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CASE REPORT

A Taiwanese woman with Dowling-Degos disease: An electron microscopic study with pathophysiological significance

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ABSTRACT

Herein we report a rare case of classical Dowling-Degos disease (DDD) in a Taiwanese woman. A 23-year-old Taiwanese woman presented with generalized hyperpigmentation in irregular and reticulated shapes that she had had since junior high school. Her mother and two sisters had also developed similar pigmentations, starting during their teenage years. The patient did not have previous skin lesions or a history of trauma. She did not have any nail or hair abnormalities. Viewed through a microscope, the hyperpigmented area was found to have elongated rete ridges, the tips of which were found to have a concentration of melanin. Based on the disease onset, family history, clinical and histopathological manifestations, the patient was diagnosed as having DDD. We performed an electron microscopic study revealing a greater number of mature melanosomes in the keratinocytes in the pigmented skin than in those in the nonpigmented skin. The numbers of melanosomes in the melanocytes were similar in both types of skin. This is the first direct comparison of ultrastructural features in pigmented and uninvolved skin in Taiwanese with DDD. We follow the discussion of the case with the differential diagnosis and genetic abnormalities of diseases with reticulate pigmentations. This case report reminds us that keratin 5/14 plays a role in both keratinocyte integrity and melanin transfer.

Introduction

Dowling-Degos disease (DDD) is an autosomal dominant disease that usually presents with reticulated pigmentations predominantly located in major flexural skin beginning in the teenage years.[1] It is also known as reticular pigmented anomaly of the flexures or postpubertal reticulate hyperpigmentation. These lesions are reticular and dark brown. Microscopically, there is a filiform epidermal down growth of epidermal rete ridges, with a concentration of melanin at the tips, without an increase in numbers of melanocytes. The genetic abnormalities of DDD are not unique to one gene. For example, genetic studies from affected families have identified mutations[2] and deletions[3] in the keratin 5 locus in DDD. However, Li et al found a gene locus responsible for DDD that maps to chromosome 17p13.3 in a Chinese family with DDD.[4] Thus, there appears to be phenotypic and genotypic heterogenecity in the pathogenesis of DDD.

Case report

A 23-year-old female presented to our dermatology outpatient clinic with the chief complaint of reticulated hyperpigmentation with irregular shapes, which she had had since junior high school (Figure 1A). According to the patient, her mother and sisters had also developed similar hyperpigmentation starting in their teenage years. She had neither previous skin lesions nor trauma history. The pigmented lesions were neither pruritic nor painful. There were no nail or hair abnormalities. Her mother, and her older and younger sisters had similar skin manifestations; however, her father and her brother did not have any abnormal hyperpigmentations (Figure 2). Skin biopsy over her hyperpigmented area revealed typical features of DDD, including filiform down growth of rete ridges and a concentration of melanin at the tips of the rete ridges (Figure 1B).

Further microscopic examination showed no significant changes in DOPA-reactive melanocytes (data not shown). Fontana-Masson stain showed that melanin expression was increased in the lesional skin (upper left, Figure 3). The patient was diagnosed with

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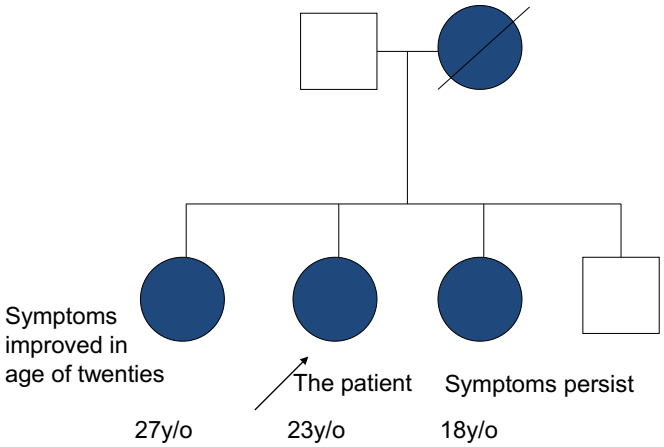

Figure 1 Family pedigree of the patient with Dowling-Degos disease.

DDD considering the disease onset, family history, clinical and histopathological manifestations. We then used a transmission electron microscope to identify whether the generation and maturation of melanosomes in lesional skin were different from those in normal skin.

Ultrastructurally, keratinocytes are readily recognized by the presence of keratin tonofilaments. Melanocytes are recognized by the presence of melanosomes in different stages without tonofilaments and desomosomes.[5] Melanosomes in different stages are distinguished by the presence of pigments, the structure and arrangements of internal membranes.[6] We counted and compared the numbers of mature melanosomes in melanocytes and the numbers of stage IV melanosomes among the mature melanosomes in basal and suprabasal keratinocytes.

Lesional skin and normal skin melanocytes had a similar number and proportion of mature melanosomes and had similar distributions and shapes. The percentage of mature melanosome among the total melanosomes was similar in melanocytes. In lesional skin, particularly in the portion of epidermal projection, the basal keratinocytes contained a significant percentage of Stage IV melanosomes among the mature melanosomes (Stage III and Stage IV). The relative percentage of Stage IV melanosomes among the mature melanosomes was significantly higher in the suprabasal keratinocytes in lesional skin than in the keratinocytes in normal skin. The similar numbers of melanosomes in melanocytes and the increased percentages of Stage IV melanosomes among mature melanosomes in suprabasal and basal keratinocytes suggest that the hyperpigmentations in the lesional skin of DDD might result from abnormalities in melanosome transfer and/or melanosome

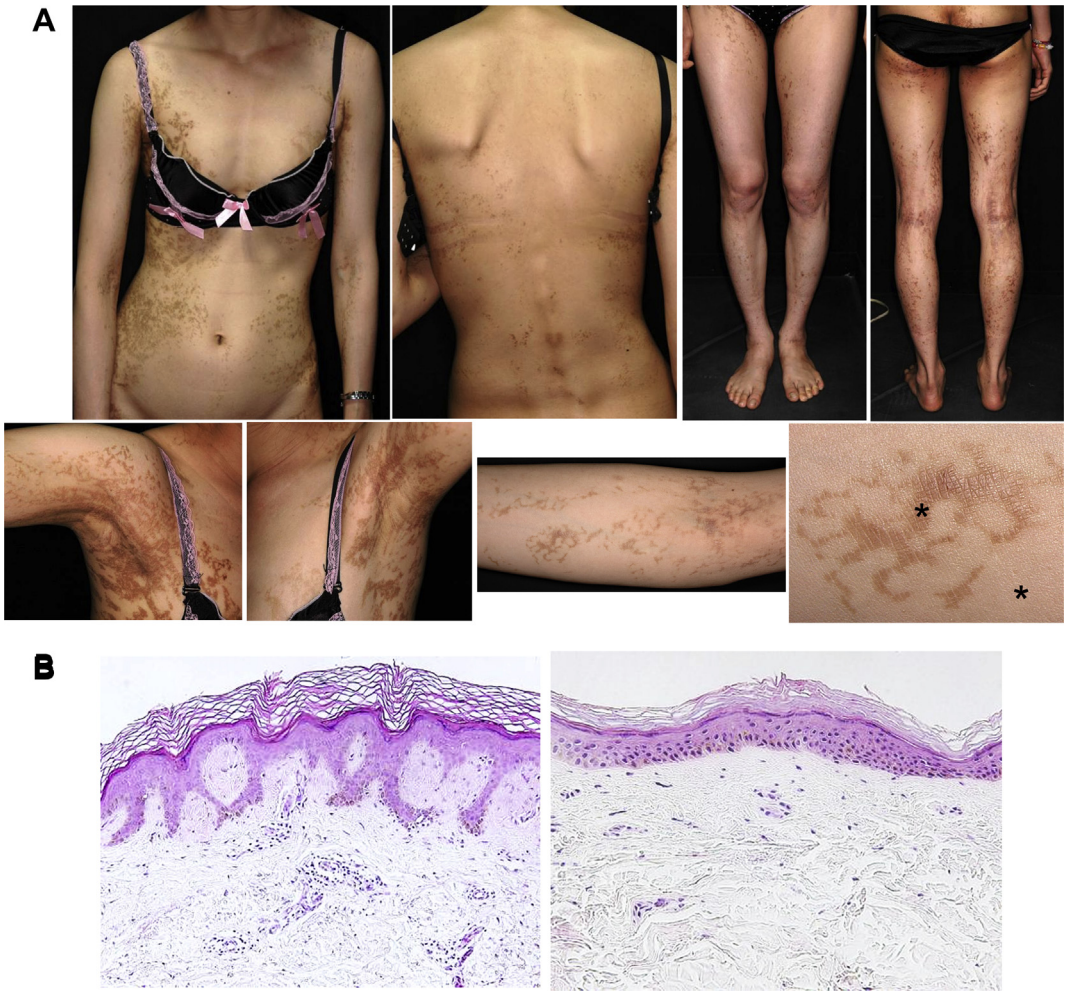

Figure 2 (A) Clinical features of a Taiwanese woman with Dowling-Degos disease. There was increased reticulate pigmentation in the flexural skin. * Indicates biopsy areas. (B) Histological and electron microscopic features of the lesional vs. nonlesional skin of the patient with Dowling-Degos disease. There was a filiform down growth of rete ridges and concentration of melanin at the tips of the rete ridges.