Darier’s Disease: A Rare Disorder of Keratinisation. Case Report and Review of Literature

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Abstract: Background: Darier’s disease or Keratosis Follicularis, is a rare autosomal dominant disorder which is characterised clinically by appearance of multiple pruritic, discrete, scaly papules affecting seborrhoeic areas coupled with palmar pits, nail changes and mucosal involvement. Histopathology of the lesions show suprabasal clefts with acantholytic and dyskeratotic cells, etc. Both sexes are equally affected. The clinical features include hyperkeratotic, waxy papules, skin coloured plaques or minute acanthomas on front of chest, retroauricular areas and central T zone of face. The nail changes show short and wide nails, white and red longitudinal bands, V-shaped notch and scalloping of distal nail plate and subungual hyperkeratosis. The palmar pits are pathognomonic. Darier’s disease is characterized by hyperkeratotic papules that coalesce into plaques and occur primarily in seborrhoeic, but also in intertriginous areas. On rare occasion the clinical pictures is dominated by skin fragility with painful erosions and fissure. Histology shows dyskeratosis in spinous layer (corps and ronds) and Stratum Corneum (grains), Supra basal acantholysis and clefts (lacunae). The underlying dermal papillae, covered by a single layer of epithelium (stratum basale), project into these clefts and form villous like structures. A large keratin plug, often showing focal parakeratosis, over lies each lesion. Hyper keratosis is common.

Keywords: Autosomal dominant, palmar pits, suprabasal clefts, Darier’s disease, keratosis follicularis, acantholysis, dyskeratosis

1. Case Report

Here we are presenting a case of 62 year old female who had come with complaints of skin lesions on neck, abdomen, axilla and groin on and off since eight years associated with itching. Symptoms used to be more severe during summers. On cutaneous examination, there was multiple hyper pigmented macerated papules to plaques which were ill defined on neck, bilateral inguinal region and left axilla. Nails showed longitudinal streaks. No history of oozing or discharge of pus from the lesion. Biopsy was done and sent for histopathological examination.

On histopathological examination, epidermis showed irregular acanthosis with focal area showing parabasal clefts and papillary projection with single layer of basal cells. Many dispersed epidermal cells with loss of intercellular bridges and occasional acantholytic cells were seen within the lacunae. Stratum granulosum and stratum corneum showed “corps ronds” having pale nucleus surrounded by clear hallow. Stratum corneum also showed plump, elongated nucleus with dense homogenous eosinophilic cytoplasm (GRAINS). Dermis showed scanty chronic inflammatory cell infiltrate.

Because of the above findings, diagnosis of Darier’s disease was made.
2. Discussion

Darier’s disease is a rare keratinisation disorder. Reported prevalence varies from 1 in 1, 00,000 in Denmark, 1.3 in 100,000 (Croatia), 1.8 in 100,000 (central England) and 3.3 in 100,000 in western Scotland. The incidence of disease reported to be 4 new cases per million, over 10 years. The disease is due to mutation in the gene ATP2A2, at chromosome 12q23-24.1. The gene encodes the SERCA2 pump, a Calcium pump. SERCA2b, which is abundantly expressed in epidermis and its appendages, shows significant correlation between the clinical presentation of Darier’s disease and intensity of histological features.

Histologically the disease needs differentiation from benign familial pemphigus, Grover’s disease and pemphigus vulgaris. Immunofluorescence of skin biopsy differentiate different acantholytic disorders.

Electron microscopy reveals loss of desmosomes, breakdown of desmosome keratin intermediate filament attachment and perinuclear aggregates of keratin intermediate filaments. The differential diagnosis includes Acne Vulgaris, seborrheic dermatitis, Acanthosis nigricans, Confluent reticulate papillomatosis, Prurigo pigmentosa and reticulate erythematous mucinous syndrome. In Acanthosis nigricans, lesions are more pigmented. Confluent reticulate papillomatosis, lesions are flat and confined to the upper trunk. The harshness of papules on palpation helps to distinguish it from visually similar conditions like Prurigo pigmentosa and reticulate erythematous mucinous syndrome.

More than 113 familial and sporadic mutations in ATP2A2 have been identified. Attempts at genotype-phenotype correlations have not been successful. Family members with confirmed identical ATP2A2 mutations can exhibit differences in clinical severity of disease. Suggest that other genes or environmental factors affect the expression of Darier’s disease.

3. Conclusions

Darier’s disease is a rare autosomal dominant disorder with ATP2A2 mutation. Mutations affect activity of the endoplasmic ATPase isoform. Whether there is an exact correlation between activity of the ATPase and phenotype of the disease remains unclear and demands further investigations.

References


