts of steatocystoma has been the subject of speculation. Hashimoto et al. (1964) and Moldenhauer & Seidel (1973) think the cyst is a hamartoma, whereas a number of authors have considered the lesion to be a retention cyst. Ultrastructural studies (Hashimoto et al. 1964, Perrot et al. 1973) have not been helpful. The histology of the lesions is distinct and diagnostic, and the distribution of sebaceous glands seen in our patient (Fig. 3) fulfills the criterion for diagnosis. Although nail biopsy is difficult, this has been accomplished by a few authors, and the histology of the lesions described (Forslind et al. 1973, Colombi et al. 1974, Pierson et al. 1975).

Complications include infection and malignant degeneration of a cyst (Harper & Davis 1971). Associated conditions include cataracts and deafness (Butterworth & Strean 1962), mental retardation and microcephaly (Niebauer 1968) and hydrocephaly (Laing et al. 1966). It is not clear whether these associated conditions are more than incidental findings. On the other hand, changes in the hair are reported regularly, and add to the impression that the condition is a fundamental disorder of the integument, involving epithelium, mucosa, subcutaneous tissue, hair, nails and sebaceous glands, and that expressivity of the various manifestations of the syndrome is highly variable.

Acknowledgments

The studies in these patients were carried out in the Clinical Research Center of the University Hospital. Dr. Thomas A. Cortese, Jr. referred the family, and Dr. Ira K. Brandt called the diagnosis to our attention.

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Unusual association of Saethre-Chotzen syndrome and congenital adrenal hyperplasia

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This report describes and discusses the very rare occurrence of two heritable traits, the Saethre-Chotzen syndrome and congenital adrenal hyperplasia (21 hydroxylase deficiency, salt-losing type) in a female infant whose father presents the clinical manifestations of Saethre-Chotzen syndrome. Family study revealed no other instances of the recessively inherited adrenogenital syndrome. Other literature cases combining acrocephalosyndactyly and urogenital anomalies are discussed and compared.

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The Saethre-Chotzen syndrome is a rare form of autosomal dominant acrocephalosyndactyly (ACS), first described in 1931 by Saethre, and 1 year later by Chotzen (1932). Since that time, additional reports have appeared in the literature (Waardenburg 1934b, Moffie 1950, Waardenburg et al. 1961, Pfeiffer 1969, Temtamy & Mc Kusick 1969, Aase & Smith 1970, Bartsocas et al. 1970, Kernohan et al. 1970, Kreiborg et al. 1972 and Pantke et al. 1975). Pantke et al. (1975) claimed to have identified in the literature 86 previously unrecognized cases. If that is true, this syndrome may well be the most common of all the ACSs, of which McKusick (1975) lists five types. This disorder is characterized by acrocephaly with asymmetry of the neurocranium and face, low-set frontal hairline, ptosis of the eyelids, defects of the vertebral column and variable degrees of soft tissue syndactyly of the fingers and toes. Additional findings observed are hypertelorism, proptosis, a highly arched and narrow palate, conductive hearing loss, cryptorchidism and mental retardation.

Congenital adrenal hyperplasia is an uncommon but well characterized syndrome involving several different inborn errors of steroid metabolism (Bongiovani & Root 1963a, 1963b and 1963c), each one presenting with a specific pattern of steroid alteration resulting from the particular enzyme defect.

This paper discusses what appears to be the first documented instance of simultaneous occurrence of the Saethre-Chotzen syndrome and congenital adrenal hyperplasia in the same patient.

Case Reports

Case 1: The proposita was first seen at 12 days of age because of cranial asymmetry, ambiguous genitalia and failure to thrive. The pregnancy was uneventful and the proposita's birth weight was 2.72 kg. The