

Development of Multiple Pigmented Nevii Within Segmental Nevus Depigmentosus

Nevus depigmentosus is a stable and well-circumscribed congenital hypomelanosis that may be in an isolated, dermatomal or systemic form. An 18-yr-old Korean man with segmental nevus depigmentosus developed multiple pigmented nevi which were present only within the confines of the leukoderma. Histologic and electron microscopic studies rendered a diagnosis of nevus depigmentosus with dysplastic nevus to the patient. The genetic alteration of melanocytes in the hypopigmented lesion is assumed to have resulted in the development of multiple pigmented nevi.

Key Words : *Nevus, Pigmented; Hypopigmentation; Dysplastic Nevus Syndrome*

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Received : 22 January 2001
Accepted : 16 April 2001

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INTRODUCTION

The clinical feature of nevus depigmentosus (ND) is quite characteristic and defined as a congenital nonprogressive hypopigmented macule or patch that is stable in its relative size and distribution throughout life (1). In some patients with hypomelanosis of Ito or piebaldism, acquired pigmented macules may occur. It has been reported that inactive cells might become functional to produce contraction of hypomelanotic areas (2-4). However, this is caused by a gradual "fading" in which the streaks acquire the same level of pigmentation as the surrounding skin. Herein we report a patient whose achromic nevi underwent an unusual change, the development of multiple pigmented nevi.

CASE REPORT

An 18-yr-old man sought a medical attention for the evaluation of black macules on the hypopigmented patch on the entire left lower extremity. The hypopigmented lesion has been present since his birth and no alterations in distribution or in texture had been noticed. Psychomotor and musculoskeletal developments were normal. There was no family history of similar cutaneous findings or melanoma. Physical examination revealed 20 hyperpigmented macules within the lower portion of the leukoderma, which appeared around his school age and showed gradually increase in size and num-

ber. Hyperpigmented macules had irregular borders, haphazard mixture of tan, brown, and black in colors, and an indistinct margin with a size range of 3 to 8 mm in diameter (Fig. 1, 2).

Skin biopsy specimens were taken from the hypopigmented patches and hyperpigmented macules. In the hypopigmented patch, melanocytes were seldomly detected, even with S-100 stain and showed a markedly decreased basal pigmentation with Fontana-Masson stain. DOPA reaction showed the decreased number of melanocytes that were less reactive than normal. Electron microscopy of the hypopigmented lesion revealed poorly matured melanocytes with stubby dendrites and with a decreased number of melanosomes, although there was no change in their size. The number of melanosomes was markedly reduced in keratinocytes and they were present as a single unit (Fig. 3A-C). Histological examination from the hyperpigmented macules within hypopigmented patch showed elongated rete ridges and poorly circumscribed nests of atypical melanocytes with bridging between rete ridges, which were consistent with dysplastic nevus (Fig. 3D). Those atypical nevus cells were positive for both S-100 protein and HMB-45 monoclonal antibody reaction stains.

DISCUSSION

Nevus depigmentosus is an uncommon congenital nonfamilial hypopigmented macule or patch that is stable in its

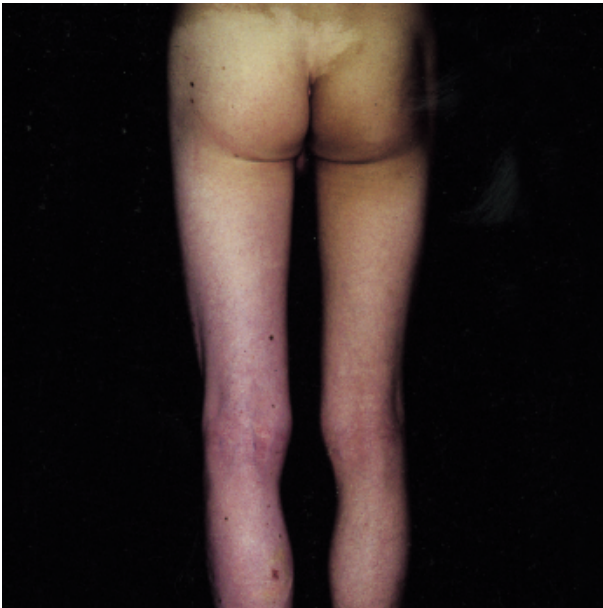


Fig. 1. Multiple scattered brown to black pigmented macules on the segmental hypopigmented patch along the right lower extremity and buttock.

relative size and distribution throughout life. Three different patterns of ND have been recognized (5): an isolated, circular, or rectangular area of hypomelanosis distributed anywhere on the body, especially on the trunk; a typical dermatomal pattern of hypomelanosis; a dermatomal pattern in which the hypomelanosis is a bizarre, sharply angulated streak, almost like an artificial white paint or in whorls of hypomelanosis, roughly following Blaschko's lines (5), which has also been described as *incontinentia pigmenti achromians* of Ito. Under Wood's lamp examination, the lesion showed an off-white accentuation, in contrast to the chalky-white accentuation observed in vitiligo. Histopathologically, the number of melanocytes is normal or decreased, depending on the series of patients, but DOPA reactivity is consistently reduced (6-9). Melanosomes are normal in their size, shape, and internal structures and the melanization is normal or decreased. Melanosomes are occasionally aggregated in melanocytes and present in reduced numbers in keratinocytes. ND is caused by a functional alteration of melanocytes, which interfere with the synthesis of normal melanosomes and subsequent transport to neighboring keratinocytes (1). In this case melanocytes are present but still immature and not active enough to produce visible melanin. There is a great reduction of melanosomes in the melanocytes and keratinocytes. Many non-ellipsoidal lamellar melanosomes were recognized in melanocytes.

There has been only two reported cases of multiple pigmented lentiginos within achromic nevi (10). The authors considered this change as a different form of "repigmentation" and proposed that it should be from the reversion of

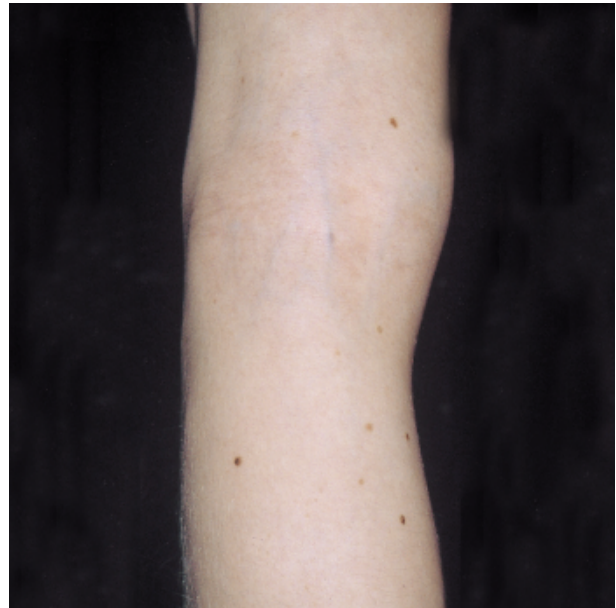


Fig. 2. Closer view of hyperpigmented macules shows their variations in size and shape. Note areas of leukotrichia on the leukoderma.

mutation in one of the genes involved in pigmentation. Occasionally, repigmentation has been also observed within the achromic patches of piebaldism (3, 4). Fukai *et al.* (4) suggested the hyperpigmented spot confined to piebald skin, should be induced by sunlight. They occurred as a result of accelerated melanin production of the melanocytes that had been inactive. This process of pigmentation seemed to be different from the normal differentiation or maturation of melanocytes and/or melanoblasts, suggested by the abnormal morphology of the melanosomes.

Melanin is thought to serve its role in photoprotection. The ability of melanin to play a protective role is supported by epidemiological and experimental evidences. Individuals with a dark skin are known to be less susceptible to the damaging effects of UV light and have a lower incidence of skin cancers than individuals with a fair skin (11-13). Many investigators have proposed that main function of melanin should be to protect from the damaging effects of UV radiation. This was possible through quenching oxygen radicals and acting as a sunscreen (14, 15). We believe that the functional alteration of melanocytes in the hypopigmented lesion impaired this protective function of normal melanosomes and thereby caused the DNA damage. These effects ultimately resulted in the development of dysplastic nevus. Dysplastic nevi occur in 2% to 5% of the normal population and are reported to be associated with 20% to 33% of malignant melanomas (16-18). Although the exact risks are unknown, a seven-fold increase of risk and 6% cumulative risk have been estimated for persons with dysplastic moles and without a family history (19). We encouraged the patient a full skin exami-

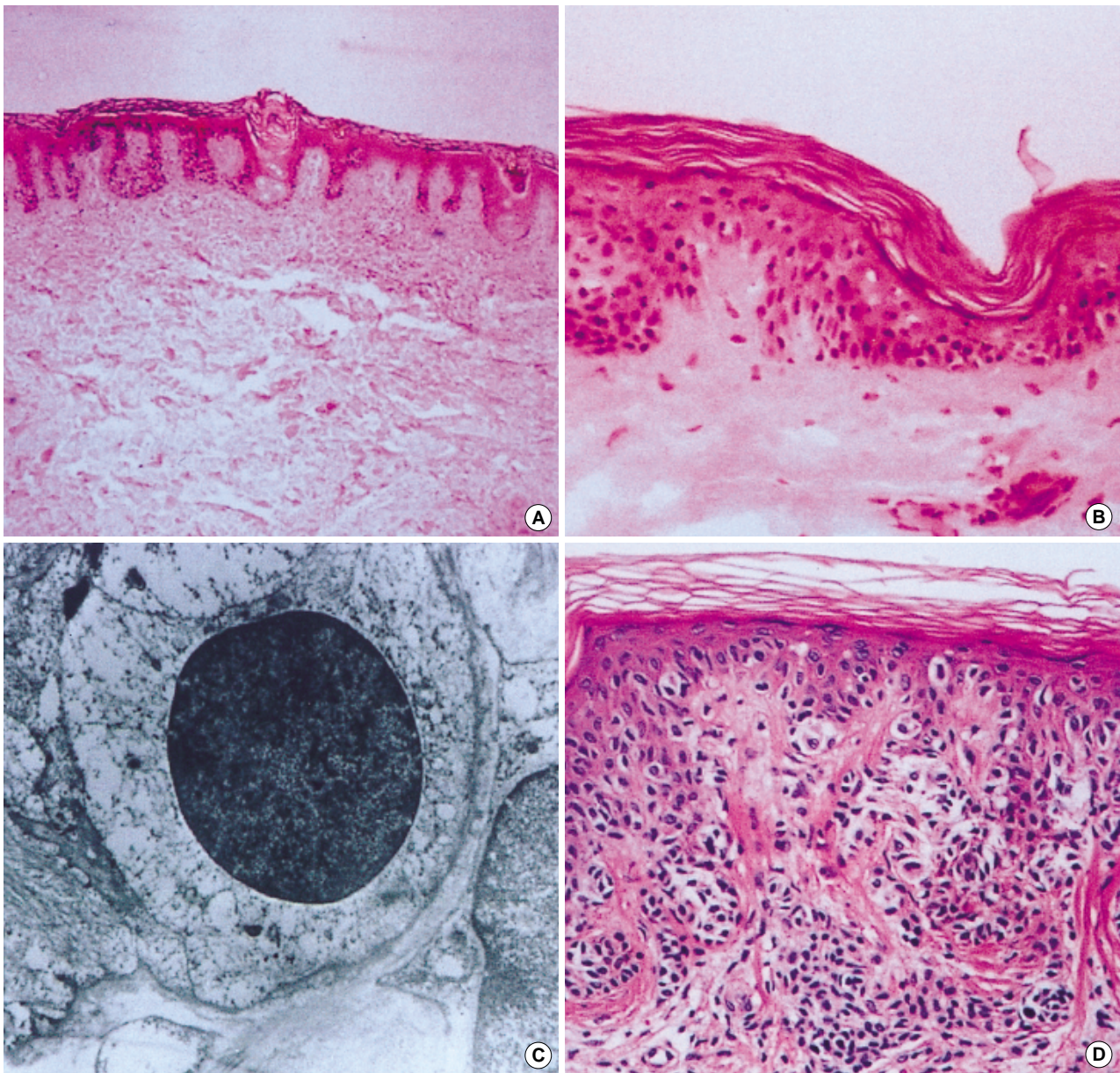


Fig. 3. **A:** Relatively small and well-circumscribed nevus confined to the epidermis. No basal melanocytic pigmentation is seen in the peripheral area (Fontana-Masson stain $\times 40$). **B:** Histological features of hypopigmented lesion show decreased melanocyte number and activity in the dermoepidermal junction (DOPA stain $\times 100$). **C:** Electron microscopic finding of melanocytes in depigmented lesional skin. The number of melanosomes within a melanocyte is decreased (original magnification, $\times 7,500$). **D:** In the junctional compartment of the nevus, the epidermal rete ridges are elongated, and there are lentiginous melanocytic dysplasia and atypia, which are consistent with dysplastic nevus (H&E $\times 100$).

nation by a physician at least twice a year, or more often if any increase in number or change in nature of the nevi are noticed. We also counseled him to minimize the exposure to sunlight. We recommend an excision for progressive nevi but, do not advocate a prophylactic removal of large numbers of nevi.

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