Dowling–Degos disease with reticulate acropigmentation of Kitamura: Extended spectrum of a single entity

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ABSTRACT

Dowling–Degos disease (DDD) and reticulate acropigmentation of Kitamura (RAK) are rare genodermatoses inherited as an autosomal dominant trait with variable penetrance. They are considered to be part of a spectrum of reticulate pigmentary dermatoses, characterized by the presence of hyperpigmented macules coalescing in a reticular fashion. The authors describe a 28-year-old male patient having hyperpigmented macules on the axillae, neck and face, reticulate acropigmentation of dorsum of the hands, forearms and feet, palmar pitting, and comedo-like lesions over back. The patient showed the unique clinical as well as histopathological overlap of both the rare diseases (DDD and RAK), substantiating the hypothesis that they represent two different features of a single entity with variable phenotypic expression.

Key words: Dowling–Degos disease, reticulate acropigmentation of Kitamura, reticulate pigmentary dermatoses

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INTRODUCTION

Reticulate pigmentary dermatoses (RPDs) are a group of uncommon disorders characterized by ephelid-like hyperpigmented macules coalescing to form reticular pattern, sometimes associated with scattered hypopigmented macules. Most of the classifications of RPDs rely on the sites of predilection, morphology, and arrangement of the lesions and the presence of hypopigmented lesions. Common RPDs include reticulate acropigmentation of Dohi, reticulate acral pigmentation of Kitamura [RAK]), Reticulate pigmented anomaly of the flexures (Dowling–Degos disease [DDD]), dyskeratosis congenita, Naegeli–Franceschetti–Jadassohn syndrome, dermatopathia pigmentosa reticularis, confluent and reticulate papillomatosis of Gougerot and Carteaud, dyschromatosis universalis hereditaria, and others.[1]

DDD was described initially by Dowling and Freudenthal in 1938 and Degos and Ossipowski in 1954. Later in 1978, Wilson Jones and Grice portrayed DDD as "demonstrating dusky dappled disfigurements and dark dot depressions and disclosing digitate downgrowths delving dermally".[2] RAK was first described by Kitamura and Akamatsu in 1943 in Japanese patients.

DDD and RAK are both rare genodermatoses following autosomal dominant pattern of inheritance with variable penetrance that predominantly affect the flexures and the extremities, respectively. Rebora and Crovato in 1983 first suspected that DDD and RAK were different phenotypic expressions of the same disease on the basis of their striking clinical and histopathological similarities.[3] Other authors have further emphasized on this overlap.[4,5] Literature search revealed only few (less than 50 families) with overlap features. We report a similar interesting case with the clinicohistopathological features of both disorders.

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CASE REPORT

A 28-year-old Indian male presented with multiple asymptomatic hyperpigmented macules over flexors, trunk, face, and extremities. The macules initially appeared on dorsum of both hands and feet during childhood and then on the extensor aspect of both forearms and legs. Gradually freckle-like lesions appeared on axillae, groin, and forehead around the age of 22 years, which progressed to the upper back, flexural aspects of forearms, inner aspects of thighs, nape, and lateral aspects of the neck. Interestingly, the interval between extensor and flexor involvement of the forearms was about 15 years; the evolution of lesions was characteristically distal in first 15 years then gradually became proximal. There was no history of similar lesions among the family members.

The mucocutaneous examination revealed numerous symmetrical brownish hyperpigmented macules, 1–2 mm in size in axillae, groin, flexor and extensor aspects of both forearms, dorsae of hands and feet, both shins and inner aspects of thighs [Figure 1a and b]. The lesions on the dorsae of hands, feet, and forearms were atrophic, whereas reticulate pattern was most pronounced on axillae, groins, and distal areas including proximal palms. Few darkly pigmented comedo-like papules and few atrophic scars were noticeable over upper back and neck [Figure 1c]. In addition, there were multiple palmar pits present with breaks in proximal palmer ridges. Multiple pitted follicular scars were also noted on bilateral malar, mandibular, and perioral regions of face with no antecedent history of acne over same sites. An accessory tragus on left side was an incidental finding.

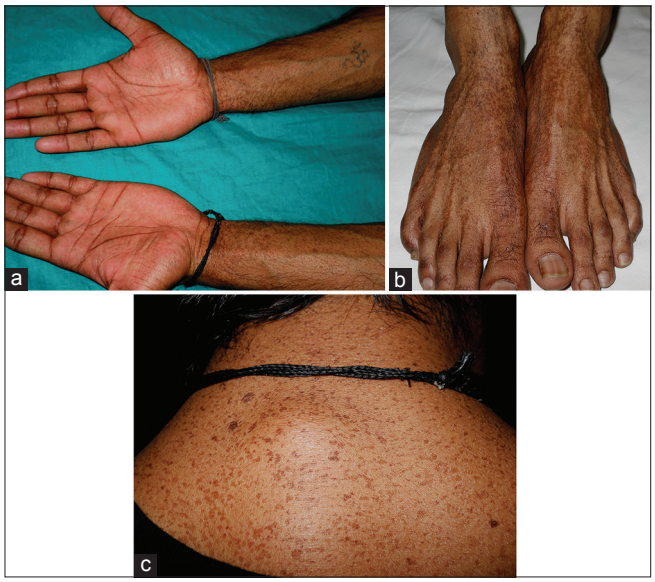

Figure 1: (a) Hyperpigmented macules over flexor aspect of forearms. (b) Hyperpigmented macules over dorsum of feet. (c) Hyperpigmented macules over back and dark dot follicles

Histopathological examination of skin biopsy taken from nape of neck revealed circumscribed foci of epidermal proliferation in the form of elongated and confluent rete ridges, which displayed antler-like branching at places. The proliferation of rete ridges was most prominent around plugged and dilated follicular infundibula. The tips of rete pegs were hypermelanotic owing to concentrated pigment, which was also scattered within the papillary dermal macrophages [Figure 2a]. Biopsy taken from dorsal aspect of forearm revealed histopathology almost similar to that of biopsy taken from nape of neck except mild perivascular lymphocytic infiltrates [Figure 2b]. These features are consistent with DDD. Genetic study to identify hereditary pattern or possible mutations could not be performed due to limited resources.

DISCUSSION

DDD, also known as reticulate pigmented anomaly of the flexures is characterized by a dysfunctional mutation in the keratin-5 (KRT5) on chromosome 12q gene, leading to abnormal pilosebaceous epithelial proliferation.[6,7] It classically manifests as an acquired progressive hyperpigmentation seen in females in their third or fourth decade. The sites involved are predominantly flexures (axillae, groins, intergluteal and inframammary folds, anticubital fossa, neck), whereas trunk, arms, face, scalp, and genitalia are also involved in some cases. Isolated involvement of the genitalia has also been reported.[8] Common additional findings include pitted follicular perioral and facial scars in patients with no previous history of acne and hyperkeratotic comedone-like follicular papules in the neck and/or back (dark dot follicles). Although usually asymptomatic, pruritus of the affected areas may be the only symptom.

Several recent reports have described an association of DDD with epidermal cysts, multiple keratoacanthomas, squamous cell carcinoma, abscess, hidradenitis suppurativa, seborrheic keratosis, and pilonidal cysts. Our case may be unique as having an accessory tragus; a condition apparently not previously reported.

Histopathological findings include acanthotic epidermis with irregular elongated rete ridges as filiform downgrowth in digitiform pattern (antler-like branching), keratin cysts in the epidermis

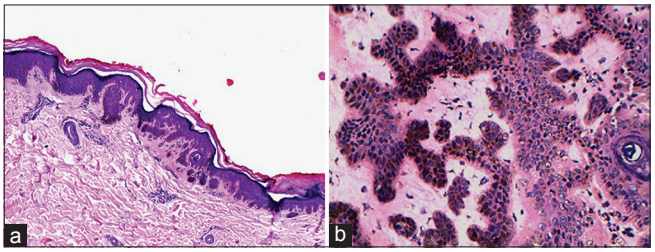

Figure 2: (a) Elongated and confluent rete ridges with antler-like branching and dilated follicular infundibula x10. (b) Elongated rete ridges with mild perivascular lymphocytic infiltrates x40

and dilated follicular infundibula. Suprapapillary epidermal thinning may also be seen. Diffuse deposits of melanin are found in the basal layer and varying quantities of melanophages in the papillary dermis with no quantitative increase in the number of melanocytes. Moderate hyperkeratosis, perivascular lymphohistiocytic infiltration within superficial dermis, and deep dermal fibrosis along with elongated rete ridges are additional features.

On the other hand, RAK usually manifests in first two decades of life and characterized by atrophic, slightly angulated freckle-like hyperpigmented macules in a symmetrical reticulate pattern on the acral skin (dorsum of hands and feet), which may further progress up to the proximal aspects of limbs, neck, and occasionally face.[9] The macules darken with time and continued sun exposure. Palmoplantar pits and breaks in the epidermal ridge pattern are also typical. Earlier the RAK cases were a majority from Japan but now the cases have increasingly been reported from rest of the world. Most of these have pointed toward autosomal dominant pattern of inheritance with variable penetrance, however, some intriguing patterns have been reported casting doubts about its pattern of transmission.[10] Histopathology is very similar to that of DDD, although epidermal atrophy, melanin incontinence, and perivascular lymphocytic infiltrate are more pronounced while lacking the antler-like pattern of the epithelial proliferation; however, these features are no longer regarded as distinguishing features.

There has been increasing reports of DDD–RAK overlap in the literature and some authors even suggest the term "Dowling–Degos syndrome" encompassing DDD, RAK, Haber syndrome, and acropigmentation of Dohi.[3-5,11] However, there are suggestions regarding the possibility of a chance association of multiple dermatoses, or atypical extensions of a single disease.

The case we report also showed acral hyperpigmentation, palmar pits, and breaks in dermatoglyphics similar to that of RAK and flexural macular lesions, comedo-like papules, and follicular pitted scars over the face, which were closely identical to that of DDD. Interestingly, the patient developed features of RAK in the first decade of life and of DDD in the third decade of life. There was no similar history of pigmentary lesions in the family, suggesting the sporadic nature of the disease.

The other RPDs such as Haber's syndrome[12] and Galli–Galli disease[13] were excluded due to the absence of persistent facial erythema or rosacea-like features and absence of acantholysis histopathologically, respectively. Other dyschromias such as dyschromatosis universalis hereditaria (DUH), and dyschromatosis symmetrica hereditaria (DSH) present as mottled hyperpigmentation and hypopigmented macules. The generalized variant of DDD has been described in the literature having hypopigmented or erythematous macules and papules but our case did not have such presentation.[14]

Hypopigmented macules have been noted in DDD-overlap cases also from India previously.[15] It may be emphasized that this case does not seem to be an incidental coexistence of DDD and RAK as we noted the classical histopathological findings of DDD at a site of classical RAK involvement. (dorsal aspect of hands). Moreover, atrophic macules were present even in the flexural aspects of forearms and DDD lesions, pointing to a true overlap. A similar blend has been described earlier.[3-5,10]

There is one recent study that analyzed the gene abnormalities of DDD and RAK. The authors concluded that the two might be different entities; however, they have referred to only 6 and 11 cases of DDD and RAK, respectively, where they mention three different gene defects localized in DDD and one in RAK. The involvement of multiple genes in genetically studied cases of DDD could also point to the polygenetic nature of the disease and admits possible allowance of RAK genes also in the same clinical spectrum. Again, as the mentioned cases in that study had relatively distinct clinical features of either type of manifestation, the explanation of other reported overlap cases would need the presumed co-existence of the two very rare genetic diseases together that would be statistically very unlikely.[16]

In summary, our case connects to the hypothesis that overlaps between DDD and RAK might be a single complex disease showing its different facets at different time points. However, more evidence might be needed to reach a definite conclusion.

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Conflicts of interest
There are no conflicts of interest.

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