Halo neurofibroma is a rare benign tumor. In the past, 3 cases of multiple halo neurofibromas and 1 case of a solitary halo neurofibroma have been reported. The neurofibroma is characterized by a skin-colored, dome-shaped soft papule or a nodule surrounded by hypopigmented macules. The pathogenesis of neuroectodermally derived tumors associated with halo phenomenon is still poorly understood. We report a case of a 46-year-old female with a solitary halo neurofibroma and discuss the possible causes. (Dermatol Sinica 27: 181-185, 2009)

Key words: Neurofibrom, Halo phenomenon, Halo neurofibroma

INTRODUCTION

A nevocellular nevus surrounded by hypomelanotic macules is clinically designated as a “halo nevus” or leukoderma acquisitum centrifugum, and this condition first described by Sutton in 1916.1 In some intra-dermal tumors such as neurofibromas, neural nevi, blue nevi, and metastatic malignant melanomas, the epidermal melanin overlying the tumor lesion is depleted or absent.1,2

The halo neurofibroma is a very rare type of benign tumor. Thus far, only 3 cases of multiple halo neurofibromas associated with neurofibromatosis have been reported in the literature.1,2 In 1965, Kopf et al. reported a case of a solitary halo neurofibroma.1 Here, we report the case of a 46-year-old female with a solitary halo neurofibroma on her chin.

CASE REPORT

A 46-year-old female visited our outpatient department because she had an asymptomatic tumor on her chin, which she had first noted when she was 16 years old. Physical examination of the skin revealed the presence of a skin-colored, dome-shaped, soft papule, approximately 6 mm in size, on the right side of the chin; the papule was surrounded by a halo ring with a width of 5 mm (Fig. 1). The central soft tumor had developed 30 years earlier, and depigmented macules had gradually developed over the next 10 years. No other similar skin lesions or café-au-lait macules were observed. The patient had no family history of neurofibromatosis, vitiligo, or any autoimmune disease. Suspecting a diagnosis of halo nevus, we obtained a skin biopsy specimen from the papule and stained it with hematoxylin-eosin.
Histological examination revealed diffuse spindle cells interspersed with wavy collagenous strands and scattered mast cells (Fig. 2). The tumor was diagnosed as a solitary cutaneous extraneural diffuse neurofibroma.

We performed immunohistochemical examinations for Fontana-Masson stain, HMB-45, neuron-specific enolase (NSE), and S-100. Staining with Fontana-Masson did not reveal any melanin granules in the basal layer of the epidermis. Further, HMB-45 was not detected. These results suggested that melanocytes were absent in the epidermis and dermis. The tumor cells stained positive for S-100. Axons were uniformly distributed along with the collagenous strands, as revealed by NSE staining (Fig. 3). We diagnosed the patient with solitary neurofibroma associated with the halo phenomenon.

The primary nodule on the patient’s chin was excised, after which the patient was treated at the outpatient clinic for the depigmented macules; the macules were treated as vitiligo is, with topical steroid application. During the 1-year follow-up visit, the lesions were reassessed, and new hypopigmented macules were noted over the angle of the mouth on the right side (Fig. 4). No changes have been noted in the primary depigmented macules over the past 2 years.

DISCUSSION

Neurofibromas arise in the nerves. Cutaneous neurofibromas are usually 2–20 mm in diameter and may develop as solitary or multiple tumors. They manifest as protuberant or pedunculated, considerably soft, and skin-colored or reddish-brown papules or nodules. Localized forms of the tumors typically do not have any internal manifestations. Neurofibromatosis is an autosomal-dominant inherited syndrome that affects the skin, bones, and nervous system. Histologically, neurofibromas are composed of Schwann cells, fibroblasts, endothelial cells, perineural fibroblasts, mast cells, and axons. They are circumscribed but not encapsulated. Thus, during clinical examinations for tumors that are encircled by a hypopigmentation zone, differential diagnoses of halo neurofibroma, neural nevus, melanoma, blue nevus, epithelioid cell nevus, and spindle cell nevus...
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should be considered. The histological findings of neurofibromas include a deficiency in or the absence of melanin in the skin epidermis.

The pathogenesis of neuroectoderm-derived tumors associated with the halo phenomenon remains largely unclear. However, the available evidence suggests that it may involve both specific antibodies and T cells.

The possibility of circulating antibodies causing halo nevi was first recognized by Copeman et al., who evaluated patients with halo nevi who produced antibodies against the cytoplasmic antigens of melanoma cells. Nevus cells are destroyed through cell-mediated cytotoxicity, and this in turn triggers antibody production. This mechanism may be associated with the immune response to melanomas. Bystryn suggested that the mechanism may represent an immune response that is triggered by autoantigens common to normal melanocytes and melanoma cells and that causes cross reactions between these two cell types.

Lucchese et al. reported that the recognition of the tyrosinase autoantigen by the immune system follows the same molecular pattern in the sera of vitiligo and melanoma patients.

Although melanocytes are absent in both halo nevi and in vitiligo-affected regions, the available evidence is insufficient for halo nevus to be regarded as a form of vitiligo. In fact, human leukocyte antigens (HLAs) produced in patients with vitiligo vulgaris differ from those produced in patients with halo nevi associated with vitiligo; this suggests that these two conditions have distinct pathogenic mechanisms.

However, the findings reported for a case of giant congenital nevocytic nevus with neurotization and the onset of vitiligo and those reported for cases of multiple neurofibromas associated with the halo phenomenon and generalized vitiligo in patients with neurofibromatosis suggest that the relationship between vitiligo and multiple neurofibromas may be similar to that between vitiligo and halo nevus. In addition, since Schwann cells and melanocytes both originate from the neural crest, the immunological responses induced in patients with neurofibromas associated with the halo phenomenon may be similar to those in patients with generalized vitiligo.

Multiple neurofibromas associated with the halo phenomenon have been identified in patients with neurofibromatosis. These pa-

Fig. 3
Diffuse cytoplasmic staining of tumor cells to S-100 protein (A, x400) and scattered cytoplasmic staining of tumor cells to NSE stain. (B, x100)

Fig. 4
The scar of the previous operation on the depigmented macule and the new hypopigmented macules observed over the mouth angle. (lower lip)
Patients had the neurofibromas since childhood and had developed vitiligo many years later. Hypopigmented macules were present on the neurofibroma sites as well as the normal skin. The reasons for neurofibromas resulting in vitiligo and for the 2 distinct diseases developing in a single patient remain unknown. In the present case, new hypopigmented macules developed over the angle of the mouth on the right side, after the halo phenomenon had been managed. Moreover, halo nevus predicted the onset of vitiligo, as was the case in previous studies on patients with this condition. Further investigations on the specific underlying mechanism are required to explain the concomitant development of the halo phenomenon and vitiligo in patients with neurofibromas.

REFERENCES
單一病灶的光暈神經纖維瘤
-病例報告

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光暈的神經纖維瘤是十分罕見的皮膚良性腫瘤。過去只有三個多發性光暈神經纖維瘤和一個單一病灶的光暈神經纖維瘤的個案。臨床上可看到一個皮膚顏色、半球形、軟的丘疹或結節，旁邊圍繞著白色斑塊。神經外胚層腫瘤形成光暈現象的病理機轉並不清楚。我們在此報告一例發生在46歲女性的單一病灶的光暈神經纖維瘤個案並探討其可能原因。（中華皮誌：27: 181-185, 2009）