Single Case

Darier's Disease: Report of a Case with Facial Involvement

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Keywords

Corps ronds and grains · Darier-White disease · Dyskeratosis follicularis · Hyperkeratotic papule · Keratosis follicularis · Leonine facies

Abstract

Darier's disease is a relatively rare autosomal dominant genodermatosis with a defect in the desmosomal attachment due to a mutation in the *ATP2A2* gene. The condition is characterized by multiple hyperkeratotic papules predominantly in seborrheic areas on the head, neck, and trunk, with less frequent involvement of the oral mucosa. Histopathologically, the lesions reveal suprabasal clefts in the epithelium with acantholytic and dyskeratotic cells. Facial involvement in Darier's disease is one of the common presenting features. However, it has been once reported in a severe, chronic form as leonine facies in a long-standing case. To raise awareness of facial involvement in Darier's disease, we herein report a 65-year-old female patient with prominent facial lesions.

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Introduction

Darier's disease, also known as keratosis follicularis, dyskeratosis follicularis, or Darier-White disease, is a relatively rare autosomal dominant skin disorder with abnormal keratinization and loss of epithelial adhesion. Its prevalence in the population ranges from 1:30,000 to 1:100,000, with no gender difference [1, 2]. Although this condition is a dominant genetic inheritance, the report of sporadic cases is approximately 40–50% [3], presumably of new mutation or incomplete penetrance. The characteristic feature of this disease is the presence of multiple, skin-colored to yellow-brown, hyperkeratotic papules predominantly in seborrheic areas, such as the face and upper trunk. Facial lesions may later develop leonine facies that is considered a rare presentation of Darier's disease and has been reported in only one earlier case so far. We herein report a case of Darier's disease with an explicit facial involvement in a 65-year-old Thai woman.

Case Report

A 65-year-old Thai woman developed multiple pruritic papules on the face, both ears, neck, and upper chest since puberty. The patient also complained of pruritus and odor of the lesions, which was aggravated by sunlight, heat, and sweating. No family member was diagnosed with hereditary diseases and had similar lesions. Physical examination revealed multiple skin-colored hyperkeratotic papules coalescing into plaques, leading to thickened skin with ridges and furrows on the face (Fig. 1). On both ears, neck, and upper chest, there were multiple, skin-colored to brownish, hyperkeratotic papules, some of which coalesced and developed plaques (Fig. 2). Examination of the scalp, palmoplantar areas, nails, and oral mucosa was unremarkable.

Histopathological examination revealed hyperkeratosis, hypergranulosis, and papillated epidermal hyperplasia. There were multiple discrete zones of suprabasal clefts with acanthosis, dyskeratotic cells in the stratum spinosum and stratum granulosum described as "corps ronds," and parakeratotic cells in the stratum corneum which resemble "corps grains" or focal acanthotic dyskeratosis (Fig. 3). Based on the history, physical examination, and histopathological findings, the diagnosis of Darier's disease was made for this patient. The patient was given 5% lactic acid cream and 10% urea cream to apply on the lesions twice daily along with advice on improvement of general hygiene, avoidance of sunlight and heat, and genetic counseling. Follow-up 8 weeks later showed mild improvement.

Discussion

Darier's disease was first described by Prince Marrow in 1886 and later independently described by Darier and White in 1889 [4]. The condition is a genodermatosis with an autosomal dominant inheritance caused by a mutation in the *ATP2A2* gene, at chromosome 12q23–12q24 [2, 5]. This gene encodes the sarcoplasmic endoplasmic reticulum Ca^{2+} ATPase type 2 protein (SERCA2), which is a calcium pump widely expressed in the skin. The main function of SERCA2 is transporting Ca^{2+} from cytosol to the lumen of endoplasmic reticulum,

where Ca^{2+} can be stored. A defect of SERCA2 leads to a deficiency of Ca^{2+} at the cell membrane, particularly in desmosomes, resulting in impaired cell-to-cell adhesion and induction of apoptosis.

The characteristic feature of Darier's disease includes the presence of multiple, skin-colored to yellow-brown, hyperkeratotic papules distributed in seborrheic areas, such as the head, neck, and trunk. Other clinical findings include flexural vegetative lesions, wart-like papules on the dorsal side of the hands and feet, palmoplantar pits, red and white longitudinal bands and distal wedge shape of the nail plate, and cobblestone papules on the oral mucosa [6–8]. In addition to classic manifestations, long-standing facial lesions may later develop skin thickening with ridges and furrows on the face compatible with leonine facies. The development of leonine facies could be explained by the long duration of untreated disease, leading to multiple confluent hyperkeratotic papules and plaques on the face, forming ridges and furrows.

Leonine facies or leontiasis is rare and corresponds to the morphologic manifestation of thickening and increased furrowing of the face due to skin infiltrations, leading to a lion-like appearance. This clinical finding is commonly associated with lepromatous leprosy and cutaneous T-cell lymphoma. Diseases reported to manifest leonine facies are summarized in Table 1. To our knowledge, the first case of Darier's disease presenting with leonine facies was reported by Mohammadi et al. [9] in 2018. They reported this rare manifestation in a 67-year-old man in association with cutis verticis gyrata.

Histopathological features of Darier's disease include acantholysis and dyskeratosis represented by corps ronds and corps grains [3, 7]. Corps ronds locate in the granular cell layer of the epidermis and present central round dyskeratotic basophilic masses surrounded by a clear halo-like zone. Electron microscopy demonstrates loss of desmosomes, breakdown of keratin intermediate filament attachment, and perinuclear aggregation of keratin intermediate filaments [10].

Treatment of Darier's disease remains a challenge due to a lack of validated curative treatment option. Several treatments have been reported in the literature; however, they provide limited effectiveness. Topical application of corticosteroids or retinoids is considered as first-line treatment. Systemic retinoids could be considered in severe and extensive cases. Sunscreen and emollients are also crucial. Other modalities reported in the literature include dermabrasion, electrosurgery, ablative lasers, photodynamic therapy, and surgical excision [11].

Due to the rarity of leonine facies in Darier's disease, physicians might be unaware of this unique feature. We report a case of Darier's disease presenting with prominent facial lesions to emphasize to physicians to consider this condition as one of the differential diagnoses. It is important to recognize this manifestation, especially in patients without classic clinical presentation, to implement earlier diagnosis, management, and appropriate counseling to patients and their family members with this genodermatosis.

Statement of Ethics

The patient provided written informed consent to perform all necessary investigations, to take clinical photographs, and use them for research purposes and publication. The patient understood that her name and initials will not be published and due efforts will be made to

conceal her identity. This case report was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

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Author Contributions

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of the manuscript, take responsibility for the integrity of the work as a whole, and gave final approval to the version to be published.

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Fig. 1. Multiple skin-colored hyperkeratotic papules coalescing into plaques on the face, leading to a lion-like appearance.

Fig. 2. Multiple, skin-colored to brownish, hyperkeratotic papules on the neck and upper chest.

Fig. 3. Suprabasal clefts with acanthosis dyskeratotic cells in the stratum spinosum and stratum granulosum. Hematoxylin-eosin stain. Original magnification, $\times 400$.

Table 1. Conditions reported to manifest leonine facies

Infections	Neoplastic	Syndromes
Leishmaniasis	Carcinoid syndrome	Infantile systemic hyalinosis
Leprosy	Epidermal nevi	Keratosis-ichthyosis-deafness syndrome
<i>Mycobacterium tuberculosis</i>	Hair follicle hamartoma	Lipoid proteinosis
Onchocerciasis	Keratoacanthomas	Mucopolysaccharidoses
Paget's disease of the bone	Leukemia cutis	Mucopolysaccharidoses
Syphilis	Lymphoma	Multicentric reticulohistiocytosis
Trichodysplasia spinulosa	Metastatic breast carcinoma	Neurofibromatosis
Inflammatory diseases	Mycosis fungoides	Pachydermoperiostosis
Lymphocytoma cutis	Plasmacytomas	Polyostotic fibrous dysplasia of the facial bones
Sarcoidosis	Subcutaneous eosinophilic necrosis with myelodysplastic syndrome	Familial sebaceous hyperplasia
Infiltrative diseases	Trichoepitheliomas	Setleis syndrome
Amyloidosis	Metabolic	Steatocystoma multiplex
Langerhans cell histiocytosis	Acromegaly	Winchester syndrome
Scleromyxedema	Cretinism	
Xanthoma disseminatum	Cryoglobulinemia	Drugs
Allergic contact dermatitis	Nodular xanthomatosis	Phenytoin hypersensitivity syndrome
Vascular	Primary cutaneous diseases	Photodermatoses
Angiolymphoid hyperplasia with eosinophilia	Alopecia mucinosa	Actinic reticuloid
Port wine stain	Darier's disease	Exogenous agents
	Rosacea	Airborne ragweed contact dermatitis