Guttate Leukoderma in Darier Disease: A Rare Presentation

Sir,
A 50-year-old female presented with chief complaints of asymptomatic multiple red-brown raised keratotic lesions along with hypopigmented lesions all over body since 20 years. Keratotic lesions started from face and gradually involved bilateral arms, hands, abdomen, back, and feet in symmetrical fashion. She gave history of photosensitivity and heat intolerance. There was no history of seizures, mental retardation, or developmental delay. There was family history of similar lesions in mother since birth. Reportedly mother had leukodermic macules in addition to classic keratotic papules. Systemic examination was unremarkable. On dermatological examination, multiple red-brown rough keratotic papules were present on face involving forehead, malar areas and chin, chest, abdomen, back, extensor aspect of bilateral upper limbs, dorsal aspect of bilateral hands, and feet. Multiple hypopigmented to depigmented perifollicular macules of size varying from 2 to 5 mm were present on chest, abdomen, back, and anterior aspect of bilateral thighs [Figures 1 and 2]. Focal palmar keratoderma involving hypothenar eminence was present along with multiple pits on thenar eminence of both palms [Figure 3]. On nail examination, longitudinal ridging and v-nick were present [Figure 4]. Oral mucosa was spared.

On histopathology of hyperkeratotic papules, epidermis showed hyperkeratosis with follicular plugging. Few corps ronds are seen in the granular layer and basal layer showed clefting and presence of mixed inflammatory infiltrate, which is reaching in upper dermis [Figure 5]. Histopathology from hypopigmented lesion showed thinned out epidermis with mild spongiosis. Dermis reveals dense collagen bundles and sparse lymphomononuclear infiltrate [Figure 6]. Based on the clinical and histopathological findings, the diagnosis of Darier disease (DD) with guttate leukoderma was made. Patient was started on Acitretin 25 mg twice daily along with topical sunscreen and topical retinoids and asked to follow up after 3 weeks.

DD [keratosis follicularis] is an autosomal dominant disorder of keratinization with characteristic dermatological findings, such as keratotic papules on the seborrheic...
regions, brittle nails, and longitudinal erythronychia, palmoplantar pitting, and cobblestoning in oral mucosa.[1]

Several variants of DD have been reported, including the guttate hypopigmented, vesiculobullous, acral hemorrhagic, acneiform comedonal, cornifying, and segmental or linear variants.[2] Small leukodermic macules were first described by Goodall and Richmond in a patient of DD in 1965.[3] Hypopigmented macules in DD is rare. 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.[4]

Etiopathogenesis is currently unknown. Some authors considered guttate leukoderma as postinflammatory or subclinical form of DD; however, the increasing number of reported cases devoid of papular lesions or macules evolving into hyperkeratotic papules refute the above hypothesis.[2] Another proposed hypothesis is dysregulated melanin transfer due to lack of keratinocyte adhesion caused by the ATP2A2 gene mutation leading to guttate leukoderma.[5]

According to Tolat et al., familial hypopigmented Darier’s differ from usual Darier by involvement of gluteal region and back.[6] In our patient also, back was involved along with palmar and nail involvement.

Histological examinations of hypopigmented DD variant vary from barely seeing any typical disease features to classic dyskeratosis with the presence of corps ronds and grains and acantholysis.[5]

Guttate leukoderma in DD may be misdiagnosed as tinea versicolor, lichen sclerosus, idiopathic guttate hypomelanosis, or follicular vitiligo.[3] Exogenous lichen sclerosus atrophicans (LSA) presents with pruritic, porcelain-white, shiny slightly elevated interfollicular papules; however, in our patient, lesions were non shiny, non atrophic perifollicular macules with absence of pruritus, wrinkling, and telangiectasia. Moreover, lesions are generally grouped in LSA and often coalesce into larger plaques; however, in our patient, lesions were present since a long time with no coalescing; so, diagnosis of LSA was unlikely. Moreover, classical histopathological features of marked hyperkeratosis, follicular plugging, and band-like infiltrate were absent, which ruled out possibility of extragenital LSA. Lesions were nonscaly; coup d’ongle sign and KOH microscopy were negative, so Pityriasis versicolor was ruled out. Follicular vitiligo was ruled out since lesions were not milky white and due to absence of convex hypopigmented border. Idiopathic guttate hypomelanosis was excluded based on age of onset and distribution of lesions. Lesions were present

Figure 1: Multiple hypopigmented macules along with keratotic lesions on the trunk

Figure 2: Close-up view showing hypopigmented lesions along with keratotic lesions on trunk
since childhood and mainly involve non-sun exposed areas. Treatment modalities include emollients, topical steroids and calcineurin inhibitors, topical 5-fluorouracil, oral retinoids, laser treatments, and surgery.[2] Increasing awareness regarding guttate leukodermic variant of DD is important to prevent misdiagnosis and for appropriate management.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not
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be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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