Palmoplantar Eccrine Syringofibroadenomatosis with Hypotrichosis, an Incomplete Form of Schöpf Syndrome: Report of a Taiwanese Case with Occurrence of Bullous Pemphigoid

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Eccrine syringofibroadenoma is a rare benign cutaneous adnexal lesion of acrosyringeal origin. It has polymorphous clinical manifestation ranging from a solitary nodule or papule to multiple lesions, especially in the palmoplantar location. We describe a 31 year-old man with cutaneous manifestation of palmoplantar keratoderma with little or no clinical itch or pain, simultaneously accompanied with progressive alopecia and hair thinning since his early 20s. No family history or other symptoms and signs implying ectodermal dysplasia can be identified. Interestingly, 10 years after the onset of bilateral palmoplantar keratoderma, generalized bullous pemphigoid occurred at the age of 30, and was then cured with steroid treatment. A skin biopsy from the plantar foot showed hyperkeratosis, acanthosis, and epithelial anastomosing cords and strands of cuboidal cells extending down into the dermis and containing ductal structures, in association with a fibrovascular stroma. Response to occlusive steroid and keratolytic therapy was not satisfactory. The first Taiwanese case of multiple eccrine syringofibroadenomas as an incomplete form of Schöpf syndrome with the coexistence of bullous pemphigoid is herein presented. This diagnosis should be considered when patients present with chronic asymptomatic and refractory palmoplantar keratoderma. (Dermatol Sinica 25: 219-225, 2007)

Key words: Eccrine syringofibroadenoma, Schöpf syndrome, Bullous pemphigoid

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INTRODUCTION

Eccrine syringofibroadenoma (ESFA) is a rare eccrine tumor that has variable clinical features. Different subtypes of ESFA are proposed, and among them, the association with Schöpf syndrome (Schöpf-Schulz-Passarge syndrome) has been well documented. Schöpf syndrome is a rare ectodermal dysplastic genodermatosis. Although the inheritance of Schöpf syndrome is autosomal recessive in most cases, autosomal dominant transmission has been reported. It is characterized by palmoplantar keratoderma, eyelid apocrine hidrocystomas, hypodontia, hypotrichosis and hypoplastic nails. Several cutaneous tumors including eccrine syringofibroadenomas, eccrine poromas, follicular tumors, squamous cell carcinomas, and basal cell carcinoma have been found to appear during the disease course. We herein report the first Taiwanese case in a 31-year-old man of multiple ESFA (eccrine syringofibroadenomatosis) as an incomplete form of Schöpf syndrome, and with a history of bullous pemphigoid at the age of 30.

CASE REPORT

A 30-year-old man presented with diffuse redness and scaling of the palms and soles (Fig. 1), accompanied with multiple shallow erosions for about 10 years. Deterioration of the skin lesions with increased thickness and scales was noted in recent months. No obvious itch nor pain was noted. In addition, progressive hair loss and thinning of hair occurred along with the change in the hands and feet. Sweating was normal. He was the second child born to unrelated, normal-appearing parents and no similar condition could be identified in his family.
members or relatives. No other systemic diseases was told except for end stage renal disease with hemodialysis for several years, hepatitis C virus infection and generalized tense bullae formation about a year ago (Fig. 2). Bullous pemphigoid was diagnosed in our hospital and was proved by skin biopsy with subepidermal bullae (Fig. 3) and positive linear IgG deposits in the basement membrane (Fig. 4). The indirect immunofluorescent study showed negative findings in both anti-basement membrane zone and anti-intercellular space antibody. Bullous pemphigoid subsided gradually after systemic steroid, methylprednisolone 8mg per day, and potent topical steroid treatment. Hyperkeratotic eczema and pompholyx in both hands and feet were told when he visited local dermatologic clinics, however, the response to steroid or keratolytic agents was not good. The physical examination revealed palmoplantar keratoderma; some showed thick erythematos plaques of reticulate patterns and scales. Alopecia in the whole scalp was found; residual hairs were left mainly in the posterior scalp (Fig. 5). The eyebrows and eyelashes were preserved. Otherwise, no nail dystrophy, no early loss of teeth, no anhidrosis, no hearing loss nor ocular problems were revealed. Skin biopsy in the plantar foot was performed. Light microscopy demonstrated hyperkeratosis, acanthosis and irregular anastomosing cords of epithelial cells extending from epidermis into papillary dermis (Fig. 6A). The stroma is rich in fibrous tissue and dilated capillaries (Fig. 6B). The tumor cells had pale cytoplasm and oval to round nuclei. There were no atypical cells or palisade arrangement. Duct-like luminal structures lined with an eosinophilic cuticle suggestive of eccrine sweat ducts were seen within the cords of cells (Fig. 6B). The patient then received topical keratolytic and steroid occlusive treatment, followed by Erbium laser, but the response was not satisfactory.

DISCUSSION

ESFA was first described by Mascaro in 1963, characterized as a solitary nodule. To date,

Fig. 3
Subepidermal cleft with infiltration of lymphocytes, neutrophils and eosinophils in the bulla cavity and upper dermis. (H&E, x100)

Fig. 4
Direct immunofluorescent study showed positive linear IgG deposit in the basement membrane zone. (x200)

Fig. 5
Alopecia in the whole scalp with residual hairs in the posterior scalp.
nearly 50 cases were reported in the literature. It is considered as a rare benign cutaneous adnexal lesion that occurs predominantly in patients over 40 years of age. The polymorphous clinical features vary from a solitary nodule or tumor to multiple lesions with a linear or palmo-plantar distribution; the latter is often referred to as eccrine syringofibroadenomatosis. Despite the clinical presentation may differ, the histopathology is unique and similar in all lesions. Because of the clinical polymorphism, it is still unclear whether ESFA represents a neoplasm, a hamartoma, or reactive eccrine hyperplasia.

ESFA is characteristically composed of anastomosing cords and strands of cuboidal acrosyringeal cells containing ductal structures, embedded in a fibrovascular stroma. It should be differentiated from other tumors of acrosyringeal origin like eccrine poroma and hidroacanthoma simplex, and tumors like fibroepithelioma of Pinkus and tumor of follicular infundibulum. Eccrine poroma is characterized by solid masses of uniform small cuboidal cells extending down the dermis, whereas hidroacanthoma simplex presents with intraepidermal nests of uniform cuboidal cells possibly containing duct-like slits or round lumina. Fibroepithelioma of Pinkus has long, thin, branching anastomosing strands of basal cell carcinoma embedded in a fibrous stroma. Tumor of follicular infundibulum shows plate-like growth of epithelial cells in the upper dermis extending parallel to the epidermis. Peripheral cell layers of the plate also show palisading.

In 1997, Starink proposed a classification consisting of the following subtypes: (1) Solitary ESFA; (2) Multiple ESFA in the Scho¨pf Syndrome; (3) Multiple ESFA without associated cutaneous findings; (4) Non-familial unilateral linear ESFA (sometimes referred to as naevoid ESFA).

In our case, the patient had multiple ESFA manifested as palmoplantar keratoderma and alopecia in the scalp without other ectodermal dysplasia. This is compatible with the classification of multiple ESFA without associated cutaneous findings. ESFA without associated cutaneous findings was considered to represent a forme fruste or an incomplete form of the Scho¨pf syndrome. Including our patient, there are 8 cases of ESFA as an incomplete form of Scho¨pf Syndrome reported to date. (Table 1) Most of the patients were males, except one being female. No patient younger than 30 years old were found. Almost all of them had nonfamilial palmoplantar lesions although lesions may also appear in the face, trunk and proximal limbs. No significant multiple associated findings, except that one patient had also glaucoma, chronic sinusitis, otitis media and gastrointestinal polyposis. Renal disease was found in 2 patients. Renal disease including chronic
Table. 1 Review of Multiple Eccrine Syringofibroadenoma as an Incomplete Form of Schöpf Syndrome

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Age/sex</th>
<th>Location</th>
<th>Cutaneous manifestation</th>
<th>Duration (years)</th>
<th>Disease association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goldner (1970)</td>
<td>65/F</td>
<td>Palms, soles</td>
<td>Multiple papules</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Sanusi (1988)</td>
<td>71/M</td>
<td>Both hands</td>
<td>Multiple papules</td>
<td>N.A.</td>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>Hara (1992)</td>
<td>63/M</td>
<td>Hands, feet, legs, arms, trunk, face</td>
<td>Multiple papules</td>
<td>30</td>
<td>Glaucoma, chronic infections, gastrointestinal polyposis</td>
</tr>
<tr>
<td>Lui (1992)</td>
<td>56/M</td>
<td>Palms, soles, shins</td>
<td>Palmoplantar keratoderma, Multiple papules</td>
<td>12</td>
<td>Diabetes mellitus, multiple BCCs</td>
</tr>
<tr>
<td>Ochonisky (1994)</td>
<td>30/M</td>
<td>Soles</td>
<td>Multiple papules, spongy plaques</td>
<td>6</td>
<td>Diabetes mellitus, recurrent infections</td>
</tr>
<tr>
<td>Gambini (1995)</td>
<td>40/M</td>
<td>Legs</td>
<td>Verrucous plaques</td>
<td>N.A.</td>
<td>Psoriasis</td>
</tr>
<tr>
<td>Starink (1997)</td>
<td>76/M</td>
<td>Palms, soles</td>
<td>Palmoplantar keratoderma</td>
<td>29</td>
<td>Chronic renal failure</td>
</tr>
<tr>
<td>Present case</td>
<td>31/M</td>
<td>Palms, soles</td>
<td>Palmoplantar keratoderma, scalp alopecia</td>
<td>10</td>
<td>End stage renal disease, hepatitis C, bullous pemphigoid</td>
</tr>
</tbody>
</table>

N.A.: not available.
Duration: symptom duration before diagnosis
BCCs: Basal cell carcinomas
renal failure and end stage renal disease with hemodialysis was also found in 2 patients too.\(^7\) The disease course seemed persistent and prolonged; duration of ESFA were mostly 10 years or more in cases whose data were available (Table 1). Unlike all other cases of multiple ESFA as an incomplete form of Schöpf syndrome whose cutaneous manifestation was limited in the skin, our patient also suffered from progressive alopecia with hair thinning since his early 20s. Nevertheless, no other manifestation of ectodermal dysplasia was found. His nails and teeth were still preserved and appeared normal. In Starink’s opinion, there are adequate evidence to firmly establish multiple palmo-plantar ESFA as a new and consistent cutaneous marker of the Schöpf syndrome.\(^7\)

In recent years, a new subtype of ESFA associated with dermatoses has been identified. They were termed reactive ESFA\(^12\) because they appeared after inflammatory or neoplastic dermatoses like bullous pemphigoid,\(^4,\)\(^13\) squamous cell carcinoma,\(^14\) burn scar ulcer,\(^15\) and lichen plans.\(^16\) ESFA may have occurred as a consequence of recurrent eccrine duct remodeling. Indeed, eccrine ductal proliferation as a result of prior ductal disruption is a common response observed during wound healing and in inflammatory or neoplastic skin disorders.\(^17\)

In literature, there were 2 men and 1 woman reported to be reactive ESFA associated with bullous pemphigoid (BP).\(^4,\)\(^11\) Their ages were all more than 60 years old. Multiple ESFA appeared 2-3 months after BP subsided. The ESFA were all in palmo-plantar location, the same as our patient. The bullae and erythematous skin lesions, when mentioned, covered almost the whole body including the palms and soles. BP in the aforementioned 3 patients and the present one responded well to systemic steroid therapy. Although our patient had both ESFA and BP, however, the ESFA in this 31 year-old man has long been noted, about 10 years earlier before the onset of BP. Besides, no obvious bullae were found in the palmo-plantar area when BP took place in this patient. As a result, our case cannot be classified as reactive ESFA. Although BP may appear at any age groups, it is still uncommon to see BP appearing at an early age of 30. The presentation of ESFA followed by BP in our patient is first to be reported in the literature.

In terms of the therapeutic choices for ESFA, few has been mentioned. If it’s a single solitary lesion or multiple lesions with limited extent, surgical excision, liquid nitrogen or laser ablation may be adequate. However, if the involvement is extensive, or if it manifests as palmo-plantar keratoderma, currently, no effective treatment is available. In our experience, the response to topical steroid and keratolytic therapy is poor. Erbium laser had been tried, but the patient lost follow up afterwards due to unsatisfactory improvement.

In summary, we report the first Taiwanese case of multiple eccrine syringofibroadenomas as an incomplete form of Schöpf syndrome. This patient was unique because he had multiple ESFA with progressive scalp alopecia, and was followed by bullous pemphigoid. This has never been reported in the literature. Due to the clinical manifestation of keratoderma, misdiagnosis often occurs. Nevertheless, lack of clinical itch or pain, and the poor response to steroid and keratolytic agent can be a clue to arrange skin biopsy for clarification. The palmo-plantar ESFA should remind us to search for the potential existence of Schöpf syndrome. Further research to elucidate the cause and pathophysiology of ESFA may render more effective management of the disease.

REFERENCES


