Dowling-Degos Disease: Case Report and Literature Review.

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ABSTRACT:

MANEEPRASOPCHOKE P, PATTANAPRICHAKUL P. DOWLING-DEGOS DISEASE: CASE REPORT AND LITERATURE REVIEW. THAI J DERMATOL 2017; 33: 267-274.

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Dowling-Degos disease (DDD), a rare autosomal dominant inherited genodermatosis, commonly affects post-pubertal individuals by presence of progressive reticulated hyperpigmentation and small hyperkeratotic papules predominantly at flexural area and skin folds. Involvement of face, trunk and extremities has also been reported. We report a case of 65-year-old woman with underlying disease of Schizophrenia, who presented with asymptomatic hyperpigmented lesions on the abdomen, both axilla, inframammary regions and both groins for 20 years. The patient reported having similar cutaneous findings in her mother who had passed away a long time ago. Histopathologic findings revealed digitate downward growth of rete ridges with some horn pseudocysts and basal hyperpigmentation without acantholysis.

Key words: Dowling-Degos disease, reticulate pigmentation

บทคัดย่อ :

พิชญา มณีประสพโชค เพ็ญวดี พัฒนปรีชากุล รายงานผู้ป่วยโรค DOWLING-DEGOS

วารสารโรคผิวหนัง 2560; 33: 267-274.

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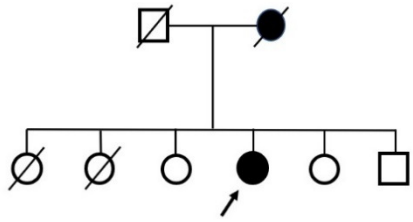
โรค Dowling-Degos เป็นโรคที่ทำให้เกิดรอยดำลักษณะเป็นร่างแหบริเวณตำแหน่งซอกพับต่างๆของร่างกาย โดยทั่วไปมักจะไม่มีอาการ อย่างไรก็ตามมีรายงานว่าสามารถพบลักษณะรอยโรคที่บริเวณใบหน้า ลำตัว และแขนขาได้ รายงานฉบับนี้เป็นการนำเสนอผู้ป่วยหญิงอายุ 65 ปี มีโรคประจำตัวเป็นโรคจิตเภท มาด้วยรอยดำลักษณะเป็นร่างแห ที่บริเวณท้อง, รักแร้, ใต้ราวนมและขาหนีบทั้ง 2 ข้าง มาเป็นเวลา 20 ปี นอกจากนี้พบว่ามารดามีประวัติมีลักษณะผื่นเช่นเดียวกับผู้ป่วย จากผลการตรวจทางพยาธิวิทยา พบลักษณะของ digitate downward growth of rete ridges และพบว่ามี horn pseudocysts และ basal hyperpigmentation โดยที่ไม่พบ acantholysis

คำสำคัญ: Dowling-Degos disease, รอยดำลักษณะเป็นร่างแห

Case report

A 65-year-old Thai female presented with 20-year history of progressive, reticulate, brownish patches without any other symptoms associated with the lesions on the skin. She reported the similar lesions appeared in her mother who had already passed away more than twenty years ago. She has four sisters and one younger brother and none of them experience this similar lesion until now. (See family pedigree)



The patient has been diagnosed of Schizophrenia for thirty years. The patient has been treated with long-term oral risperidone and recently-added clorazepate according to the disease activity which has been in partial remission for many years. Despite asymptomatic presentation of the skin pigmentation, the patient and the family were concerned with the progressivity and extensive distribution of the lesion. Therefore, the patient sister insisted to escort her to see dermatologist for evaluation of this condition. On physical examination, a good conscious, well cooperated, Thai woman with large-reticulated hyperpigmented patches with few comedo-like lesions on the abdomen extended to involve both inframammary region. There are also similar lesions on both axilla, genitalia and both groins. Ill-defined hyperpigmented patches of the forehead and perioral area without perioral pitted scar. Mucosa, hair, nail and other system are unremarkable. Skin biopsy was performed at the pigmented patch on the abdomen and revealed downward epidermal hyperplasia with basal hyperpigmentation and focally presence of horn pseudocysts without acantholysis. Mild superficial perivascular lymphocytic infiltrate is present with minimal melanin incontinence in papillary dermis. According to clinical findings and histological examination as mentioned, the

diagnosis of Dowling-Degos disease has been concluded. We were unable to obtain genetic studies from this patient.

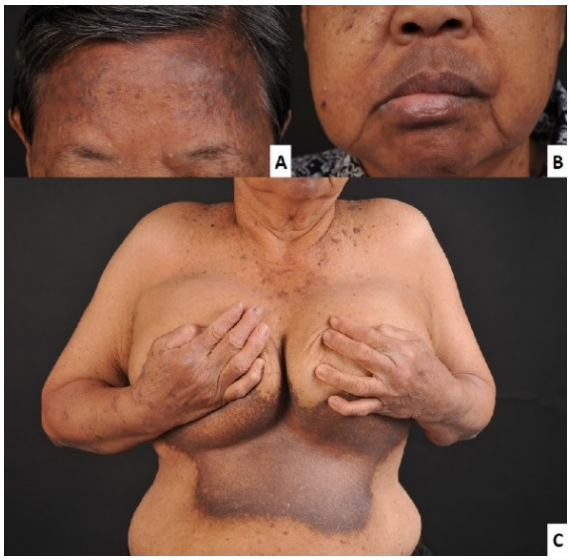


Figure 1.1 A-C; Reticulated hyperpigmented patches on forehead, perioral and inframammary involving abdomen

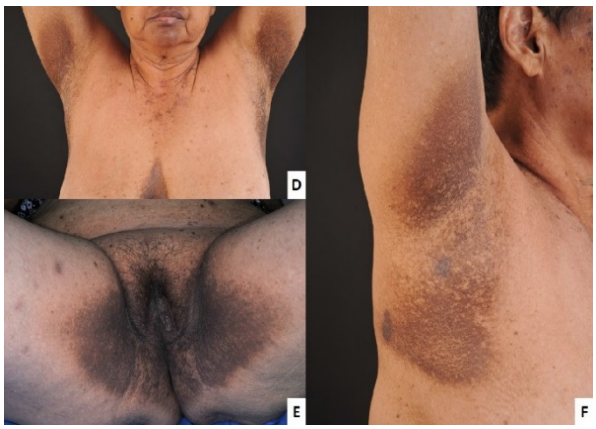


Figure 1.2 D-F; Flexural reticulate hyperpigmentation on both axilla, inguinal regions and genitalia

Discussion

Dowling-Degos disease (DDD) was first described as a distinct genodermatosis in 1938 and 1954 by Degos and Dowling.[1,2] The disease is characterized by flexural pigmented reticulate macules and patches with comedo-like papules on the back and the neck and perioral pitted scars in some cases. Most of the patients are asymptomatic, however, pruritus of affected flexural areas may be the sole symptom in DDD. Dowling-Degos disease is slowly progressive but not life threatening and most of the cases experience the onset at puberty and early adolescent.[3] The disease appears to be an autosomal dominant inheritance with major gene mutation has been documented as loss-of-function mutation in keratin 5 gene (*KRT5*) which also expressed in its acantholytic variant, Galli-Galli disease.[4-6] Moreover, mutations in *POGLUT1* or *POFUT1* gene has been found in DDD which lacks *KRT5* mutation.[7,8] DDD has been found to affect both sexes equally but a female predominance has been noted in some surveys.[9]

A rare association has been described in DDD with several conditions including hidradenitis suppurativa with multiple epidermal cysts, multiple keratoacanthoma, multiple seborrheic keratosis, reticulate acropigmentation of Kitamura, and Darier disease.[10-13] The novel mutation has been found in *PSENEN*, encoding protein presenilin enhancer gamma-secretase

subunit. Four families of *PSENEN* mutation carriers presented a phenotype combining

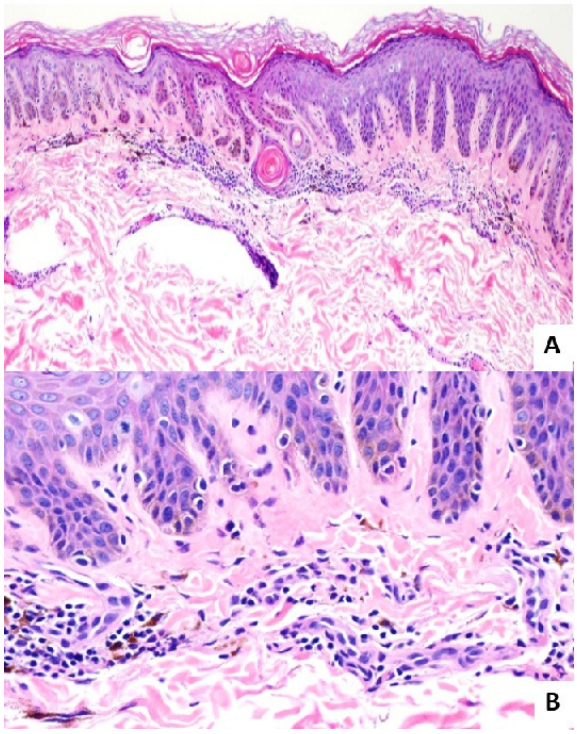


Figure 2; Histological examination reveals elongated, thinning rete ridges with basal hyperpigmentation and few horn pseudocysts with superficial perivascular infiltrate of lymphocytes, melanophages and melanin in papillary dermis.

Dowling-Degos disease and hidradenitis suppurativa. Notch signaling may play a role in pathogenesis of this condition.[14]

The clinical presentation may be varying from classic DDD that intense involvement with a brownish black color patches and mottled hyperpigmentation on flexural area to less severe conditions as stippled brown shades. Rarely, the macules may be hypopigmented. In addition, generalized DDD has the characteristic of classic DDD and generalized reticulate hyperpigmentation at trunk and limb, as observed in our case.[15] Usually, verrucous papillomatosis is not present, as might be seen in acanthosis nigricans. If the patches are palpable, it is because of lichenification from external rubbing and at times wrinkled appearance may be observed. The margins may show tiny pigmented comedones.[16] Moreover, speckled macules involving the dorsum of the hands, the proximal nail folds, or the scrotum, diffuse penile pigmentation may be seen. Genital involvement in both sex has been reported.[17,18]

Differential diagnosis of DDD includes it acantholytic variant namely Galli-Galli disease, reticulate acropigmentation of Kitamura, Haber syndrome, epidermolysis bullosa simplex with mottled pigmentation, reticulate hyperpigmentation in systemic sclerosis, confluent and reticulate papillomatosis of Gougerot-Carteaud; all of which share similar and overlap features of reticulate or mottled hyperpigmentation. List of differential diagnosis is shown in Table 1.

Table 1 Table of differential diagnosis

Disease	Inheritance	Genetic defect	Clinical appearance	Histopathology
DDD	AD/sporadic	KRT 5, POGLUT1, POFUT1, PSENEN	Adult and early adolescent onset with flexural reticulated hyperpigmentation, comedone-like papules and perioral pitted scars	Thin proliferative rete ridges, basal hyperpigmentation with follicular plugging and pseudocyts
Galli-Galli disease	AD/sporadic	KRT 5	Adult and early adolescent onset with macular and papular reticulate hyperpigmentation at flexural areas	Similar to DDD, with suprabasal acantholysis
Kitamura's disease[22]	AD	ADAM 10	Starts in first or second decade of life with atrophic acral reticulate pigmentation and palmar pits	Epidermal atrophy with elongation and thinning of the rete ridges with basal hyperpigmentation
Haber syndrome[23]	AD	Possible same disorder as DDD	Childhood onset with rosacea-like facial eruption, reticulated hyperpigmentation of flexures, comedones on the back and neck, and pitted facial scars	Elongation of rete ridges with suprapapillary thinning, basal hyperpigmentation, and dilated follicles
EBS with mottled pigmentation	AD/sporadic	KRT 5	Begins in infancy with erosions or blisters after minor injury or friction with a mottled pigmentation of trunk and limbs	Cell-poor subepidermal separation with focal basal hyperpigmentation and melanin incontinence without an inflammatory infiltrate
SSc with reticulate hyperpigmentation[24]	Sporadic	-	Adult onset with progressive thickening of skin and fibrosis of internal organ, Raynaud's phenomenon, reticulate pigmentation predominantly on the trunk	Thickening and hyalinization of dermis and subcutaneous fat with atrophy of adnexal structure and focal basal hyperpigmentation

Disease	Inheritance	Genetic defect	Clinical appearance	Histopathology
Confluent and reticulate papillomatosis of Gougerot-Carteaud	Sporadic	-	Usually adult onset with reticulated hyperpigmentated patches on trunk	Church-spire appearance of papillomatosis without basal hyperpigmentation nor acanthosis. Occasional presence of *Malassezia* yeasts
Acanthosis nigricans[2]	AD/sporadic	Sometimes FGFR3	Adolescent or adult onset with dark, velvety thicken skin in flexural area.	Church-spire papillomatosis without acanthosis nor basal hyperpigmentation

DDD = Dowling-Degos disease, EBS = epidermolysis bullosa simplex, SSc = systemic sclerosis, AD = autosomal dominant, KRT = keratin, POGLUT1 = Protein O-Glucosyltransferase 1, POFUT1 = Protein O-Fucosyltransferase 1, ADAM 10 = ADAM metallopeptidase domain 10, FGFR3 = fibroblast growth factor receptor 3.

Histopathologically in Dowling-Degos disease, elongation of rete ridges with basal pigmentation and thinning of the suprapapillary epithelium, melanin incontinence, and perivascular lymphohistiocytic infiltration is present. The elongated proliferations are composed of regular pigmented basal keratinocytes.[9]

To date, there has been no effective medical treatment for DDD. Topical retinoic acids, topical steroids, hydroquinone, and systemic retinoids have been used without definite success. Laser treatment, such as fractional Er: Yag laser in combination with Q-switched Nd: YAG, fractional carbon dioxide laser, and intense pulsed light, has been reported to show favorable outcome is some cases of DDD.[19-21]

Our present DDD patient has been evaluated for the other cause of cutaneous hyperpigmentation which show no association with either the underlying disease of Schizophrenia or her previous and current medication. After informing the patient and a caregiver of the definite diagnosis of her cutaneous condition, there is no further treatment due to the patient's understanding and education of non-life-threatening condition of DDD.

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