Darier's Disease: A rare genodermatosis

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Abstract
Darier's disease or darier white disease or keratosis follicularis is a rare inherited autosomal dominant genodermatosis which are clinically characterized by multiple hyperpigmented, firm , greasy, warty lesion usually in seborrhoeic distribution. They also show palmar pits, and mucosal involvement. Histologically they present with suprabasal splitting of epidermis with presence of acnatholytic and dyskeratotic cells. we report a case of a female of 30years old who shows clinical and histological features of dariers disease.

Keywords: Genodermatosis , Darier's disease, Keratotic papules, Dyskeratosis, Hyperpigmented papules.

Case Report
30 year old female patient presented to dermatology OPD with complaints of dark raised lesion over face, neck, upper back and lower limb. The lesion was also present on the abdomen (Fig. 1). The lesion became itchy and infected during summer. Illness started during her teens and with multiple hyperpigmented warty lesions over the face, neck, upper back and lower limb.On examination she has multiple hyperpigmented warty papules and macules over face, neck (Fig. 2) upper back and lower limb.Nails showed diffuse light and dark longitudinal bands. She had diffuse scalp hair loss. Blood count, sugar, urea, creatinine were all normal.

Skin biopsy was taken from lesion on right side of abdomen and sent for histopathological examination showed stratified squamous epithelium with hyperkeratosis, focal vertical parakeratosis (Fig. 3), spongiosis (Fig. 5)with suprabasal splitting of epidermis, focal acantholysis, areas of dyskeratosis forming corps, ronds and grains (Fig. 4) with underlying dermis shows perivascular lymphocytic inflammatory infiltrate.

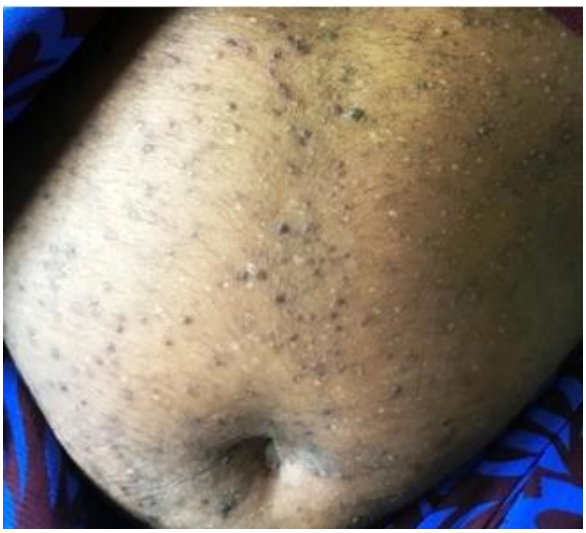

Fig. 1: Multiple hyperkeratotic papules and plaques over abdomen

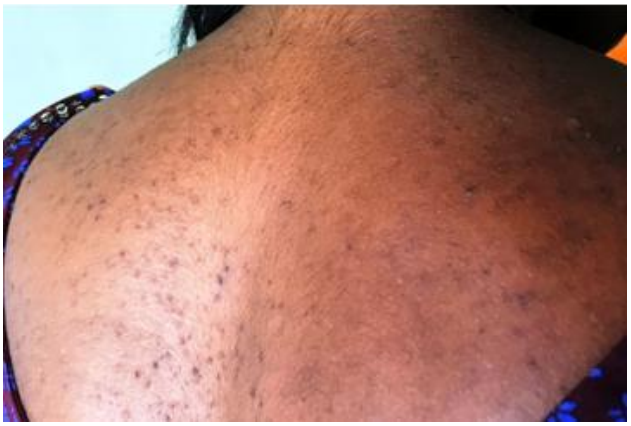

Fig. 2: Presence of warty plaques over the upper back area

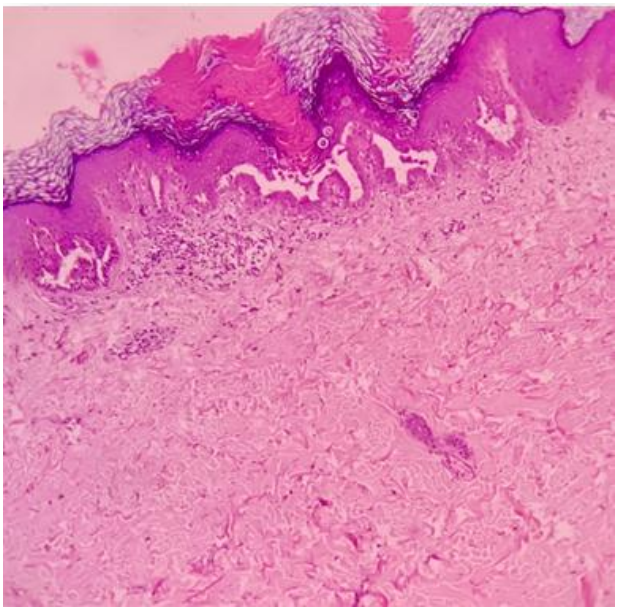

Fig. 3: Photomicrograph showing hyperkeratosis, parakeratosis (H&E stain x100 magnification)

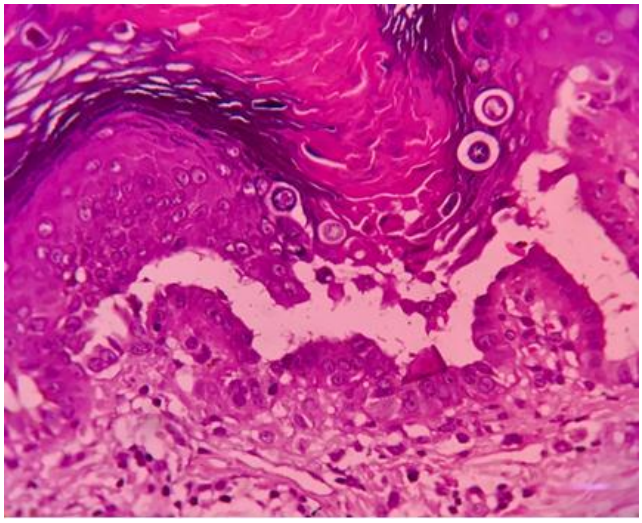

Fig. 4: Photomicrograph showing suprabasal splitting of epidermis with dyskeratotic cells like corps and ronds (H & E stain x400 magnification)

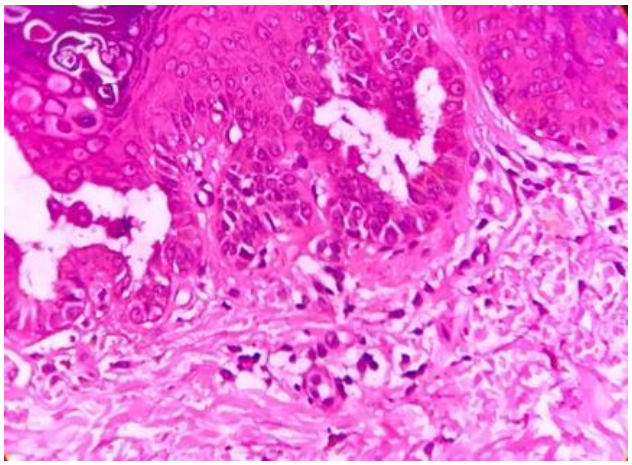

Fig. 5: Focal spongiosis and areas of papillomatosis seen. (H&E X400 magnification)

Discussion

Darier's disease or keratosis follicularis - a rare disorder of keratinisation the incidence of which is around 4 cases per million, over 10 years. Mutation in the gene ATP2A2, at chromosome 12q23–24 1.3 is the causal insult for the disease to occur.[1,2] The gene encodes SERCA2 (sarcoplasmic/ endoplasmic reticulum Ca+2 ATPase type 2 protein), a calcium pump. an isoform of SERCA2 is SERCA2b, which is more abundantly expressed including epidermis. The diasease occurs due to a reduction in function of SERCA2b causing an abnormal intracellular Ca+2 signaling and abnormal organisation or complex maturation which are responsible for cell adhesion. The clinical variants are of disease manifestation– (a) hypertrophic, (b) vesiculobullous (c) linear or zosteriform. Histological features are, abnormal presence of cleavage, acantholysis, papillary proliferation into the clefts, premature keratinization, presence of villi, corps, ronds and grains which are seen in the granular layer and horny layer respectively. Lacunae are seen between the epidermal cells due to impaired desmosomes. Underlying dermal layer is are covered by stratum basale projecting into the clefts and forming villus-like structures.[3]

The differential diagnosis includes acanthosis nigricans, confluent reticulate papillomatosis, seborrheic dermatitis, prurigo pigmentosa acne vulgaris and reticulate erythematomucinous syndrome. Features which differentiates these conditions from dariers are as follows. Hyperpigmented lesions are present in acanthosis nigricans. Flat lesions and distribution over upper trunk is a distinguishing feature of confluent reticulate papilomatosis. Palpatory findings such as harsh papules differentiates it from prurigo pigmentosa and reticulate erythematomucinous syndrome which appear similar on inspection. Benign familial phemphigous, pemphigus vulgaris, Warty Dyskeratoma, Acantholytic Dyskeratosis are the histological differentials for Dariers.In familial Benign Pemphigus the supra basal separation appears as a bulla ,large area of epidermis is affected by Acantholysis, Corps Ronds and Grains are not prominent. Warty Dyskeratoma shows a cup shaped invagination connecting with Epidermis and Corps & Ronds are seen only in the upper portion. Acantholytic Dyskeratosis shoes suprabasal cleft with overlying Acantholysis and Dyskeratotic cells. Pemphigus Vulgaris shows a suprabasilar bullae with a single row of keratinocytes and there is acantholysis in the follicular infundibula. Immunofluroscence can differentiate among different acantholytic disorders.[4]

General measures such as hygienic practices, wearing loose and free clothes preferably cotton, avoiding excess heat, sunlight and use of sunscreens. Urea and lactic acid containing moisturisers and topical retinoids can decrease scaling and hyperkeratosis.[5] Oral retinoids aids in reducing the keratinisation, smoothening of papules and also helps to reduce odor. Antibiotics and antivirals may be required to suppress secondary bacterial and viral infections. Other modalities of treatment includes dermabrasion, electrosurgery, laser ablations of recalcitrant plaques. Photodynamic therapy and surgical excision of thickened plaques has also been reported.[6]

Irrespective of patients presentation and treatment all patients should undergo genetic counseling and should be clearly explained regarding the risks of genetic transmission. In case of oral lesions a biopsy is mandatory for final diagnosis and the patient might need a dermatological examination based on the result. Patients should be counseled regarding the complications of this disorder and the required care. Psychological evaluation and counseling may be required in severe forms, hence efficient management of the disease requires a multidisciplinary approach.

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