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Hereditary Palmoplantar Keratoderma in the Northernmost County of Sweden

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A papular and a diffuse variety of hereditary palmoplantar keratoderma (Unna Thost) are described. It was not possible to demonstrate any histopathological differences between the two varieties. Of the patients examined 36.2% were found to have dermatophytosis in addition to hereditary palmoplantar keratoderma. The hyperkeratosis was smooth and uniform in both varieties. When scaling and fissuring did occur they were signs of dermatophytosis and not part of the clinical picture. The examination of biopsies stained with H&E and PAS showed that dermatophytosis in patients with hereditary palmoplantar keratoderma, especially those with recurrent vesicular eruptions, gave rise to a histopathological picture which was, in some respects, similar to that of acute vesicular eczema. *Key words: Hereditary palmoplantar keratoderma; Clinical picture; Dermatophytosis; Histopathology.* (Received September 18, 1984.)

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Earlier descriptions of HPPK of the Unna Thost variety, usually based on a limited number of patients, have shown that this frequently encountered genodermatosis possesses an autosomal dominant mode of inheritance (1, 2, 3). Equally distributed between the sexes, it is the most frequently found keratoderma, occurring worldwide, though uncommon in the negro. The frequency generally quoted is that from Northern Ireland of 1 : 40000 (4). It has, however, recently been shown to be 1 : 12 000 in Slovenia (Yugoslavia) (5) and 1 : 300 among adolescents in the county situated immediately to the south of the area from which patients included in the present study were taken (6). In Norrbotten (the northernmost county of Sweden) a frequency of 1 : 200 among school children was reported in 1967 (7). The clinical picture differed from those previously described, and it was therefore considered of interest to reinvestigate and further study the patients of this county.

MATERIAL AND METHODS

Two groups of patients with HPPK were included in the material for the clinical description. The first group came from a follow up investigation performed about 20 years after the first genetic study (7). Relatives of the original 87 propositi constituted the second group. Forty-four (51%) of those, 17 men and 27 women, average age 34 years (range 30–41 years) were included in the first group. Of the remaining 43, 34 lived outside the county, 4 did not keep their appointments at the department, 2 were dead, 1 had emigrated to the USA and 2 could not be found. Of the relatives, 91 were selected according to a randomized scheme, 31 men, average age 43 years (range 16–70 years), 36 women, average age 42 years (range 17–68 years) and 24 children, average age 7 years (range 1–15 years).

After pretreatment of lesions with ethanol-ether, material for culture of fungi was collected by use of a curette and inoculated on Sabouraud's glucose agar without cycloheximide (8, 9, 10). Biopsies from the medial side of the foot, 1 cm within the demarcation of hyperkeratosis corresponding to the

Abbreviations: Hereditary palmoplantar keratoderma: HPPK.

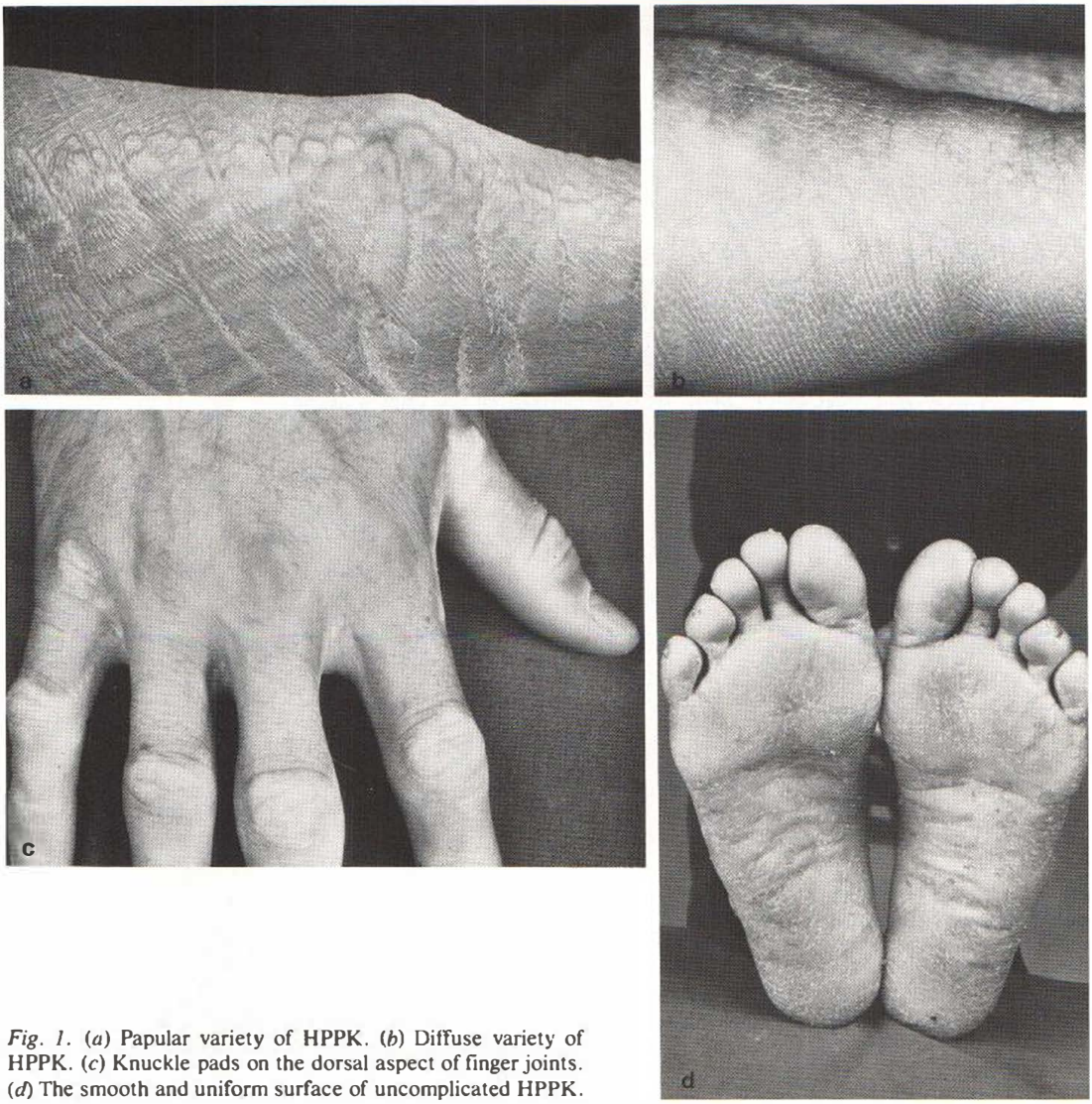

Fig. 1. (*a*) Papular variety of HPPK. (*b*) Diffuse variety of HPPK. (*c*) Knuckle pads on the dorsal aspect of finger joints. (*d*) The smooth and uniform surface of uncomplicated HPPK.

metacarpophalangeal joint of the first toe were taken from 39 patients of the second group. They were fixed and stained with H&E and with PAS for the demonstration of fungal elements. The chi-square test was used for statistical calculations.

RESULTS

Two types of HPPK with different clinical pictures could be distinguished, one diffuse with a distinct demarcation and one characterized by a papular border between hyperkeratotic and normal skin (Fig. 1 *a*, *b*). Knuckle pads, commonly located to the dorsal aspects of the finger joints were frequently found in the latter type (Fig. 1 *c*). The papular variety was more often observed among children, developing into the diffuse variety with increasing age (Table I). Hyperkeratosis was smooth and uniform in both varieties, with a colour

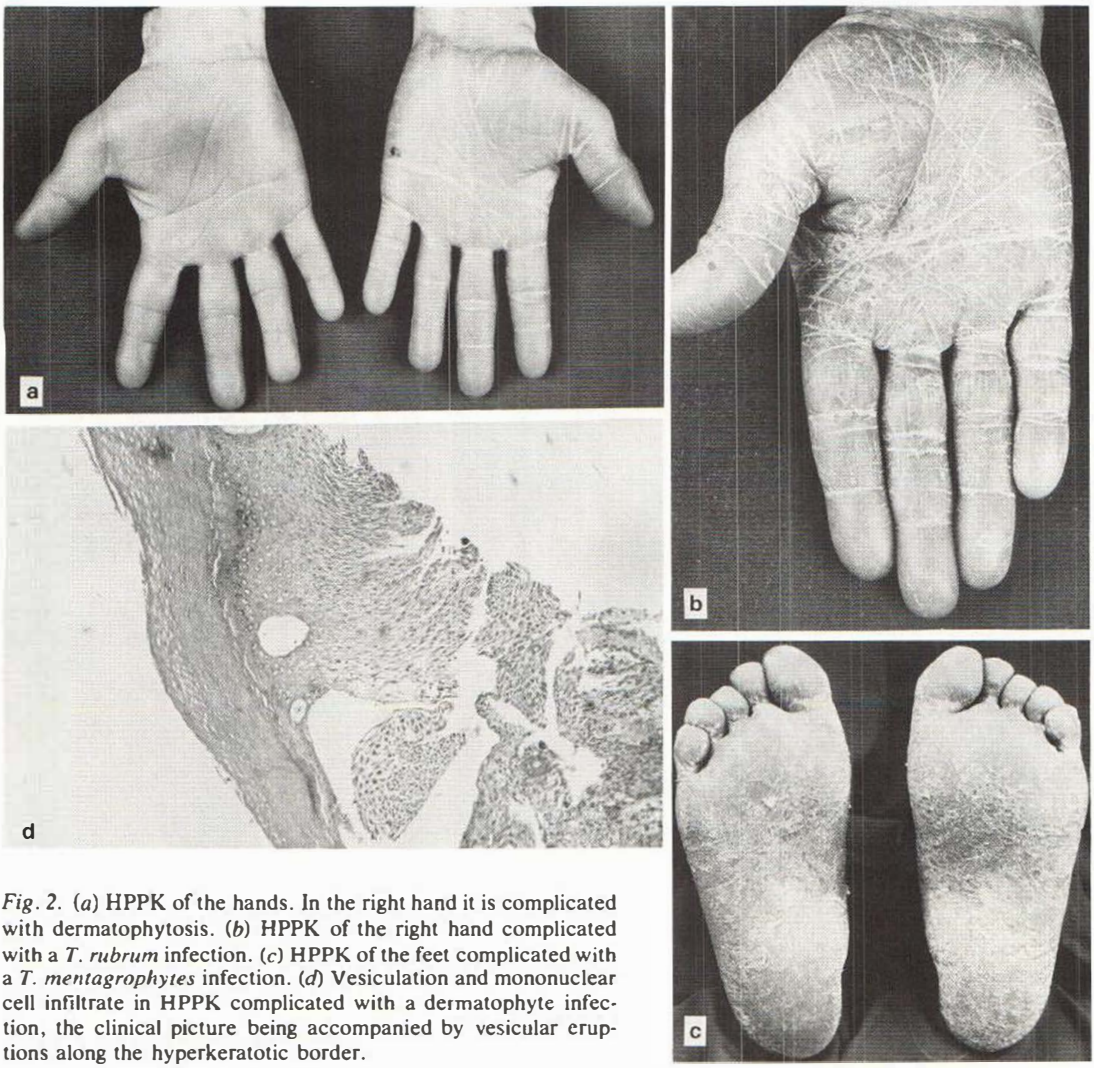

Fig. 2. (*a*) HPPK of the hands. In the right hand it is complicated with dermatophytosis. (*b*) HPPK of the right hand complicated with a *T. rubrum* infection. (*c*) HPPK of the feet complicated with a *T. mentagrophytes* infection. (*d*) Vesiculation and mononuclear cell infiltrate in HPPK complicated with a dermatophyte infection, the clinical picture being accompanied by vesicular eruptions along the hyperkeratotic border.

ranging from that of normal skin to yellow depending on the thickness of the horny layer (Fig. 1 *d*). Hyperhidrosis commonly reported to accompancy HPPK (11), occurred more often in men than in women and children, disappearing with increasing age in the majority of cases (Table I).

In the second group 65 % of the men, 22 % of the women and 21 % of the children were shown to have dermatophytosis, giving a frequency of 33/91 (36.2 %) (Fig. 2 *a*, *b*, *c*) (12, 13). The distribution of fungi cultured in patients with HPPK was compared to the total number of cultures performed at the department during the same period. *T. mentagrophytes* was found far more often in patients with HPPK than in those without ($p<0.01$). Scaling and itching were predominant features in 23 out of the 33 patients examined 1983 (70 %), accompanied by a red eczematous zone outside the demarcation of hyperkeratosis. However, these symptoms were lacking in 3 men, 4 women and 3 children, diagnosis being made only after the results of the mycological investigation had been studied. Five (15 %)

Table I. *The frequency of different clinical signs in patients suffering from hereditary palmoplantar keratoderma*

Patients were divided into two groups. The first group included patients belonging to a genetic study performed in 1967, of whom 51% were reexamined during 1982 and 1983. The second group was represented by relatives to the first group and were examined in 1983

	First group (n=44)													
	1st examination (1967)				2nd examination (1982–83)				Second group (n=91). Examined 1983					
	Men (n=17)		Women (n=27)		Men (n=17)		Women (n=27)		Men (n=31)		Women (n=36)		Children (n=24)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Papular variety	11	65	17	63	4	24	7	26	8	26	15	41	11	46
Diffuse variety	6	35	10	37	13	76	20	74	23	74	21	58	14	58
Hyperhidrosis	6	35	9	33	7	41	9	33	19	61	16	43	9	38
Scaling and fissuring	2	12	0	0	9	47	6	22	16	52	5	14	3	13
Dermatophytosis	Cultures were not performed in 1967				10	59	4	23	20	65	8	22	5	21

patients had dermatophytosis on both hands and feet, the remaining 28 were affected on the feet only. Onychomycosis was found in 6/33 (18%). A history of recurrent vesicular eruptions along the hyperkeratotic border was obtained in 26/33 (79%) patients with and 10/58 (17%) patients without dermatophytosis. Thus, such eruptions occur more often in patients with dermatophyte infections than in those without ($p<0.01$).

Histopathological examination of biopsies from 39 patients of whom 23 (59%) had dermatophytosis as demonstrated by conventional culture showed 38 to have orthohyperkeratosis and normogranulosis. Parakeratosis was demonstrated in 4 biopsies, elongation of the rete ridges in 2 and focal spongiosis and verruciform hyperkeratosis in 1 biopsy each. Hyphae were found in 14 biopsies and spores in 6 localized to the upper 2/3 of the horny layer. In 11 biopsies a dermoepidermal mononuclear cell infiltrate could be demonstrated and hyphae were found in 9 of these. Biopsies from 4 patients contained vesiculation and intracellular vacuolation in addition to an epidermal mononuclear cell infiltrate. In the same biopsies hyphae could be demonstrated in the horny layer (Fig. 2*d*). These patients were found to have vesicular eruptions along the hyperkeratotic border when clinically examined.

DISCUSSION

In previous publications a rough surfaced type of HPPK with scaling and fissuring and a smooth surfaced variety lacking these features have been described (14, 15). A differentiation between these two forms was impossible in the present material, which was instead subdivided into a papular and a diffuse variety. The papular type was most often seen in children and adolescents, being replaced by the diffuse type later in life. The hyperkeratosis was smooth and uniform in both varieties. When scaling and fissuring did occur they

were generally signs of dermatophytosis and disappeared after treatment (16). Hyperhidrosis was more often found in men than in women and children and showed a tendency to decrease with increasing age (Table I).

T. mentagrophytes has recently been shown to be a weaker antibody inducer than *T. rubrum* and *E. floccosum* in patients with HPPK (17). This may help to explain the predominance of *T. mentagrophytes* in these patients. Vesicular eruptions along the hyperkeratotic border are probably dermatophytid reactions, mediated by IgG (17). Symptomless carriers of dermatophytes or latent dermatophytosis were seldom found, and in patients with HPPK these conditions should be interpreted as a resting state of hyphae and spores in the thick horny layer.

The histopathological picture of HPPK, uncomplicated by dermatophytosis does not differ from earlier description (18). In patients suffering from dermatophytosis together with vesicular eruptions, it was however found to be similar to acute vesicular eczema. This study has shown that HPPK in Norrbotten is found in a papular and diffuse variety both of which have a smooth and uniform hyperkeratotic surface. Scaling and fissuring were seen amongst cases infected with dermatophytes, i.e. complications, that are consequently considered to be clinical signs of dermatophytosis and not part of the clinical picture of HPPK.

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