Ann Dermatol Vol. 23, No. 2, 2011 DOI: 10.5021/ad.2011.23.2.205

CASE REPORT

A Case of Dowling-Degos Disease on the Vulva

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Dowling-Degos disease (DDD) is an autosomal dominant genodermatosis and this disease is a genetically determined disturbance of epidermal proliferation. It is characterized by acquired, slowly progressive pigmented lesions that primarily involve the great skin folds and flexural areas such as the axilla, neck, limb flexures, the inframammary area and the inguinal folds. The vulva is an unusual location for DDD. A 41-year-old woman presented with a 10-year history of multiple, small, reticulated and brownish macules distributed symmetrically on the bilateral external genital regions. We found no other similarly pigmented skin lesions on her body, including the flexural areas. There was no known family history of similar eruptions or pigmentary changes. The histologic examination showed irregular rete ridge elongation with a filiform or antler-like pattern and basilar hyperpigmentation on the tips. Fontana-Masson staining showed increased pigmentation of the rete ridges and the S100 protein staining did not reveal an increased number of melanocytes in the epidermis. From these findings, we diagnosed this lesion as DDD. **(Ann Dermatol 23(2) 205～208, 2011)**

-Keywords-
Dowling-Degos disease, Pigmented skin lesion, Vulva

INTRODUCTION

Dowling-Degos disease (DDD) is also known as reticulate pigmented anomaly of the flexures, and this is a rare autosomal dominant genodermatosis that causes abnormal epidermal proliferation[1]. It is characterized by acquired, slowly progressive pigmented lesions that primarily involve the great skin folds and flexural areas such as the axilla and inguinal folds[2]. However, there have only been a few previous case reports of DDD on the vulva in the dermatologic literature. We report here on a case of DDD on the vulva of a 41-year-old woman.

CASE REPORT

A 41-year-old woman presented with a 10-year history of numerous small, hyperpigmented macules in a reticular pattern on the bilateral external genital regions. We found no other similarly pigmented skin lesions on her body, including the skin folds and flexural areas (Fig. 1). Her medical history was unremarkable and there was no known family history of similar eruptions or pigmentary changes. On the physical examination, there were multiple, small, reticulated and confluent brownish macules distributed symmetrically on the vulva. Histologic examination showed irregular, filiform epidermal elongation of the rete ridges with a concentration of melanin at the tips (Fig. 2A, B). Fontana-Masson staining showed that the hyperpigmentation was mainly limited to the filiform downgrowths (Fig. 2C). The S100 protein staining did not reveal an increased number of melanocytes in the epidermis (Fig. 2D). From these findings, we diagnosed these lesions as DDD.

DISCUSSION

DDD is an autosomal dominant genodermatosis that is characterized by acquired, slowly progressive pigmented lesions that primarily involve the large body folds and flexural areas such as the axilla, neck, limb flexures, the inframammary area and the inguinal folds[1,2]. It can occasionally appear on the wrist, face and scalp[3]. Involvement of the genitalia, and particularly pigmented

Received March 26, 2010, Revised April 26, 2010, Accepted for publication April 28, 2010

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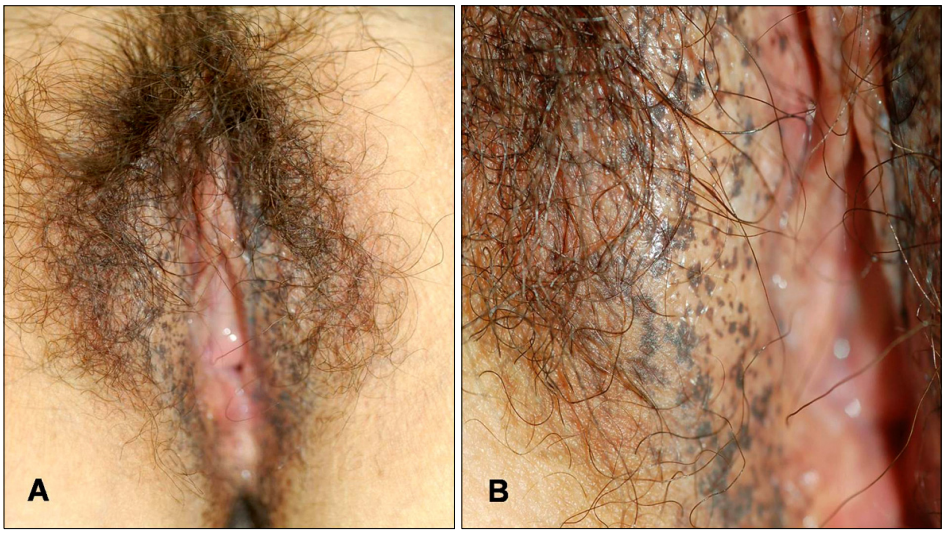

Fig. 1. (A) Multiple hyperpigmented brownish macules located symmetrically on the bilateral external genital area. (B) A close up view of the reticulate pigmented lesion.

lesions of the vulva, has been rarely reported[1-3]. The reported cases are summarized in Table 1[2,4-6]. The disease is more common in women, it presents in adult life and most frequently in the fourth decade[7]. It usually presents as numerous, small, round pigmented macules that resemble freckles[8]. The pigmentation is symmetrical and progressive[2,8]. The degree of pigmentation varies, but in some patients the lesions are almost confluent, giving a brown or black lace-like pattern[8]. The other features that can be present in DDD are scattered comedo-like lesions and pitted acneiform scars[1,8]. In our patient, we saw the characteristic features of multiple, small reticulated and brownish macules distributed symmetrically on the bilateral external genital regions.

DDD is believed to be a part of a disease spectrum that includes reticulate acropigmentation of Kitamura (RAK), Haber's syndrome (HS) and reticulate acropigmentation of Dohi (RAD)[1,3,7]. These may be variants of the same entity with similar clinicopathological features and they overlap in some cases[1]. The genetic defect of DDD has not yet been well defined[9]. A recently reported series described the loss of function mutations in the KRT5 gene encoding keratin K5 in two German pedigrees[10]. KRT5 gene mutations have previously been recognized as being involved in the pathogenesis of epidermolysis bullosa simplex[9,10]. However, no association between DDD and epidermolysis bullosa simplex has been reported[9].

Histopathologically, DDD shows pigmented epidermal rete ridge elongation with a filiform or antler-like pattern and variable basilar hypepigmentation on the tips[1]. Involvement of the follicular infundibulum, thinning of the suprapapillary epithelium, moderate hyperkeratosis and dermal melanosis have all been observed[1,3,6,8]. The pigmentation is present as finely dispersed melanin granules scattered uniformly throughout the cytoplasm of the cells[6]. Fontana-Masson staining reveals that the hyperpigmentation is limited mainly to the epidermal downgrowths. S100 protein staining reveals no increase in the number of melanocytes, and this substantiates that the pigmentation is likely not due to an increased density of melanocytes[3,11]. The histologic examination for our patient revealed irregular, filiform epidermal elongations of hyperpigmented rete ridges with a concentration of melanin at the tips. No increase in the number of melanocytes was noted on the S100 protein staining.

The differential diagnosis includes lentigo simplex, senile lentigo, adenoid seborrheic keratosis and other hereditary pigmented anomalies[2,6]. Usually there are only a few scattered lesions in lentigo simplex, without a predilection for areas of sun exposure[12,13]. They are small, symmetric and well-circumscribed macules that are evenly pigmented, but they vary individually from brown to black[13]. However, the absence of melanocytic hyperplasia rules out the possibility of a lentigo simplex or other similar melanocytic lesions[12,14]. The involvement of the infundibulum of the hair follicle is a unique and distinctive feature of the reticular pigmented anomaly: it is not seen in seborrheic keratosis, epidermal nevus or any other lesions[12]. In addition, hereditary pigmented anomalies such as RAK, HS and RAD need to be differentiated from DDD. A summary of the differences among them is presented in Table 2[1,3,7,15].

Many treatment options have been tried for DDD, but no treatment has been effective in eliminating the lesion[16]. Depigmenting agents such as hydroquinone, as well as systemic and topical retinoids, have been used and reported on anecdotally[4,11,17]. Altomare et al.[18] reported a temporary therapeutic benefit after using topical adapa-

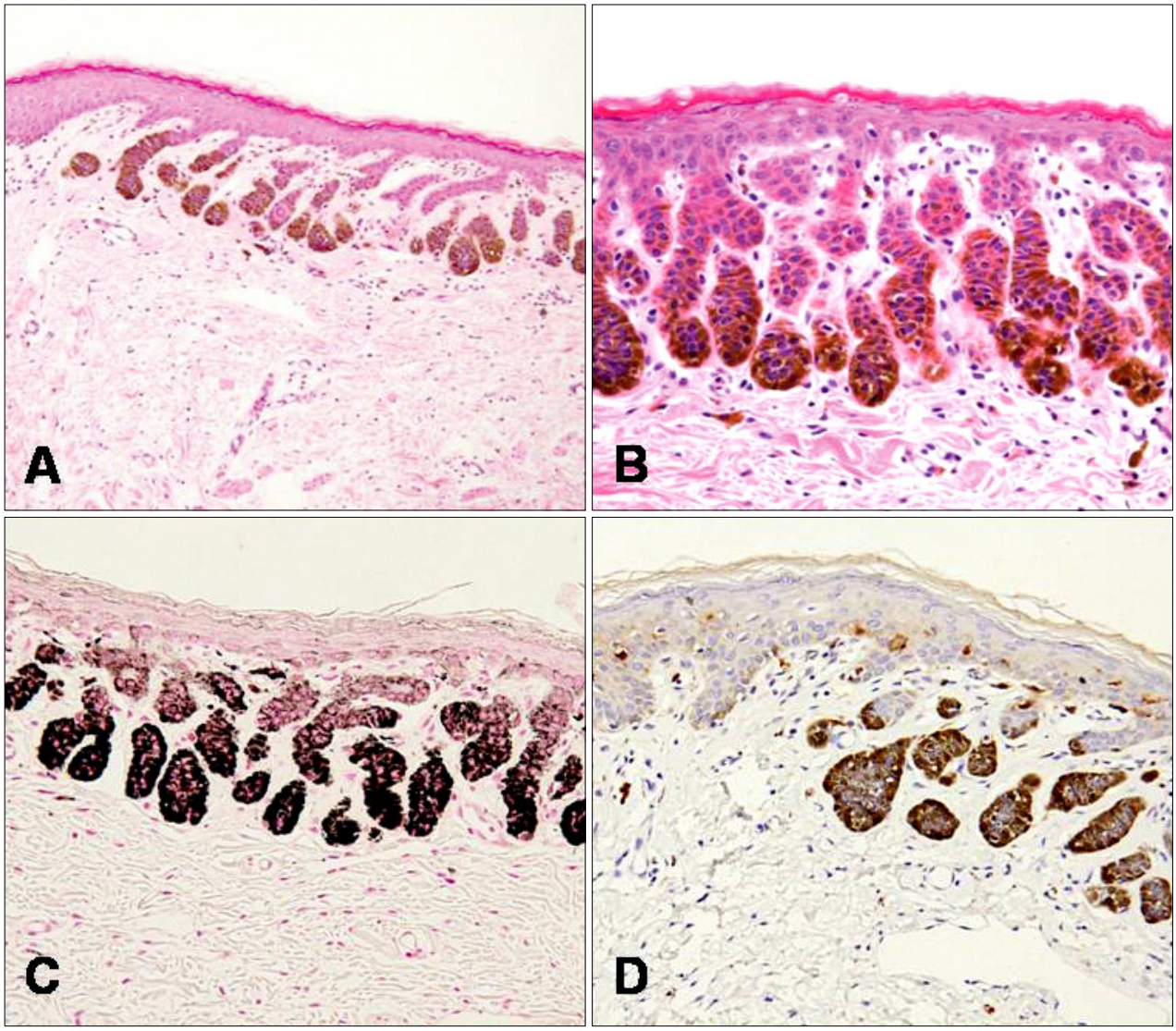

Fig. 2. (A) The epidermal downgrowths showed a filiform or antler-like pattern with irregular elongation of the rete ridges in the lesion (H&E, ×100). (B) There is increased melanin pigment at the tips of the epidermis (H&E, ×200). (C) There is increased pigmentation of the rete ridges on Fontana-Masson staining (Fontana-Masson, ×200). (D) Compared with perilesional normal skin, the S100 protein staining reveals no increase in the number of melanocytes (S100 protein, ×200).

Table 1. Summary of reported cases of DDD on the vulva

Author	Sex/Age	Onset	Family history	Distribution
Jones and Grice[4] (1978)	F/65	Adulthood	+	Axillae, inguinal folds and vulva
	F/52	32 years ago	+	Axillae, inguinal folds and vulva
Milde et al.[5] (1992)	F/40	2 years ago	−	Vulva, perianal area
	F/46	Unknown	−	Vulva
O'Goshi et al.[6] (2001)	F/55	5 years ago	−	Vulva
Massone and Hofmann-Wellenhof[2] (2008)	F/51	Several years ago	−	Vulva
This case	F/41	10 years ago	−	Vulva

DDD: Dowling-Degos disease.

Table 2. Differential diagnosis of DDD, RAK, HS and RAD

Disease	Inheritance	Age at onset	Clinical findings	Histologic findings
DDD	AD	Fourth decade	Acquired pigmented reticulate macules of the flexures Comedo-like lesions on the neck or back & pitted oral scars	Filiform or antler-like epidermal down-growths with basilar hyperpigmentation Dermal melanosis
RAK	AD	First & second decades	Reticulated & pigmented macules on acral area, especially on the dorsum of the hands and feet	Elongation of the rete ridge with basilar hyperpigmentation Epidermal atrophy
HS	AD	Childhood	Pigmented keratotic papules mainly in the axilla but also on neck & trunk Pitted scars on the face	Downward budding of the epidermis & follicular keratotic plug
RAD	AD (AR)	Infancy & early childhood	Reticulated hyper-pigmented & hypo-pigmented macules on the dorsa of the hands and feet	In hyperpigmentation: increased melanin pigments at basal layer & through epidermis In hypopigmentation: decreased or absent of melanin pigments No increase in the number of melanocytes

DDD: Dowling-Degos disease, RAK: reticulate acropigmentation of Kitamura, HS: Haber's syndrome, RAD: reticulate acropigmentation of Dohi, AD: autosomal dominant, AR: autosomal recessive.

lene. Various laser systems, and especially CO_2 and Er:YAG lasers, have been proven to be effective[11,17]. In our case, the patient applied topical agents containing tretinoin, hydroquinone and fluocinolone acetonide (Tri-luma®), but the patient failed to appear for follow-up.

In conclusion, we clinically observed a case of DDD arising on the vulva. This is a rare case in the dermatologic literature, but physicians should consider DDD in the differential diagnosis of pigmented skin diseases.

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