

Dowling-Degos disease: a rare spectrum of the reticulate pigmentary disorders.

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ABSTRACT :

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Dowling-Degos disease (DDD) is a rare genetic disorder of the skin. It is characterized by reticulate brownish pigmentation predominantly in flexural areas, comedo-like papules on the back and neck and pitted perioral or facial scars. We reported a case presented with hyperpigmented macules in his axillae, cubital fossae, popliteal fossae, neck, face, back and dorsa of both hands. There were comedo-like papules and pitted scars at his upper back. The histopathology shows the characteristic findings of Dowling-Degos disease including lentiginous hyperplasia with thinning of the suprapapillary plates and increased pigmentation of the basal layer. Various similar conditions should be considered in the differential diagnosis. At present, most of the treatment options are not satisfactory.

Key words: Dowling-Degos-Disease, hyperpigmentation, reticulate

บทคัดย่อ :

ขวลิศ ทรัพย์ศรีสัญชัย, นฤมล ศิลปอาษา รายงานผู้ป่วย DOWLING-DEGOS DISEASE 1 รายซึ่งเป็นกลุ่มโรคที่มีรอยดำเป็นร่างแหและพบได้น้อย วารสารโรคผิวหนัง 2555; 28: 204-208.

ภาควิชาดจวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล

โรค Dowling-Degos เป็นโรคทางพันธุกรรมที่พบได้ยาก มีลักษณะสำคัญคือมีผื่นสีน้ำตาลคล้ายร่างแห พบมากที่บริเวณซอกพับของร่างกาย มีตุ่มคล้ายหัวสิวที่หลังและคอ และพบหลุมแผลเป็นที่รอบปากหรือที่หน้า คณะผู้ประพันธ์ได้นำเสนอผู้ป่วย 1 รายที่มีผื่นดำที่ซอกรักแร้ ซอกพับแขน ซอกพับขา คอ หน้า หลัง และ หลังมือทั้งสองข้าง ตรวจพบตุ่มคล้ายหัวสิวและหลุมแผลเป็นที่บริเวณหลัง ลักษณะทางพยาธิวิทยาที่จำเพาะของโรค Dowling-Degos จะพบการงอกยาวลงมาของหนังกำพร้าและการเพิ่มจำนวนเซลล์สร้างเม็ดสีร่วมกับมีการบางลงของบริเวณเหนือต่อปาปิลลาและมีการเพิ่มขึ้นของเม็ดสีที่บริเวณชั้นเบสัลของชั้นหนังกำพร้า มีกลุ่มโรคหลายกลุ่มที่ต้องพิจารณาในการวินิจฉัยแยกโรค ปัจจุบันทางเลือกในการรักษายังไม่เป็นที่น่าพอใจ

คำสำคัญ: Dowling-Degos disease, ภาวะเพิ่มขึ้นของเม็ดสี, ร่างแห

Introduction

Dowling-Degos disease (DDD) is a rare genetic disorder of the skin. It is characterized by reticulated brownish pigmentation predominantly in flexural areas, comedo-like papules on the back and neck and pitted perioral or facial scars.¹ It is also mentioned as "Reticulate pigmented anomaly of the flexures".² The histopathology is very characteristic which shows basal hyperpigmentation, dilated follicle, fingerlike projections of the rete ridges with thinning of the suprapapillary plates, resulting in an "antler-like" pattern.³ Herein, the authors report a case with classical manifestations and review of the literature.



Figure 1 Reticulated brownish macules at upper back (A), right cubital fossa (B) and right axilla (C). Pitted scars are located at upper back (A).

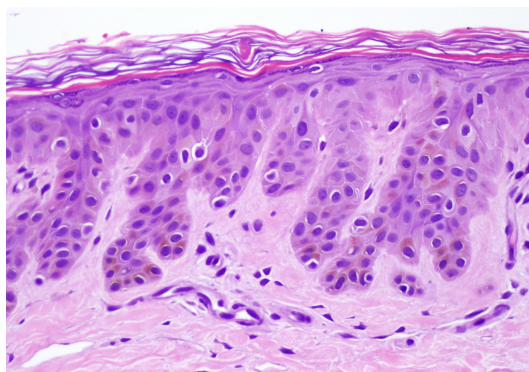


Figure 2 Skin biopsy from upper back, epidermis reveals normal basket weave keratin with lentiginous hyperplasia and basal hyperpigmentation. (Haematoxylin-eosin, original magnification $\times 40$)

Case report

A 25 year-old man visited the Dermatology Department in February 2012 for evaluation of progressive macular pigmentation in his flexural areas, dorsa of both hands, upper back and face. The dark macules were initially detected after birth at his axillae. His mother, but none of the siblings, also had similar lesions. Physical examination revealed numerous small, 2–4 mm in diameter, round brownish macules located on his axillae, cubital fossae, popliteal fossae, neck, face, back and dorsa of both hands. (Figure 1) The macules were arranged in a reticulate pattern without hypopigmented lesions. There were comedo-like papules and pitted scars on his upper back. Periorificial pits and palmar pits were absent. The mucous membrane was unaffected. For a variety of reasons his relatives had not been submitted to clinical evaluation.

Histopathology from skin at the back revealed normal basket weave keratin with lentiginous hyperplasia and basal hyperpigmentation. Many of the epithelium strands have only 2–3 cell layers thick. Melanocyte number was normal with no nest of melanocyte. (Figure 2) We were unable to obtain genetic studies on the patient.

Discussion

DDD is a rare autosomal dominant condition with variable penetrance that often presents in early adulthood. It was first described by Dowling GB and Freudenthal W in 1938 as a benign form of acanthosis nigricans.¹ In 1954, Degos and Ossipowski firstly introduced the aspect of reticulate pigmentation and termed “dermatose reticulée des plis”.⁴ Jones and Grice reviewed related literature in 1978 in their description of 10 patients with the disorder and suggested the name “Dowling–Degos disease”.¹ Until present, there has been no report of classical case of DDD from Thailand in the international literature.

The pathogenesis of DDD involved in the loss of expression mutation in the keratin 5 gene (*KRT5*) which is a component of cell adhesion and melanosome transport and transfer.⁶ Anyway, some patients had no mutation of *KRT5* gene suggesting an etiological heterogeneity of the disease.⁶ Recently, Li et al. found a gene locus mapping to chromosome 17p13.3 in some cases of DDD.⁷

The disease affects both genders, although a female preponderance has been noted in some studies.³ Classic

DDD is characterized by hyperpigmented, 2 - 3 mm. macules and minimally elevated papules on flexures, such as the axilla, neck, limb flexures, and inguinal folds in a reticulate pattern.^{1,8} The lesions can spread to the face, chest, perineum, and wrists.⁸ The reticulate pigmentation can be pruritic. Comedones and pitted scars commonly occur around the lateral margins of the mouth, but can involve other areas of the face, neck, axillae, thighs and back. The DDD lesion at vulva which is rarely affected site had been reported.⁹ Palmar pits may be seen especially patients with an overlap of classic DDD and reticulate acropigmentation of Kitamura (RAPK). Rarely, erythematous macules and papules can occur as initial manifestations of DDD.¹⁰ Hypopigmented lesions resembling dyschromatosis symmetrica hereditaria (DSH) or dyschromatosis universalis hereditaria (DUH) have been reported in patients with generalized DDD.¹¹ These lesions do not change with sun exposure, anyway heat can aggravate DDD.¹² DDD had been reported in one case received psoralen photochemotherapy (PUVA) for 8 years.¹³

The conditions associated with DDD include hidradenitis suppurativa, mental retardation, trichilemmal cysts, multiple keratoacanthomas, multiple epidermal cysts and perianal squamous cell carcinoma. These can be explained by the defect in pilosebaceous epithelial proliferation.^{1,9,13-16}

The differential diagnoses of DDD are various including Galli-Galli disease, Harber's disease, acanthosis nigricans and other genetic pigmentary

disorders, such as RAPK, DSH, DUH.³ Galli-Galli disease is an acantholytic variant of DDD.¹⁷ It results from of a loss of epidermal cell stability due to a keratin 5 (*KRT5*) defect. Clinical presentation is similar to DDD but erythematous, scaly papules can be found on the trunk and proximal extremities. The histopathology of Galli-Galli disease shows foci of acantholysis.¹⁸ Harber's disease is a rare genodermatosis with early rosacea-like rash associated with comedones, cribiform scar, keratotic lesions, reticulate pigmentation on trunk, axillae and proximal extremities.¹⁹

RAPK is a sporadic autosomal dominant disease of unknown origin. It consists of hyperpigmented atrophic macules on the backs of the hands and feet with palmar and plantar pits. The lesions darken with time and worsen with sun exposure.²⁰ DSH is an autosomal dominant inheritance characterized by pinpoint, hyperpigmented, and hypopigmented macules limited largely to the dorsal aspects of the hand and feet. DUH is characterized by pigmented flecks and spots over the body, not limiting to the flexural areas.²⁰ These conditions are less similar to our patient.

The histopathology of DDD was very characteristic, showing dilated follicle, finger-like projections of the rete ridges with thinning of the suprapapillary plates, resulting in an "antler-like" pattern and basal hyperpigmentation.³ Perivascular lympho-histiocytic dermal infiltrations and dermal fibrosis along elongated rete ridges are observed. Also, intra-epidermal keratin cysts may be prominent.¹⁰ An increased number of

melanophages has been found, with no quantitative increase in the number of melanocytes.³ The dermatoscopic features of papules in DDD reveals brown star shape which considered as a characteristic feature.²¹

In regard to the treatment of DDD, the therapeutic options are unfulfilled and the results are poor. Temporary good results have been reported with the use of topical corticosteroids, bleaching agents, topical adapalene.²² There was a report of the treatment with Er:YAG laser, pulse energy between 1,000 and 1,200 mJ, three consecutive passes, which showed good result.²³

Conclusions

Dowling-degos disease is a rare reticulate pigmentary disease. Various similar conditions should be considered in the differential diagnosis. At present, most of the treatment options are not satisfactory.

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