

Generalised Dowling-Degos Disease: A Rare Variant with Hypopigmented Macules

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Abstract

Dowling Degos disease is characterised by hyperpigmented macules arranged in a reticulate pattern in the flexures. The rare hypopigmented variant shows characteristic acanthosis with antler like rete ridges but with pigment only at the tips of the rete ridges. We describe here a rare variant with coexistence of characteristic reticulate hyperpigmentation and hypopigmented macules, which has been described as generalised Dowling Degos disease.

Keywords: Dowling Degos disease; Hypopigmented; Generalised

Introduction

Dowling Degos disease (DDD) is an autosomal dominant disorder characterised by predominantly flexural pigmented reticulate macules and comedone like papules/ pitted scars on the face, neck and back [1]. Hypopigmented macules have been rarely described in DDD occurring either 1) as an isolated variant or 2) in addition to the typical flexural reticulate pigmented anomaly (described as a generalised variant of DDD) [2-5].

Case Report

A 38 year old female presented with multiple, tiny, light coloured flat lesions over the abdomen of 2 years duration. She also complained of multiple, tiny, dark coloured, flat lesions since one and half years, which initially appeared over the neck and chest and gradually involved the inframammary region, back, bilateral axillae and groins. She also gave history of multiple acne like lesions over the face since 15 years, which subsequently caused scarring. There was no history of similar lesions in other family members.

Cutaneous examination revealed multiple brown macules, distributed over the face, neck, chest, back, bilateral axillae and groins interspersed with pitted scars (Figure 1). There were multiple, hypopigmented to depigmented macules scattered in a confetti like pattern over the lower abdomen (Figure 2). Multiple comedone like lesions and pitted scars were present over the face and upper back. Oral mucosa, palms, soles and nails were normal. Based on the clinical features, a differential diagnosis of Dowling Degos disease and Dyschromatosis Universalis Hereditaria was considered.

Histopathological examination of the biopsy from the hyperpigmented macule over the right axilla showed acanthosis with marked and irregular elongation of thin, branching rete ridges (Antler's sign) with dermal delving and increased pigmentation throughout the basal layer and follicular plugging (Figure 3). Skin biopsy from the hypopigmented macule over the lower abdomen also showed elongation of the rete ridges but with pigmentation limited only to the tips of the rete pegs and decreased/absent pigmentation at other areas of the basal layer (Figure 4). The acanthosis and elongation of rete ridges, though typical were much lesser in the hypopigmented macule compared to the hyperpigmented macule. The presence of melanin throughout the basal layer in the hyperpigmented macule contrasting with pigment only at the tips of the rete ridges was confirmed on Fontana- Masson stain (Figure 5). These features were consistent with the diagnosis of generalised Dowling Degos disease. Patient was treated with topical Tretinoin (0.025%), although with unsatisfactory results.

Discussion: Dowling-Degos disease (Synonyms: Reticulate

pigmented anomaly of the flexures, dark dot disease) was first described by Dowling and Freudenthal in 1938 and by Degos and Ossipowski in 1954.

DDD has been reported to be caused by loss of function mutations in the keratin 5 gene (KRT5) situated in the keratin gene cluster on 12q13, resulting in haploinsufficiency [4,6]. However KRT5 mutations are absent in almost half of the familial as well as sporadic cases [3,7]. Recently mutations in *POFUT1* (encoding Protein O- fucosyltransferase 1) and *POGLUT1* (encoding Protein O- Glucosyltransferase 1) have been identified in this group of patients [7-9]. A possible genotype-phenotype correlation has been recorded with predominant involvement of non-flexural areas in patients with *POGLUT 1* mutation compared to those with KRT5 mutation.



Figure 1: Multiple discrete hyperpigmented macules with pitted scars on neck, chest (A), back (B), both axillae (C&D). Prominent comedone like lesions and pitted scars on back (B).

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Figure 2: Multiple discrete hypopigmented to depigmented macules on abdomen.

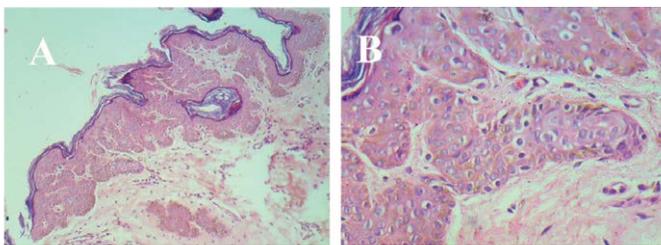


Figure 3: Skin biopsy from hyperpigmented macule in axilla (H&E Stain): 10x (A) and 40x (B): showing multiple finger like downgrowths of the epidermis with increased melanin pigmentation throughout the basal layers.

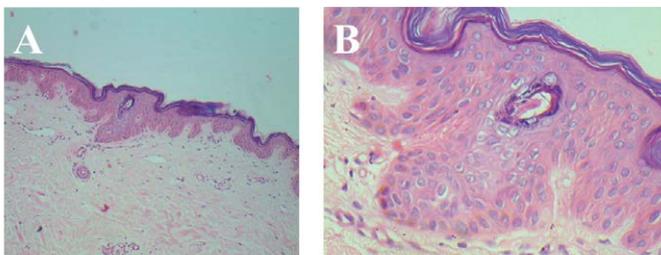


Figure 4: Skin biopsy from hypopigmented macule on abdomen (H&E Stain): 10X (A) and 40X (B): showing finger like downgrowths of the epidermis with melanin pigmentation only at the tips of the rete ridges.

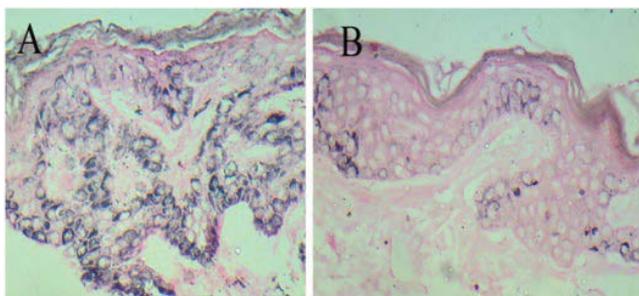


Figure 5: Skin biopsy from hyperpigmented macule (A) and hypopigmented macule (B): Fontana-Masson stain: (A): showing marked melanin pigmentation throughout the basal layers, (B): showing melanin pigmentation only at the tips of the rete ridges.

Although, DDD typically affects the flexural sites of axillae and groins, involvement of other sites such as vulva, back and scalp can occur. Rare variants including an asymmetrical pattern and follicular variant have been described. Occasionally DDD has been reported to be associated with hidradenitis suppurativa, epidermal cysts and keratoacanthoma. DDD also has been reported in association with other reticulate pigmentary disorders including reticulate acropigmentation of Kitamura (RAPK) and Dyschromatosis universalis hereditaria (DUH). However it is possible that these cases may be variants of DDD and not co-occurrence of two disorders.

Histopathological features of DDD include a distinctive type of acanthosis characterised by irregular elongation of thin branching rete ridges which tend to join giving a characteristic “deer antler” like appearance. There is increased melanin in the basal layers especially at the tips of the rete ridges. Follicular plugging may be observed occasionally. A histopathological variant of DDD is Galli- Galli disease, which is characterised by suprabasal acantholysis.

Hypopigmented lesions have been only rarely described in DDD. There is a single case report of DDD in an African- American woman presenting only as hypopigmented macules [2]. A generalised variant of DDD has been described mostly in Asians with hypopigmented lesions in addition to the classical reticulate pigmented pattern. The histopathological features of the hypopigmented lesions are similar to that seen in the hyperpigmented macules of DDD, with both showing the classical acanthosis and differing only in the distribution and amount of melanin pigment which is present only at the tips of the rete ridges in hypopigmented lesions. Wu and Lin reported that hyperpigmented macule had lesser degree of acanthosis compared to the hypopigmented macule [3]. However the reverse was observed in our case; the hyperpigmented macule showed more marked acanthosis compared to the hypopigmented macule. Interestingly, few of the cases of DDD described with hypopigmented lesions have shown suprabasal acantholysis (Galli- Galli variant), thus prompting the hypothesis that hypopigmentation may be an expression of subclinical acantholysis [3,10]. Our case however, did not show any evidence of suprabasal acantholysis. Another hypothesis for coexistence of hypopigmented as well as hyperpigmented lesions in DDD has been explained by Li et al., who identified *POFUT1* mutation in two Chinese families of generalised DDD. Based on the functional analysis of *POFUT1* and its role in melanin synthesis and transfer in a zebrafish model, they suggested that hypopigmented macules in DDD result from an impaired ability to synthesize melanin in melanocytes with loss-of-function mutation in *POFUT1*. Notably, a common mutation in exon1 of *KRT5* gene [c.C10T (p.Gln4X)] has been reported in two cases of DDD with hypopigmented lesions, one of which was a Galli-Galli variant [4,10]. These examples point to the possibility of specific genotypes causing hypopigmented lesions in DDD.

Also, important to note is that generalised DDD needs to be differentiated from 1. Dyschromatosis universalis hereditaria (DUH) which is also characterised by generalised mottled pigmentation (Hyper and hypo-pigmented macules) and 2. Acropigmentation of Dohi, which is characterised by hyperpigmented and hypopigmented macules on the dorsal aspects of the extremities. Histopathology can easily differentiate DUH as well as Acropigmentation of Dohi from DDD as both of them lack the characteristic pattern of acanthosis seen in DDD. DUH and acropigmentation of Dohi are distinct reticulate pigmentary disorders caused by proven specific gene defects (*ABCB6* and *ADAR1* respectively).

This case thus highlights the rare occurrence of hypopigmented

macules in a case of Dowling-Degos disease and the importance of differentiating this variant of Dowling-Degos disease from other reticulate pigmentary disorders with hypo- and hyperpigmentary macules.

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