DARIER'S DISEASE

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Summary

Two patients suffering from Darier's disease are described. They had characteristic cutaneous, mucous membrane and nail changes. The skin lesions improved with oral therapy of vitamin A. One patient developed bilateral paresis of lower extremities. This feature has not been described in Darier's disease so far to our knowledge. The exact cause of this could not be ascertained. The pertinent literature is briefly reviewed.

Darier's disease is a rare hereditary disorder of keratinization characterised by symmetrically distributed, pinhead to pea-sized, skin-coloured or brownish, greasy, crusted, predominantly follicular papules and vegetating masses which show a predilection for the seborrhoeic sites of the body. This disorder usually manifests in childhood and gradually becomes progressive with exacerbations in summer and remissions in winter. The exact aetiology of this condition is not clear but an autosomal dominant gene is held responsible for the transmission. Several other factors such as sunlight, disturbance of vitamin A metabolism and abnormal activity of sebaceous glands have been implicated but their exact role is not clear[1].

Darier[2] in 1889 described this entity under the name of "psorospermosis" and proposed a parasitic aetiology for this considering the dyskeratotic cells seen in histologic sections as parasites. In the same year White[3] also reported a patient with similar clinical picture under the name of keratosis follicularis. After studying a second patient in 1890 White[4] pointed out the genetic nature of this disorder. Hence this disorder is often referred to as Darier-White disease. We are describing here two patients with Darier's disease who attended the skin out-patient clinic of S. S. Hospital, Institute of Medical Sciences, Varanasi.

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Case Reports

Case No. 1: A 22 years old male patient reported with the complaint of moderately itchy and scaly lesions over the face and extremities of 5 years' duration.

There was no history of application of oils or greases. The lesions used to improve considerably in winter and aggravate during summer. No other member in the family was having similar lesions. There was no history of drug intake.

Examination revealed multiple, discrete, symmetrical, dry, crusted, brownish, hyperkeratotic, follicular papules of 2–4 mm diameter situated on the periorbital region, nasolabial folds, axillae, extensor aspects of upper extremities, groins, thighs, knees,

ankles and dorsae of the feet (Fig. 1 Page No. 98). Multiple punctate whitish papules were noted on the buccal mucosa and hard palate. Hyperkeratosis was seen on both palms and soles. The nails appeared brittle. Longitudinal ridging and subungual hyperkeratosis were seen on the 2nd and 3rd finger nails of the right hand. Systemic examination revealed no abnormality.

Investigations :- Haemogramme : NAD. X-ray chest : Normal.

Histopathology :- Section from one of the lesions on right thigh revealed marked hyperkeratosis, keratotic plugging, acanthosis, suprabasal lacunae and multiple corps ronds and grains in the prickle cell layer (Fig. 3 Page No. 98). In the dermis there were foci of non-specific inflammatory infiltration.

The patient was kept on oral therapy with vitamin A 100,000 units twice daily. The skin lesions improved considerably after one month of this therapy but unfortunately patient developed bilateral paresis of both lower limbs. Examination by neurologist could not reveal any specific cause for this. X-rays of long bones were normal. There were no signs of hypervitaminosis A. Serum vitamin A level could not be estimated. Patient was advised to stop vitamin A therapy but the paresis remained unchanged even after three months.

No. 2 :–A 15 years old female reported with the complaint of multiple, asymptomatic lesions on the forehead, chest and extremities of 7 years' duration. No other member in the family was having similar lesions.

Examination revealed lesions similar to those described in the first patient; on the forehead, retroauricular areas, sides of the neck, chest, abdomen, back, perianal region and extensor aspects of extremities.

(Fig. 2 Page No. 98). Other features noted were numerous, tiny, punctate, whitish papules on the mucosa of hard palate, palmoplantar hyperkeratosis and sub-ungual hyperkeratosis of the finger nails. Systemic examination revealed no abnormality.

Investigations:-Haemogramme: NAD. X-ray chest and long bones NAD.

Histopathology :- The features were typical of Darier's disease.

Skin lesions improved markedly in three months with oral therapy of vitamin A 100,000 units twice daily.

Discussion

Darier's disease is an autosomal dominant disorder but cases may occur sporadically, and are then attributed to spontaneous mutation of the gene[5]. In our patients the disease manifested in the form of isolated cases. The characteristic lesions in Darier's disease are firm, greasy, crusted, hyperkeratotic follicular papules usually on the seborrhoeic sites of the body. Mucous membrane lesions are reported to be uncommon but may occur in many affected and some normal relatives of the affected as whitish, umbellicated or cobble - stone like papules on the palate, tongue, buccal mucosa, vulva, oesophagus or rectum[5]. Nails may be brittle and dry with longitudinal ridging and subungual hyperkeratosis. Palmoplantar keratoderma is also mentioned to occur in 10% of the cases. These characteristic cutaneous, mucous membrane and nail lesions were observed in our patients also.

Other features reported to occur in Darier's disease are haemorrhagic macules on the extremities, discrete papules resembling acrokeratosis verruciformis on the backs of feet and hands, punctate keratosis of palms and soles, genital hypoplasia, mental retardation, short stature, fibrosis in

the lungs and cystic lesions in the long bones of the extremities[5,6]. An association of Darier's disease with familial benign chronic pemphigus of Hailey and Hailey and Fordyce disease was reported [7,8]. None of these features were observed in our cases.

Bilateral paresis of lower extremities was observed in case No. 1. To our knowledge, this feature has not been recorded so far in Darier's disease, whether this paresis was part of the disease process or merely a coincidental feature or due to some other cause is not known.

Histologically, Darier's disease presents a characteristic appearance.

The pathogenesis of Darier's disease is far from clear. Increased mitotic activity was found in the upper two layers above the basal layer and this is presumed to be responsible for the clinically evident hyperkeratosis[9]. Electron microscopic studies of Charles[10] in 1961 and Caufield and Wilgram[11] in 1963 revealed that the primary fault in Darier's diseases lies in the desmosome-tonofilament complex and the detachment of tonofilaments from desmosomes precede separation of cells in the acantholytic process. More recently Mann and Haye [12] in 1970 reported that the main fault in this disorder may be in the formation and maintenance of the intercellular contact layer. According to these authors stretching of the tonofilaments and desmosomes followed by the loss of intercellular contact layer and splitting of the desmosomes is the sequence of events in the mechanism of acantholysis.

REFERENCES

1. Butterworth T and Strean LP: Keratosis Follicularis. Clinical Genodermatology, The Williams and Wilkins Company, Baltimore, 1962, p. 40.
2. Darier J: Psorospermose folliculaire vegetantae. Ann Derm Syph, 10: 597, 1889. Quoted by 9.
3. White JC: A case of keratosis (ichthyosis) follicularis. J Cutan Genito-Urin Dis., 7: 201, 1889. Quoted by 9.
4. White JC: Keratosis follicularis; a second case. J Cutan Genito-Urin Dis., 8: 13, 1890.
5. Rook A, Wilkinson DS and Ebling FJG: Darier's disease. Text Book of Dermatology, 2nd Edition, Blackwell Scientific Publications, Oxford, p. 1169.
6. Thambiah AS, Sridhar Rao U, Annamalai R et al: Darier's disease with cystic changes in the bones, Brit J Derm, 78: 87, 1966.
7. Ganor S and Sagher F: Keratosis Follicularis and Familial benign chronic pemphigus (Hailey-Hailey) in the same patient, Brit J Derm, 77: 24, 1965.
8. Sardari Lal and Velou A: Darier's disease and Fordyce disease, Indian J Derm Vener., 33: 153, 1967.
9. Frost P: Darier white disease (Keratosis follicularis). Dermatology in General Medicine. Ed: Fitzpatrick TB, Arndt KA and Clark WH et al: McGraw-Hill Book Company, New York, 1971, p. 266.
10. Charles A: An electron microscopic study of Darier's disease. Dermatologica, 122: 107, 1961.
11. Caufield JB and Wilgram GF: An electron microscopic study of Dyskeratosis and Acantholysis in Darier's disease, J Invest Derm., 41: 57 1963.
12. Mann PR and Haye KR: An electron microscopic study of acantholytic and dyskeratotic processes in Darier's disease, Brit J Derm., 82: 561, 1970.