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Case Report

A Case Report on Darier Disease

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Abstract

Darier disease is rare autosomal dominant disease characterized by the loss of adhesion between epidermal cells and by abnormal keratinization. Mutations in the ATP2A2 gene cause Darier disease. Clinical manifestations of DD was summarised as acantholysis, hyperkeratotic lesions, hyper or hypomelanotic macules, in some cases mucous membranes and nails are also affected. Symptomatic therapy was given with antibiotics, retinoids, emollients, topical steroids. There is no cure for darier disease but treatment was given for symptomatic relief. The patient should receive genetic counselling with information on the inherited condition and risk of transmission to the offspring.

Keywords: *Darier Disease; Hyperkeratosis; Mutation; Keratinisation; Retinoids*

Introduction

Darier disease (DD) is a rare autosomal dominant genetic disorder characterized predominantly by scaly or crusted papules or by wart-like blemishes on the body. Some patients were suffered with the disease even one parent had disease. Some others may suffer as a result of new mutations in the gene like in people with no history of the disorder in their family. It usually first diagnosed in late childhood or early adulthood and frequently affected areas include scalp, forehead, upper arms, chest, back, knees, elbows, and/or behind the ear. It was otherwise called as 'keratosis follicularis' or 'Darier white disease'. Darier disease was initially described by Prince Marrow in 1886 and it was first reported independently by Darier and White in 1889 [1]. The prevalence of this disorder in the population is 1:100,000, most often affecting males [2]. Mostly patients will develop more blemishes during the summer when they are excessively exposed to heat and humidity. Other factors that causes increase in blemishes includes UV light, minor injury or friction, such as rubbing or scratching; and ingestion of certain medications.

DD was clinically classified into three types namely hypertrophic, vesiculobullous, linear or zosteriform [1]. The major difference between the histologic features of the hyperkeratotic papules and those of the vesicles or bullae was the size of the lacunae. Linear or segmental form shows blemishes on localized areas of the skin but not wide spreaded. Some people with the linear form have nail abnormalities only on one side of the body [3]. Diagnosis was done based on physical examination and family history but skin biopsy was the preferred option.

Case Report

A 40 year old female patient was admitted in the department of dermatology in a tertiary care teaching hospital with chief complaints of skin lesions started over face and foot gradually spread to all over the body since 5 years. She was an epileptic patient on treatment with phenytoin and escitalopram since 10 years. Cutaneous examination shows hyperkeratotic plaques over face, soles and palms. Multiple depigmented and hypomelanotic macules were observed over abdomen. Nails were V shaped and splitting, fissuring was present. Her hair and mucosa was normal. Skin biopsy reveals hyperkeratotic stratified lining the lesion with subepidermal area showing keratosis with follicular plugging suggestive of keratosis follicularis. Liver function tests and renal function tests were in normal ranges. Presently she was prescribed with Amoxyclav, vitamin A, D, C supplements orally and soframycin, white field ointment for topical application. Antiepileptic drugs were using as usual.

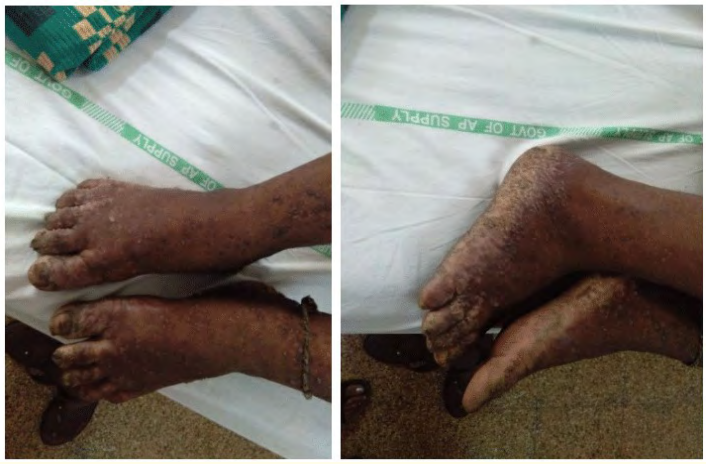

Figure 1, 2: *Hyperkeratotic plaques on legs.*

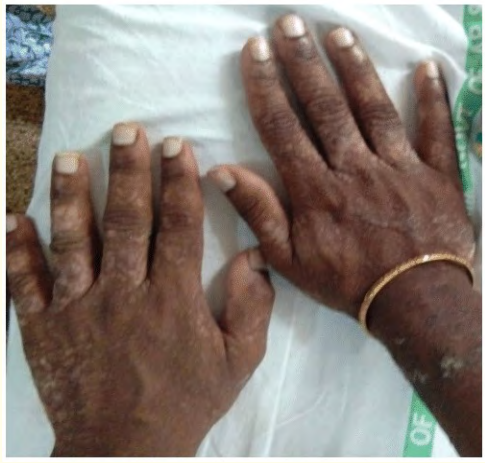

Figure 3: *Hypopigmented macules on palms.*

Discussion

Darier disease is rare autosomal dominant disease characterized by the loss of adhesion between epidermal cells and by abnormal keratinization. Mutations of the *ATP2A2* gene is the main reason for Darier disease. This gene provides instructions for producing an enzyme SERCA2 which acts as a pump that helps to control the level of calcium ions inside cells, particularly in the endoplasmic reticulum and the sarcoplasmic reticulum. Mutations in the *ATP2A2* gene result in insufficient amounts of functional SERCA2 enzyme. A lack of SERCA2 enzyme reduces calcium levels in the endoplasmic reticulum, causing it to become dysfunctional. This abnormal intracellular Ca^{+2} signalling results in irregular organisation or maturation of complexes accountable for cell adhesion. Hence the key pathology of DD are Abnormal keratinocyte-keratinocyte adhesions and aberrant epidermal keratinisation [4]. The clinical severity of the disease depends on range of reduction in functional SERCA2 enzyme.

Histologically biopsy of skin shows abnormal premature keratinisation or dyskeratosis or hyperkeratosis, presence of cleavage, acantholysis, an upward proliferation of papillae into the clefts, presence of elongated papillae, corps, ronds in the granular layer. Lacunae are formed which are small suprabasal separations between epidermal cells result of impaired desmosomes. A large keratin plug, with focal parakeratosis, was present over lesions. Hyperkeratosis is the key pathological feature of DD. Electron microscopy discloses loss or breakdown of desmosomes keratin filament attachment and perinuclear aggregates of filaments. Clinical manifestations of DD was summarised as acantholysis, hyperkeratotic lesions, hyper or hypomelanotic macules, in some cases mucous membranes and nails are also affected. Diagnosis of DD was primarily done based on cutaneous manifestations and family history of the patient. Skin biopsy and genetic testing was helpful in confirming the Darier disease. Some other dermatological disorders mimic the signs and symptoms of darier disease with slight difference like in acanthosis nigricans, lesions are more pigmented. Confluent reticulate papillomatosis lesions are flat and seen only to upper trunk. palpation of papules helps to distinguish it from prurigo pigmentosa and reticulate erythematous mucinosis syndrome based on harshness [1,5,6].

Measures needed to control Darier disease include using sunscreen, wearing cool cotton clothing, and avoiding hot surroundings. Moisturizers with urea or lactic acid can reduce scaling. A low- or mid-potency topical steroid is sometimes useful for inflammation. If bacterial overgrowth is suspected or there is a lot of crusting, use antibiotics and astringents. Topical medications may include topical retinoids adapalene, tretinoin. Other medications include acitretin, isotretinoin, cyclosporine, or oral retinoids (e.g. acitretin, isotretinoin). Oral retinoids have been the most effective medical treatment for Darier disease, leading to reduction of symptoms in 90% of affected people. However, prolonged use is limited due to adverse effects [7].

Conclusion

There is no cure for darier disease but treatment was given for symptomatic relief. The patient should receive genetic counselling with information of inheritance pattern to the offspring. A biopsy is fundamental for final diagnosis. Patients should be enlightened with the complications preventive measures of Darier disease.

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