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Acral Peeling Skin Syndrome: A Rare Genetic Disorder

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Abstract

Acral Peeling Skin Syndrome (APSS) is a genetic disorder occurs due to mutation in the TGM2 and CSTA gene. Common clinical manifestations are recurrent blisters and erosion on the palm and soles. A 30-year-old male who had symptoms since 12-years came to OPD with complaint of recurrent blisters and peeling of palm skin. Skin biopsy was taken and sent for fungal and histopathological examination. The clinical and histological examinations were consistent with a diagnosis of APSS. It may pose a diagnosis challenge because of its rarity and similarities with other exfoliating skin disorders. Hence, constellate features of clinical history, histopathology examination, and genetic testing will aid in an accurate diagnosis.

Keywords:acral peeling skin syndrome (APSS), genetic, TGM2, CSTA, gene, blister, histopathology

Introduction

APSS is a rare autosomal recessive disorder with peeling of skin from the hands and feet. Localized and generalized types are the two principal classified forms. The APSS is believed to be a localized variant.[1] The both forms of APSS show the same level of blistering in the epidermis at the stratum granulosum and stratum corneum junction. in ultra-structural and light microscopic studies.[2] The genetic defect of acral peeling syndrome is located on chromosome 15 (at 15q15.2).[3] It is caused by mutations in the TGM5 gene and the CSTA gene. APSS is present with blisters and erosion on the palms and soles, which are the most common clinical manifestations. These symptoms are not limited to the dorsal aspect of the hands and feet. The hot temperature, high humidity, and friction may aggravate the condition. Due to its low incidence and little or no clinical repercussion, it tends to be underdiagnosed or incorrectly diagnosed as epidermolysis bullosa simplex. The primary aim of treatment is to prevent skin damage and manage symptoms as they occur.[1,2,3]

Herein, we present a rare case of APSS in a 30-year-old male who had symptoms since 12-years.

Case Report

A 30-year-old male washer man presented to outpatient department with complaint of repetitive shedding of skin from acral area since 12 years. On detailed history patient revealed life long history of superficial skin peeling, vesiculation, and burning sensation on the palmer aspect of hands and feet. All these events are provoked by soaking of hands and feet in water or during perspiration. They had a tendency to heal spontaneously within 2 to 3 days. There was no evidence of oozing and scarring. General and systemic examination revealed no abnormality. He was unaware of any allergies and did not take any medication regularly. The patient's family history was unremarkable.

Examination of his foot and hands reveals bilateral asymmetrical superficial erosions and areas of desquamation on the dorsal, palmar and plantar aspect of both hands and feet (Fig.1), whereas other parts of body and mucosal surface remained unaffected. Samples for fungal culture and potassium hydroxide preparation were negative. Blood tests including complete blood count, ESR, C-reactive protein level were within normal limit.

Biopsy was taken from both hands and feet and was fixed in formalin and embedded in paraffin. Histological examination shows characteristic separation between the granular and corneal layers without inflammation. Stratum corneum layer above the plane of separation shows several layers of large round pale cells with edematous and less compact appearance (Figs.2.a&2.b). The clinical and histological examinations were consistent with a diagnosis of APSS. Genetic analysis shows mutation in TGM 5 and CSTA gene.

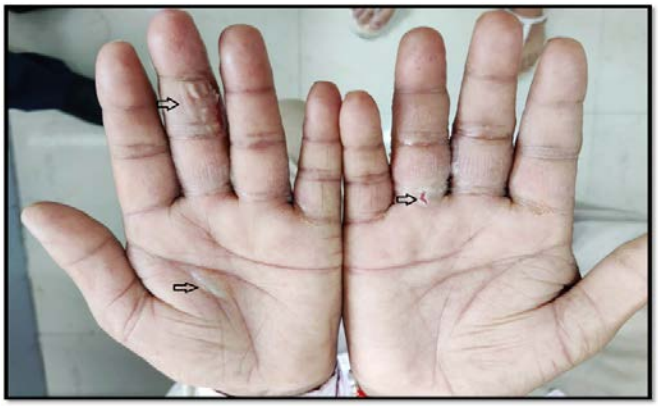

Figure.1: Flaccid blister (arrow) on the right ring finger, left middle finger, and left palm.

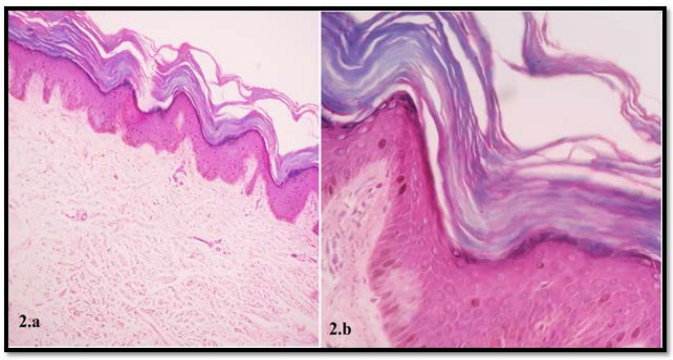

Figure.2.a & 2.b: Separation between the corneal and granular layers of the epidermis. Hematoxylin and eosin (H&E).

Discussion

APSS is a clinical variant of the rare recurrent genetic exfoliative dermatosis known as peeling skin syndrome. It is an autosomal recessive disorder considered to be a localised type which, unlike the generalised form, predominantly involves hands and feet.[4,5] It was first described by Fox in 1921, and he introduced the term keratolysis exfoliativa congenital.[6]

Later, in 1982, Levy and Goldsmith coined the new term "peeling skin syndrome".[7] There are two clinical variants of acral peeling skin syndrome, namely: generalised and localised.[8,9,10] Generalized variety have been further subdivided on the basis of the presence of signs of inflammation like erythema into two subtypes, type A

and type B. Type A is non-inflammatory, and type B is an inflammatory form.[11] A new subtype, type C, was introduced by Mevorah et al., which starts in infancy and is characterised by atopy, itching, and the presence of circular erythematous patches that are encircled by areas of peeling.[12] Acral peeling skin syndrome is an autosomal recessive disorder in which skin peeling is limited to the hands and feet.[4,5] It is caused by mutations in the transglutaminase 5 (TGM5) gene and, less frequently, in the cystatin A (CSTA) gene.[3,13] TG5 is expressed in the corneal layer and is responsible for the formation of crosslinks between key proteins in the cornification process (loricrin, involucrin, filaggrin, and others); it is also essential for the maintenance of an intact corneal layer.[3,14,15] The underlying genetic mechanism was elucidated by Cassidy et al. in 2005.[3] It is characterised by the formation of blisters and superficial peeling of the skin of the palms and soles, leaving a painless residual erythema that heals without scarring. These clinical manifestations are exacerbated by humidity and physical factors like trauma or friction. Otherwise, generally symptoms are absent or mild. The characteristic histopathological finding in APSS is separation between the granular and corneal layers. Another common finding seen in the stratum corneum above the plane of separation with the granular layer is the presence of several layers of cells of atypical appearance, comprising of large, round, pale cells with an edematous and less compact appearance.[15,16]

APSS manifests mostly in early childhood. Our patient is one of the few adult-onset cases ever reported, confirming suggestions that the onset of clinical presentation may be variable.[4,9,17,18] The most common clinical differentials include contact dermatitis, exfoliative skin disorders such as keratolytic winter erythema (Oudtshoorn disease), Netherton syndrome, and epidermolysis bullosa simplex.[19] When epidermolysis bullosa is not confirmed by mutations in corresponding genes in suspected cases, screening for TGM5 mutations is recommended.[20] Therefore, history and physical examination are only suggestive. Histopathologic examination of skin biopsy and genetic studies can confirm the diagnosis of APSS. Currently, effective treatment for APSS is not available.[17]

Therefore, treatment is mostly symptomatic and includes protection from heat, humidity, and trauma, predominantly pressure and friction. In some individuals, topical emollients and keratolytic agents may be helpful. Other treatment modalities such as methotrexate, ultraviolet B phototherapy, isotretinoin, and corticosteroids seem to be ineffective.[16] Considering the current lack of an effective treatment, genetic counselling is mandatory, as this promotes patient understanding of the condition and helps patients cope.[21]

Conclusion

Acral skin peeling syndrome is a genetic disorder characterized by recurrent spontaneous exfoliation limited to the limbs. It may pose a diagnosis challenge because of its rarity and similarities with other exfoliating skin disorders. Clinical history, histology, and genetic testing will aid in an accurate diagnosis.

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