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Case Report

Extensive darier's disease with pityriasis amiantacea, alopecia and congenital facial nerve palsy

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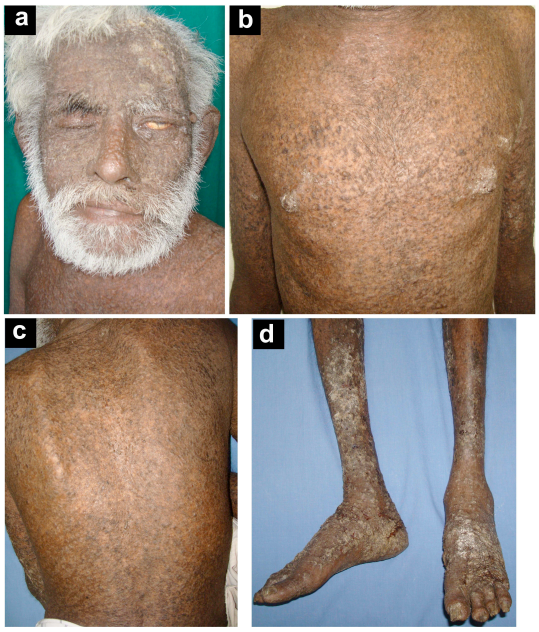
Abstract

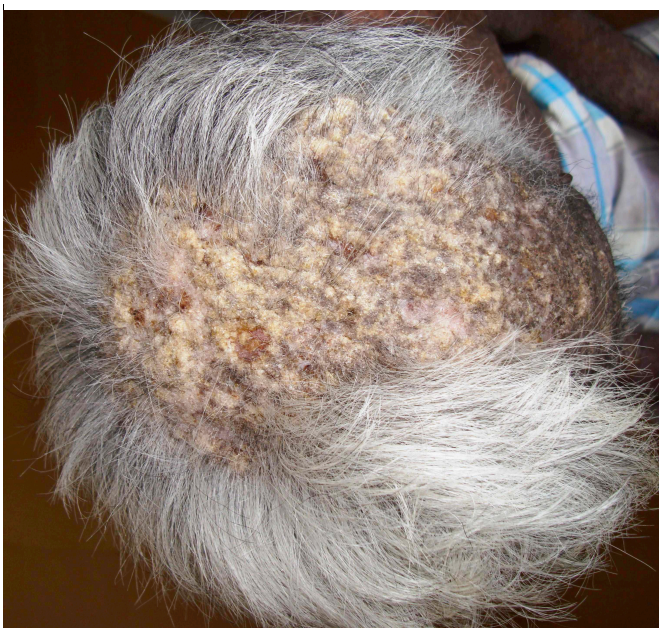
We present a 65-year-old man with Darier disease with pityriasis amiantacea on the scalp, alopecia, and congenital facial nerve palsy.

Introduction

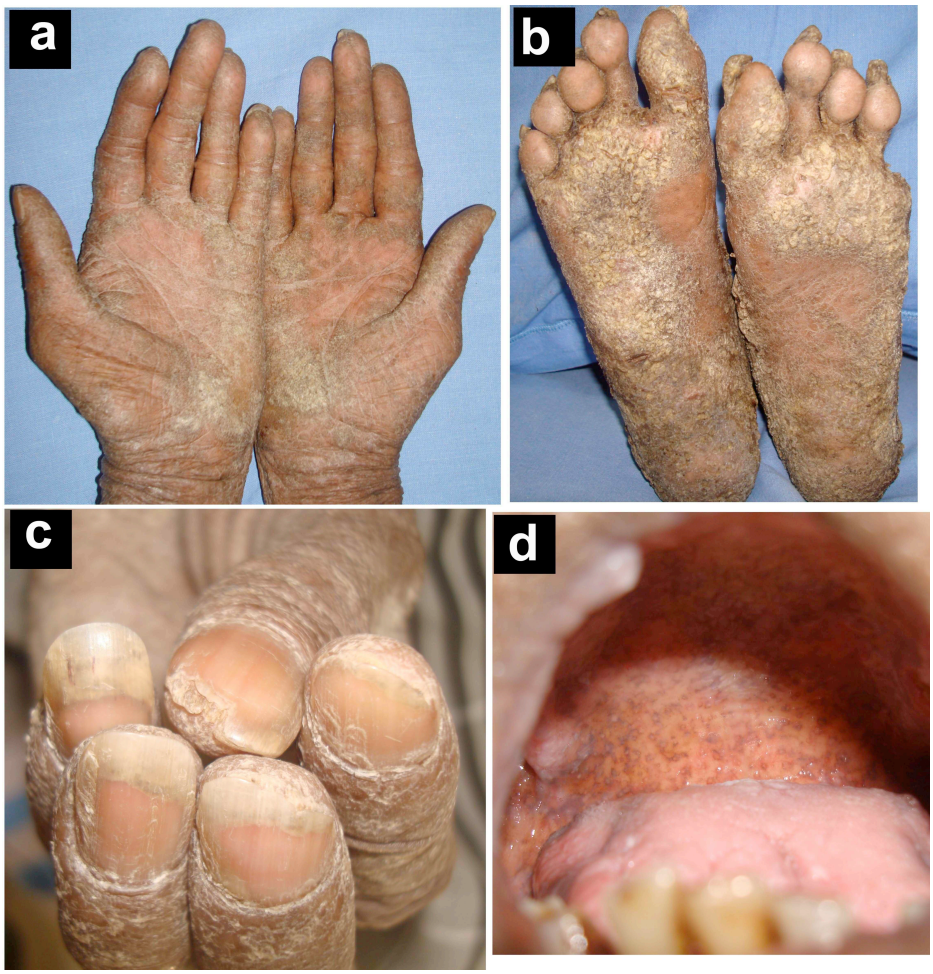
Darier disease is a rare autosomal dominant genodermatosis related to defective function of the sarco/endoplasmic reticulum Ca^{2+}-ATPase-2, which is responsible for acantholytic dyskeratosis in the histopathology [1,2]. The most common clinical manifestation is seen as skin-colored to brown, hyperkeratotic, greasy papules that coalesce into warty plaques commonly involving the seborrheic areas of the trunk, face, and scalp along with typical nail and oral mucosal changes [3]. Several other morphological variants have been described. Universal involvement of the entire skin integument is rare. Involvement of the scalp may be severe, but loss of hair is rare [1]. Pityriasis amiantacea-like scales on the scalp was described in a single case report of Darier disease [4]. Herein, we describe a rare case of extensive Darier's disease with pityriasis amiantacea on the scalp with alopecia and congenital facial nerve palsy. Our patient was treated with low-dose isotretinoin, which improved his skin lesions.Case Report

A 65-year-old man presented with a history of itchy, scaly, warty lesions all over the body since 14 years of age. He was born out of a non-consanguineous marriage. There was no history of similar illness in any of his family members. His lesions initially started on the scalp and chest and gradually spread all over the trunk and limbs. He also noticed that the disease was severe during summer with recurrent episodes of foul smelling discharge from the lesions. He also complained that the scaling was severe in the scalp associated with localized areas of hair loss. He also had deviation of his angle of the mouth to the right side and inability to completely close his left eye since birth. His left little toe was amputated a few years back because of a spreading infection. There was no history of any psychiatric illness or epilepsy.

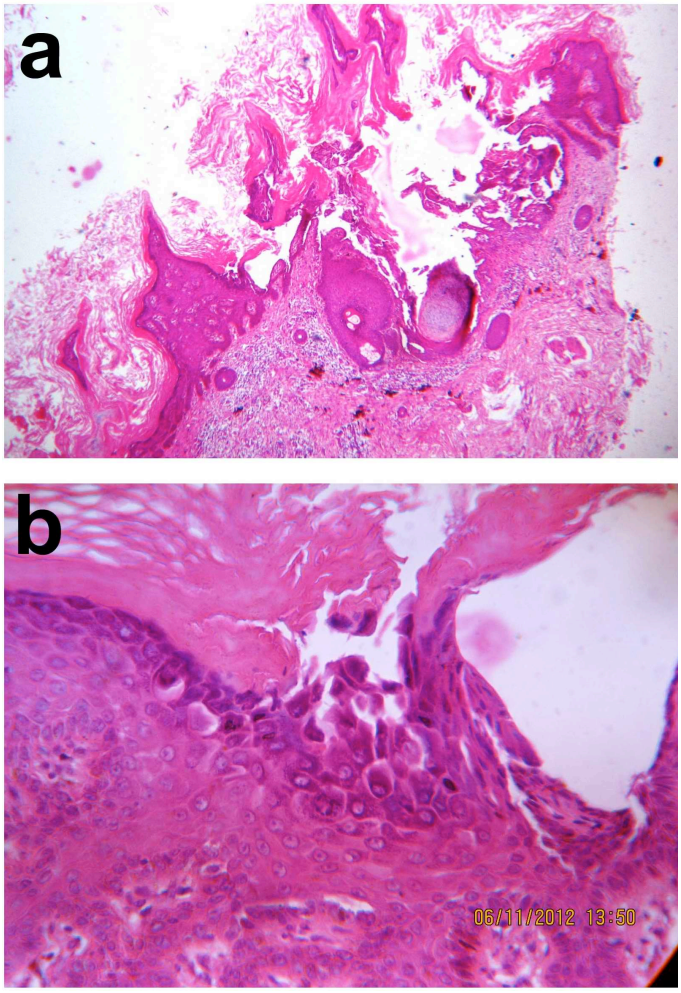




Examination revealed brown-to-pigmented greasy papules and coalescing plaques involving the entire skin surface including the scalp, palms, soles, and genitalia (Figure 1). Lesions of the upper and lower limbs were predominantly hyperkeratotic. The scaling was significantly marked and adherent in some areas on the scalp, forehead, face, around the nipples, anterior axillary folds, dorsa of hands and feet, and the groin. On the scalp, the scales were thick, asbestos-like, and surrounded and bound by tufts of hairs. There was also alopecia on the vertex and left fronto-temporal scalp (Figure 2). Palms showed hyperkeratotic, scaly plaques and keratin-filled pits (Figure 3a). Thick, hyperkeratotic scaling was seen on the soles (Figure 3b). The left little toe was absent owing to amputation. Finger nails showed 'V'-notching of distal free edge, longitudinal red bands and alternating red and white bands, and onycholysis (Figure 3c). All the toenails were dystrophic with thickening of the nail plate, increased curvature, and subungual hyperkeratosis. The oral mucosa showed multiple cobblestone pattern of papules in the hard palate and the tongue showed fissuring (Figure 3d). There was also a lower motor neuron type of left sided facial nerve palsy characterized by the inability to close his left eye fully and deviation of the angle of the mouth to the right side (Figure 1a). Examination of the other cranial nerves was normal. Systemic examination was also normal.



Complete blood count and routine biochemical investigations were within normal range. Histopathology of a skin biopsy specimen showed hyperkeratosis, focal parakeratosis, acanthosis, papillomatosis, suprabasal and intraepidermal clefts, villi, (Figure 4a), and dyskeratotic cells ('corps ronds' and 'grains') in the upper stratum malphigii and corneum layer (Figure 4b). The dermis showed a mild perivascular inflammatory infiltrate. Based on the above findings a diagnosis of Darier disease was made. He was treated with a 2 month course of oral isotretinoin (0.5 mg/Kg) after which scaling and the papules decreased. However, owing to financial constraints isotretinoin could not be continued.



Discussion

Darier disease (OMIM # 124200), also known as keratosis follicularis, Darier-White disease, and Psorospermose Folliculaire Vegetante, was described independently by White and Darier in 1889. It is caused by heterozygous mutation in the ATP2A2 gene on chromosome 12q23-q24.1 encoding for the sarco/endoplasmic reticulum Ca^{2+}-ATPase-2 (SERCA-2) [5]. Insufficient function of SERCA-2b leads to abnormal intracellular Ca^{2+} signaling, notably of the endoplasmic reticulum. The result is a loss of suprabasilar cell adhesion (acantholysis) and an induction of apoptosis (dyskeratosis) [2]. It has complete penetrance and variable expressivity in adults [5]. The disease rarely, if ever, skips a generation [3]. Sporadic cases are also common [1]. Some relatives may only display very minor features of Darier disease, such as acrokeratosis verruciformis or nail changes and are unaware of their condition [3].

The papules usually become apparent in the second or third decade, but can be first seen from the age of 4 years to elderly patients [3]. The lesions of Darier disease are skin-colored to brown, hyperkeratotic, greasy papules that coalesce into warty plaques commonly involving the seborrheic areas of the trunk and face, especially the scalp margins, temples, ears, and scalp [1,5]. Involvement of the hands, producing lesions resembling acrokeratosis verruciformis of Hopf, is seen in the majority of patients [6]. The most common complaint associated with the disease is itching, with exacerbations attributed to heat, sweating, sunlight, lithium, steroid therapy, stress, and menstruation [3]. Nail changes include ‘V’-notching of distal free edge, longitudinal erythronychia, alternating bands of longitudinal leuconychia and erythronychia (known as “candy-cane” appearance), subungual hyperkeratosis, and brittle nail [7]. The pathognomonic nail sign is the combination of a red and white sandwich of streaks associated with a V-shaped notch [3]. Mucous membrane lesions occur as white umbilicated/cobblestone papules affecting the palate, tongue, buccal mucosa, gums, epiglottis, and pharyngeal walls [1]. The heavy scalp crusting imparts a characteristic spiny feel. The hair on the scalp is usually preserved, but occasional scarring alopecia may occur, which was seen in our case [1]. Punctate keratoses occur on the palms and soles, sometimes with a pathognomonic central depression or pit [1]. *Café-au-lait* macules and guttate leucoderma (mostly in a perifollicular distribution in darker skin types) are unusual cutaneous features [1,3]. The hypomelanotic macules may precede the typical greasy papules or occur concurrently [3]. This shows acantholytic dyskeratosis on histopathology, which was the reason why Cornelison et al [8] considered guttate leucoderma to be a form of subclinical Darier disease.

Variants include hypertrophic, vesiculobullous, linear, unilateral, zosteriform, localized (acral, vulva, breats, cervix), and ‘groversid’ variant (smooth papules) [1,3,6]. Other unusual forms are cornifying, comedonal, mosaic, and hemorrhagic [1]. The

cornifying type has markedly hyperkeratotic plaques occurring on non-flexural sites, usually the lower limbs [3]. Erythroderma related to Darier disease is rare. In a study of 247 cases of erythroderma by Vasconcellos et al, only one case was owing to Darier disease [9].

Pityriasis amiantacea is a distinct clinical appearance of the scalp characterized by thick, silvery, adherent, asbestos-like scales, which surround and bind down tufts of hair [10]. It may represent a particular reaction pattern to various inflammatory scalp diseases like psoriasis, seborrheic dermatitis, lichen planus, lichen simplex chronicus, and superficial fungal or pyogenic infection. Pityriasis amiantacea as a manifestation of Darier disease has been described in a single case report by Hussain et al in a 12-year-old girl, in whom it was the sole manifestation of the disease [4]. Our case of Darier disease also had pityriasis amiantacea on the scalp, which is considered to be a rare occurrence.

Darier disease has been associated with neuropsychiatric manifestations like bipolar affective disorders, schizophrenia, psychosis, and suicidal tendencies [11]. Plantar keratoderma, epidermal cysts, dermatofibroma protuberans, verrucae, cutis verticis gyrata, leprosy, and gynecomastia have been described associated with Darier disease [1]. Association with congenital facial nerve palsy in our case could be a coincidental finding.

The characteristic change in the histopathology of Darier disease is acantholytic dyskeratosis [3]. Acantholysis leads to the formation of suprabasal clefts (lacunae) and proliferation of a single layer of basal cells into the cleft, known as villi [1]. A thick orthokeratotic hyperkeratosis and focal parakeratosis are also seen. Two characteristic types of dyskeratotic cells are present – *corps ronds* and *grains*. The *corps ronds* are found as solitary cells or sometimes as small groups of separated cells in the upper malpighian layer and stratum corneum. They have a small pyknotic nucleus, a clear perinuclear halo, and brightly eosinophilic cytoplasm. The *grains* are small cells with elongated nuclei and scant cytoplasm in the upper layers of the epidermis [6].

Treatment for Darier disease has consisted of topical retinoids, tacrolimus, topical 5-fluorouracil, calcipotriol, and oral retinoids [1,3,5,12]. Resistant cases have also responded to oral cyclosporine and oral contraceptive pills [1]. There are reports of surgical treatment of Darier disease using dermabrasion, electrosurgery, and cryosurgery. Er:YAG and CO2 laser ablation have shown clinical efficacy, although this treatment is associated with greater risks and a longer down time. Treatment with the flashlamp-pumped pulsed-dye laser has been shown to improve Darier disease [13]. Studies investigating photodynamic therapy with aminolevulinic acid have had variable results [14]. Our patient responded favorably to a short-term course of isotretinoin therapy with good improvement in his skin condition.

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Legends to the figures

Figure 1a Skin lesions on the face and left sided facial nerve palsy. Skin lesions on the trunk (**Figure 1b, 1c)** and lower limbs (**Figure 1d**).

Figure 2 Pityriasis amiantacea on scalp with alopecia

Figure 3 a & b Palmar and plantar lesions, Nail changes (**Figure 3c**) and palatal cobble-stone papules (**Figure 3d**).

Figure 4a Histopathology of a skin showing hyperkeratosis, focal parakeratosis, acanthosis, papillomatosis, suprabasal and intraepidermal clefts, and villi (H&E, X40). **Figure 4b** 'Corps ronds' and 'grains' in the upper stratum malphigii and corneum layer (H&E, X400).