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Adult-Onset Acral Peeling Skin Syndrome in a Non-Identical Twin: A Case Report in South Africa

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 44
Final Diagnosis: Acral peeeling skin syndrome
Symptoms: Recurrent skin exfoliation
Medication: —
Clinical Procedure: Skin biopsy
Specialty: Dermatology

Objective: Rare disease

Background: Acral peeling skin syndrome is a rare autosomal recessive disorder in which skin exfoliation is limited to the hands and feet. While it typically manifests from early childhood, in this first reported case from South Africa, the patient did not manifest clinically until the fourth decade of life.

Case Report: A 44-year-old woman of African descent, 1 of a set of non-identical twins, presented with recurrent episodes of skin peeling of the upper and lower limbs. The first episode occurred 4 years prior, followed by perennial skin peeling during the spring seasons. She was not on treatment for any chronic disease and reported no exposure to chemicals or other irritants. The family, including the non-identical twin sister, has no history of skin disorders and the patient's HIV antibody test was negative. At presentation, physical examination revealed ongoing exfoliation with new skin formation on the palms and soles. The mucous membranes and nails were spared. Other systems were normal. Skin biopsy taken from the palms confirmed peeling skin syndrome. The patient was managed with topical aqueous cream and analgesics. She was briefly counseled on the nature and prognosis of the disease, and referred for genetic testing and counseling. On follow-up, she continues to have skin peeling once or twice a year.

Conclusions: This first reported case of this rare disease in South Africa contributes to the growing body of literature on the disease and highlights the need for clinicians to be aware of its variable clinical onset.

MeSH Keywords: Adult • Dermatitis, Exfoliative • Hand Dermatoses • Leg Dermatoses • Twins, Dizygotic

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/892110

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Background

Acral peeling skin syndrome is a clinical variant of the rare, genetic, and recurrent exfoliative dermatosis known as peeling skin syndrome. It is an autosomal recessive disorder in which, unlike the generalized form, skin peeling is limited to the hands and feet [1,2]. The overwhelming majority of reported cases started manifesting clinically from early childhood and occurred in singleton patients. In addition, no variant of peeling skin syndrome has ever been reported in South Africa. In this article, we report the first documented case of acral peeling skin syndrome in South Africa, in a female non-identical twin, whose first episode of skin peeling was in the fourth decade of life.

Case Report

A 44-year-old woman of African descent presented with recurrent episodes of skin peeling of the upper and lower limbs. The first episode occurred at the age of 40 and was followed by perennial skin peeling, mostly during the spring seasons. She reported no exposure to chemicals or other skin irritants that could suggest contact dermatitis. She was not on any treatment for chronic diseases and her HIV antibody test was negative. Prior to presentation at our clinic, no definitive assessment had been made, and treatments received elsewhere were largely unsuccessful. The patient is an academic support staff at a University and is 1 of a set of non-identical twins. She is a mother of 2 children and neither the twin sister nor any of her family reported any history of skin diseases.

Her episodes of skin exfoliation usually start with pain and swelling of the limbs, followed by peeling and new skin growth underneath the peeled skin. The peeling starts from the elbows and extends towards the tip of the fingers, and from the buttocks, extending to the toes. The nail beds were spared.

Physical examination at presentation revealed ongoing exfoliation with new skin formation on the palms of the hands and soles of the feet. There were areas of thickened and keratinized skin with mild non-pitting swelling in the hands and feet (Figures 1 and 2). The mucous membranes were spared and other organ systems were normal.

A probable assessment of acral peeling skin syndrome was initially made, which was later confirmed on histology of skin biopsies taken from the palms (Figure 3). The patient was managed with topical aqueous cream and analgesics. She was briefly counseled on the nature and prognosis of the disease, and referred for genetic counselling and testing at a tertiary unit. Follow-up shows that she continues to have recurrent exfoliation, the last episode being early 2014.

Discussion

Peeling skin syndrome was first described by Fox as congenital ichthyosiform erythroderma in 1921 [3]. However, in 1982, Levy and Goldsmith introduced the term “peeling skin syndrome” [4]. There are 2 clinical variants of peeling skin syndrome, namely: Generalized and Acral peeling skin syndrome [3,5,6]. All variants are autosomal recessive and a detailed family history of skin exfoliation is therefore crucial. Depending on type, mutations in the CDSN or TGM5 or CSTA genes are implicated [1]. These genes play roles in the adhesive interactions between corneocytes and their mutation results in cleavage of the stratum corneum from the stratum granulosum, a phenomenon that explains the skin exfoliation.

Unlike the generalized variants, which involve most parts of the body [2,7,8], skin peeling in the acral variant is limited to the hands and feet [3]. Clinically, peeling may be accompanied by burning sensation, tenderness, and erythema of the limbs. However, there are no nail changes or blister formation.

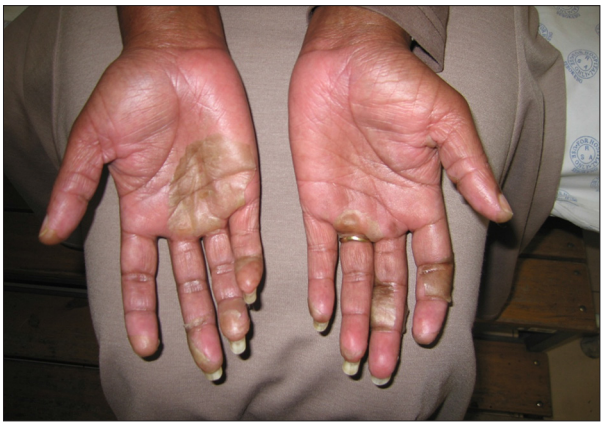


Figure 1. Photograph of both hands. Note the erythema, swelling and remnant peeling of the skin of both hands.

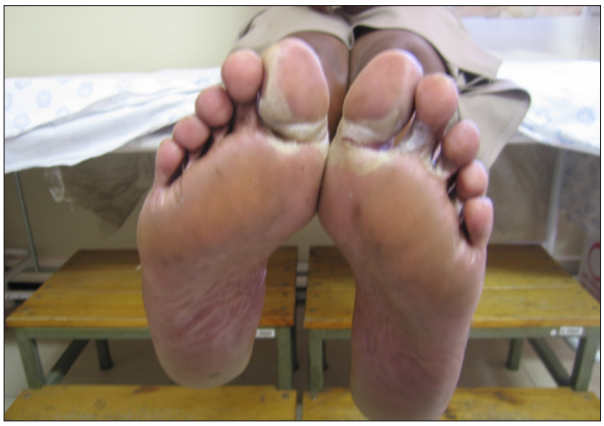
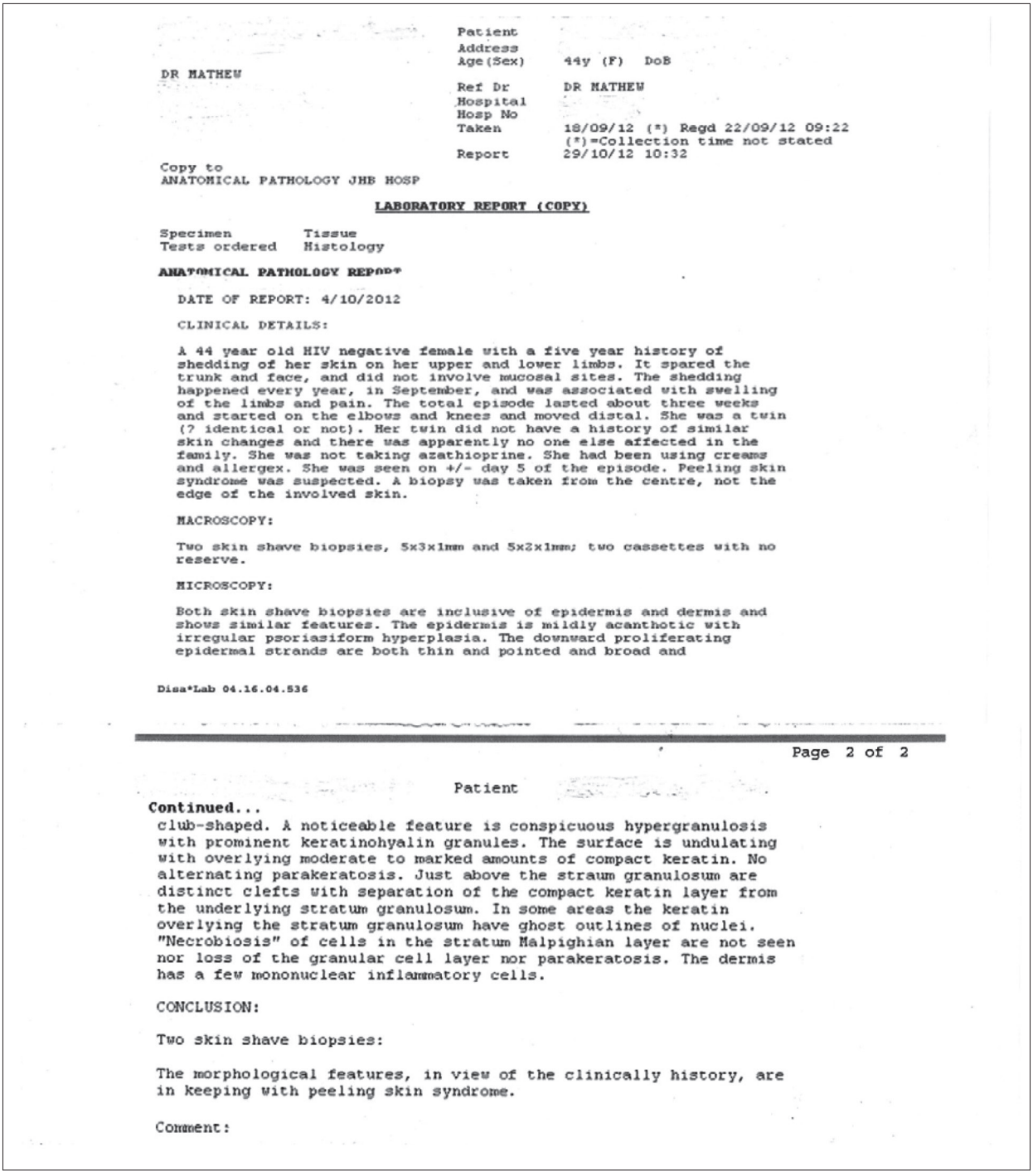


Figure 2. Photograph of both feet. Note the erythema and remnant peeling of the toes.



Patient
Address
Age(Sex) 44y (F) DoB

DR MATHEW

Ref Dr DR MATHEW
Hospital
Hosp No
Taken 18/09/12 (*) Regd 22/09/12 09:22
(*)=Collection time not stated
Report 29/10/12 10:32

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ANATOMICAL PATHOLOGY JHB HOSP

LABORATORY REPORT (COPY)

Specimen Tissue
Tests ordered Histology

ANATOMICAL PATHOLOGY REPORT

DATE OF REPORT: 4/10/2012

CLINICAL DETAILS:

A 44 year old HIV negative female with a five year history of shedding of her skin on her upper and lower limbs. It spared the trunk and face, and did not involve mucosal sites. The shedding happened every year, in September, and was associated with swelling of the limbs and pain. The total episode lasted about three weeks and started on the elbows and knees and moved distal. She was a twin (? identical or not). Her twin did not have a history of similar skin changes and there was apparently no one else affected in the family. She was not taking azathioprine. She had been using creams and allergex. She was seen on +/- day 5 of the episode. Peeling skin syndrome was suspected. A biopsy was taken from the centre, not the edge of the involved skin.

MACROSCOPY:

Two skin shave biopsies, 5x3x1mm and 5x2x1mm; two cassettes with no reserve.

MICROSCOPY:

Both skin shave biopsies are inclusive of epidermis and dermis and shows similar features. The epidermis is mildly acanthotic with irregular psoriasiform hyperplasia. The downward proliferating epidermal strands are both thin and pointed and broad and

Disa*Lab 04.16.04.536

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Patient

Continued...

club-shaped. A noticeable feature is conspicuous hypergranulosis with prominent keratinohyalin granules. The surface is undulating with overlying moderate to marked amounts of compact keratin. No alternating parakeratosis. Just above the straum granulosum are distinct clefts with separation of the compact keratin layer from the underlying stratum granulosum. In some areas the keratin overlying the stratum granulosum have ghost outlines of nuclei. "Necrobiosis" of cells in the stratum Malpighian layer are not seen nor loss of the granular cell layer nor parakeratosis. The dermis has a few mononuclear inflammatory cells.

CONCLUSION:

Two skin shave biopsies:

The morphological features, in view of the clinically history, are in keeping with peeling skin syndrome.

Comment:

Figure 3. Histology report.

Environmental factors such as high temperature and humidity may aggravate the symptoms [9], as seen in this patient, in whom peeling episodes occur just after winter. Although the palms of the hand and soles of the feet may be hyperkeratotic in the generalized variant, the limbs are usually spared from peeling [10].

Most cases of acral peeling skin syndrome manifest in early childhood [1] and our patient is one of the few adult-onset cases ever reported, confirming suggestions that the onset of clinical presentation may be variable [5,9,11].

Apart from differentiating acral peeling skin syndrome from contact dermatitis, in which there is a history of exposure to

a skin irritant, it is important to exclude other exfoliative skin disorders such as Keratolytic winter erythema (Oudtshoorn disease), Netherton syndrome, and Epidermolysis bullosa simplex. Oudtshoorn disease is an autosomal dominant disorder that causes peeling of the palms and soles of the feet during winter and occurs exclusively among the Afrikaner settler population of the Western Cape in South Africa [12]. However, our patient is a black South African woman and has no mixed ancestry. She also has no family history of exfoliative skin diseases, contrary to expectations in an autosomal dominant disease. Netherton syndrome is an autosomal recessive, exfoliative skin disorder usually diagnosed in early childhood like peeling skin syndrome. However, it is characterized by increased risks of fatality in early childhood and patients with this syndrome are highly unlikely to survive to adulthood [2,13,14]. Its clinical features include: atopy, raised IgE, eosinophilia, generalized erythema, susceptibility to recurrent infections, poor thermoregulation, scaling, and the typical hair follicle anomalies referred to as "Bamboo hair" [2,11,15]. Except for the skin peeling and erythema, other clinical features of Netherton syndrome were absent in our patient. Although epidermolysis bullosa simplex has been reported to resemble acral peeling skin syndrome, the later is an autosomal dominant disease characterized by bullae or blisters formation and the genetic mutations implicated are in the KRT5, KRT14, or PLEC genes [1]. Our patient did not present with bullae.

History and physical examination are only suggestive, and diagnosis of acral is only confirmed by histology of skin biopsy and genetic studies. Histology typically shows hyperkeratosis, psoriasiform hyperplasia, hypergranulosis with keratinohyalin granules and cleavage of the stratum corneum from the stratum granulosum – a key histological feature of peeling skin syndrome.

Genetic studies and testing show an autosomal recessive pattern and are important for identifying mutations and for profiling risks of transmitting mutant genes to future generations. This is especially crucial in populations where consanguineous marriages are practiced. Genetic mutations in the TGM5 or CSTA genes are implicated in acral peeling skin syndrome, while of the 2 generalized variants, only the type B, inflammatory generalized type, has been associated with a homozygous non-sense mutation in the CSDN gene (which encodes corneodesmosin) [9,15,16].

There is currently no effective treatment for acral peeling skin syndrome [17]. Treatments with analgesics, emollients, antihistamines, keratolytics, methotrexate, steroids, isotretinoin, and ultraviolet rays have all been tried with limited successes [17]. Until there is adequate understanding of the etiology of peeling skin syndrome sufficient to inform the development of effective treatment, management remains symptomatic. Considering the current lack of an effective treatment, genetic counseling is mandatory, as this promotes patient understanding of the condition and helps patients to cope [18].

Conclusions

This first reported case of acral peeling skin syndrome in South Africa highlights the variable clinical onset of this rare skin disease. While its rarity and similarities with other exfoliating skin disorders may pose a challenge to prompt diagnosis, a history of recurrent spontaneous exfoliations limited to the limbs should raise the possibility of acral peeling skin syndrome.

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