

## CASE REPORT

# Cutaneous Malignant Melanoma Associated with Papillary Thyroid Cancer

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As the survival from cutaneous malignant melanoma and its clinical concerns have been steadily increasing, the possibility has been raised of an increased risk of second primary cancers in the patients with malignant melanoma. Especially, recent studies have identified an association between cutaneous malignant melanoma and thyroid carcinoma. We here report on a case of cutaneous malignant melanoma that developed in a 61-year-old female patient who had hypothyroidism caused by papillary thyroid carcinoma. We suggest that the individuals who have cutaneous malignant melanoma may be predisposed to other primary cancers and especially thyroid carcinoma. Continuous monitoring of the thyroid function in melanoma patients is required because hypothyroidism can worsen due to malignant melanoma and this is probably associated with thyroid carcinoma. (*Ann Dermatol* 22(3) 370~372, 2010)

**-Keywords-**

Hypothyroidism, Melanoma, Papillary thyroid carcinoma

## INTRODUCTION

Cutaneous malignant melanoma is an uncommon tumor that arises from melanocytes and the melanocytes originate from the neural crest. As the survival from cutaneous malignant melanoma has increased, so too have the clinical concerns because the possibility has been raised of an increased risk of second primary cancers

in the patients with malignant melanoma<sup>1</sup>. Especially, recent studies have identified an association between cutaneous malignant melanoma and thyroid carcinoma<sup>2,3</sup>. There may be a genetic link between cutaneous melanoma and thyroid carcinoma due to the high prevalence of a mutation in the BRAF oncogene. Furthermore, a recent study reported a higher than expected prevalence of hypothyroidism among the patients with cutaneous melanoma, and both melanocyte-stimulating hormone and thyroid-stimulating hormone act upon the melanocytes and thyroid cells.

We report here on a case of cutaneous malignant melanoma that developed in 61-year-old female patient who had hypothyroidism caused by papillary thyroid carcinoma. We suggest that the individuals who have cutaneous malignant melanoma may be predisposed to having other primary cancers.

## CASE REPORT

A 61-year-old female presented with a 5-year history of a solitary 1.0×1.0 cm sized denuded black-colored nodule with 2.5×2.0 cm sized surrounding ill-demarcated mottled patches on the left heel, and the papules and patches had enlarged during the previous 2 months (Fig. 1). The histological finding of the skin biopsy revealed scattered or nested atypical melanocytes that were arranged in a pagetoid pattern in the epidermis. In the dermis, the tumor cells made up nests of anaplastic epithelioid cells with melanin pigments, and dilated vascular channels were also observed (Fig. 2). The immunohistochemical staining for S-100 protein and HMB45 was positive. After the lesions were confirmed as cutaneous malignant melanoma (T3bN0M0, Stage IIB), we operated and performed surgical excision and a partial skin graft. The dissected sentinel lymph node in the left

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inguinal area was negative for metastasis. The pre-operative routine laboratory findings were within the normal limits, except for the thyroid functional test and

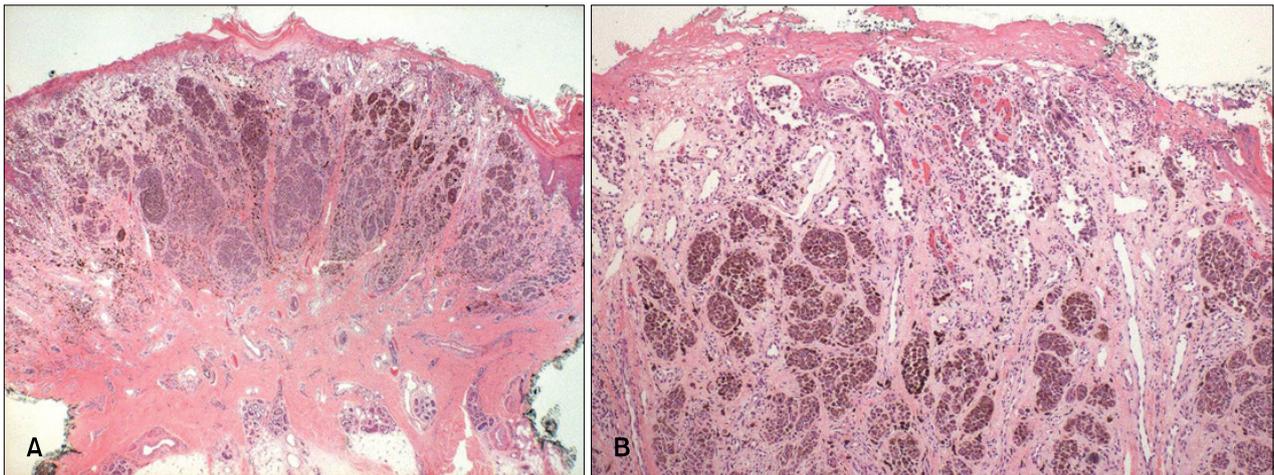


**Fig. 1.** The 1.0×1.0 cm sized solitary black-colored nodule with 2.5×2.0 cm sized surrounded ill-demarcated mottled patches on the left heel.

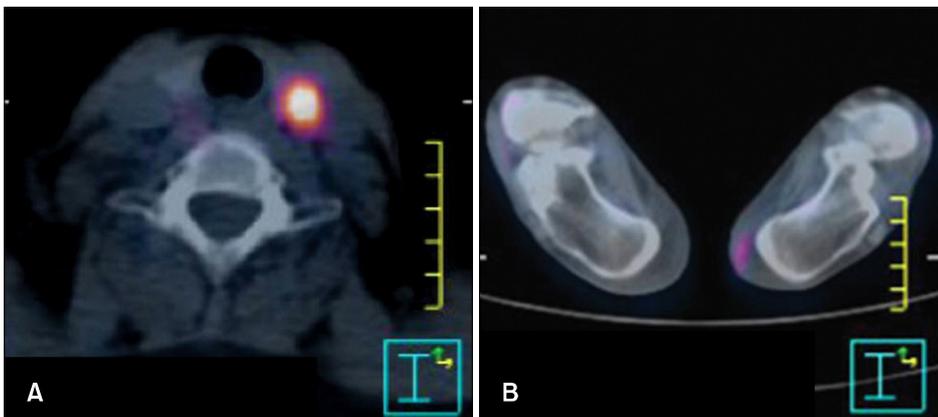
the latter had been within the normal limits 2 years ago. The thyroid stimulating hormone level (TSH: 6.2 mIU/L [normal range: 0.17~5.00 mIU/L]) was increased and the free T3 (1.5 pg/ml [normal range: 1.62~3.8 pg/ml]) and free T4 levels (0.7 ng/dl [normal range: 0.89~1.80 ng/dl]) were decreased. Fine needle aspiration was then done due to the abnormal indications of the thyroid both on the PET-CT scan and the thyroid ultrasonographic examination, which were both performed to evaluate for metastasis (Fig. 3). Papillary carcinoma was confirmed in the left lobe of the thyroid, and so we performed total thyroidectomy. We have not detected any indications of relapse during 24 months of follow-up both for the thyroid carcinoma and the cutaneous melanoma.

## DISCUSSION

Cutaneous malignant melanoma is a malignant tumor that originates from melanocytes. The incidence of cutaneous



**Fig. 2.** (A) The histopathologic findings show scattered or nested atypical melanocytes that are arranged in a pagetoid pattern (H&E stain, ×12.5). (B) The high power view reveals nests of anaplastic epithelioid cells with melanin pigment in the tumor and dilated, enlarged vascular channels in the dermis (H&E stain, ×40).



**Fig. 3.** The PET-CT scan finding shows focal hot lesions are checked (A) in the left lobe of the thyroid and (B) the soft tissue on the heel of the left foot.

malignant melanoma has recently risen in Korea<sup>4</sup>. As the survival of patients with malignant melanoma increases, it is known that the patients with cutaneous malignant melanoma are more susceptible to other primary cancers<sup>1</sup>. The incidence of a secondly primary cancer, except other skin cancers, is 1.5~20% for patients with malignant melanoma<sup>4</sup>. Especially, neural cancer, malignant lymphoma, breast cancer, head and neck cancer, uterine cancer, ovarian cancer, testicular cancer and gastrointestinal cancer have a higher risk of occurrence in patients with malignant melanoma<sup>4</sup>. Several recent studies have reported on the association between malignant melanoma and thyroid cancer<sup>2,3</sup>. Especially, superficial spreading melanoma is often accompanied with thyroid cancer, but more research on the subtypes of melanoma and thyroid cancer must be done since only a few comparative analyses on this association have been reported. The mechanism for this is uncertain, and there is little in terms of the epidemiology to support an association between hypothyroidism and melanoma. In a recent study, the overall prevalence of hypothyroidism (7%) in patients with malignant melanoma was greater than expected (4.6%) with statistical significance ( $p < 0.001$ ), and the risk was higher in males<sup>2</sup>. Additionally, Shah et al.<sup>2</sup> reported that hypothyroidism is more frequently occurred in patients with head and neck sited melanoma than that was originated from other anatomical sites. Some studies have reported that TSH is more likely to be expressed by dysplastic nevi than by benign nevi, and the dysplastic nevi of melanoma patients have a higher TSH expression than that of healthy individuals. Thus, TSH has been implicated in the malignant transformation of melanocytes to melanoma, and TSH stimulates the growth of melanoma cells<sup>5,6</sup>. On the other hand, the possibility has been suggested that the melanoma induces the thyroid dysfunction and this leads to hypothyroidism under the condition of low circulating thyroid hormone levels and concomitantly elevated TSH levels, although an autoimmune mechanism has also been suggested<sup>2</sup>. Moreover, the rearrangement of the RET proto-oncogene and mutation of the BRAF ontogeny, which are known to be

the causes of papillary thyroid carcinoma, are observed in cutaneous malignant melanoma. It seems that the BRAF oncogene plays a key role in the development of these two kinds of tumors<sup>3,7</sup>.

As the patients with hypothyroidism have a higher risk of malignant melanoma, we need to keep a close watch on the development of pigmented skin lesions in these patients. Continuous monitoring of the thyroid function in melanoma patients is required because hypothyroidism can worsen due to malignant melanoma and this probably is associated with thyroid carcinoma, like in our case<sup>2,5</sup>. More research is needed on the effects of TSH suppression with using thyroid hormone for the treatment of cutaneous malignant melanoma. We report here on a case of cutaneous malignant melanoma that was accompanied by papillary thyroid carcinoma in a 61-year-old female.

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