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Palmoplantar hyperkeratosis with short stature, facial dysmorphism, and hypodontia—a new syndrome?: case report

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Abstract

In this study, a possible new syndrome affecting 18 members of a family spanning 4 generations is described. The main features include palmoplantar hyperkeratosis, proportionate short stature, facial dysmorphism, clinodactyly, epilepsy, deafness, and hypodontia. This syndrome is inherited in an autosomal dominant manner with a high degree of penetrance but variable expressivity. This syndrome differs markedly from the autosomal recessive types of palmoplantar hyperkeratosis such as Papillon-Lefèvre syndrome which shows premature loss of both dentitions. It is also distinct from other previously described cases of autosomal dominant forms of palmoplantar hyperkeratosis such as the Unna-Thost syndrome in that it presents short stature, facial dysmorphism, and hypodontia. These features which previously have not been associated with palmoplantar hyperkeratosis suggest that this may be a new syndrome.

Hyperkeratosis of the skin may result from both acquired and hereditary causes. Acquired hyperkeratosis of the palms and soles may result from severe physical work, neurodermatitis, contact dermatitis, psoriasis, tertiary syphilis, fungal infections, and arsenal keratoderma (Fred et al. 1964). Inherited types of palmoplantar keratoderma are classified into a few groups based on the mode of inheritance and clinical presentations including dental features. The syndromes presenting with diffuse-type hyperkeratosis are shown in Table 1 (next page).

In dentistry, the most well known of these conditions is the Papillon-Lefèvre syndrome which is inherited in an autosomal recessive mode and characterized by diffuse palmoplantar hyperkeratosis and generalized, rapidly progressive periodontitis resulting in the early loss of both primary and permanent dentitions (Haneke, 1979; Gorlin et al. 1964; Vrahopoulos 1988). Less well known are the syndromes known as Mal de Meleda (Jee et al. 1985) keratosis palmaris et plantaris (KPP), also called Unna-Thost syndrome or tylosis (Dencer 1953; Stern et al. 1984) as well as Richner-Hanhart syndrome, a form of tyrosinemia (Stern et al. 1984). These 3 conditions differ from the Papillon-Lefèvre syndrome in that early loss of the teeth is not a notable feature. In addition, the Mal de Meleda and the Richner-Hanhart syndromes are inherited in an autosomal recessive manner which distinguishes them from the Unna-Thost syndrome, an autosomal dominant condition (Bergfeld et al. 1982).

The medical literature reveals that the autosomal dominant form of palmoplantar keratoderma is a heterogeneous group of disorders with many variants from the original syndrome described by Thost in 1880 and Unna in 1886 (Cockayne 1933). In most of these variants as well as in the original syndrome, dental findings were unremarkable. In this study, a family with autosomal dominant palmoplantar hyperkeratosis accompanied by hypodontia is described. The facial dysmorphism and hypodontia present in this family suggest it to be a new syndrome.

Case Report

The proband was a 10-year-old Caucasian male referred to the University Dental School by his pediatrician for dental assessment. His medical condition was at that time undiagnosed.

The patient was the product of a nonconsanguinous marriage, born 4 weeks prematurely after an uncomplicated pregnancy with breech delivery and birth weight of 1079 g. Neonatal complications included respiratory distress requiring mechanical ventilation, inguinal hernia, and undescended testes which were corrected surgically. Eye lashes, eyebrows, and fingernails were absent at birth.

The patient showed frontal bossing and hypertelorism (Fig 1, next page). Hypertelorism canthi was confirmed by measurements of the outer canthi, inner canthi, and interpapillary distance which gave values of 9.5, 3.5, and 58.0 cm, respectively. These values

were all > 97th percentile for a 5-year-old (Smith 1982). In addition, abnormal hair whorls and a low posterior hair line were observed.

Moderate diffuse hyperkeratosis of the palms of the hands and soles of the feet were noted shortly after birth (Fig 2). In addition, hypoplasia of the nails was observed, ranging from severe hypoplasia in the fifth finger to mild hypoplasia in the others.

The patient was of proportionate short stature with height 106.6 cm (< 3rd percentile), weight 17.6 kg (< 3rd percentile), and head circumference 49.5 cm (3rd percentile). Clinodactyly of the fifth finger on both hands was noted (Fig 2). A hand/wrist radiograph at age 9 years, 6 months revealed a delayed bone age of approximately 4 years, 6 months. Skull radiographs were normal.

Mild mental retardation was noted (the patient attended a special school). In addition, there was bilateral mild conductive hearing loss. Petit mal epilepsy was diagnosed recently with an EEG consisting of 8-9 cycles/sec activity present bilaterally at 30-60 mV. It was controlled adequately by carbamazepine.

Metabolic screens of plasma and urine revealed no biochemical abnormalities. Banded chromosomal analysis was normal.

Extraoral examination revealed that the patient had incompetent lips and a Class II malocclusion with

Table 1. Types of Inherited Diffuse Forms of Palmoplantar Keratoderma

Syndrome	*Mode of Inheritance*	*Associated General Features*	*Dental Features*
Papillon-Lefevre	Autosomal recessive	Hyperhidrosis Dysplastic nails Arachnodactyly Susceptibility to infections Physical retardation Mental retardation Calcification in falx cerebri	Hyperkeratosis of attached gingiva Exfolation of primary and permanent teeth soon after eruption
Mal de Meleda	Autosomal recessive	Onychodystrophy	No oral findings reported
Keratosis Palmaris et Plantaris (KPP or tylosis)	Autosomal dominant	Carcinoma of skin and esophagus Hyperhidrosis Dysplastic nails Optic atrophy Mental retardation Oxycephaly Clubbing of fingers Clinodactyly Deafness	Hyperkeratosis of attached gingiva
Richner-Hanhart	Autosomal recessive	Tyrosinemia, corneal dystrophy,brachy-phalanges, mental retardation	No oral findings reported
This report	Autosomal dominant	Small stature Facial dysmorphism Clinodactyly Dysplastic nails Deafness Epilepsy	Hypodontia Enamel hypoplasia Fusion of teeth Taurodontism Anterior open bite

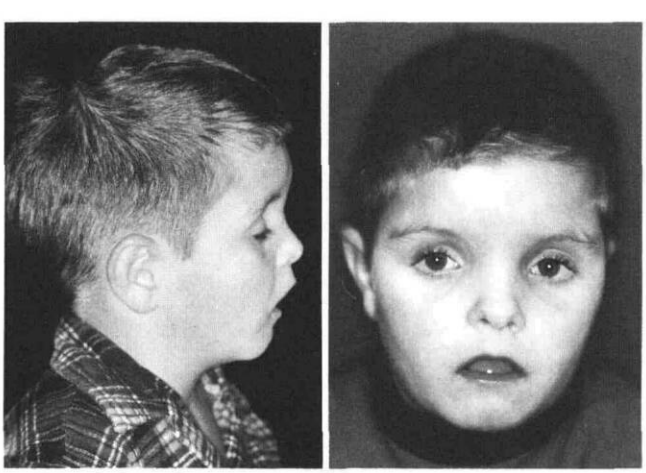

Fig 1. Facial views of proband showing hypertelorism, frontal bossing, and low hair line.

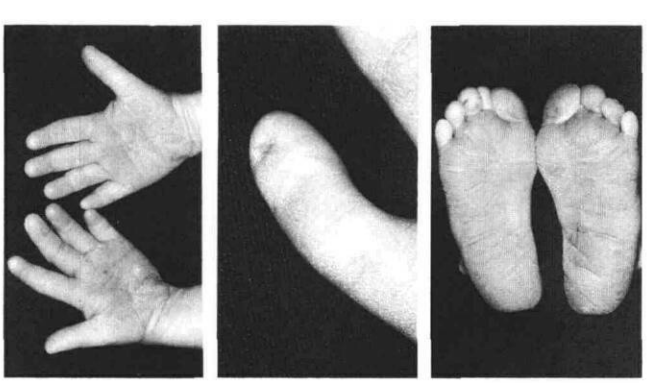

Fig 2. Hands and feet of proband showing palmoplantar hyperkeratosis. Clinodactyly of the fifth finger also is shown. Note hypoplastic fingernail.

overjet of 10 mm and a large anterior open bite which was accompanied by an anterior tongue thrust habit present at rest position as well as during swallowing and speech.

Intraoral examination (Fig 3) revealed the following teeth to be present:

16	55	54	53	52	21	62	63	64	65	26	
46	85	84	83	41	31	32	73	74	75	36	

Enamel hypoplasia manifested as a depressed area of missing labial enamel was noted on the mandibular left central incisor and the left maxillary central incisor showed diffuse enamel opacity. All other erupted teeth were clinically normal.

Periodontal examination revealed poor oral hygiene and marked gingivitis. Periodontal probing did not reveal any pockets greater than 3 mm and no abnormal mobility was detected. In addition, no hyperkeratinization of the gingiva was noted.

An orthopantograph (Fig 4) and occlusal radiographs (Fig 5) confirmed agenesis of the permanent maxillary lateral incisors and the mandibular left central incisor. In addition permanent first molars showed radiographic evidence of taurodontism. Radiographs revealed that all other permanent teeth except the third molars appeared to be developing normally. No abnormalities were noted from bite-wing radiographs.

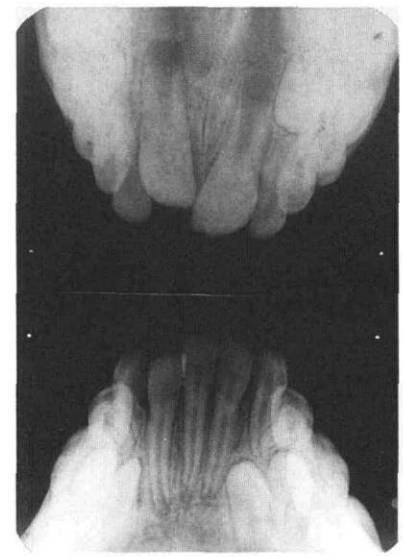

FIG 5. Mandibular and maxillary occlusographs of proband confirm the absence of the maxillary permanent lateral incisors and the mandibular left lateral incisor.

Family Pedigree

A family pedigree chart showing 18 affected members spanning 4 generations is illustrated (Fig 6). In the present family the children have inherited the condition from the father and an autosomal dominant mode of inheritance with a high degree of penetrance is evident. Apart from the proband, his siblings, and parents, the other family members were diagnosed from history, particularly in relation to palmoplantar hyperkeratosis.

The patient had 2 brothers, ages 3 and 10 years, and a 4-year-old sister. All siblings presented for dental examination. The findings are shown on the next page in

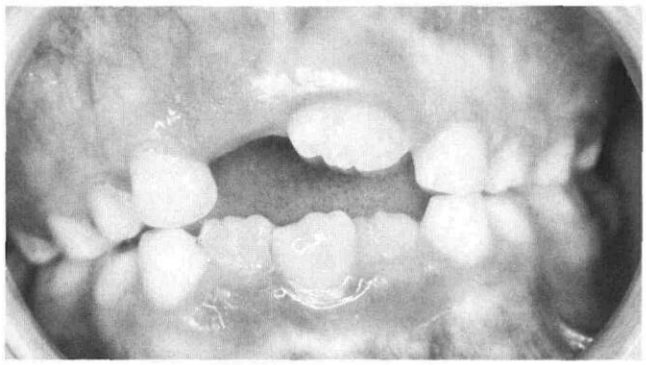

FIG 3. Intraoral view of proband showing the anterior teeth. Enamel hypoplasia of the mandibular left central incisor is evident.

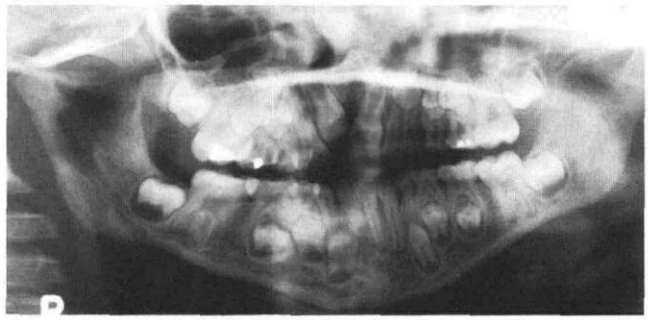

Fig 4. Orthopantograph of the proband illustrating the missing mandibular permanent lateral incisor and the maxillary permanent lateral incisors.

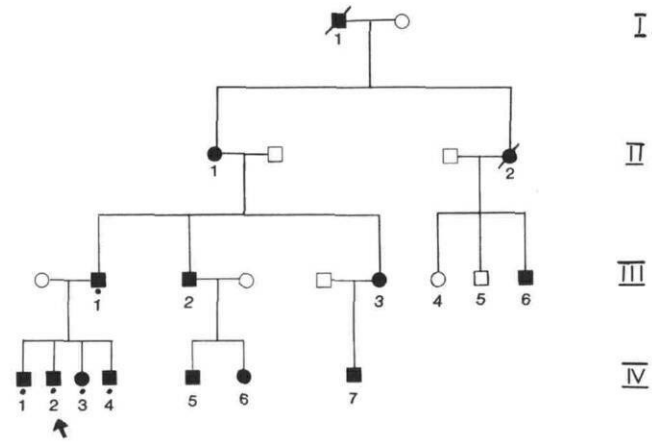

FIG 6. Pedigree of the family (4 generations). Those members diagnosed from history all have palmoplantar hyperkeratosis which is a feature easily distinguished by nonprofessionals.

○ unaffected female (by history

□ unaffected male (by history)

● affected female (by history)

■ affected male (by history)

● affected female (by examination)

■ affected male (by examination)

deceased

Table 2. Hyperkeratosis of the palms and soles appeared to be a prominent feature in all siblings. Other dysmorphic features noted in the proband such as small stature, hypertelorism, clinodactyly, hypoplastic nails, and low hair line also were noted in all siblings. In addition, the eldest sibling shared further similar medical findings with the index case such as low birth weight, premature birth, and petit mal epilepsy.

Dental examination of the siblings revealed that all had agenesis of some permanent teeth. These missing teeth included mandibular incisors in both brothers and maxillary lateral incisors in the sister. The eldest sibling also presented with a macrodont maxillary central left incisor which has a distinct labial groove from the gingival margin to the incisal edge (Fig 7). This feature, together with the fact that the maxillary left lateral incisor was absent, indicated that fusion of the central and lateral incisors may have occurred. Periapical radiographs which revealed a single large pulp chamber further suggest true fusion of the incisors. This sibling also showed enamel hypoplasia manifested as loss of enamel on the fused tooth surface as well as enamel opacities on the labial surfaces of the right central incisor and the permanent first molars.

The mother (age 34 years), who wore a partial upper denture, had only a few teeth at examination, the others having been lost through decay. Apparently she had complete sets of primary and permanent teeth and there was no family history of agenesis.

The father (age 36 years) presented with marked diffuse hyperkeratosis of the palms and soles which had been present since birth. He also suffered mild epilepsy, mild hypertension which did not require treatment, and chronic bronchitis from cigarette smoking. He was of normal stature (height 154.0 cm, weight 107 kg) and no craniofacial dysmorphological features were noted. Dental examination revealed all permanent teeth to be present except for the mandibular left second and third molars. According to the father, these teeth were extracted for extensive caries. Unrestored proximal carious lesions were noted in several teeth. Periodontal probing revealed the presence of generalized pockets of > 5 mm around most teeth and several teeth had moderate mobility. A diastema was noted between the maxillary central incisors. A Class II malocclusion was present with increased overbite and overjet.

TABLE 2. Clinical Presentations of Affected Family Members

	Family Member				
Dysmorphic Feature	*Father*	*Sib 1*	*Proband*	*Sib 2*	*Sib 3*
Small stature		√	√	√	√
Hypertelorism		√	√	√	√
Hyperkeratosis of palms & soles	√	√	√	√	√
Clinodactyly		√	√	√	√
Dysplastic nails		√	√	√	√
Low hair line		√	√	√	√
Abnormal hair whorls		√	√	√	√
Skin tags on ear		√			
Medical findings					
Low birth weight		√	√		
Premature birth		√	√		
Deafness		√	√		
Epilepsy	√	√	√		
Dental findings					
Missing teeth		√	√	√	√
Taurodontism			√		
Enamel hypoplasia		√	√		
Fusion of teeth		√			
Anterior open bite			√		
Tongue thrust			√		

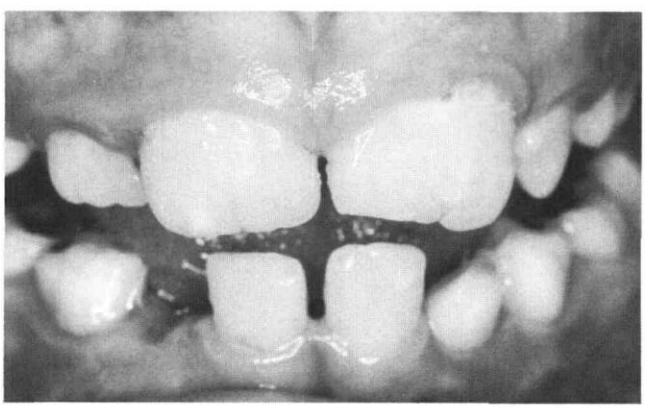

FIG 7. Anterior teeth of first sibling showing fused maxillary permanent left central and lateral incisors and the missing mandibular permanent lateral incisors.

Discussion

Palmoplantar hyperkeratosis is a feature of many acquired and genetic disorders. Inherited conditions usually are identified by their mode of inheritance, phenotype, and associated features because the underlying defect is seldom known (Der Kaloustian and Kruban 1979; Demis et al. 1982).

Dental abnormalities may be important diagnostic features in many of these conditions as in other syndromes (Gorlin et al. 1976; Seow et al. 1985; Seow and Latham 1986). For example, in two autosomal recessive types of hyperkeratosis, different dental presentations are noted. In the Papillon-Lefèvre syndrome, severe periodontitis and premature loss of both dentitions are constant findings, whereas in the Mal de Meleda

disorder the teeth are apparently normal (Jee et al. 1985). Also, severe enamel hypoplasia was noted in a new autosomal dominant type of palmoplantar hyperkeratosis associated with corneal changes, short stature, brachydactyly, and premature birth (Stern et al. 1984). However, hypodontia has not been associated with the autosomal dominant form of palmoplantar hyperkeratosis before, although it has been reported in autosomal recessive forms of hyperkeratosis associated with ectodermal dysplasia (Egelund and Frentz 1982).

In the present study, hypodontia, enamel hypoplasia, craniofacial dysmorphism, deafness, small stature, epilepsy, and clinodactyly are associated with an autosomal dominant form of palmoplantar hyperkeratosis. As hypodontia and craniofacial dysmorphism have not been associated with palmoplantar hyperkeratosis before, the present family may represent a new genetic syndrome. Searches carried out on 2 dysmorphology computer databases (The London Dysmorphology Database—Winter R and Baraitser M; Pictures of Standardized Syndromes and Undiagnosed Malformations, Murdoch Institute for Research into Birth Defects, Melbourne, Australia) revealed no similar syndrome previously reported.

The apparent lack of facial dysmorphism and hypodontia in the father may indicate variability in expressivity of the phenotype in this syndrome. It is also possible that hypodontia may be inherited as an isolated trait. However, since skin and teeth are derived from similar structures, it is most likely that in this case, hypodontia is related to the hyperkeratosis condition.

As the present condition is inherited in an autosomal dominant manner, it may represent a variant of the Unna-Thost syndrome. This condition is also known as KPP or tylosis (Dencer 1953). However, large studies on patients classically affected by the Unna-Thost syndrome (Nielsen 1985a) did not report other defects associated with the disorder apart from squamous cell carcinoma of the esophagus and skin (Howell-Evans et al. 1958; Shine and Allison 1966; Yesudian et al. 1980) and dermatophytosis (Nielsen 1985b).

A study of current literature on the autosomal dominant forms of palmoplantar hyperkeratosis reveals a few other conditions which could possibly be related to the present syndrome. Stern et al. (1984) reported on an autosomal dominant syndrome characterized by unique corneal epithelial changes, diffuse palmoplantar hyperkeratosis, distal onycholysis, brachydactyly, short stature, premature birth, and severe enamel hypoplasia. Also, clinodactyly associated with the autosomal dominant form of palmoplantar hyperkeratosis was found in families studied by Aguirre-Negrete et al. (1981), Hernandez et al. (1982), and Anderson and Klintworth (1961). In addition, deafness also has been reported in 10 cases in one family showing the autosomal dominant palmoplantar hyperkeratosis by Bititci (1975), as well as by Hatamochi et al. (1982).

Metabolic disorders such as tyrosinemia type 2 (tyrosinosis, Richner-Hanhart syndrome) produce palmoplantar hyperkeratosis; however, these conditions were excluded in the present family from metabolic studies and lack of corneal opacities as well as the fact that these conditions usually are inherited in an autosomal recessive manner.

In conclusion, this possibly new syndrome further expands the panorama of diverse clinical conditions presenting with palmoplantar hyperkeratosis.

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Did you know...

- The growth rate of the dentist population is expected to exceed that of the population as a whole, according to the government's Health Resources and Services, in a report to Congress.
- The number of dentists will increase 9% by the year 2000 while population growth overall will be 6%, the report said. At the same time, dental school enrollment is dropping, declining 64% between 1975-76 and 1986-87, according to the report.
- The number of female dentists has nearly doubled since the early 80s, according to a researcher at the Health Resources and Services Administration. That's a faster growth rate than for female physicians, pharmacists, or veterinarians.
- Napoleon's toothbrush was sold last October 27, according to the Hermann Historica auction house in Munich. The toothbrush, a silver- and gold-plated toothbrush belonging to the French emperor and decorated with Bonaparte's coat of arms, was pocketed by a British officer after the Battle of Waterloo, according to a *Chicago Tribune* report. One of the officer's heirs is selling the artifact.