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# Punctate Palmoplantar Keratoderma Associated with Morbus Bechterew and HLA B 27

## *A Family Study*

P. GAMBORG NIELSEN

*Department of Dermatology, Central Hospital, Halmstad, Sweden*

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Four patients in a family with punctate palmoplantar keratoderma (Buschke-Fischer) associated with Morbus Bechterew and HLA B 27 in 3 of the family members are reported. Without severe side effect, the proband was successfully treated with 50 mg etretinate per day for 6 weeks *Key word: Etretinate.* (Received December 8, 1987.)

P. Gamborg Nielsen, Department of Dermatology, Central Hospital, S-301 85 Halmstad, Sweden.

Punctate palmoplantar keratoderma was probably first described by Davies-Colley in 1879 under the designation "disseminated clavus of hands and feet" (1). In 1910 this keratinization disorder was recorded by Buschke & Fischer as "keratodermia maculosa dissiminata palmaris et plantaris", and 2 years later in 1912 Brauer demonstrated the hereditary nature of a disease with a similar clinical picture (2, 3). Consequently, it was named "keratoderma hereditarium dissipatum palmare et plantare (Brauer)". A great number of confusing designations for this clinical picture have characterized the nomenclature during the following years. Most authors, however, agree that the sporadic form first described by Buschke & Fischer and the familial form later described by Brauer are one and the same disease, and are, therefore, in consequence called "punctate palmoplantar keratoderma (Buschke–Fischer)" (4). Although most cases have not been associated with a familial history of the disease, the cases of a few affected families have been reported; the consensus is that the mode of transmission in those cases is that of an autosomal dominant inheritance (5).

Generally, punctate palmoplantar keratoderma (Buschke–Fischer) is considered to be rare. In previously performed investigations, patients with punctate palmoplantar keratoderma constituted a heterogeneous group, including sporadic and familial cases as well as cases of keratosis punctata of the palmar creases (6, 7). Therefore, it was rather difficult to estimate exactly any prevalence, but among dermatological out-patients approximately 1 : 2 000 has been mentioned (8). However, since the lesions are usually asymptomatic, it is conceivable that the majority of persons with the condition do not seek medical consultation (9).

Punctate palmoplantar keratoderma (Buschke–Fischer) is characterized by numerous small, hard round or oval, yellow horny papules, irregularly distributed on palms and soles. They vary in size between 2 and 10 mm or more in diameter and tend to be larger when subjected to trauma. The lesions first develop at any time between the ages of 10 and 45, but usually between 15 and 30 years. In most patients the condition is an asymptomatic, incidental finding, but some patients experience tenderness when pressure is applied to the lesions. The disease has been reported to exist in all human races (10).

The cause of the disorder is not known, but a dual influence of genetic and environmental factors may trigger off the disease in many cases (11). A strong association between punctate

palmoplantar keratoderma and hard manual labour has even been postulated. Hyperhidrosis does not accompany this disorder. Previously, it has been stated that the prevalence of dermatophytosis in patients with diffuse palmoplantar keratoderma of the Unna-Thost variety was 36.7%, but in punctate palmoplantar keratoderma, affinity to dermatophytes has not been demonstrated (12).

According to the literature, associated features are rare, and more often reported together with the sporadic form than with the familial form (13) (Table I). It was, therefore, considered of interest to report a family study of punctate palmoplantar keratoderma (Buschke–Fischer) associated with HLA B 27 and Mb. Bechterew.

## CASE REPORTS

The proband was a 64-year-old man, who was admitted to the Department of Dermatology in 1976. From 1946 he suffered from Mb. Bechterew. A correct clinical diagnosis of his cutaneous disorder was, however, not made before 1978, when it was established that he suffered from a punctate palmoplantar keratoderma (Fig. 1).

In 1987 the patient was readmitted to the department of dermatology and the diagnosis punctate palmoplantar keratoderma of the variety, first described by Buschke & Fischer was verified. The keratoderma appeared at an age of 30 years with wart-like, punctate projections arising from the palms and 1–2 years later from the soles. The lesions were larger on the soles than those on the palms and were localized predominantly to the heels and to the thenar and hypothenar prominences. The individual lesions varied between 1 and 3 mm in size on palms (Fig. 2) and even larger, though fewer, on the soles. The dorsal aspects of hands and feet were not involved and spreading of hyperkeratotic lesions to other parts of the skin could not be demonstrated. Sensibility of the skin on palms and soles was normal. Nails, hair, teeth and eyes were unaffected and hyperhidrosis was not found.

Since 1946 the patient suffered from Mb. Bechterew and typical ossifications of the anterior longitudinal ligaments, corresponding to the thoracic and lumbar parts of the vertebral column was shown by radiologic examination. The sacro-iliac joints were normal. Association with HLA B 27 was demonstrated in 1987 (25).

At the clinical examination *Epidermophyton floccosum* was cultured from soles and the dermatophyte infection was successfully treated with topical econazole nitrate (Pevaryl®).

A punch biopsy from a lesion localized on the right palm showed marked hyperkeratosis with depression of the underlying malphigian layer below the level of epidermis. An increased thickness of the granular layer was likewise demonstrated. The dermis was free of any inflammatory infiltrate and except for slight dilatated subepidermal capillaries, no further diagnostic changes were demonstrated. The histopathologic picture was therefore compatible with that of punctate palmoplantar keratoderma of the Buschke–Fischer variety.

The patient was married to a healthy woman free from hyperkeratotic lesions or Mb. Bechterew, and association to HLA B 27 could not be demonstrated. Marriage resulted in 4 children, 3 boys born 1952,

Table I. *Punctate palmoplantar keratoderma (Buschke–Fischer) and associated features*

| Skeleton | | Skin, hair and nails | | Mucous membranes | | Miscellaneous types | |
|---|---|---|---|---|---|---|---|
| Sporadic | Familial | Sporadic | Familial | Sporadic | Familial | Sporadic | Familial |
| | HLA B 27 and Mb. Bechterew | Truncal lesions (14)<br>Hypopigmentation (15)<br>Blisters (16) | Atopy (8)<br>Nail dystrophies (4)<br>Basal cell carcinomas (17)<br>Squamous cell carcinomas (17)<br>Multiple lipomas (18) | Oral leukoplakia and esophageal carcinoma (19)<br>Esophageal squamous cell carcinoma (20)<br>Carcinoma of the stomach (21) | Adenocarcinoma of the colon (22)<br>Duodenal ulcers (23) | Endocrinological and trophoneurotical disorders (4)<br>Carcinoma of the lung (17)<br>Carcinoma of the breast (17)<br>Hepatic cirrhosis (24) | |

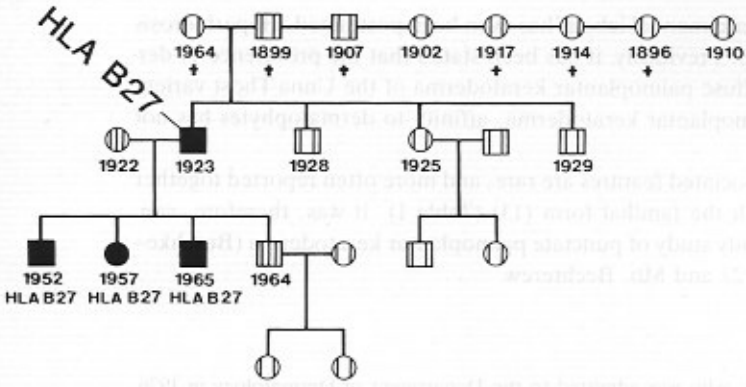
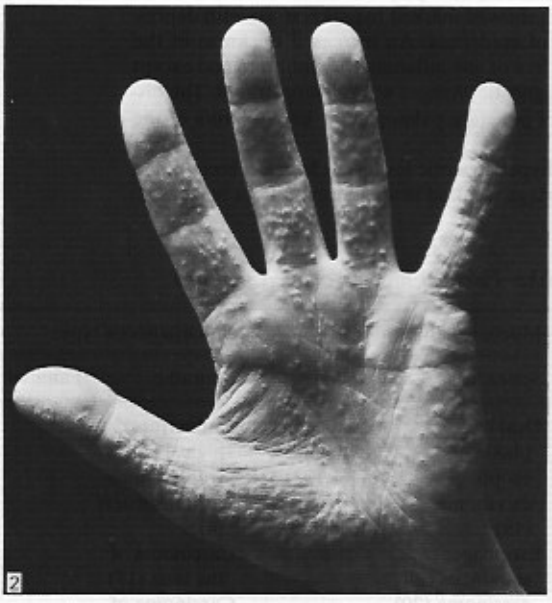



*Fig. 1.* Pedigree of the family with punctate palmoplantar keratoderma of the Buschke–Fischer variety associated with Mb. Bechterew and HLA B 27.

1955 and 1964 and 1 girl, born 1957. Three of these children suffered from punctate palmoplantar keratoderma and Mb. Bechterew with or without radiologic changes (Fig. 1).

The son born 1952 developed punctate palmoplantar keratoderma at the age of 17 years. At the age of 20 years he was suffering from back pain and stiffness of the vertebral column. Radiologic examination of the vertebral column proved normal, but an incipient ossification of the sacro-iliac joints could be demonstrated. Association to HLA B 27 was found. At the clinical examination of palms and soles, punctate lesions were less pronounced than those of the proband. In other respects, however, the clinical examination was normal.

The son born 1955 had a very slight punctate palmoplantar keratoderma on the palms, which ap-



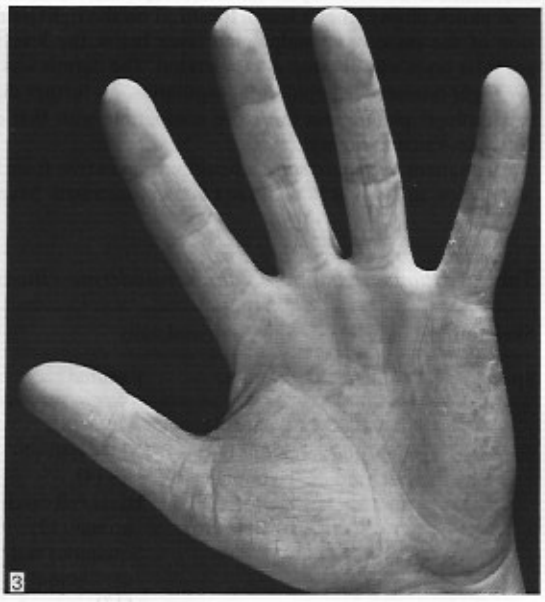




*Fig. 2.* Left hand of the proband with punctate palmoplantar keratoderma of the Buschke-Fischer variety.

*Fig. 3.* Left hand of the proband with punctate palmoplantar keratoderma of the Buschke-Fischer variety after treatment with etretinate (Tigason® 50 mg a day) for 6 weeks.

peared at the age of 20 years. He was unaffected on the soles and the remaining skin was normal. He had never suffered from back pain, but the radiologic examination revealed inflammatory changes with widening of the joint space in both sacro-iliac joints. This patient was HLA B 27 positive too.

The daughter, born 1957, had a slight punctate palmoplantar keratoderma on both palms and soles, which she had contracted at the age of 18 years. From the age of 16 years she had suffered from low back pain, but the radiologic examination performed in 1987 did not show any radiologic changes of the vertebral column or sacro-iliac joints. She was HLA B 27 positive.

The son born in 1964 was healthy, with negative HLA B 27. He was married to a healthy woman and their children are so far unaffected.

The proband was successfully treated with etretinate (Tigason®) 50 mg a day for 6 weeks (Fig. 3) (26). The patient discontinued the treatment because of a dry mouth and scaling of the lips. Laboratory examinations during the treatment period were within normal limits but, one month after he had ceased the treatment, lesions had recurred.

## DISCUSSION

Owing to confusing information about classification of punctate palmoplantar keratoderma in the literature, it has been difficult to estimate its incidence. However, according to a questionnaire answered by 26 Swedish dermatological departments, it appeared that among 270 000 patients visiting the clinics during 1985, 25 suffered from punctate palmoplantar keratoderma of the Buschke–Fischer variety. Patients were equally distributed among the counties of Sweden, in contrast to hereditary palmoplantar keratoderma of the Unna-Thost variety, which is restricted to the northernmost counties of the country (12). The frequency of punctate palmoplantar keratoderma (Buschke–Fischer) was estimated to approximately 1 : 10 000 admitted patients. Most cases were sporadic, and according to the questionnaire a dominant mode of inheritance was documented in only 6 cases (27). Among sporadic cases, some with the clinical picture of punctate palmoplantar keratoderma (Buschke–Fischer) have been classified as an acquired form, even though no history of previous arsenical therapy was reported. In this group a late onset between 40 and 80 years of age has been recorded, but according to the generally accepted classification, these cases should probably also be designated sporadic cases of the Buschke–Fischer variety. Most likely such cases are produced by a combined influence of genetic and environmental factors, which may even explain the late onset of the disease.

Associated features occur more often in sporadic than in familial cases and they have also been difficult to prove. The association between punctate palmoplantar keratoderma (Buschke–Fischer) and Mb. Bechterew and HLA B 27 may be true, but a genetic coincidence should not be excluded.

Successful treatment of punctate palmoplantar keratoderma with etrinate has previously been reported (26) and confirms the effect of this drug on hyperkeratotic lesions.

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