Spontaneous Involution of Congenital Melanocytic Nevus With Halo Phenomenon

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Abstract: Congenital melanocytic nevus (CMN) is a neural crest-derived hamartoma, which appear at or soon after birth. CMN has a dynamic course and may show variable changes over time, including spontaneous involution. Spontaneous involution of CMN is a rare phenomenon and is often reported in association with halo phenomenon or vitiligo. The mechanism of halo phenomenon is yet to be investigated but is suggested to be a destruction of melanocytes by immune responses of cytotoxic T cells or IgM autoantibodies. Here, the authors report an interesting case of spontaneously regressed medium-sized CMN with halo phenomenon and without vitiligo, which provides evidence that cytotoxic T cells account for the halo formation and pigmentary regression of CMN.

Key Words: congenital melanocytic nevus, cellular immunity, halo phenomenon, involution, vitiligo

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INTRODUCTION

Congenital melanocytic nevus (CMN) is considered to be a neural crest-derived hamartoma, which appears at or soon after birth,[1] with incidence of 0.2–2.1 in neonates.[2] CMN has a dynamic course and may change over time. It can increase in size, become darker in color, become hairy, or even lose its pigmentation.[3] Spontaneous involution of CMN is a rare phenomenon, and it is often reported in association with halo phenomenon or vitiligo.[4–7]

The halo nevus or leukoderma acquisitum centrifugum, also called as Sutton nevus, is usually observed around congenital or acquired melanocytic nevi.[4] Halo phenomenon may also develop around Mongolian spot, café au lait macules, neurofibroma, basal cell carcinoma, seborrheic keratosis, histiocytoma, and flat warts.[8] The clinical manifestation of halo phenomenon is characterized by progressive lightening of the color, disappearance of central nevus afterwards, and persistence of hypopigmentation.[5]

To date, the mechanism of halo phenomenon is suggested to be a destruction of melanocytes by immune responses of cytotoxic T cells or IgM autoantibodies. Musette et al[9] reported local proliferation of T-cell clones activated by common nevus antigens found in different halo nevi of the same patient. However, few reports about concomitant onset of vitiligo and halo nevus suggest that immunological factors may play a crucial role.[10]

Here, we report a case of medium-sized CMN with halo phenomenon and pigmentary regression without vitiligo development in a young girl. Its histopathologic findings provide evidence that cytotoxic T cells account for the halo formation and pigmentary regression of CMN.

CASE REPORT

A 13-year-old girl visited our department for evaluation of a melanocytic nevus, which appeared since birth and showed progressive depigmentation for 5 years. On physical examination, a white to grayish, 10 × 7 cm sized, irregularly bordered patch with brown to tan colored macules inside the patch was observed (Fig. 1). There was no erythema in the lesion, and the patient did not complain of any subjective symptom. The child did not have any medical history and a familial history of CMN. No other depigmented lesion was noticed by full skin examination. Histopathologic examination from the center of depigmented patch showed nests and cords of nevus cells that do not contain melanin pigment in the mid-to-deep dermis, confirming the diagnosis of CMN (Fig. 2A). Dense infiltration of mononuclear cells around the nevus cells in superficial dermis and periadnexal structures was also seen (Fig. 2B). No nevus cell showed a sign of cellular atypia. Immunohistochemistry showed

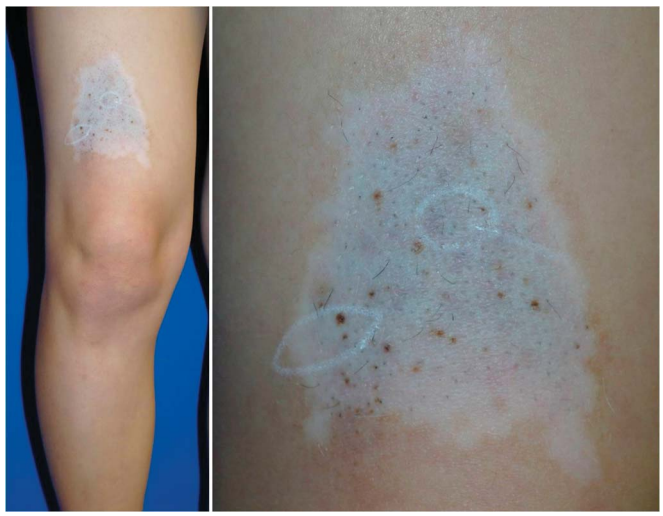

FIGURE 1. Clinical appearance of the skin lesion. A white to grayish, 10 × 7 cm sized, irregularly bordered patch with brown to tan colored macules inside the patch was observed.

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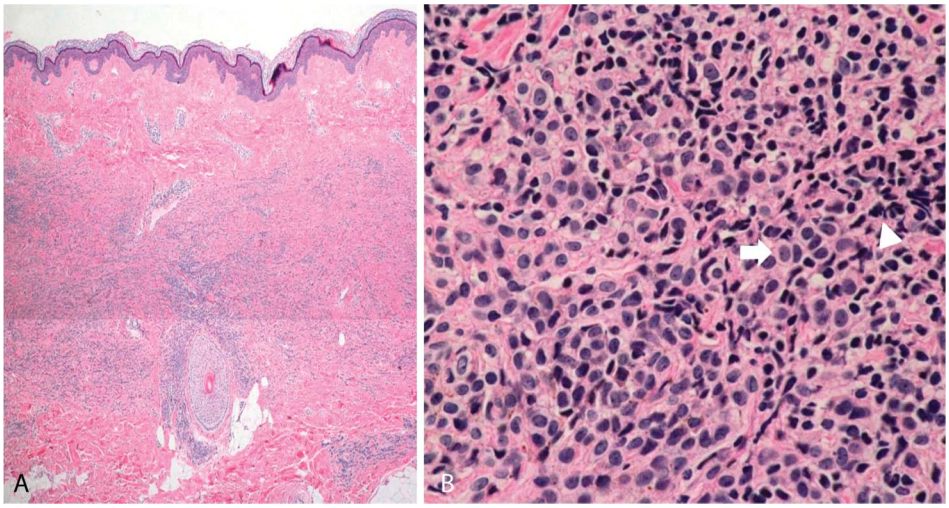

FIGURE 2. Histopathologic examination from the center of depigmented patch. A, Nests and cords of nevus cells not containing melanin pigment were seen in the mid-to-deep dermis. B, Dense mononuclear cell (arrow head) infiltrated around the nevus cells (arrow) in superficial dermis and periadnexal structures. Hematoxylin and eosin, original magnification: (A) ×40; (B) ×400.

positive staining for S100 and MART-1 but negative for HMB-45 in nevus cells. Cells labeled with Ki-67 revealed to be less than 2% of total nevus cells. The immunophenotype analysis of the mononuclear infiltrate revealed that the cells were composed predominantly of CD5-positive T cells, and CD4:CD8 ratio was approximately 1:6. Only few cells were CD20 positive (Fig. 3). Although the lesion showed no risk for malignancy, the patient was recommended a total excision of the lesion for cosmetic improvement and was referred to plastic surgery department. However, she was not able to be followed up.

DISCUSSION

CMN is common and occurs in 0.6–1.6 of 5 newborns.[11] Few reports about spontaneous regression of CMN are published, and regression of medium-sized CMN is known to be even less common than that of larger variants.[12] Most CMN cases with spontaneous regression and halo phenomenon are associated with development of vitiligo at a distant site.[4–6,11] Spontaneous regression of CMN without halo formation is a more exceptional case.[13]

The exact pathogenesis of halo phenomenon or spontaneous regression of CMN is unknown. In both halo nevus and vitiligo, mononuclear cell infiltration in close contact with ultrastructurally damaged melanocytes[14] was seen histopathologically. Eighty percent of the mononuclear infiltrate was found to be T lymphocytes with a relatively high percentage of suppressor/cytotoxic T cells.[15] Nevomelanocytes of halo nevus express major histocompatibility complex class I

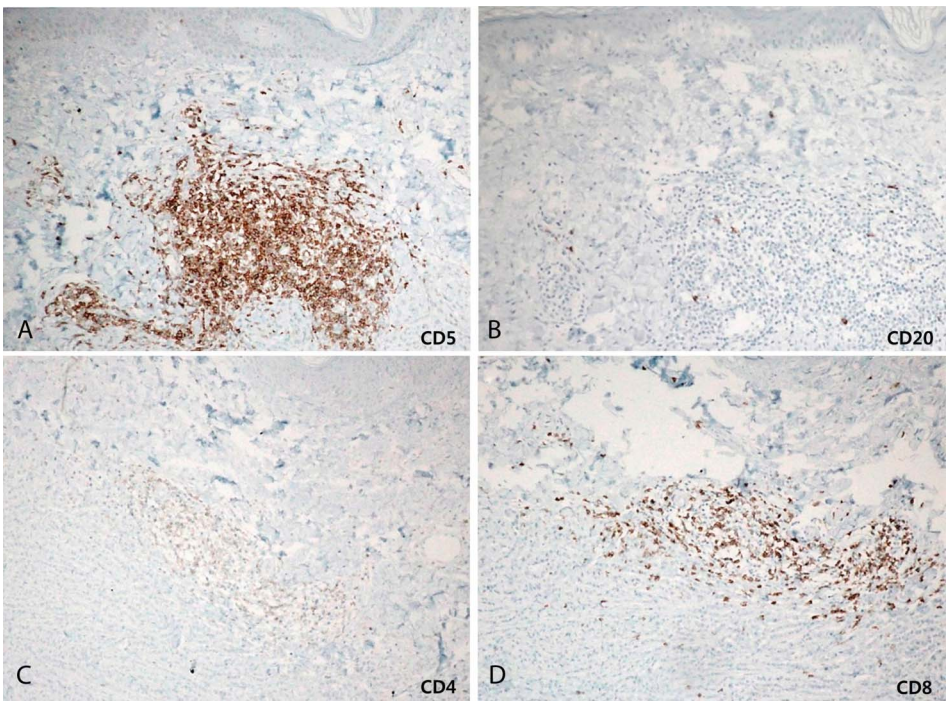

FIGURE 3. A, The immunophenotype analysis of the mononuclear infiltrate revealed that the cells were composed predominantly of CD5-positive T cells. B, Few cells were CD20-positive B cells. C and D, CD4:CD8 ratio was approximately 1:6. (A) CD5, ×200; (B) CD20, ×200; (C) CD4, ×200; (D) CD8, ×200.

(HLA-A, HLA-B, HLA-C) antigens that allow them to be recognized by cytotoxic T lymphocytes and attack them.[15] However, IgM or IgG autoantibodies against melanocytes have been found in the serum of patients with both halo nevi and vitiligo, suggesting that humoral immune reaction accounts for the destruction of melanocytes.[16–18] CMN with halo phenomenon we report here belongs to the inflammatory type of halo nevus, which is characterized by the presence of a marked mononuclear inflammatory infiltrate.[18] By immunophenotype analysis, we could see that the majority of the infiltrated inflammatory cells were T cells with relatively high proportion of $CD8^+$ T cells, and this could be an another example of evidence that cytotoxic T-cell immunity plays an important role in the regression and halo phenomenon of CMN. Another interesting finding of our case was that the mononuclear infiltrate was concentrated at the upper dermis and periadnexal areas. This could be explained by the target specificity of nevus cells recognized by T cells, and the expression of the determinants may be greater in the upper dermis and periadnexal areas.[18]

There have been several reports about the association of halo nevi and malignant melanoma,[19,20] which support the hypothesis that cytotoxic lymphocytes attack both melanoma cells and nevomelanocytes sharing antigenic determinants. Although such cases are rarely described, in case of CMN that shows pigmentary regression, biopsy must be performed to find out the presence of any malignant change with a careful whole body inspection.[21] In our case, there was no malignant change of nevus cells by histopathologic examination or other suspicious lesion by physical examination.

Here, we report an interesting case that could be an additional evidence for the role of cytotoxic T-cell immunity in regression and halo phenomenon in CMN and that there is a target specificity of nevus cells to be recognized by T cells.

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