Hereditary palmoplantar keratoderma type papulosa in Slovenia

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A B S T R A C T

Background: Hereditary palmoplantar keratodermas (HPPK) are relatively frequent in Slovenia; however, the papulosa type of HPPK is rare. Epidemiological data are scarce; a population study in Croatia revealed a prevalence of 1.17/100,000 inhabitants. According to the preliminary data, it seems that HPPK papulosa is more common in Slovenia than in other countries. Efforts were made to identify all patients with HPPK papulosa in Slovenia.

Patients and Methods: Existing hospital and outpatient records served as a starting point. Patients and their relatives were invited for examination. When necessary for preparing pedigrees, we visited patients.

Results: Altogether 66 patients were observed, giving a prevalence of 3.3/100,000 inhabitants. 62 patients belonged to 11 unrelated families with two or more affected members and there were also four isolated cases. Our investigation points to an autosomal dominant mode of inheritance. All of the routine biochemical and hematologic tests were within normal limits. No malignancies were observed, nor were such data revealed in patients' histories. Thickened nail-plates were observed in three patients.

Conclusions: The prevalence of HPPK papulosa in Slovenia is higher than in other countries studied. Further loci mentioned in literature suggest a genetic heterogeneity in this condition.

K E Y W O R D S

keratoderma, palmoplantar, papulosa, heredity, epidemiological study, Slovenia

Introduction

HPPK papulosa (Buschke-Fischer-Brauer) is a rare form of HPPK and was described by Buschke and Fischer in 1910 (1) and Brauer in 1913 (2). The epidemiological data are inconsistent. A larger population study in Croatia showed a prevalence of 1.17/100,000 inhabitants (3).

Clinically, the condition is characterized by numerous, irregularly distributed, verrucous hyperkeratotic papules on the palms and soles, sometimes indistinguishable from common warts, various forms of acquired punctate keratoderma, as well as papules from other similar conditions (Fig. 1). The papules vary in size and appearance, and often tend to coalesce over pressure points. In a number of cases, the diagnosis was made coincidentally

because many patients do not complain about being troubled by the hyperkeratotic lesions.

Histopathology revealed a typical, sharply demarcated hyperkeratosis and acanthosis with hypergranulosis, without a notable inflammatory infiltrate in the papillary dermis (Fig. 2).

An autosomal dominant mode of inheritance with age-dependent penetrance is usually observed. The age of onset is primarily between 10 and 40 years. This exhibits the greatest variation in morphology among all of the HPPKs, but minimal phenotypic variation within single pedigrees.

The molecular basis of the disease has still not been definitely established. In a previous study, the keratin gene clusters on chromosomes 12 and 17 were excluded as candidate genes (4). Later, the cause of this condition was attributed to chromosome 8q24, whereas Martinez-Mir et al. located the responsible locus to chromosome 15q22–q24 (5). Zhang et al. incriminated a locus on chromosome 8q24.13–8q24.21 in a Chinese pedigree (6), and a more recent study revealed the gene causing PPK papulosa to be on a 5.06-cM interval at 15q22.2–15q22.31 (7). Such data suggest possible genetic heterogeneity of this disorder.

Patients and methods

We present clinical data on 66 patients with HPPK papulosa, Buschke-Fischer-Brauer type, from Slovenia. Existing hospital and outpatient records served as a starting point (8, 9). Patients and their relatives were invited for examination, and visiting patients at their homes enabled us to prepare pedigrees in certain instances. Efforts were made to include all patients with the HPPK papulosa type in Slovenia. The diagnosis was established clinically and through patient histories. A skin biopsy was performed in all clinically doubtful cases. The data were entered into prepared questionnaires.

Results

Altogether, 66 patients were found, giving Slovenia a prevalence of 3.3/100,000 inhabitants: 38 (57.7%) males and 28 (42.3%) females.

Two or more affected members were found in the eleven families. An autosomal dominant mode of inheritance was confirmed. There were also four isolated cases.

Nineteen patients were clinically examined, and all displayed typical palmoplantar lesions. Thickened nail-plates were observed in three patients. There was no palmoplantar hyperhidrosis or further skin changes.

In 10 patients (52.63%) the age of onset was between 20 and 40 years, in 3 patients (15.83%) the condition appeared before age ten, and in six cases (31.56%) clinical symptoms became evident during the first year of life.

Discussion

Although there are no data on the prevalence of papulosa-type HPPK in various populations, it seems that this rare disorder is relatively frequent in Slovenia. Recent reports revealed different genetic loci for PPK papulosa in a Chinese pedigree. Genotyping of markers in this region

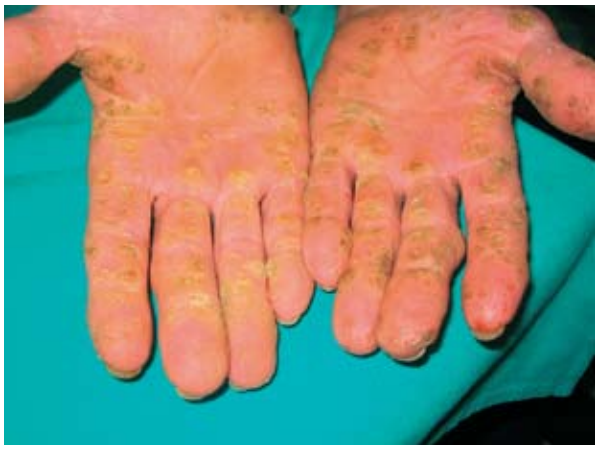

Fig. 1. HPPK papulosa: numerous hyperkeratotic papules on the hand.

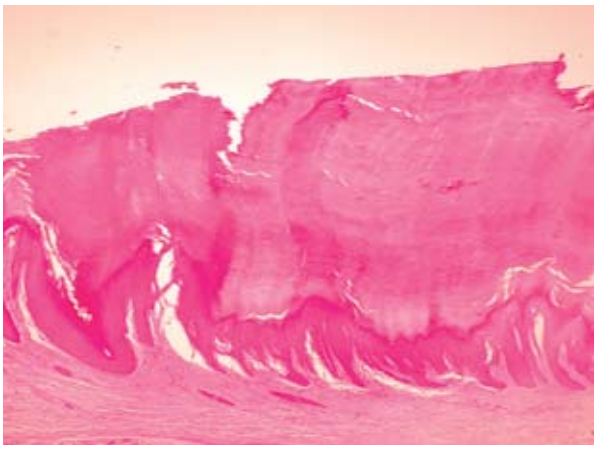

Fig. 2. HPPK papulosa: sharply demarcated hyperkeratosis and acanthosis with hypergranulosis, without a notable inflammatory infiltrate in the papillary dermis (HE 20×).

failed to confirm cosegregation of the disease in the pedigrees. As mentioned in the literature, the various genetic loci suggest genetic heterogeneity for this condition.

The study of this condition is further complicated by the various synonyms that have been used for it: keratoma dissipatum hereditarium palmare et plantare (Brauer), keratodermia maculosa disseminata symmetrica palmaris et plantaris (Buschke-Fischer), disseminated clavus of the hands and feet, papulotranslucent acrokeratoderma, Davis-Colley syndrome, keratodermia palmoplantaris punctata, and others. These synonyms are descriptive and rather confusing. The lesions are punctate or papular at the onset, but later may become verrucous; thus the term PPK verrucose is probably more suitable.

Conclusion

HPPK type papulosa is a rare condition. Available data suggest that the incidence of 3.3 per 100,000 inhabitants in Slovenia is probably the highest reported in a population.

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