Transgrediens et progrediens palmoplantar keratoderma of Sybert: Four cases in a single family

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Conflicts of interest: None to declare

Received: 28 February 2016
Accepted: 17 March 2016

Palmoplantar keratoderma of Sybert (PPK of Sybert) or Sybert's keratoderma was first documented by Virginia Sybert in 1988. Due to the high degree of similarity, it was previously considered to be Greither's keratoderma, an established entity at that time. Currently, clinical and ultrastructural studies distinguish between the two disorders. Sybert's keratoderma is an extremely rare type of keratoderma with an autosomal dominant mode of inheritance caused by mutations to the keratin 1 gene along with severe bilateral involvement of the palms and soles with a tendency for proximal extension and natal cleft in the absence of systemic manifestation. To the best of our knowledge, there are less than 20 cases of PPK of Sybert reported in the literature. Here we discuss an extremely rare familial PPK of Sybert that has affected 4 family members. The cases presented with symmetrical, severe involvement of their palms, soles, and knees with the development of pseudoainhum and autoamputation of the fingers and/or toes.

Keywords: autoamputation, Greither, palmoplantar keratoderma of Sybert, pseudoainhum

Iran J Dermatol 2016; 19: 60-64

INTRODUCTION

Palmoplantar keratoderma of Sybert (PPK of Sybert) or Sybert's keratoderma was first described in 1988 by Virginia Sybert, an American dermatologist and medical geneticist [1]. Due to the high degree of similarity with Greither keratoderma, it was previously considered to be Greither's keratoderma. Currently, clinical and ultrastructural studies distinguish between these two disorders. An extremely rare type of PPK with an autosomal dominant mode of inheritance, bilateral severe involvement of the palms and soles in a glove-and-stocking pattern with a tendency to extend to the knees, elbows, and natal cleft in the absence of systemic manifestations [1-3].

CASE REPORT

The nuclear family consisted of six members with four siblings, from which two brothers (18 and 10 years of age), their 20-year-old older sister, and 45-year-old mother presented to our outpatient Department of Dermatology. The family members had similar lesions, thickening and scaling on their hands, feet, knees, and perioral erythema since infancy. There was a history of progression of the lesions and history of consanguinity between parents was absent. The father (50 years of age) and one female sibling (14 years of age) were normal.

On cutaneous examination, we observed bilateral symmetrical hyperkeratosis on the palms, soles, dorsa of the hands, feet, and knees in all affected individuals. There was pseudoainhum formation of both little fingers of the youngest male child and autoamputation of little toe/s were seen in the other three affected family members (Figures 1-4). There was evidence of scaling, hyperhidrosis, maceration, and fissuring on the palms and soles. Natal cleft and shins were also involved in the two male siblings; the female members refused examinations of the genital or perigenital areas. Additionally, all affected members had perioral erythema. Examination revealed a normal cutaneous

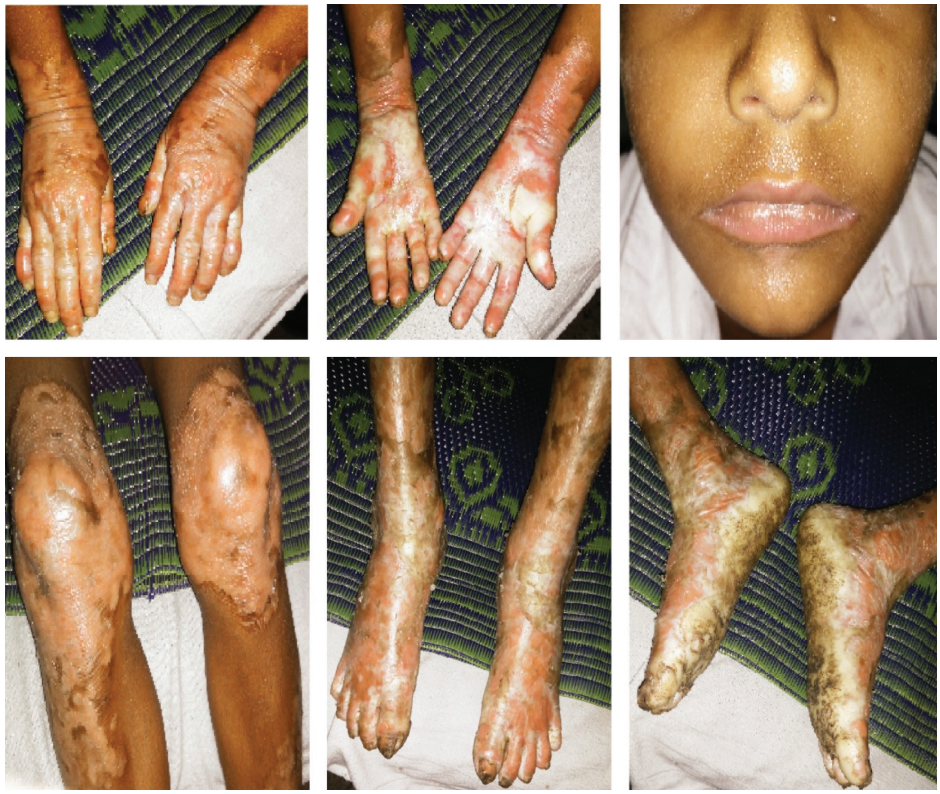

Figure 1. The 10-year old youngest sibling with Hyperkeratotic macerated plaques on both palms and soles that extended to the dorsal surface, shins and knees with pseudoainhum on both little fingers and hyperhidrosis.

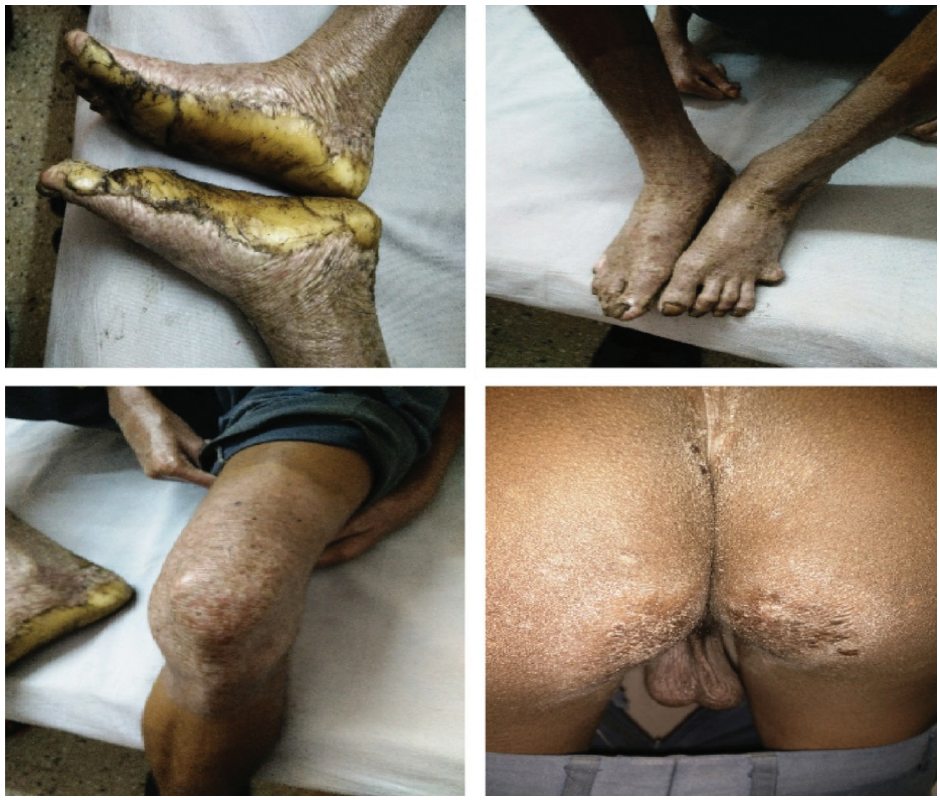

Figure 2. The 18-year old elder brother had similar lesions on his hands, feet, knees, and natal cleft with autoamputation of the left little toe.

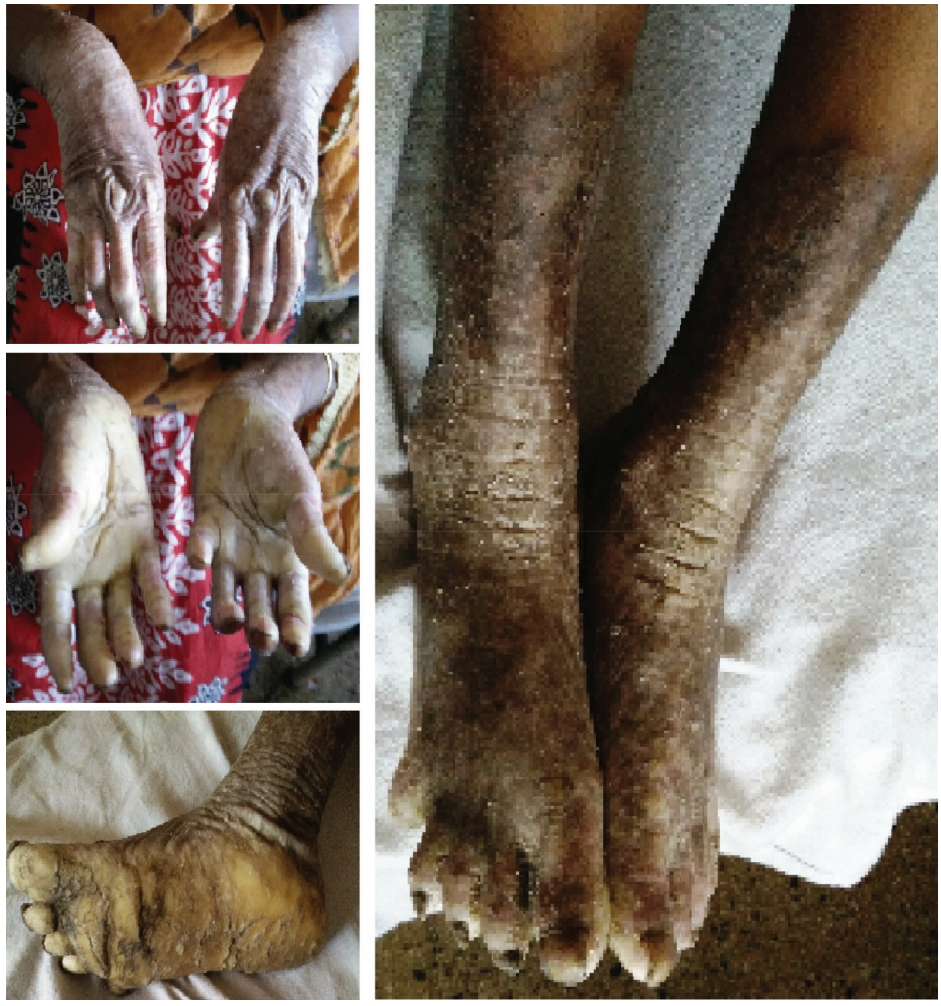

Figure 3. The 20-year old older sister with development of sclerodactyly, amputation of the right little toe, and transgredient nature of the palmoplantar lesions.

area. There was no peripheral sensory loss or motor weakness. Examination of the eyes, hair, and teeth was normal, however the nails of the fingers and toes were found to be dystrophic along with yellowish-brown discoloration, subungual hyperkeratosis, and onychogryphosis. There was no hearing loss in any of the patients.

Systemic examination did not reveal any abnormalities and routine laboratory parameters were within normal limits.

Histopathologic examination of the punch biopsy sample taken from the palm from the dorsa of the mother's right hand revealed marked orthohyperkeratosis, hypergranulosis and acanthosis without vacuolar or granular degeneration, and papillomatosis in the epidermis (Figure 5). There were sparse lymphocytic infiltrates in the papillary dermisseen. Further investigations that include electron microscopy and genetic mapping could not be performed because of the high cost and lack of this facility in our hospital.

Based on the autosomal dominant mode of an inheritance pattern in this family, clinical features and histopathological findings, we diagnosed this family with PPK of Sybert. The patients began emollients, topical keratolytics, and oral isotretinoin with a recommendation for follow up at monthly intervals.

DISCUSSION

Hereditary palmoplantar keratodermas are a heterogeneous group of ectodermal dysplastic disorders characterized by a variable degree of hyperkeratosis of the palms and soles [3-9]. The mode of inheritance may be autosomal dominant,

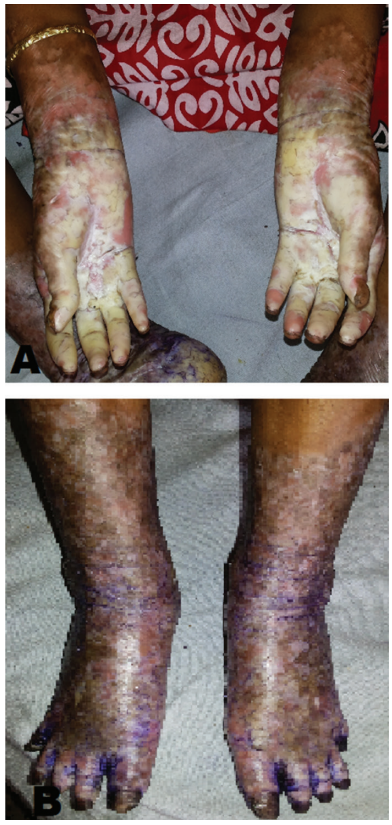

Figure 4. The 45-year old mother with typical palmoplantar involvement and progredient nature of this disease that led to sclerodactyly and autoamputation of both little toes.

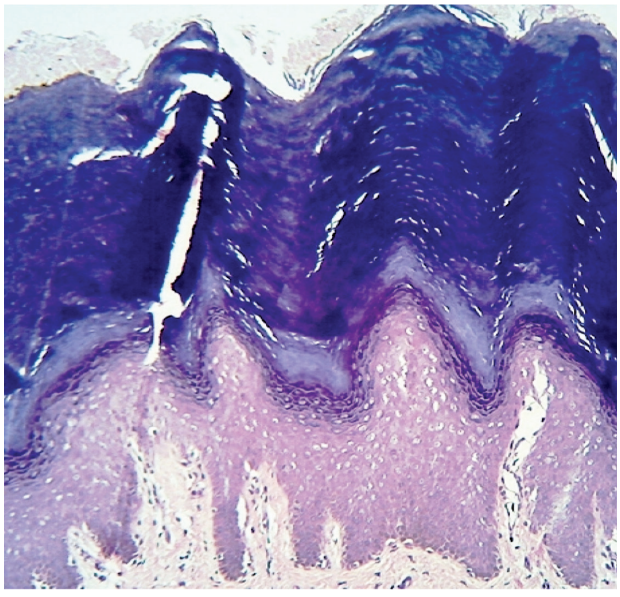

Figure 5. Marked orthohyperkeratosis, hypergranulosis, and acanthosis without vacuolar or granular degeneration (epidermolysis) and mild papillomatosis (H & E, 40×).

autosomal recessive, or X-linked [3]. The various presentations and overlapping clinical features has led to the classification of PPK into three types based on pattern and distribution - diffuse, focal and punctate [4]. Focal and punctate types usually remain localized on the palms and soles whereas the diffuse variety can have a wide array of presentation. Therefore, depending upon the histopathological features, spread, complications, and mode of inheritance, diffuse PPK is further subclassified into many subtypes. Epidermolytic hyperkeratosis (granular degeneration) has historically been divided into epidermolytic PPK (i.e., Vorner's keratoderma) and non-epidermolytic PPK. Extension to other contiguous sites (wrist, dorsa of the hands, elbows and knees), and presence of cicatrization has led to the categorization of transgredient (i.e., Loricrin keratoderma, Greither's, Sybert's keratoderma, Mal de Meleda, Olmsted syndrome, Huriez syndrome, Gamborg-Nielsen type PPK, and Nagashima type PPK) and non-transgredient (i.e., Vorner's keratoderma and Thost-Unna keratoderma). Based on the mode of inheritance, autosomal recessive PPK includes Mal de Meleda, Nagashima type PPK, Olmsted syndrome, and Gamborg-Nielsen type PPK. However, autosomal dominant PPK consist of Vorner, Thost-Unna, Huriez, Loricin, Greither, and Sybert keratoderma. Keratodermas are also classified into three groups based on extracutaneous features: simple; complex type with involvement of skin adnexal structures, hair and teeth; and syndromic (associated with malignancy, hearing loss or cardiac abnormalities) [5].

It is very difficult to confirm a diagnosis of PKK due to the wide spectrum of PPKs, their rarity, various means of clinical presentations, overlapping features in patients, and non-specific histopathological findings. Genetic testing has undoubtedly aided in diagnosis, however this is a heterogeneous group of disorders. Hence, multiple genes have been implicated in the development of PPKs and mutations in a single gene can result in different types of PPKs. After correlating the clinical, histopathological, and electron microscopic analyses along with a genetic study, a more accurate diagnosis of specific type of PPK can be made. Practically, with the help of clinical characteristics of pattern, distribution and extension, histopathology and inheritance pattern in a family, differentials can be excluded to reach the most probable diagnosis as in the current case

of PPK of Sybert [6]. Palmoplantar keratoderma of Sybert is an extremely rare autosomal dominant, diffuse, non-epidermolytic, transgredient PPK characterized by symmetric severe involvement of the whole palmoplantar surface in a glove-and-stocking distribution that extends to the elbow, knees, posterior aspects of the forearms, shins, groins, and natal cleft and a pseudoainhum formation which leads to autoamputation of the toes [1].

In the last 27 years after the initial documentation in 1988, a few similar cases of PPK have been reported from different areas of the world. These cases did not fit into either Mal de Meleda or Greither keratoderma hence, they were considered a distinct entity of Sybert keratoderma. The differing features of PPK of Sybert from the above mentioned closest differential diagnosis include autosomal dominant inheritance (unlike Mal de Meleda), severe palmoplantar hyperkeratosis with transgrediens, earlier onset, progression with age (progrediens), pseudoainhum, and autoamputation of the toes (unlike Greither keratoderma) [7,8].

Although histopathological evaluation is not specific, the presence of lipid-laden cells in the stratum corneum is remarkable [9]. Ultrastructural studies by electron microscopy do not demonstrate abnormal keratins other than those associated with hyperproliferation. However, the association of filaggrin and keratin filaments are disturbed with abnormal distribution and structure of keratohyalin granules [1,9]. Definite genetic linkage is not known and PPK of Sybert appears to not be a keratin disorder but keratin 1 gene on chromosome 12q has been held responsible so far [3,9,10].

As with other PPKs, treatment by emollients, topical retinoids, keratolytics, and topical glucocorticoids have some degree of success. However, the best results have been seen only with oral retinoids [1,10].

We reported a familial incidence of PPK of Sybert with well supportive clinical and histopathological features. We hope that this case report helps the dermatologists to avoid misdiagnosis of the is rare disease.

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