Epidermolytic Palmoplantar Keratoderma (Vorner's Keratoderma)

Dr. K. H. Mak

Date:	14 April, 1999
Venue:	Yaumatei Skin Centre
Organizer:	Social Hygiene Service, DH; Clinco-pathological Seminar

CASE SUMMARY

History

A 17-year-old male student developed thick skin over his palms and soles since few months of age. It did not cause any symptom or functional disability. Blistering occurred occasionally in summer time. There was no palmoplantar hyperhidrosis. No other area was involved and the patient had normal development. The patient was the only child of the family. His mother had similar problems but her siblings and parents were unaffected.

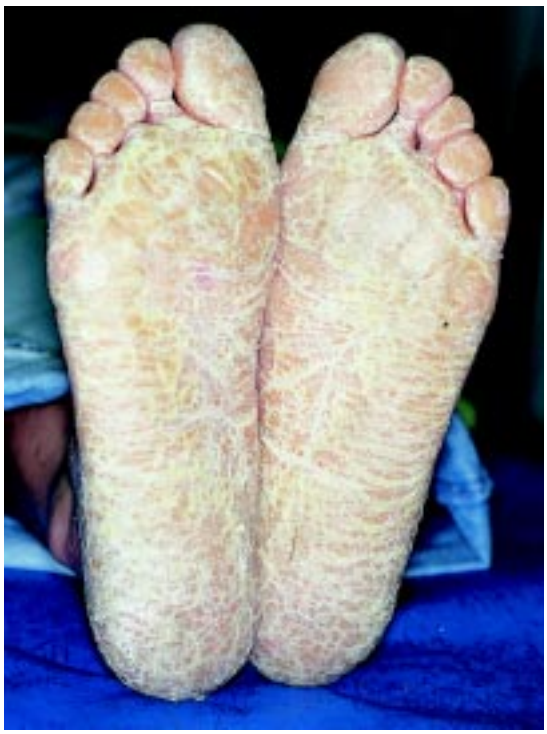

Figure 1: Diffuse hyperkeratosis of soles

Physical examination

There was thick, yellow, waxy and diffuse keratosis on the palms and soles (Figure 1), extending to the lateral surfaces. It was demarcated sharply with an erythematous rim (Figure 2). Knuckle pads were present and there was mild flexion contracture of the distal interphalangeal joints of fingers (Figure 3). There was no other hyperkeratotic area noted over the elbows and knees. Nails, teeth and hair were normal. A congenital melanocytic nevus of 2cm in diameter was incidentally found on the right side of his chin.

Similar features could be detected in his mother but the erythematous margin was less marked and the flexion contracture of finger joints was more pronounced.

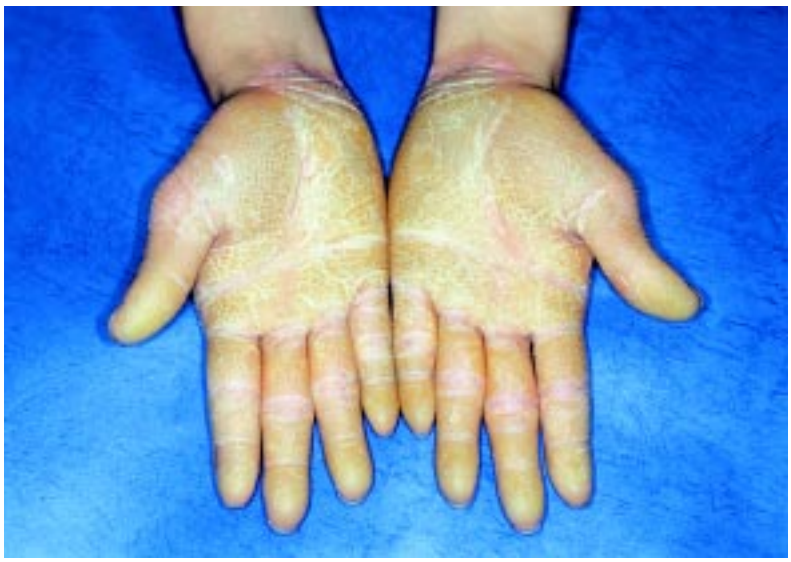

Figure 2: Diffuse hyperkeratosis of palms with an erythematous rim over the wrists

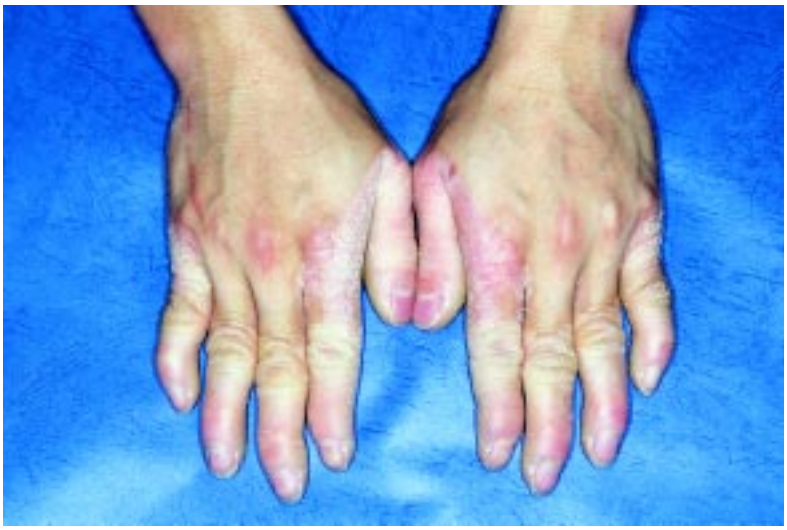

Figure 3: Knuckle pads and mild flexion contracture of finger joints shown with no transgrediens

Clinical diagnosis

The clinical diagnosis is a diffuse non-mutilating type of hereditary palmoplantar keratoderma.

Investigations

Skin biopsy of his palm showed marked orthokeratotic hyperkeratosis with epidermolysis of upper and mid-epidermis. There is elongation of rete ridges and sparse superficial perivascular lymphocytic infiltrate. The diagnosis is consistent with palmoplantar keratoderma of Vorner type.

Treatment

The patient was advised on manual paring. He was treated with 3% salicylic acid ointment and 10% urea cream topically. Response was unsatisfactory and treatment with systemic retinoid was being considered.

REVIEW ON HEREDITARY EPIDERMOLYTIC PALMOPLANTAR KERATODERMA (HEPPK)

Hereditary epidermolytic palmoplantar keratoderma or Vorner's keratoderma is a rare genodermatosis first described by Vorner in 1901.[1] Clinically, this cannot be distinguished from Unna-Thost keratoderma which is non-epidermolytic in histology. Both entities are autosomal dominantly inherited and manifested as diffuse palmoplantar keratoderma (PPK) without transgrediens (extension to the dorsal surfaces) or associated ectodermal features. To-date, at least 33 families with this disorder and 11 sporadic cases were reported.[2] It was once believed that Unna-Thost keratoderma was the commonest hereditary PPK. However, in 1988, Hamm and colleagues noted the features of epidermolytic hyperkeratosis in 12 out of 21 patients with diffuse PPK.[3] Besides, re-investigation of family originally seen by Thost also revealed the epidermolytic features.[3] It is likely that the true frequency of Vorner's keratoderma was under-estimated in the past and this entity may actually be the most frequent type of hereditary PPK.

Genetics

There is a remarkable consistency of mutations identified in families of Vorner's keratoderma. The mutated gene encodes acidic keratin, keratin 9, which is located in chromosome 17q. Keratin 9 is a palm and sole-specific keratin.[4,5] This explains why the site of involvement is restricted to palm and sole.

Clinical features

The keratoderma usually presents in infancy. Initially there is a palmoplantar erythema that is soon covered by thick and horny layer. The hyperkeratosis is diffuse, thick and uniform. Fissuring is sometimes present. It may extend to the lateral surfaces with a sharp demarcation and an erythematous rim. Knuckle pads

are usually present. Some patients have hyperhidrosis that is more consistantly seen in Unna-Thost keratoderma. Blistering can be a feature but is infrequent. Vorner's keratoderma runs a stable course, that is, the lesions remain unchanged throughout life. Therefore, it is regarded as a 'non-progrediens, non-transgrediens' type of PPK.

Histopathology

It demonstrates the features of epidermolytic hyperkeratosis. There is orthokeratotic hyperkeratosis, hypergranulosis, acanthosis and a reticulated pattern of suprabasal epidermis due to intercellular and cellular edema. Keratinocytes of the granular and spinous layers show severe vacuolization and contain clumps of irregular eosinophilic granules. Ultrastructural studies have shown that the intracytoplasmic inclusions seen on light microscopy are composed of abnormal aggregates of tonofilament and enlarged keratohyalin granules.

Epidermolytic hyperkeratosis is suggested to be an expression of keratin abnormality and is not unique for Vorner's keratoderma. It is also present in other hereditary disorders such as bullous congenital icthyosiform erythroderma, icthyosis bullosa of Siemens, subgroup of epidermal naevus and hereditary painful callosities. It can be acquired or an incidental finding in epidermolytic acanthoma, seborrheic wart, melanocytic and actinic lesions, squamous cell carcinoma, epidermal and pilar cysts; and occasionally in normal oral mucosa.

Differential diagnosis

Clinically, it is impossible to distinguish Vorner's from Unna-Thost keratoderma. However, differentiation from other types of PPK is not difficult due to the presence of diffuse palmoplantar involvement without transgrediens or constriction bands of digits (pseudoainhum), its dominant inheritance and the absence of associated ectodermal features (Table 1).

Table 1. Hereditary palmoplantar keratoderma[8,10]

	Inheritance	*No associated ectodermal features*	*With associated ectodermal features*
Diffuse	AD	**Unna-Thost** (NEPPK) **Greither** (transgrediens +) **Vorner** (EPPK) **Sybert** (mutilating)	**Vohwinkel** (mutilating, starfish-shaped hyperkeratosis) **Huriez** (sclerodactyly) **Clouston** (hydrotic ectodermal dysplasia)
	AR	**Mal de Meleda** (transgrediens+) **Gamborg Nielsen** (mutilating) **Acral keratoderma** (diffuse and striate, mutilating)	**Papillon-Lefevre** (periodontitis) **Bureau-Barriere-Thomas** (clubbing and skeletal deformity)
Focal (nummular/ striate)	AD	**Wachters** (focal NEPPK) **Hereditary painful callosities** (focal EPPK) **Striate PPK**	**Richner-Hanhart** (oculocutaneous tyrosinaemia) **Pachyonychia congenita** **PPK and oral hyperkeratosis** **Howel-Evans** (PPK with oesophageal cancer)
	AR		**Pachyonychia congenita** **Jakac-Wolf** (papuloverrucous)
Punctate	AD	**Bushke-Fischer-Brauer disease** **Acrokeratoelastoidosis** (with elastorrhexis) **Focal acral hyperkeratoisis**	**Hanhart** (with lipomata)
	AR		**Schopf-Schulz-Passarge** (syndrome with cystic eyelids, hypodontia and hypotrichosis)

Treatment

Regular manual paring and use of topical keratolytics (salicylic acid 6-10% in white soft paraffin or 35-70% propylene glycol) with or without occlusion may reduce the thickness of keratoderma. Associated secondary dermatophyte infections should be watched out for and treated accordingly. Topical retinoid is not useful as reported. Acitretin, at the dosage of 0.5-1mg/kg/day, is helpful. However, patients may find it intolerable since loss of thick keratin can give rise to a tender, insufficiently keratinized base with hyperaesthesia.[6,7] Condition recurs upon withdrawal of treatment. To avoid long term toxicity of treatment, intermittent therapy (for example, 4 months 'on' and 2 months 'off') may also achieve good control of symptoms.[8] Topical calcipotriol was reported to be useful in a patient.[9] With the advent of molecular biology, the keratin gene mutations of more and more inherited PPK have been identified. This may allow the future development of specific gene-targeted pharmacological therapies in inherited keratodermas.[8]

Discussion

There was query if epidermolytic hyperkeratosis can be present in other inherited keratodermas. According to the literature, it can be present in another entity called the hereditary painful callosities (PPK nummularis) which presents with focal, painful keratoderma without associated features. There was also one case of oculocutaneous tyrosinosis (Richner-Hanhart) which showed a circumscribed PPK with epidermolytic keratoderma that regressed in response to appropriate diet.[7,10]

Question was raised concerning the clinical characteristics of Howel-Evans syndrome. Howel-Evans first reported 2 Liverpool families in 1958 with high incidence of oesophageal carcinoma in tylotic members. Although originally described as tylosis or diffuse, non-epidermolytic PPK, reappraisal of the affected family has shown that lesions predominantly affect the pressure points of the sole, not the palm, and therefore the lesions should be considered as focal PPK.[11] There was also variable oral leukokeratosis and follicular prominence. Thirty seven percents of affected family members developed oesophageal cancer 30-40 years later. The locus of affected gene is on chromosome 17q23, a site of no known candidate genes. It was labeled the TOCG locus (for tylosis with oesophageal cancer). Another German-American family had been reported to have an increased risk (38 fold) of oesophageal cancer associated with a focal keratoderma with oral leukokeratosis.[12]

Learning points:
Vorner's epidermolytic PPK is an autosomal dominantly inherited, diffuse keratoderma without transgrediens or associated ectodermal features. This condition may respond to oral retinoid.

References

1. Vorner H. Zur Kenntniss des Keratoma hereditarium palmare et plantare. Ach Dermatol Syph 1901;56:3-37.
2. Requena L, Schoendorff C, Sanchez YE. Hereditary epidermolytic palmoplantar keratoderma (Vorner type) - report of a family and review of literature. Clin Exp Dermatol 1991; 16:383-8.
3. Hamm H, Happle R, Butterfass T, Traupe H. Epidermolytic palmoplantar keratoderma of Vorner, is it the most frequent type of hereditary palmoplantar keratoderma? Dermatologica 1988;177:138-45.
4. Bonifas JM, Matsumura K, Chen MA. Mutations of keratin 9 in two families with palmoplantar epidermolytic hyperkeratosis. J Invest Dermatol 1994;103(4):474-7.
5. Reis A, Hennies HC, Langbein L, et al. Keratin 9 gene mutations in epidermolytic palmoplantar keratoderma. Nature Genet 1994; 6:174-9.
6. Fritsch P, Honigsmann H, Jaschke E. Epidermolytic hereditary palmoplantar keratoderma. Report of a family and treatment with an oral aromatic retinoid. Br J Dermatol 1978;99(5): 561-8.
7. Kanitakis J, Tsoitis G, Kanitakis C. Hereditary epidermolytic palmoplantar keratoderma (Vorner type). Report of a familial case and review of the literature. J Am Acad Dermatol 1987; 17(3):414-22.
8. Ratnavel RC, Griffiths WAD. The inherited palmoplantar keratodermas. Br J Dermatol 1997;137:485-90.
9. Lucker GP, Van de Kerkhof PC, Steiljen PM. Topical calcipotriol in the treatment of epidermolytic palmoplantar keratoderma of Vorner. Br J Dermatol 1994;130:543-6.
10. Lucker GP, Van de Kerkhof PC, Steijlen PM. The hereditary palmoplantar keratoses: an updated review and classificaion. Br J Dermatol 1994;131(1):1-14.
11. Ellis A, Field EA, Field JK, et al. Tylosis associated with carcinoma of the oesophagus and oral leukoplakia in a large Liverpool family: a review of six generations. Eur J Cancer Oral Oncol 1994;30:102-12.
12. Stevens HP, Kelsall DP, Bryant SP, et al. Linkage of an American pedigree with palmoplantar keratoderma and malignancy (palmoplantar ectodermal dysplasia type III) to 17q24. Arch Dermatol 1996;132:1-12.