Familial Case of Darier Disease with Guttate Leukoderma: A Case Series from India

Sir,

Darier disease [DD; Darier-White disease or (dys) keratosis follicularis], is an autosomal dominant disorder of keratinization with characteristic dermatologic findings such as keratotic papules on the seborrheic regions, brittle nails and longitudinal erythronychia, and palmoplantar pitting. Hypopigmented macules (guttate leukoderma or predominantly "idiopathic guttate hypomelanosis") is known to be a rare finding in certain disorders of keratinization, e.g., DD, Grover disease, and Cole disease (guttate hypopigmentation with palmoplantar hyperkeratosis).[1,2] Here, we report 2 new cases of this association.

A 45-year-old male presented to the dermatology outpatient department (OPD) with his two daughters and a son. The father had chief complaints of dark brown keratotic papules, sized 1–2 mm on the skin of his head and neck area, chest, back, and shin since approximately 25 years. These lesions had coalesced to form plaques in some areas. On the head and neck, lesions were present predominantly in the scalp, forehead, and temporal regions [Figure 1a], behind the ears, and nasolabial folds. A secondarily infected plaque was present on the left shin. Palmoplantar hyperkeratosis with palmar pitting was present. Nails were dystrophic with erythronychia and V-shaped nick [Figure 1b]. Orodental hygiene was poor and buccal mucosa had whitish papules with leukokeratosis, suggestive of mucosal involvement. Based on classic presentation, a clinical diagnosis of DD was considered and a skin biopsy was taken from the back (index case). The pathological findings included focal suprabasal clefting with a thickened stratum corneum. Few dyskeratotic cells, with "corps ronds" and "grains" were also identified in epidermis consistent with the diagnosis of DD [Figure 1c and d]. The elder daughter, aged 18 years, started developing similar keratotic papules on the neck and trunk since last 3 years with leukoderma-like macules (guttate leukoderma) on the trunk since 4 years [Figure 2]. The younger daughter, aged 16 years, also started developing similar papular lesions since the last 2 years on the neck and trunk, with pitting of palms and nail involvement but no guttate leukoderma. The 12-year-old son of the index case also had brown papules on the forehead along with guttate leukoderma on back [Figure 3]. On enquiring the family history, there were no similar complaints in sibling of the index case; however, the deceased father of the index case had a similar (undiagnosed) disease. Thus, the pedigree chart [Figure 4] suggested the autosomal dominant inheritance of the illness. The index case was treated with isotretinoin 20 mg twice a day, and his daughters and son with topical retinoids, which was supplemented with supportive treatment including moisturizers, sun protection, and counselling for preventing infections and exacerbation.

Figure 1: Index case. Dark brown keratotic papular lesions in temporal region behind the ear (a), nail involvement showing dystrophy, erythronychia, and a V-shaped nick (b), histopathological features of index case showing focal suprabasal clefting with a thickened stratum corneum and dyskeratotic cells, with "corps ronds" and "grains" in epidermis (c and d). (Hematoxylin and eosin stain, original magnification c – ×40, d – ×400)

Guttate leukoderma or hypopigmented macules, as seen in two of our patients, has been reported primarily

Figure 2: Elder daughter. Keratotic lesions with guttate leukoderma on the abdomen

Figure 3: Son. Guttate leukoderma on the back

in high skin phototypes IV to VI and is considered a manifestation of DD in the dark-skinned, though it is considered to be a rare finding. It was first described by Goodall and Richmond in a patient of DD in 1965 (quoted in[1]). Terrom *et al*. in a recent review on this association identified only 21 cases of DD with guttate leukoderma in the English- and French-language literature reported till now.[1] One case of DD associated with guttate leukoderma was reported by Sharma *et al*. from India in 2016.[3] Gupta *et al*. more recently reported another Indian patient of DD with guttate leukoderma following the lines of Blascho.[4] In DD, guttate leukoderma usually appears during the first two decades of life, usually some years before the brown keratotic papular lesions appear. Guttate leukoderma is stable over time and does not respond to therapy for DD. The etiopathogenesis of guttate leukoderma in DD is not clearly understood. Various hypotheses have been proposed e.g., the macules are proposed to be a subclinical form of papules of DD. Impaired transfer of melanin to keratinocytes has also been suggested. Leukodermic macules have also been proposed to be postinflammatory.[3] However, this is untenable in view of the persistent nature of these lesions. Though most of the patients reported till recently were of African origin, the few cases in other races and recently reported cases from India,[3,4] including our two patients, clearly indicate that this presentation is usually missed clinically, and may be more common than recognized.

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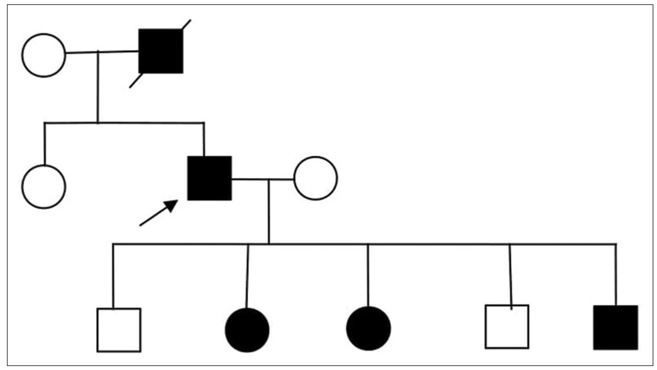

Figure 4: Pedigree chart

Conflicts of interest

There are no conflicts of interest.

Naveen Kumar Kansal, Neirita Hazarika, Shalinee Rao[1]

Departments of Dermatology and Venereology and [1]Pathology and Laboratory Medicine, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India

Address for correspondence:
Dr. Naveen Kumar Kansal,
Department of Dermatology and Venereology, All India Institute of Medical Sciences, Rishikesh - 249 203, Uttarakhand, India.
E-mail: kansalnaveen@gmail.com

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