

## Case Report

# Peeling skin syndrome: an investigational dilemma

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**Received:** 21 June 2019

**Accepted:** 30 July 2019

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### ABSTRACT

Peeling skin syndrome is a rare autosomal recessive disorder of cornification that starts either at birth or later in childhood, characterized by widespread painless peeling of the skin in superficial sheets. We report the case of a 13-year-old boy who presented with asymptomatic peeling of skin since birth. Sheets of skin were peeling from the neck, trunk and extremities following mild friction or rubbing, with sparing of palms and soles. The case is being reported due to its rarity.

**Keywords:** Acral, Inflammatory, Non-inflammatory, Peeling skin syndrome

### INTRODUCTION

Peeling skin syndrome (PSS) is a heterogeneous group of rare autosomal recessive disorders characterized by superficial painless peeling of the skin without mucosal fragility.<sup>1</sup> Two forms of PSS are recognized, namely, Acral PSS (APSS; OMIM 609796) and generalized PSS (OMIM 270300). APSS is a localized form of PSS characterized by skin peeling mainly on the dorsal and volar surfaces of the hands and feet.<sup>2</sup> Generalized PSS is further divided into two types, namely, noninflammatory type (type A) and inflammatory types (type B).<sup>3</sup> In both the types (A and B) skin involvement is generalized. While type A presents with asymptomatic non-inflammatory skin peeling, type B presents with erythroderma at birth, showing overlap with Comel Netherton syndrome.<sup>4</sup> Mevorah et al expanded this classification and added a new variant, type C, that starts in infancy and is characterized by atopy, itching and presence of circular erythematous patches that are encircled by areas of peeling.<sup>5</sup>

We report the case of a 13-year-old boy with asymptomatic and non-inflammatory peeling of skin since birth with sparing of palms and soles.

### CASE REPORT

A 13 year old boy was brought by his father with complaints of asymptomatic peeling of skin over the body since birth. The boy was born of a non-consanguineous marriage with no history of similar skin problem in any other member of the family. There was no history of fluid filled blisters over the body at or after birth. Peeling of skin remained all around the year with worsening in the summer. The patient was able to perform his daily activities with no restriction. On examination, he had patches of peeled off skin over the trunk and extremities (Figures 1 and 2) with total area of involvement being less than ten percent. The older lesions were healing with scab-like hyperpigmentation without scarring. Rubbing of normal appearing skin caused easy and superficial peeling with no bleeding, oozing or underlying erythema. The palms, soles and mucous membranes were uninvolved (Figures 3 and 4). Teeth and nails appeared normal. General and systemic examination revealed no abnormality. Routine hemogram and urinalysis were normal. Biopsy from the normal appearing skin over the back adjacent to the erosion showed sub-corneal cleavage in the epidermis, hypogranulosis, mild acanthosis and a normal dermis

(Figures 4 and 5). No vacuolization of granular layer was noted.



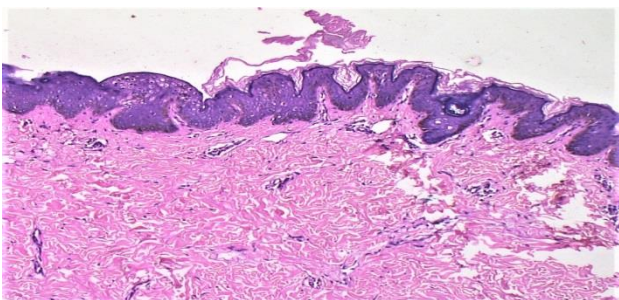
**Figure 1: Superficial peeling, erosions and crusts over trunk.**



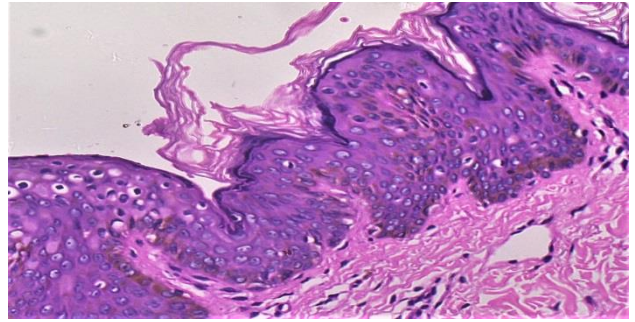
**Figure 2: Erosions and crusting around the elbow.**



**Figure 3: Sparing of palms and soles.**



**Figure 4: Subcorneal split with hypogranulosis and mild acanthosis (H and E, 10x).**



**Figure 5: Subcorneal split with hypogranulosis. Vacuolization of granular layer was not seen (H and E, 40x).**

Based on these clinical and histopathological findings, diagnosis of Type A (non-inflammatory) PSS was made. The patient was educated about avoiding exacerbating factors such as heat, friction, humidity, mechanical trauma and excessive perspiration. He was treated with emollients but continued to have asymptomatic skin peeling with the same intensity.

#### DISCUSSION

PSS is an autosomal recessive genodermatosis commonly affecting communities where consanguinity of marriage is present. It is characterised by asymptomatic shedding of sheets of skin since birth or early childhood.<sup>6</sup> It was first described by Fox as congenital ichthyosiform erythroderma in 1921.<sup>7</sup> The condition has variously been described as keratolysis exfoliativa congenita, deciduous skin, familial continual skin peeling, and continual skin peeling syndrome.<sup>7-10</sup> However in 1982, Levy et al introduced the term PSS and described a 24 year-old woman of short stature who was affected by generalised asymptomatic skin peeling since birth and also had primary amenorrhoea, sexual infantilism and anosmia.<sup>1</sup>

Various associated features such as koilonychia, distal onycholysis, chapping, keratoderma, sexual dysfunction, anosmia, keratoderma, cheilitis, keratosis pilaris, melanonychia, clubbing, hyperhidrosis and onychodystrophy have been described.<sup>11</sup> Abnormal biochemical parameters like altered tryptophan levels, aminoaciduria, high levels of serum copper, iron and iron-binding capacity, IgE and ceruloplasmin and abnormal epidermal retinoid metabolism are also reported.<sup>12,13</sup>

PSS has clinical resemblance to subcorneal pustular dermatosis, epidermolysis bullosa simplex superficialis, congenital ichthyosiform erythroderma, Netherton syndrome, pemphigus foliaceus, erythrokeratoderma like erythrokeratolysis hiemalis (Oudtshoorn disease), keratolysis exfoliativa and even exfoliation following dyshidrosis.<sup>11</sup> However, differentiation from most of these diseases can be done based on clinical features, routine laboratory tests, histopathologic and ultrastructural analysis of a skin biopsy, and mutation analysis.

Type A PSS has been shown to have its genetic basis in the CHST8 gene encoding a golgi transmembrane N-acetylgalactosamine-4-O-sulfotransferase (GALNAC4-ST1) in 2012.<sup>14</sup>

It is characterized by asymptomatic, generalized skin peeling with areas of hyper-pigmentation, without vesiculation or erythema that begins at birth or between 3 and 6 years of age. Histopathologically, there is hyperkeratosis, thinning of the granular layer, and separation of the stratum corneum from the underlying stratum granulosum or intracorneal split.<sup>15</sup> Type A PSS should be differentiated from superficial epidermolytic ichthyosis wherein superficial skin peeling described as "Mauserung phenomenon" may be observed. Lack of mutations in the KRT2 gene, absence of prominent hyperkeratotic skin changes and absence of vacuolization of the granular cell layer favour Type A PSS. Epidermolysis bullosa simplex superficialis has recently been described as a new and rare variant of Epidermolysis bullosa simplex (EBS), which mimics PSS closely but differs from it by the absence of continual skin peeling, presence of mucosal lesions, healing with milia and scarring, and autosomal dominant mode of inheritance.<sup>16</sup>

Our patient presented with asymptomatic and non-inflammatory skin peeling since birth with sparing of palms and soles, and absence of blistering, scarring or mucosal lesions. Histopathology showed characteristic sub-corneal cleavage in the epidermis, thinned out granular layer with no vacuolization and a normal dermis. These findings favoured the diagnosis of Type A PSS. Extensive investigations like ultrastructural analysis or tests to detect any rare biochemical alterations were not done in this study.

Type B is due to autosomal recessive loss-of-function mutations in CDSN encoding corneodesmosin, that maintains the structural integrity of stratum corneum.<sup>17</sup> It presents with superficial patchy peeling of the entire skin with underlying erythroderma, pruritus, and atopy.<sup>11</sup> Histologically, the epidermis is psoriasiform with an absent or reduced granular layer, with marked parakeratosis and acanthosis. The split occurs at the level of the granular layer. Mild inflammatory infiltrate in the upper dermis may be present.<sup>11</sup> Type B PSS should be differentiated from Netherton syndrome by the absence of typical hair shaft defects, normal LEKTI (lymphoepithelial-Kazal-type 5 inhibitor) staining and also appearance of the peeling lesions without double-edge scales.

Type C usually begins in infancy with erythematous patches surrounded by peeling circles. Atopy and pruritus can be noted.<sup>5</sup> Histological features of type C cases were similar to those of type B.<sup>11</sup>

Acral PSS is caused by missense mutations in TGM5 encoding transglutaminase 5.<sup>18</sup> Patients present with

superficial peeling or blistering of the dorsal surfaces of hands and feet and palms and soles, often associated with significant erythema and mild pruritus.

APSS is most frequently confused with localized epidermolysis bullosa simplex which is an autosomal dominant disorder caused by mutations in the genes KRT5 or KRT14. Ultrastructurally, the blisters are located in the basal layer of the epidermis and not in the upper epidermis as in APSS. Erythro keratolysis hiemalis, another mimicker of APSS, is inherited in an autosomal dominant pattern with cyclic erythema, hyperkeratosis, and peeling of the palms and soles, particularly during the winter. The disease-causing gene was mapped to chromosome 8p22-p23.<sup>19</sup> Keratolysis exfoliativa, occurs in young adults usually in the summer months and may be related to sweating. Lesions appear as tiny white rings or 'air bubbles', which soon rupture and peel off ('ringed keratolysis').

There is no specific therapy for PSS. Avoidance of exacerbating factors such as heat, friction, humidity, mechanical trauma and excessive perspiration, as well as daily topical application of emollients to the affected areas is the mainstay of treatment. Various treatment modalities such as topical keratolytic agents, topical calcipotriol, topical tar, topical steroid, methotrexate, and phototherapy have been used but with inconsistent results.<sup>6</sup>

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

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**Cite this article as:** Saini S, Kharkar V. Peeling skin syndrome: an investigational dilemma. *Int J Res Dermatol* 2019;5:894-7.