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REVIEW

The hereditary palmoplantar keratoses: an updated review and classification

G.P.H. LUKKER, P.C.M. VAN DE KERKHOF AND P.M. STEIJLEN
Department of Dermatology, University Hospital Nijmegen, Postbus 9101, 6500 HB Nijmegen, the Netherlands
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Summary

The palmoplantar keratoses (PPKs) comprise a heterogeneous group of disorders of keratinization, which can be subdivided into hereditary and acquired forms. Many authors have attempted to classify the hereditary forms, and most classifications have been based on the morphology, distribution, associated symptoms and mode of inheritance. Subsequently, many new forms have been recognized, and what were previously considered to be distinct types have been shown to be variants of a single type, both of which limit the usefulness of previous classifications. Hence, we propose a new, updated classification, which enables accurate diagnosis of these disorders.

The disorders known as palmoplantar keratoses (PPKs) comprise a number of different clinical entities, and there are both hereditary and acquired forms.

Hereditary forms may be localized primarily to the hands and feet or be associated with more generalized skin diseases, such as autosomal dominant ichthyosis vulgaris, bullous ichthyosiform erythroderma, lamellar ichthyosis, and erythrodermatous ichthyosis. Classification of the hereditary PPKs localized primarily to the hands and feet is difficult, because of inter- and intratriadinal variations, differences in nomenclature, and the large number of reported cases. In recent years, a number of new forms have been described, and forms which were previously considered to be distinct have been shown to be variants of the same type of keratoderma. Based on the available data, we propose an updated classification (Table 1). The most important features in the classification of PPKs are the specific morphology and distribution of the hyperkeratosis, the presence or absence of associated features, and the inheritance pattern. Additional criteria are the presence of skin lesions on areas other than the palms and soles, age at onset of the keratoderma, severity of the disease process, and the histopathological findings.

Diffuse hereditary PPKs without associated features

PPK diffusa circumscripta Unna–Thost
Diffuse PPK Unna–Thost usually presents in the first month of life, and is evident by the age of 2 in the majority of cases. An even, very thick, diffuse hyperkeratosis covers the palms and soles, starting at the margins and extending to the centre. Initially, the margins show a violaceous border, which usually disappears after several years. There is no spread on to the extensor surfaces. Aberrant keratotic lesions may appear on the dorsa of the hands and feet, and the knees and elbows. Marked hyperhidrosis is usual. The nails may be thickened. Histologically, PPK Unna–Thost is said to show non-specific changes, but there are no case reports in the literature confirming such histological findings. Until recently, diffuse PPK Unna–Thost was generally believed to be the most frequent type of hereditary PPK. Clinically, the disease is identical to PPK Vorner, which is characterized histologically by epidermolytic hyperkeratosis. In a number of cases clinically thought to have PPK Unna–Thost, the histological features were those of epidermolytic hyperkeratosis.
Reinvestigation of the family originally seen by Thost also revealed the histological features of epidermolytic hyperkeratosis. Hence, there is doubt about the existence of PPK Unna–Thost as a separate entity.

PPK transgranulare et progressivum Grethler (Fig. 1)
PPK Grethler is a diffuse PPK which extends on to the dorsa of the hands and feet (transgranulare), has a violaceous border, and is associated with hyperhidrosis.
Additional hyperkeratotic lesions can be seen on the knees and elbows, and in the region of the Achilles tendon. Worsening of the keratosis is seen
during childhood, followed by a static phase after puberty, and finally a tendency to improve in the fifth decade. It differs from the Unna–Thost variety by extending to the dorsal surfaces, and from mal de Meleda by its dominant inheritance and variable intra-familial expression. Solitary cases must be differentiated from erythrodermata.

PPK of Sybert

In 1988, Sybert described a family with a palmoplantar keratoderma which started with erythema and scaling of the palms and soles in the first year of life. The palmoplantar lesions eventually progressed to a severe diffuse hyperkeratosis, causing deformities and spontaneous amputation of the digits. In childhood, additional lesions developed in the metacarpal cleft and groins. With increasing age, hyperkeratoses developed on the elbows, knees, dorsa of the hands and feet, posterior aspects of the forearms and anterior aspects of the legs. The pedigree was consistent with an autosomal dominant mode of inheritance. This diffuse, transgrediens, mutilating PPK has to be differentiated from mal de Meleda, PPK of Gamborg Nielsen and PPK of Greither. The clinical features resemble those found in mal de Meleda which, however, is an autosomal recessive disorder. PPK of Gamborg Nielsen shows less extension on the dorsal surfaces, fewer additional hyperkeratoses, and is recessively inherited. The severity and extent of involvement are much greater than in PPK of Greither.

Mal de Meleda (keratosis extrema et keratodermia transgrediens et progressiva) [Figs 5 and 6]

This very rare disorder has, as a result of inbreeding, an endemic prevalence on the Adriatic island of Mljet.
It is characterized by a diffuse, thick hyperkeratosis with a prominent erythematous border. The thick hyperkeratosis may lead to flexion contractures. The disease has an onset in early infancy, and follows a progressive course, with extension on to the dorsal surfaces of hands and feet. Constricting bands surrounding the digits are typical, and occasionally result in spontaneous amputation. Concomitant lesions can be found on other sites, especially the elbows and knees. Perioral erythema and hyperkeratosis may be present, resembling the clinical features of Olsnian synostosis. Hyperhidrosis of the affected parts, with maceration of the hyperkeratotic masses and consequent production of a musty odour, is pronounced. Nail changes (onycholysis, nail thickening, subungual hyperkeratosis) are usually present. The disease has to be differentiated from PPK transgressens et progressus Greither and PPK of Sybert, both of which have a dominant mode of inheritance, and from PPK of Gamborg Nielsen.

**PPK Gamborg Nielsen**

Gamborg Nielsen delineated a severe form of PPK, represented by six patients in two families, who lived in the northernmost county of Sweden. This type of PPK was characterized by a very thick hyperkeratosis, distinctly demarcated from normal skin. The dorsal aspects of the finger joints were covered by hyperkeratotic plaques. A violaceous margin was present in four patients. One patient demonstrated extension of the keratoderma on to the dorsa of the hands. Another featured mutilating changes due to constricting bands surrounding the fingers. Apart from knuckle pads on the dorsa of the fingers, there were no additional hyperkeratoses. The pedigrees in both families were consistent with an autosomal recessive mode of inheritance.
elbows and knees. In one individual, the right fifth toe was missing, and a constricting band completely enclosed the base of the left fifth toe. Histology showed dyskeratotic changes without epidermal hyperkeratosis. Clinically, the keratoderma can be distinguished from PPK mutans by the presence of reticulate hyperkeratosis on the palmar surface of the fingers, the absence of starfish-shaped hyperkeratosis, and the lack of a violaceous border surrounding the palmar and planar keratoderma. In addition, the pedegree suggests an autosomal recessive inheritance pattern. The typical clinical features enable a distinction to be made between acral keratoderma and mal de Meleda.

Diffuse hereditary PPKs with associated features

PPK mutans Volwinkel

PPK Volwinkel is a diffuse PPK with a honeycombed hyperkeratosis, a violaceous border, and hyperhidrosis. It presents in infancy, and is characterized by strangulating fibrous bands leading to progressive constriction and eventual spontaneous amputation of the digits. In addition, patients may have distinctive keratotic lesions on the elbows and knees, as well as on the dorsa of the hands and feet, with a peculiar linear and starfish-shaped configuration. In one patient, grossly mutilating keratoderma was accompanied by keratosis of the groin and perianal skin. A number of associated features have been noted to occur sporadically: sloth, high-tone acoustic impairment, spastic paraplegia, myopathy, tachyphylactic dermatomes, and nail anomalies. Constriction bands on digits may occasionally occur in mal de Meleda, pachyonychia congenita, acral keratoderma, the Ohmstedt syndrome and PPK of Sybert.

Carcinoma of the oesophagus with keratosis palmaris et plantaris (Howel-Evans)

Howel-Evans et al. reported the association of palmar and plantar keratoderma with carcinoma of the oesophagus. In their study of two Liverpool families, oesophageal carcinoma occurred in 18 of 48 tyloic family members, but in only one of 87 non-tyloic members. The age of onset of the palmar and plantar hyperkeratosis was between 5 and 15 years, and the average age of onset of the oesophageal carcinoma was 43 years. Yeilding et al. described a pedigree with tylois in 22 members of a family spanning over five
generations. Of those affected, three of the fourth generation did not develop squamous carcinoma of the skin, and one of these died from carcinoma of the oesophagus. Palmoplantar keratosis was present at birth. Skin cancer developed in the second decade of life. It is possible that there is a genetic association between the state of the oesophagus and the palmoplantar keratoderma which predisposes both sites to the development of squamous carcinoma. Acquired PPK, beginning late in life and apparently not genetically determined, has also been described in association with internal malignancy.

PPK with sclerodactyly (Huriez syndrome)
The disorder first described by Huriez et al. is characterized by sclerodactyly, diffuse keratoderma of the palms and soles, nail anomalies (aplasia, ridging and clubbing) and possible malignant degeneration of the affected skin. Associated hypohidrosis is common. Another two familial cases have been reported. The

Figure 4. Hyperkeratosis, hypergranulosis and acanthosis. The granular cell layer displays numerous clumped keratohyalin granules, vacuoles and ruptured cell walls, consistent with epidermolysis hyperkeratosis (haematoxylin and eosin, x400).

Figure 5. Mal de Meleda, showing diffuse hyperkeratosis, with a prominent erythematosus rim, spreading to the dorsal surfaces, as shown in Figure 6.

Figure 6. Same patient as in Figure 5. The dorsal surfaces are covered by hyperkeratoses, which extends from the planter surfaces. The hyperkeratotic areas have erythmatous borders.
disease is present at birth, or appears in the first years of life, and persists unchanged throughout adult life. Sclerosis, in contrast, is not associated with Raynaud's phenomenon. It is the most prominent feature of the syndrome. In some severe PPKs there is a suggestion of sclerosis, but in the Hurwitz syndrome the sclerotic changes are disproportionately greater. Squamous cell carcinomas often develop in the atrophic skin, as early as the third to fourth decade of life. The Hurwitz syndrome can be distinguished from scleroderma by its onset at birth, absence of systemic signs and symptoms, lack of vasomotor phenomena, and lack of progression during adulthood.

Hidrotic ectodermal dysplasia (Clouston syndrome)

Hidrotic ectodermal dysplasia, first described by Clouston in 1928, is characterized by dystrophy of the nails, defects of the hair, and palmoplantar keratosis. There is sparsity of the hair of the scalp, face, eyebrows, eyelashes, axillae and genitilia, which varies in severity from mild thinning to complete baldness. In some cases, alopecia appears maximally soon after birth, although in the majority hair loss is gradual, less severe, and only occurs after puberty. Hyperkeratosis of the palms and soles has a papillomatous appearance, with multiple small fissures, and generally increases in severity with age. Skin thickening has also been reported on the knuckles, knees and elbows. Biochemically, a depletion of hair matrix protein, related to a disruption of sulphydryl bond formation in the keratin of the integumentary system, may account for the clinical features in hair and skin. Sensorineural deafness, polydactyly, syndactyly, finger clubbing, mental retardation, dwarfism, photophobia, and strabismus may be associated.

PPK and sensorineural deafness

Recently, Shumuk et al. described a new syndrome of diffuse palmoplantar hyperkeratosis invariably associated with a slowly progressive, bilateral, high-frequency, deafness. The onset of deafness in infancy and early childhood precedes the skin changes, and thereafter both progress slowly with age. The two abnormalities never appeared as isolated defects in the family. A combination of sensorineural hearing loss and palmoplantar keratosis has been recognized previously. A variable relationship between the inheritance of skin lesions and acoustic impairment has been reported in the Clouston syndrome, and PPK mutilans Volkmann. The Clouston syndrome also includes other ectodermal defects.

Mutilating palmar plantar keratoderm with periocular keratotic plaques (Olmsted syndrome)

Including the original description by Olmsted, there are five well documented cases of this syndrome. The syndrome consists of congenital, diffuse, sharply marginated keratoderma of the palms and soles, with flexion deformities of the digits, leading to constriction or spontaneous amputation, periocular keratosis, and onycho-dystrophy. Periostal involvement has been reported in four cases. Lecokorakytosis was present in two cases and in one patient the gums and inner thighs, ears and anterior neck. The age of 2 years. This patient also had universal alopecia, absence of a promontory tooth, joint hypermobility and, at the age of 20, linear hyperkeratotic streaks in the antecubital fossae and on the flexor aspects of the forearms. Recently, a case has been reported with a congenital non-mutilating PPK and nail dystrophy, who developed progressive perioral and perineal keratoderma and, in addition, bilateral cornal epithelial dysplasia, leading to severe corneal scarring and impairment of vision. The principal genetic syndromes to be excluded in the differential diagnosis include hidrotic ectodermal dysplasia of the Clouston type, pachyonychia congenita, mal de Meleda, and PPK of Volkmann. The condition mimics acrokeratodermatitis enteropathica, which can be excluded by determination of the plasma zinc level.

Palmoplantar keratoderm with periodontitis (Papillon-Lefavre syndrome)

The Papillon-Lefavre syndrome (PLS) is characterized by a diffuse transgrediens palmoplantar keratosis and premature loss of both the deciduous and permanent teeth. In addition to the palmoplantar hyperkeratosis, many PLS patients have scaly erythematous lesions over the knees, elbows and interdigital joints, not uncommonly misdiagnosed as psoriasis. Redness and thickening of the palms and soles usually appear in the first years of life, at the time of eruption of the deciduous teeth. A spontaneous improvement parallels the resolution of gingival inflammation after the loss of the permanent teeth. Associated hyperhidrosis causes an unpleasant odour. An increased susceptibility to infections has been observed in about 20% of PLS.
patients. The skin is reported to be the most common site affected by infections; internal organs are less frequently involved. Disorders of leucocyte function might account for the prominent gingival and cutaneous infections. Some investigators have demonstrated disturbances in both polymorphonuclear leucocyte motility and bactericidal function, or in bactericidal function alone, whereas others have not found any defects in leucocyte function. The precise underlying mechanism responsible for susceptibility to infections in PLS patients, however, remains to be determined. Histopathological changes are nonspecific. Electron microscopic features include lipid-like vacuoles in the keratinocytes and granulocytes, a reduction in tonofilaments, and irregular keratohyalin granules. A syndrome combining the features of PLS with flat feet, onychogryphosis, arachnodactyly, and acro-osteolysis, has been described in one family by several authors. PLS has to be distinguished from the Schöpf-Schulz-Passarge syndrome.

PPK with clubbing of the fingers and toes and skeletal deformity (Bureau, Barrière, Thomas)

In 1959, Bureau, Barrière and Thomas described four members of one family who presented with a diffuse, symmetrical, non-transgenetic palmo-plantar keratosis, clubbing of the fingers and toes, and skeletal changes consisting of bone hypertrophy and thinning of the cortex of long bones. Reedstrøm et al. reported two sisters with consanguineous parents, who developed palmo-plantar keratoderma in childhood, clubbing of fingers and toes, and unusual skeletal changes in the terminal phalanges. X-rays showed a peculiar deformity of the terminal phalanges. The distal ends appeared spayed, and showed marginal effects suggesting atrophy. In both of these families the PPK was accompanied by marked hyperhidrosis. Recently, a patient was described with PPK, drumstick fingers, hypotrichosis, hypohidrosis and dental dysplasia.

Nummular hereditary PPKs without associated features

Keratosis palmoplanteris varia Wachters (Fig. 7)

Originally, distinct subtypes were described by Fuhls, Brünauer, and Siemens, because of the diversity of clinical features. All of these variants, however, should be considered as one dermatosis, for which Wachters introduced the term “keratosis palmoplantaris varia.” A characteristic feature is the great inter- and intra-

Figure 7. PPK variants of Wachters, displaying characteristic nummular keraticotic plaques, mainly confined to the pressure points.

familial variability. The palmar keratoses have either a nummular, linear, membranous, fissured or periangual configuration. The keratoses on the soles always have a nummular appearance, and are localized on the pressure points. Woolly hair has been described as an associated feature in one family. Nevertheless, because of the absence of associated features in other families, PPK variants Wachters is classified in the group of nummular-linear PPKs without associated features.

Keratosis palmoplanteris nummularis (hereditary painful eczematoids) (Fig. 8)

Nummular keratotic lesions, almost exclusively located on the plantar pressure points, with pain as the major complaint, are characteristic of this disease, and have been reported in 34 patients in 14 families. The lesions usually appear when an affected child begins to walk. They progress slowly, and are often accompanied by pain. The palms may also be involved after mechanical trauma. Lesions in areas other than the palms and soles have been observed in only two patients. The major histological feature, in nearly all patients, is local epidermolytic hyperkeratosis. This disorder differs from PPK Vörné in that in the Vörné type of palmo-plantar keratosis there is diffuse palmo-plantar epidermolytic hyperkeratosis.

Nummular hereditary PPKs with associated features

Tyrosinaemia type II (Richner-Hanhart syndrome)

Tyrosinaemia type II is a rare disorder of tyrosine
metabolism, characterized clinically by focal, painful, palmoplantar keratosis, bilateral pseudokeratotic corneal ulceration and mental retardation. The typical cutaneous changes of tyrosinaemia type II consist of painful, circumscribed, hyperkeratotic plaques on the palms and soles. Occasionally, aberrant hyperkeratotic lesions are present in areas such as the elbows and knees, or even the tongue. Hyperhidrosis of the palms and soles is frequently associated. Mild herpetiform corneal erosions and dendritic ulcers develop within the first months of life, and may lead to corneal scarring and glaucoma. Skin lesions usually occur when eye lesions have developed, although the skin lesions may be present without eye lesions. Deficiency of the enzyme tyrosine aminotransferase, which leads to increased serum levels of tyrosine and phenolic acid metabolites of tyrosine, is the biochemical basis for tyrosinaemia type II. Histologically, cosinophilic cytoplasmic inclusions are present in the Malpighian layer of a thickened epidermis.

**Pachyonychia congenita** (Fig. 9)

Pachyonychia congenita was originally described by Muller in 1904, and Wilson in 1905, although the association with palmoplantar keratoderma and other ectodermal defects was first reported by Jadassohn and Lewandowski. It is characterized by discoloration and thickening of the nails, usually beginning within the first month of life. The thickening is the result of subungal hyperkeratosis, with an upward angulation of the distal part of the nail plate, whereas the lateral borders are often incurved. Dystrophy of all the nails, and dyskeratotic skin lesions are necessary to establish the diagnosis. Several subdivisions have been proposed. A retrospective study of pachyonychia congenita, performed by Feinstein et al., revealed 163 reported cases. Based on the main features found in this survey, the following classification was proposed: type I (56% of cases), hyperkeratosis of nails, palmoplantar keratosis, follicular keratosis and oral leukokeratosis; type II (23% of cases), clinical findings of type I, plus bullae of palms and soles, palmar and plantar hyperhidrosis, total or neonatal teeth, and stertor on sleep; type III (12% of cases), clinical findings of types I and II, plus angular chelitis, corneal dystrophy, cataracts, and testes anomalies; type IV (7% of cases), clinical findings of types I, II and III, plus hoarseness, mental retardation, hair anomalies and alopecia. However, we recently demonstrated that the presence of other abnormalities is not an absolute prerequisite for the diagnosis.
Histopathology of the bullae, which are quite a common manifestation, did not reveal any features of epidermal-lytic hyperkeratoses. An autosomal recessive form of the disorder has been described, and recently late-onset pachyonychia congenita has been reported.

Vocal palmpoplantar and oral mucosa hyperkeratosis syndrome

The combination of PPK and hyperkeratosis of the oral mucosa was first described by Fred et al. Raphael et al. described this combination of clinical features in a family in which there were four affected individuals. There have since been reports of kindreds in which several generations were affected. The syndrome is characterized by hyperkeratosis of the palms, soles, and oral mucosa. The hyperkeratosis is especially marked on the weight-bearing areas of the soles, areas of the palms exposed to pressure, and the labial attached gingiva. In addition to the attached gingiva, hyperkeratotic lesions develop in areas of the oral mucosa subjected to friction and irritation. The hyperkeratosis, which has a symmetrical distribution, appears in early childhood or around puberty, and the lesions increase in severity with age. However, the severity varies between individuals, and among affected members of the same family. Subungual and circumungual hyperkeratosis may be an associated feature. The syndrome has to be differentiated from others which feature hyperkeratoses of the palms and soles, and oral mucosal lesions, such as PPK Howel-Evans and pachyonychia congenita.

Keratosis palmpoplantaris papillomatosa et verrucosa

In 1975, Jakac and Wolf described a clinically distinct hereditary palmoplantar keratoderm in four members of one family. This disorder has its onset between 2 and 6 years of age, and is characterized by a verrucous-papillomatous appearance. The PPK, which has a violaceous border, and is nummular at onset, subsequently extends to cover the entire surface of the palms and soles, but does not extend beyond the palmar and plantar surfaces. The skin of the fingers and toes is atrophic, and the digits develop flexor contractures. Abnormal keratotic lesions may be present on the knees, lower arms and buttocks. Profuse hyperhidrosis, which is a constant accompanying feature of the disease, and the pronounced papillomatosis, predispose to secondary infection, and this may lead to periostitis and osteomyelitis. Although spontaneous remissions have been described, the overall clinical course is progressive. In one of the patients, gingivitis and periodontitis resulted in premature loss of teeth.

Papular hereditary PPKs without associated features

Keratosis palmpoplantaris punctata (Davies-Colley, Buschke, Fischer, Brauer) [Figs 10 and 11]

The clinical presentation of numerous tiny keratotic papules, strictly limited to the volar aspects of the hands and feet, has been designated porokeratosis punctata palmaris et plantaris, palmoplantar keratoderma acuminata, and punctate porokeratotic keratoderma, and these numerous appellations have led to much confusion. Lesions usually first develop between the second and fourth decades, with the age of onset ranging from 12 to 70 years. The popular keratodermas progress slowly, and remain asymptomatic. Despite great interfamilial clinical variation, there is uniform expression within an affected family. Localized forms limited to the palmar creases have been described. Most of the patients do not have any associated features, but ankylosing spondylitis, and facial sebaceous hyperplasia, have been reported in association with PPK punctata. In addition, a coincidental, and a possible familial, association with gastrointestinal malignancy have been discussed. Histological examination reveals a compact column of parakeratosis resembling that of a cornoid lamella, but without evidence of dyskeratosis or hydropic degeneration in the epidermis, differentiating the condition from porokeratosis.

Figure 10. Classical PPK punctata, with multiple keratotic papules covering the soles.
Figure 11. PPK punctata of the palmar creases. This rare variant of PPK punctata exhibits small keratotic papules confined to the creases.

is important because of the malignant potential of porokeratosis.143

Acrokeratoelastoidosis

In 1952, Costa described a clinical entity which he called acrokeratoelastoidosis.44,145 Clinically, the disease is characterized by small, yellowish, round to oval keratotic papules, mainly confined to the margins of the palms and soles. The keratotic papules may become confluent in the centre of the palms and soles, to produce a diffuse keratoderma. The process begins in adolescence or adult life. The number of papules gradually increases over several years. Local hyperhidrosis is present. Histologically, the disease is characterized by elastofibrosis.144,145 It must be differentiated histologically from focal acral hyperkeratosis, and clinically from degerative collagenous plaques of the hands,146 a separate acquired condition, which occurs in an older age group on the sun-exposed parts of the hands.

Focal acral hyperkeratosis (Fig. 12)

This dermatosis is clinically similar to, but histologically different from acrokeratoelastoidosis.44,147 It appears to be a focal disorder of keratinization, which has an insidious onset in childhood, reaches a maximum in early life, and causes only cosmetic embarrassment. With the exception of one Arab patient, all reported individuals have been of Negroid racial origin. In addition to the typical papules along the borders of hands and feet, hyperkeratotic papules may be present over the interphalangeal joints of the fingers and toes, and on the heels. On histological examination, there is no elast-

Figure 12. Focal acral hyperkeratosis, displaying a picture similar to acrokeratoelastoidosis, with yellowish papules mainly confined to the thenar eminence.

rhesis, and this distinguishes the disease from acrokeratoelastoidosis.

Papular hereditary PPKs with associated features

Keratosis palmoplantaris with lipomata

In 1947, Hanhart reported a family in which six members in three consecutive generations co-expressed palmoplantar keratosis with lipomata.103 The keratosis is limited to the palms, soles and volar surfaces of the fingers and toes, and consists of multiple papular keratotic lesions. Its onset is from the third decade of life onwards. The number of lipomata varies from solitary lesions to multiple lipomata in a generalized distribution. However, five members of the same family expressed only palmoplantar keratosis, suggest-
ire a coincidence of two unrelated anomalies in the 'affected' members.

**Syndrome of cystic eyelids, palmpoplantar keratosis, hypodontia and hypopituitarism (Schöpf–Schulte–Passarge syndrome)**

Schöpf et al. reported two sisters with a syndrome of cystic eyelids, hypodontia, hypopituitarism and palmpoplantar keratosis. A similar grouping of ectodermal defects was reported by Burk et al. in a man who was a sporadic case. Unique in this individual were multiple facial tumours of the follicular infundibulum (Mehregen and Butler). Happle et al. described the development of squamous cell carcinoma in association with this syndrome. The Papillon–Le Févre syndrome can be easily distinguished from this disorder. Periodontitis, which is an integral part of the PLS, was not a feature of the reported cases of the Schöpf syndrome, and eyelid cysts have not been described in the PLS.

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