Original Research Article

Indian Journal of Pathology: Research and Practice
Volume 6 Number 4, October - December 2017 (Part-II)
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.6417.48

Dowling-Degos Disease: A Clinicopathological Study

M. Supriya*, Syeda Naushaba Masood, Atiya Begum*****

*Assistant Professor **Post Graduate ***Professor, Department of Pathology, Deccan College of Medical Sciences, Santosh Nagar, Kanchanbagh, Hyderabad, Telangana 500058, India.

Abstract

Background: Dowling-Degos Disease (DDD) is a rare genetic disease of the skin having an autosomal dominant inheritance. It is grouped under reticulated pigmented anomalies and manifests as symmetric, progressive, pigmented macules over flexures, scattered comedo-like lesions and pitted acneiform scars. Histopathology is required for definitive diagnosis and to distinguish it from other reticulate pigmentary genodermatoses. *Aims:* 1. To show the existence of this rare disease in the local population. (2) To stress on the clinico-pathological correlation for the definitive diagnosis of the disease. *Materials & Methods:* Punch biopsies of skin received by the Department of Pathology over a span of two years with Dowling Degos Disease as one of the differential diagnosis, were included in the study. The biopsies were processed as per standard protocol. Diagnosis was confirmed by the histopathological examination. *Result:* A total of six cases were included in the study, out of which four were histologically confirmed as DDD and one case had features overlapping with Reticulate Acropigmentation of Kitamura (RAPK). The study showed female preponderance. Four cases had family history. The clinical and histopathological findings of each case are discussed. *Conclusion:* Dowling Degos Disease may not be a rare entity. It should be considered as one of the differential diagnoses for pigmentary disorders. With combined clinical and histopathological evaluation, more cases may come into light in the future and DDD may not remain as a rare disorder.

Keywords: Dowling-Degos Disease; Genodermatoses; Reticulate Pigmented Disorders.

Introduction

Reticulated pigmented anomalies is a broad category comprising of various dermatological conditions with clinical presentation of reticulate, retiform, or fishnet-like hyperpigmentation and histological evidence of increased intra- epidermal melanin. Dowling-Degos Disease (DDD) is one such condition included under this group [1].

Dowling-Degos Disease is a rare genetic disease of the skin having an autosomal dominant inheritance pattern. It is also called as dark dot disease [2] with heavily pigmented symmetric macules as the clinical manifestation. These macules increase in number and size, thereby coalescing on flexural skin – chiefly in the axillae and groin. Other sites include infra-mammary and inguinal folds, antecubital and popliteal fossae, and inter-gluteal clefts [1]. Gene mapping studies have shown the association of this disorder with loss-of-function mutation in the keratin 5 gene (KRT5) [3].

Dowling-Degos Disease needs to be differentiated from other genodermatoses (reticulated pigmented anomalies) such as Dyschromatosis Symmetrica Hereditaria (DSH) also called Reticulate Acropigmentation of Dohi (RAPD), Dyschromatosis Universalis Hereditaria (DUH) and Reticulate Acropigmentation of Kitamura (RAPK) [4], Galli-Galli Disease and Haber's Disease [3] as these disorders have similar clinical presentation to DDD.

Materials & Methods

This is a retrospective study done in the department of Pathology for a period of two years. Out of 365

Corresponding Author: M. Supriya, Department of Pathology, Deccan College of Medical Sciences, Santosh Nagar, Kanchanbagh, Telangana 500058, India.
E-mail: supriyamed.sunki@gmail.com

(Received on 27.08.2017, **Accepted on** 14.09.2017)

punch biopsies of skin received by the Department of Pathology in a span of two years, six cases had Dowling Degos Disease (DDD) as one of the differential diagnosis which was the principle criteria for the inclusion of these cases in our study and all the other skin biopsies were excluded .

Patient details such as age, sex, clinical history, family history, differential diagnosis and other details were noted from request forms. From the clinical information provided, none of the patients of these six cases had association with any other diseases - medical, surgical or gynecological and the routine blood investigations were within normal limits. The tissue was formalin fixed and paraffin embedded in entirety.

Sectioning and H & E staining were done as per standard protocol. Diagnosis was confirmed by histopathological examination under light microscopy. Molecular studies on these cases have not been done.

Results

Of all the skin biopsies received during the two year study period, only six had the differential diagnoses of DDD. Five cases were histologically confirmed as DDD of which one had features overlapping with Reticulate Acropigmentation of Kitamura whereas one case was diagnosed as chronic lichenoid dermatosis. Majority of the cases were in the age group of 15-30 years and mean age at presentation was 29 years. Female preponderance (60%) was present in the study.

Family history was positive in four cases (P1, 2, 3 & 5). Of these one patient (P1) gave a history of similar complaints in his mother. Other two cases (P2& 3) were of the same family (mother and son) (Table1). Case (P5) had a family history of three generations. It was noticed in the patient's grandmother (pigmented lesions all over the body similar to the patient) and her ancestors, which was passed onto the father and paternal relatives (uncles, aunts and cousins).

Table 1: Clinical & histopathological diagnosis of individual case

S. No	Age	Sex	Clinical presentation	Site of biopsy	DD	HP Diagnosis
P1.	20 y	M	Generalised hyperpigmented macules over upper limbs, trunk and neck. Family history-present	Hyperpigme-nted macule on Left fore-arm	RAPK, DSH, DDD	DDD
P2.	19 y	M	Multiple, symmetrical, reticulate hyperpigmentation on neck,wrist, hands trunk, groin ,thighs Pitted scars on bilateral palms Acneiform eruption over face (predominantly in perioral area & nasolabial folds) pinnae, upper trunk & thighs. Asymmetric hypopigmented macules present. Family history-present	a)hyperpigme-nted macule on neck & b)hyperpigme-nted macule on hand	RAPK, DDD, DUH	DDD + RAPK
P3.	49 y	F	Small round hyperpigmented macules on face, pinnae, upper trunk, thighs, axillae, infra-mammary area, groin & cubital fossae. Family history-present	Hyperpigment-ed macule on Infra Mammary.	?DDD	DDD
P4.	35 y	F	Reticulate hyperpigmented macules over face(Fig-4), upper trunk, thighs, infra-mammary folds, buttocks & vulva Hydradenitis suppurativa. Family history-absent	hyperpigmented macules on Infra Mammary.	?DDD	DDD
P5.	27 y	F	Diffuse well defined hyperpigmented macules. Few hypopigmented macules on arms Palmar pits. Family history-present	Hyperpigment-ed macule Right Infra-clavicular Area.	DDD, RAPK.	DDD
P6.	24 y	F	Hyperpigmented macules on bilateral upper limbs, neck, chest and abdomen. Family history-absent	Hyperpigment-ed macule on abdomen.	DDD, Lichenoid dermatitis	Chronic lichenoid dermatosis

Table 2: Comparison with other studies

Findings	Bhagwat et al (2009)[5]	Sharma R (1996)[6]	Wititsuwannakul et al(2013)[4]	Zimmermann et al(2011)[2]	Present study
No. of Cases	3	4	3	1	5
Age (mean)	27 yrs	19.25	63 yrs	51 yrs	29 yrs
Male: Female ratio	1:2	1:3	2:1	-	2:3
Family history	3 /4	3/3	All three cases belong to same family	+	4/5
Associations	-	Milia (in case 1)	-	-	Hidradenitissup purativa (in P4)

Table 3: Differential diagnoses of DDD and their histopathological features

Disorder	Histological Features
Dyschromatosis Symmetrica Hereditaria (DSH) Or RAPD	Increased basal pigmentation in hyperpigmented areas; Reduced pigmentation, decreased no. of melanocytes in hypopigmented areas.[3]
Dyschromatosis Universalis Hereditaria (DUH)	Variable Pigmentation Pigment incontinence.[3]
Reticulate Acropigmentation of Kitamura (RAPK)	Basal hyperpigmentation with intervening epidermal atrophy Club shaped elongations of rete ridges .[3]
Galli-Galli Disease	Suprabasal acantholytic lacunae Slightly parakeratotic roof without dyskeratosis Basal hyperpigmentation Digitate downgrowths of rete ridges.[3]
Haber's Disease	Seborrheic keratosis like papules Histologically similar to DDD, but there is presence of facial rosacea like rash – photosensitive. [2]

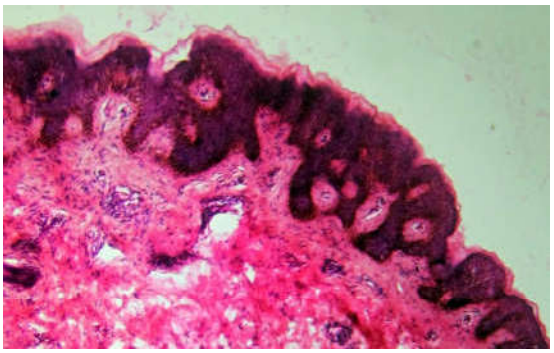

Fig. 1: Epidermis shows acanthosis with downward filiform proliferation of rete ridges associated with clubbing, budding and lateral fusion of tips. (H and E section, low power-10x)

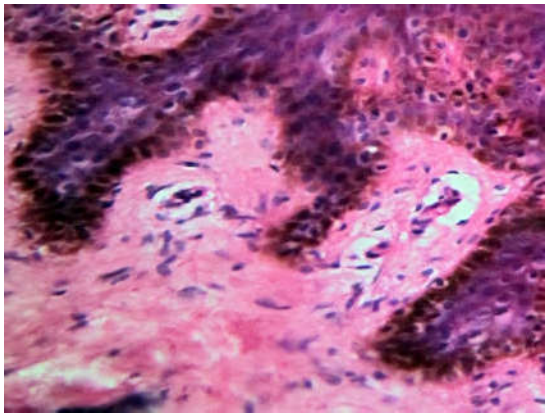

Fig. 2: Prominent pigmentation at the tips of rete ridges (H and E section, high power-40x)

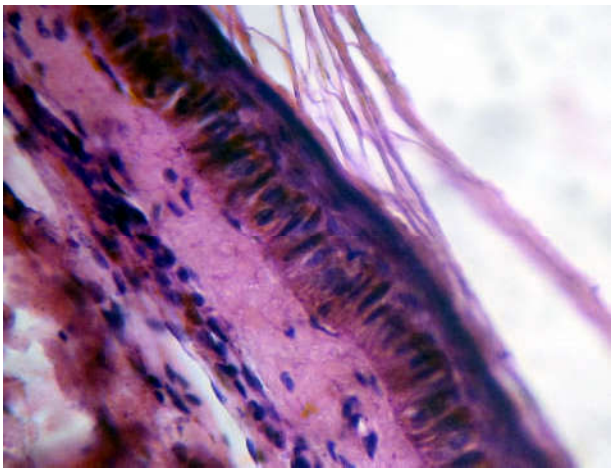

Fig. 3: Atrophy of epidermis–a feature of RAPK (H and E section, low power -10x)

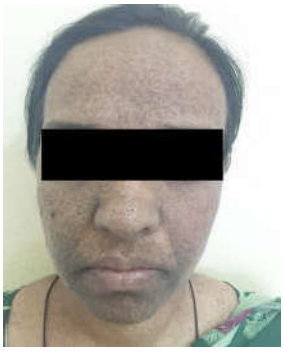

Fig. 4: Reticulate hyperpigmentation on face

In the present study, four cases (P1, P3, P4, P5) with the histolopathological diagnosis of Dowling Degos had common features of mild orthokeratotic hyperkeratosis with epidermis showing filiform proliferation of rete ridges (Fig. 1) and basal layer with prominent pigmentation, (Fig. 2) also mild to moderate peri-vascular lymphohistiocytic infiltrate is noted all the four cases irrespective of the site of biopsy (Table 1).

In Case (P2), the punch biopsy taken from neck had histological features of epidermis with filiform downgrowth of rete ridges and in that taken from the dorsum of hand showed presence of epidermal atrophy (Fig. 3). These contrasting epidermal features along with palmar pitting supported the conclusion that in this case Dowling Degos disease had overlapping features of Reticulate Acropigmentation of Kitamura (RAPK). Case P6 had no histological features of Dowling Degos and it was reported as Chronic Lichenoid dermatoses.

Discussion

Dowling Degos Disease is an autosomally inherited disorder. Though, it has been reported as a rare entity in the literature [2,3], we have received a total of five cases of DDD in a span of two years thus questioning its rarity. Fewer incidences could possibly be due to poor awareness or lack of recognition of the condition and diagnostic confusion. This disorder is shown to have female preponderance [2] which is also depicted in our study. It presents initially around puberty and thereafter it spreads [4].

The numbers of cases in our study (5cases) were comparable with the study done by Sharma R [6] (4 cases) (Table 2). The mean age of presentation was in younger adults (29yrs). In the studies done by Bhagwat et al [5] (27yrs) and Sharma R [6] (19.25) also showed the affliction in younger age group. Present study had positive family history (4 cases) which was also observed in other studies [2,4,5,6].

Genetic studies have shown polygenic inheritance of DDD. The loss of function mutation of KRT 5 (Keratin 5) gene mapped on chromosome 12q13 has been mentioned in the literature [3]. Other studies have mapped gene defects on chromosome 20q11, 17p33.3 & 3q13 [7].

Hence being a genetically inherited disease, the patients usually present with a family history. The pedigree chart of case P5 shows that the disease has not skipped any generation (dominant trait) and it has been transmitted to both male and female offsprings (autosomal – inheritance). However not all offsprings are affected as the disease has variable penetrance [2].

One case (p 4) had no positive family history which may be due to the fact that the patient is unaware of the presence of this disease or it could be of sporadic origin. Sporadic cases rarely occur and it has been reported by Mohan L et al [8].

As the present study was done retrospectively, the patients were either not traceable or were unwilling for genetic study to identify the mutations.

In the present study 5 cases were diagnosed on histopathology as Dowling Degos Disease. The classical histopathological features of DDD include moderate orthokeratosis or hyperkeratosis [2] with thinning of suprapapillary epithelium [1], are filiform or digitate or thin branch-like downgrowths of rete ridges, also described as "antler-like" pattern [2]. Increased pigmentation of basal layer, more pronounced at the tips of the rete ridges is observed. Some studies mention presence of variably dilated pilo-sebaceous follicles with follicular plugging along with comedo like lesions. Other features include melanin incontinence and mild to moderate superficial perivascular infiltrate of lymphocytes and histiocytes in papillary dermis [3]. The two common findings constantly present in all the positive cases of our study are filiform projection of rete ridges and increased pigmentation of basal layer. Thus we have arrived at a conclusion that these two features form the histologic hallmark of DDD.

One case (P2) had features of DDD overlapping with Reticulate Acropigmentation of Kitamura (RAPK). In RAPK the hyperpigmented macules are present initially on the dorsum of the hand and feet, later it progresses in a reticulate fashion involving the limbs, trunk and face [1]. Histologically the features overlap with DDD apart from the presence of epidermal atrophy [3], which is not present in DDD. The overlap in the presentation may be because DDD and RAPK are different manifestations of same entity [1]. It has also been mentioned in the study done by Muller et al, that the disease under the group of reticulate pigmentary anomalies are varying expressions of same disorder [9].

The sixth case (P6) had clinical differential diagnoses of DDD or lichenoid dermatitis. Histopathological examination of this case revealed thinning of epidermis with hyperkeratosis, parakeratosis and shortening of rete ridges along with heavy lymphocytic infiltrate in the reticular dermis and proliferating fibro-collagenous tissue in the deeper dermis, thus favouring the diagnosis of Chronic Lichenoid Dermatosis. Thus asserting the

necessity of histopathological examination and it also points out the wide range of clinical differential diagnoses.

Two forms of DDD have been described namely, Classic DDD which shows reticulate hyperpigmentation in flexural areas and Generalised DDD that shows generalised reticulate hyperpigmentation at the trunk, limbs and also reticulate hypopigmented macules unlike the classical form [4]. Our study had three cases (P1,3&4) with classic DDD and two cases (P2&5) with Generalised DDD presentation.

The less commonly associated clinical features of DDD include pitted peri-oral scars, hyperpigmented comedones, hidradenitis suppurativa, keratoacanthomas, seborrheic keratoses multiple cysts and abscesses; squamous cell carcinomas [3]. In our study one case (P4) had coexisting hidradenitis suppurativa.

The list of differential diagnoses of Dowling Degos Disease is long. In our study we are discussing those diseases which are closely related to our case series. (Table 3).

A few other differential diagnoses which have been mentioned in other studies include acanthosis nigricans [2], Familial dyskeratotic comedones and acne conglobata [5].

Conclusion

Dowling Degos Disease may not be a rare entity. It should be considered as one of the differential diagnoses for pigmentary disorders. With combined clinical and histopathological evaluation, more cases may come into light in the future and DDD may not remain as a rare disorder.

References

1. Kovarik CL, Spielvogel RL, Kantor GR. Pigmentary disorders of the skin. In:Lever's Histopathology of the skin, 10th Edition, Lippincott Williams & Wilkins; 2009.p.689-90.
2. Zimmermann CC, Sforza D, Macedo PM, Azulay-Abulafia L, Alves MFGS, Carneiro SCS. Dowling-Degos disease: classic clinical and histopathological presentation. *An Bras Dermatol* 2011;86(5):979-82.
3. Disorders of pigmentation. In: Weedon D. Skin Pathology, 3rd Edition. London: Churchill Livingstone; 2010.p.295-96.
4. Wititsuwannakul J, Noppakun N. Generalized Dowling – Degos Disease: Case Reports. *Ann Dermatol* 2013;25(3):360-3.
5. Bhagwat P V, Tophakhane R S, Shashikumar B M, Noronha T N, Naidu V. Three cases of Dowling Degos disease in two Families. *Indian J Dermatol Venerol Leprol* 2009;75:398-400.
6. Sharma R. Dowling-Degos disease. *Indian J Dermatol Venereol Leprol* 1996;62:27-9.
7. OMIM.org [Internet]. Maryland: Mckusick-Nathans Institute of Genetic Medicine. C1986-[updated 2016 Jun 23;cited 1986 Jun 23]. Available from: http://www.omim.org/entry/179850.
8. Mohan L, Bhatiya P S, Mishra R, Singh K K, M. Dowling - Degos disease. *Indian J Dermatol Venereol Leprol* 1991;57:251.
9. Muller C S L, Tremezaygues L, Pfohler C, Vogt T. The spectrum of reticulate pigment disorders of the skin revisited. *Europ J Derm* 2012;22:596-604.