Familial Occurrence of Eccrine Tumours in a Family with Ectodermal Dysplasia

HÅKAN NORDIN, TORE MÅNSSON and ÅKE SVENSSON

Department of Dermatology, Central Hospital, Kristianstad, Sweden

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In two brothers and their sister, ectodermal defects including hypodontia, onychodystrophia, trichodysplasia and palmoplantar keratosis were observed. In addition to the ectodermal dysplasia a diffuse palmoplantar eccrine hyperplasia was noted as well as tumours and cysts of eccrine origin. This seems to be the first report of familial occurrence of eccrine tumours.
Key words: Eccrine poroma; Palmoplantar eccrine hyperplasia; Cystic lesions of eyelids. (Received April 22, 1988.)

Å. Svensson, Department of Dermatology, Central Hospital, S-291 85 Kristianstad, Sweden.

Ectodermal dysplasias constitute a heterogenous group of disorders due to the variation of possible defects. Several attempts have been made to classify the conditions. Freire-Maia & Pinheiro (1) have made a classification based on certain symptoms which reflects the different developmental ectodermal defects.

In 1971, Schöpf et al. (2) described two sisters with ectodermal dysplasia presenting identical lesions: hypodontia, hypotrichosis, onychodystrophia, cystic tumours of the eyelids and palmoplantar keratosis. Burket et al. (3) reported a similar case. Recently, Font et al. (4) had a fourth case without hypotrichosis but otherwise like the other three. We present three siblings with similar ectodermal defects and in addition multiple eccrine tumours.

MATERIALS AND METHODS

Family history

Mrs R. H. (case 1) gave an excellent description of the family (Fig. 1). Her parents as well as their siblings had been normal. It was not known to her that any consanguinity existed between her parents. Two of her brothers had similar symptoms as she herself. The other two brothers and her three sisters were normal. The grandson of one of her affected brothers had a skin disease which upon examination was found to be psoriasis. The other members of the family represented in Fig. 1 had no skin disease according to Mrs R. H.

CASE REPORTS

Case 1

Mrs R. H., aged 80 years, came to us in 1984 with 6 months' duration of a fleshy tumour on her right plantar heel. Since 15 years of age she had red scaly skin in her palms and soles that easily fissured. As long as she could remember she had had poor nails. Four of her lower deciduous teeth never came, the rest were normal and lost at the age of 8–9 years. Of her permanent teeth only four cone-shaped upper incisors developed and had to be removed some years later in her youth. She always had sweated excessively in her palms and soles. After the age of 50 the sweating decreased gradually. Body sweating had always been normal. For 10–15 years she had had multiple cysts of the borders of the upper and lower eyelids recurring after incision. She did not complain of any hair problem. Hearing was normal as well as vision.

There were no signs of psychomotor disturbance.

An erythema with telangiectasia of her face was noted. Multiple skin-coloured or pale red papules and

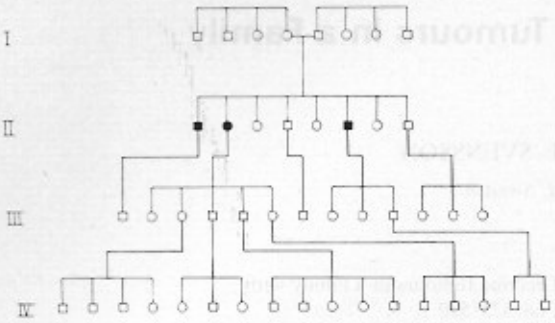

Fig. 1. Pedigree of the family. Black symbols represent the affected members.

cysts were observed in the central parts of the face especially on the eyelid margins. Her eyelashes and eyebrows were sparse but the scalp and body hair was normal with regard to her age. Microscopy of scalp hairs revealed no abnormalities.

The skin of her hands and feet was hyperkeratotic with multiple red soft macules or slightly raised papules. The finger nails, with the exception of the little fingers', showed severe dystrophy or anonychia (Fig. 2). The toe nails were somewhat thicker than normal with subungual hyperkeratosis.

On the medial aspect of her right heel some cm over the sole she had a red bulging tumour measuring about 2 cm in diameter.

Case 2

Mr E. R., brother of case 1, aged 75 years when he first visited our dermatologic department in 1986, had always had poor nails and since 14–15 years of age scaly red and easily fissurating skin of his palms and soles. His deciduous teeth all came but were small. Of his permanent teeth two lower incisors never appeared, two upper incisors were coneshaped and the rest were small and widely spaced. All his teeth were removed at the age of 28 years for aesthetic reasons. As a young man he was troubled by excessive sweating of his hands and feet. In later years the sweating had decreased. For at least 15 years he had noticed nodules on the borders of both his upper and his lower eyelids. Since 10 years he had a large

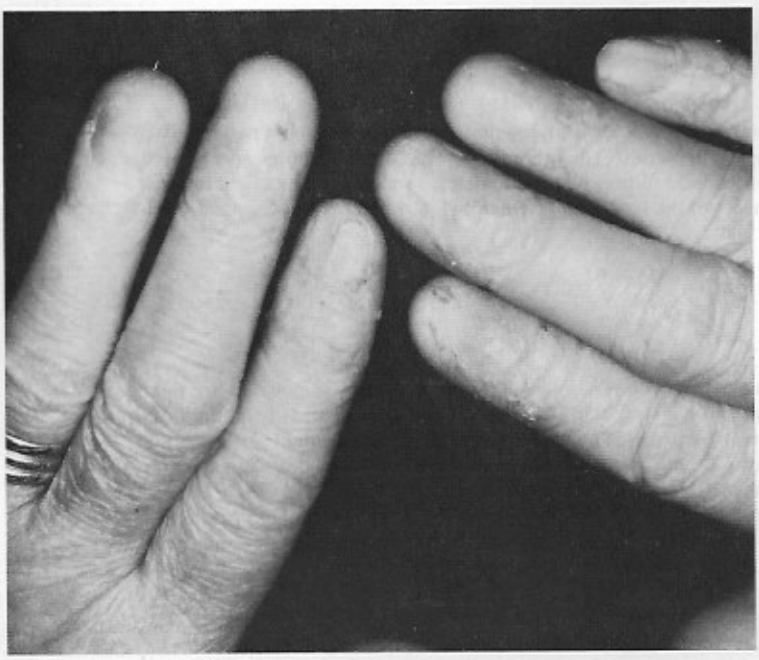

Fig. 2. Onychodystrophy of case 1 with partial anonychia.

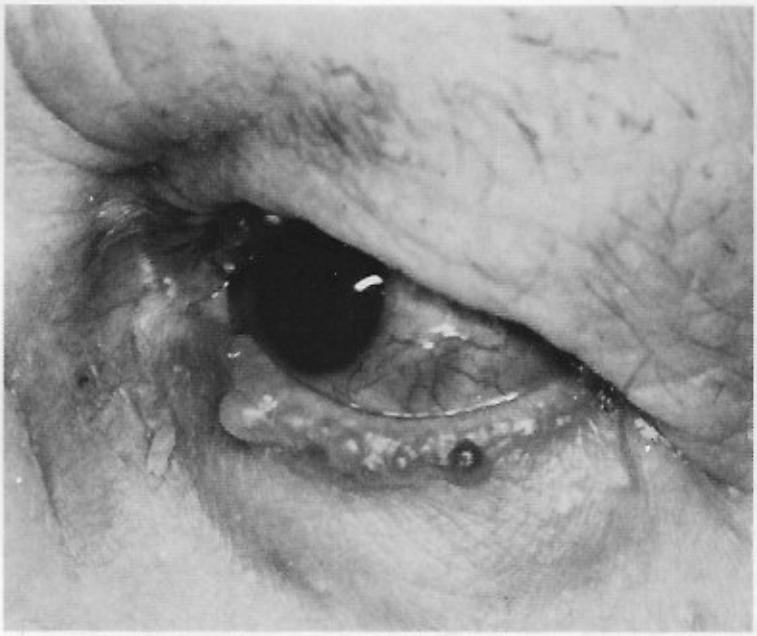

Fig. 3. Cysts on the eyelids of case 2 with sparse eyelashes and eyebrows.

slowly growing tumour on his left sole and one smaller on his left wrist. He had a progressive loss of hair of androgenic type beginning at the age of 20. Hearing and vision were normal.

On examination no psychomotor disturbance was noted. In his face a blue tinged erythema with telangiectasias was observed. Multiple cysts with the size of 1–4 mm were seen on the margins of the upper and lower eyelids (Fig. 3). His eyelashes and eyebrows were sparse and his scalp hair thin. The palms and soles were hyperkeratotic and scaling with multiple small confluent soft red patches and papules. The nails of the feet were grossly normal but those of the hands showed variable grade of dystrophy. On

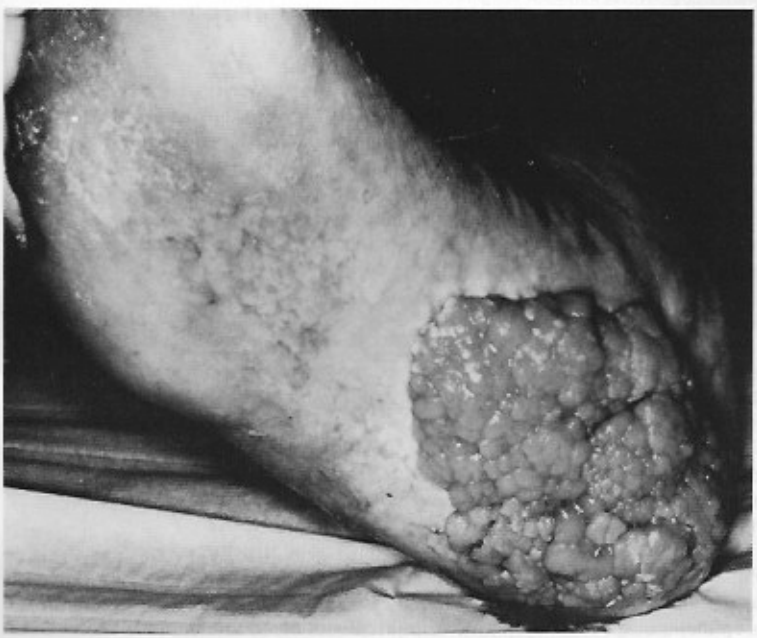

Fig. 4. Cauliflower-like tumour on the heel of case 2. The secretion from the tumour has darkened the napkin under the heel.

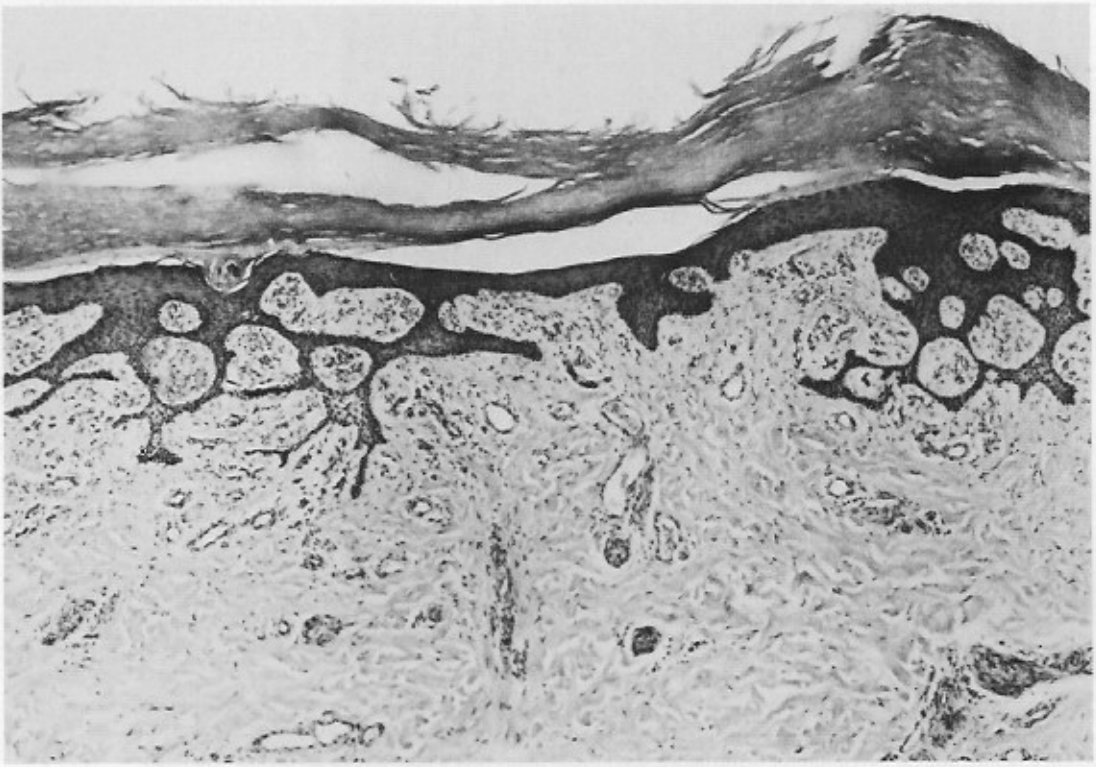

Fig. 5. Excision biopsy from the center of the sole of case 2. Basal projections with trabecular, anastomosing structures dropping down in the corium (original magnification × 40).

the medial and plantar aspects of his left heel he had a bulging red papillomatous tumour measuring 9×7 cm (Fig. 4). From the surface of the tumour a great amount of serous fluid was oozing. On his left wrist a small tumour 1 cm in diameter of similar structure was noted.

Case 3

Mr K. R., an older brother of cases 1 and 2, was 83 years of age when he died in 1979. According to the description of Mrs R. H. he had had similar nail changes and palmoplantar skin as she herself and case 2. The skin lesions were interpreted as pustulosis palmoplantaris by a general practitioner who also noted multiple cysts on the border of his upper and lower eyelids and on his cheeks.

In 1967 a small tumour of the right cheek was treated radiologically. No biopsy was done but the clinical diagnosis was basal cell epithelioma. In 1968 he had an eczema-like lesion on the volar aspect of his left wrist. After biopsy, radiation therapy was given. In 1975 a new lesion at the same site appeared and was treated with excision.

Histologic investigations

Four punch biopsies and one excision biopsy from the palms and soles of cases 1 and 2 were performed: From the hyperkeratotic epidermis, basal projections were growing down in the corium forming branching and anastomosing trabecular structures (Fig. 5). The monomorphic cells in these formations contained PAS positive material in coarse granules. Most of these strands were thin but also broad basal proliferations were noted. The cells in the periphery of these plumper structures showed a palisading tendency. In some of the epithelial cords slight central keratinisation and microcystic formations were found. In the corium there was a relative abundance of comparatively wide blood vessels.

Excised cysts of the nose of case 1 and of the eyelid of case 2: In the dermis, cystic structures were seen with walls consisting of a double layer of cuboidal or cylindric cells.

Excised tumours of the heels of cases 1 and 2 and tumour of the wrist of case 2: The surface of these tumours was covered with squamous epithelium, spotwise dysplastic or injured with blood imbibation.

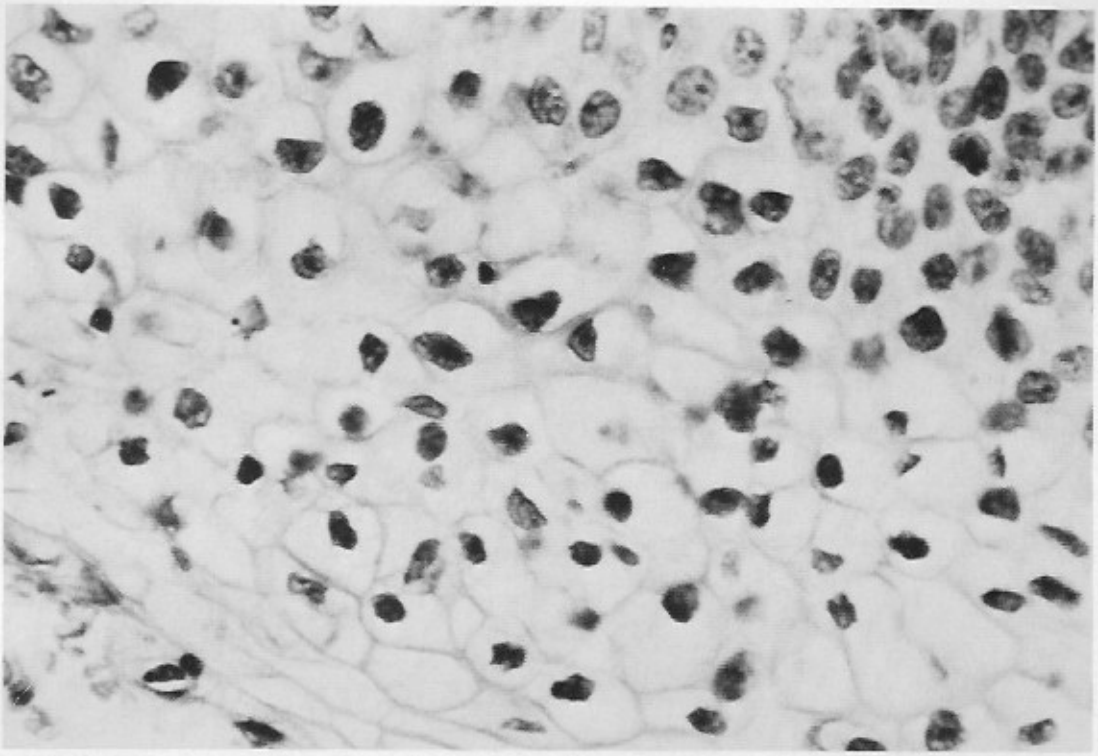

Fig. 6. High magnification of the tumour in Fig. 4 with, in the upper right hand corner, small monomorphic cells and in the center larger clear cells with sharply demarcated cell walls (original magnification × 400).

From the surface, coarse lobules were growing downward. Two types of cells were seen in the tumours. One major cell population consisted of monomorphic cells with basophilic cytoplasm and were smaller than the keratinocytes. Intermingled there were scattered groups of another cell type with clear cytoplasm and distinct cell wall (Fig. 6). Some of the tumour strands showed palisading of the peripheral cells. Ductal formations were seen sometimes lined by the large clear cells. Microcystic structures were very frequent and there were also larger cystic spaces filled with amorphous, slightly eosinophilic substance (Fig. 7). There were neither horn cysts nor follicular structures. The fibrous stroma was highly vascular with foci of chronic inflammation. In the periphery of the tumours the epithelial structures were growing in projections and anastomosing strands.

Tumour of the wrist of case 3: The excision biopsy performed in 1968 was said to show typical basal cell carcinoma but unfortunately cannot be found for reexamination. Histologic examination of the tumour excised in 1975 showed solid formations built up of small dark cells. The peripheral cell layer showed palisading arrangement. Horn cysts occurred within the tumour and the surface of the epidermis was covered by a thick horny layer.

Enzyme histochemical investigation of a punch biopsy from a red, raised patch on the heel of case 2: Examination was performed on frozen sections. Amylophosphorylase: a dominantly perinuclear activity most pronounced in superficial epidermis was found. In the upper two-thirds of the epithelial strands there was also a clear activity attenuating towards the deeper parts of the epithelial structures. Acid phosphatase: there was positivity in the epithelial cells with somewhat stronger reaction in the periphery of the epithelial strands. Alkaline phosphatase, beta-glucuronidase and aminopeptidase: the epithelium was totally negative. Succinic dehydrogenase: Positive reaction was found in the epithelial cells both superficially in epidermis and in the deep epithelial strands.

DISCUSSION

According to the classification of Freire-Maia and Pinheiro (1) the ectodermal dysplasia of our patients belongs to subgroup 1-2-3 (tricho-odonto-onychic). In addition to these

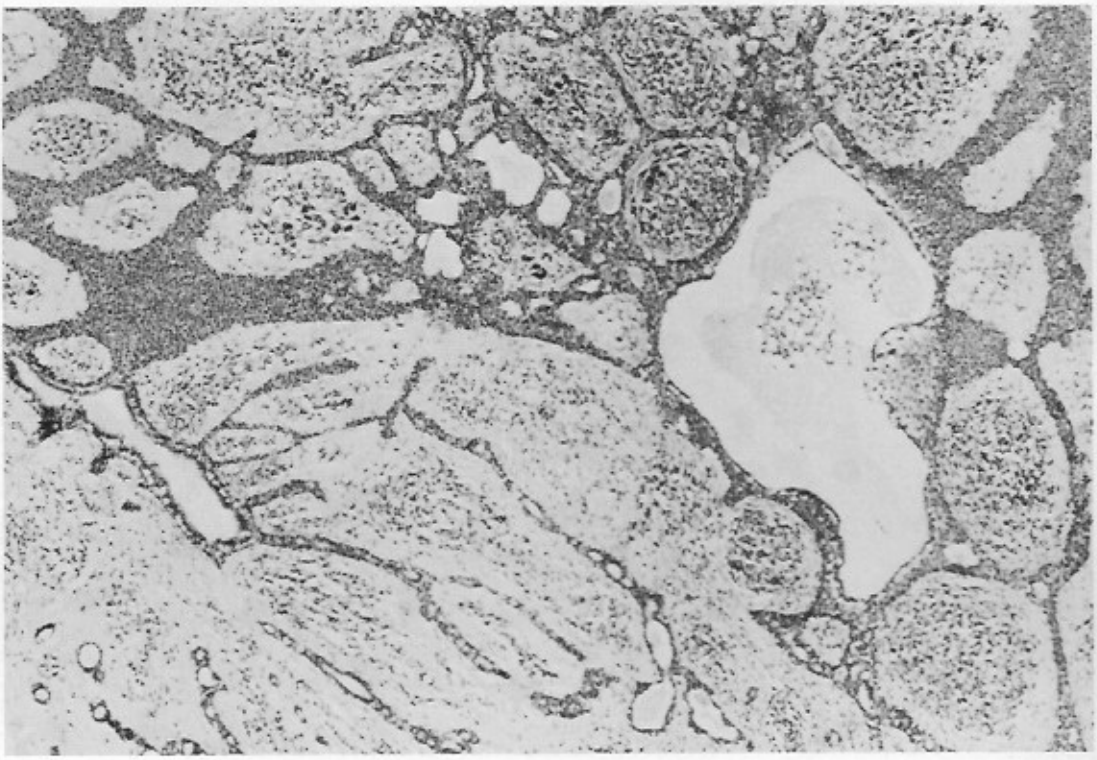

Fig. 7. Section from basal part of the tumour in Fig. 4. Larger cystic structures are visible as well as microcysts in narrow anastomosing epithelial strands (original magnification × 40).

symptoms our patients showed hyperplastic changes of epidermal structures and multiple tumours. The eccrine glands are of ectodermal origin. Therefore it can be expected that morphologic as well as functional changes in them are prone to develop in ectodermal dysplasias. Disturbance of sweating in ectodermal dysplasias is well known but histologic changes seem to be uncommon. In fact, there is only one report of morphologic changes of sweat glands in ectodermal dysplasia. Wilkinson et al. (5) reported on a woman, aged 44 years, a member of the kindred originally described by Clouston (6), who had multiple eccrine poromas.

There are only two reports of multiple eccrine poromas, however, without concomitant ectodermal dysplasia. Goldner (7) described one case and another case was presented at the XVI International congress of Dermatology in Tokyo, 1982 (8).

The scattered skin changes of the palms and soles in our patients are well consistent with eccrine poromas clinically (Fig. 8) as well as histologically (7). Furthermore, the enzyme histochemical investigations support that they were of eccrine origin (9). Whether these changes are tumours or merely hyperplastic changes constituting a component of the ectodermal dysplasia cannot be settled.

The tumourous formations of our cases must, however, be regarded as true neoplasms. Those of the heels of case 1 and 2 were strikingly similar in the microscope. The localization is typical of eccrine poromas and the tumours were mainly built up by eccrine poroma-like structures (10). Areas with clear cells and tubular ducts were, however, also seen with close resemblance to clear cell hidradenoma (11). In other areas, especially in the periphery, thin, anastomosing strands of tumour cells suggestive of fibroepithelial type of basal cell car-

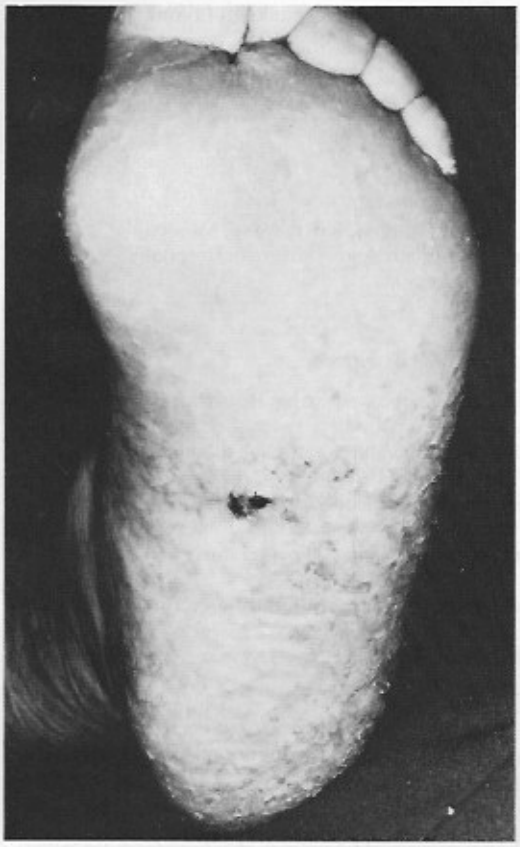

Fig. 8. Hyperkeratotic and scaling sole of case 2 with multiple fissures and papules. The black area in the center represents the biopsy site.

cinoma (12) were found and in the central parts formations reminding of regular basal cell carcinoma were seen.

Two cases of basal cell carcinoma at the site of superficial hidradenoma of the scalp have been reported (13). In another study 100 examples of syringadenoma papilliferum were examined and in 9 cases basal cell carcinoma was present in the same histological section (14).

There are many reports of basal cell carcinoma with eccrine differentiation (BCCED). These tumours are usually situated on the head or scalp (15). The eccrine differentiation of the tumours in cases 1 and 2 was obvious but the localization was different compared to that of BCCED and the histology seemed to be more complex with pronounced eccrine differentiation. It is therefore more probable that they represent tumours of eccrine origin but with partial basal cell differentiation.

The tumour of case 3 was histologically a typical basal cell carcinoma. Repeated investigations of multiple sections of the tumour could not reveal structures of eccrine type.

A classification of benign eccrine tumours according to their differentiation has been proposed (16, 17). From this point of view, the variable histology of our cases might be understood to represent different levels of maturation. The disseminated changes of the palms and soles constitute hyperplastic changes while the tumours are of true neoplastic nature showing in part adenomatous levels of differentiation as in eccrine poroma but also less organized tumour formations of clear cell hidradenoma and primordial fibroepithelioma type. The de-

velopment of different and multiple eccrine tumours in at least two siblings speaks in favour of an inherited trait with autosomal inheritance. The presence of clinical manifestations in three out of eight siblings indicates a recessive inheritance. This is in accordance with the fact that no cases have occurred in the following two generations.

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