

# 갑상샘 유두암을 닮은 전이성 흑색종의 세침 흡인 세포 소견

## -1예 보고-

울산의대 울산대학교병원 및 서울아산병원<sup>1</sup> 병리과

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### Metastatic Melanoma Mimicking a Papillary Carcinoma of the Thyroid in Fine Needle Aspiration Cytology -A Case Report-

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Metastasis to the thyroid gland is very rare in clinical practice. We recently encountered a 65-year-old woman who presented with a large thyroid nodule that mimicked the cytologic features of a papillary thyroid carcinoma on fine needle aspiration biopsy (FNAB). Although initially diagnosed as a papillary thyroid carcinoma, a thorough clinical work-up revealed multiple lesions in the bones, liver, and nasal cavity, which were confirmed as metastases of a malignant melanoma. Despite a thorough physical examination, however, the primary skin lesion could not be identified. Although FNAB shows a high degree of accuracy in diagnosing primary thyroid tumors, it is less accurate in diagnosing metastases to the thyroid gland. A thorough clinical history with appropriate immunohistochemical staining assays is necessary for the accurate diagnosis of metastatic malignant melanoma.

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**Key Words :** Malignant melanoma, Thyroid gland, Metastasis

## INTRODUCTION

Fine needle aspiration biopsy (FNAB) is the method most frequently used for the diagnosis of thyroid nodules, including nodular hyperplasia, follicular neoplasm and papillary carcinoma. Papillary carcinoma, the most common malignancy in the thyroid, possesses cytologic features, including intranuclear pseudoinclusions, intranuclear grooves and vesicular nuclei, that are usually specific for its diagnosis. In contrast, metastatic

tumors rarely mimic the cytologic features of papillary carcinoma of the thyroid in FNAB. We recently encountered a patient with a metastatic malignant melanoma from an unknown primary site that had cytologic features similar to those of papillary carcinoma. The possibility of metastatic malignant melanoma should be considered in the differential diagnosis of papillary carcinoma. Immunohistochemical staining using antibodies to S-100 protein, HMB-45, and thyroglobulin can be helpful in differential diagnosis.

## CASE

A 65-year-old woman was referred to our hospital for a thyroid nodule, plus lower back pain of 2 months' duration. A palpable 4cm-sized nodule was detected in the right lobe of the thyroid gland. FNAB was performed using a 22-gauge needle connected to a 10ml plastic syringe. 95% ethyl alcohol was used as fixative. The immediate submersion of the wet cell sample into a fixative solution was performed to prevent air drying artifact. Hematoxylin-eosin stain was done. The thyroid aspirate was cellular and showed multiple long and thick branching papillae with scattered or loosely aggregated tumor cells (Fig. 1). Normal follicular cells and focal necrotic tumor diathesis were identified in the background, but the colloid was indistinct. The papillae each consisted of a central fibrovascular stalk covered by clusters of tumor cells. The tumor cells had round or slightly oval nuclei with small amount of cytoplasm. The nuclei contained nuclear indentations or grooves with occasional intranuclear pseudoinclusions and finely granular or optically clear chromatin (Fig. 2). Prominent nucleoli were frequently noted. No intracytoplasmic brown pigment or psammomatous calcification was detected.

Although these cytologic findings were similar to those of a papillary thyroid carcinoma, radiologic exam-

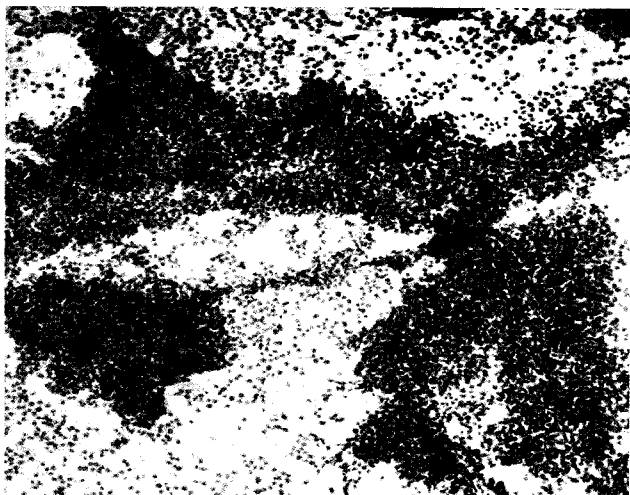


Fig. 1. Cytologic finding. Branching papillary tissue fragments were on a background of numerous aggregated or scattered oval cells, (H&E).

ination revealed disseminated metastatic tumors involving the liver, bones, nasal cavity, and thyroid. On magnetic resonance imaging, multiple lesions including a well-defined 1cm size nodule in the right lobe of the thyroid gland, multiple small nodules in the liver, and metastatic bone lesions involving cervical, thoracic, and lumbar spines with pathologic fracture were noted. Biopsies for the masses of the nasal cavity and liver were performed. Histologically, these tumors were composed of epithelioid tumor cells with intranuclear grooves and pseudoinclusions in pseudopapillary or diffuse patterns. Immunohistochemical staining showed

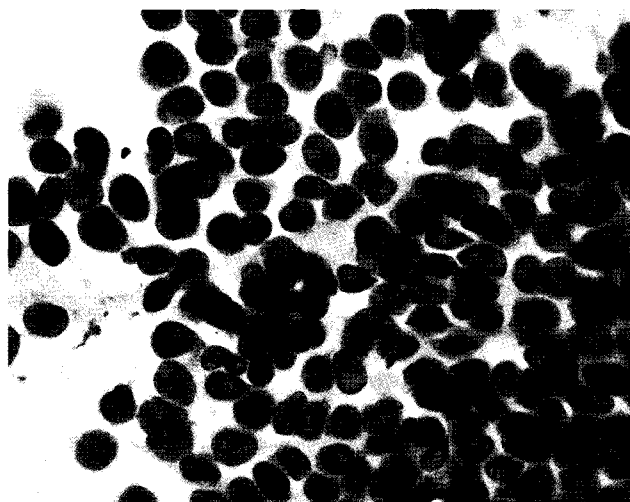


Fig. 2. Cytologic finding. Loosely cohesive tumor cells show crowded, grooved nuclei with irregular nuclear contours. Intranuclear pseudoinclusions were observed in a few cells, (H&E).

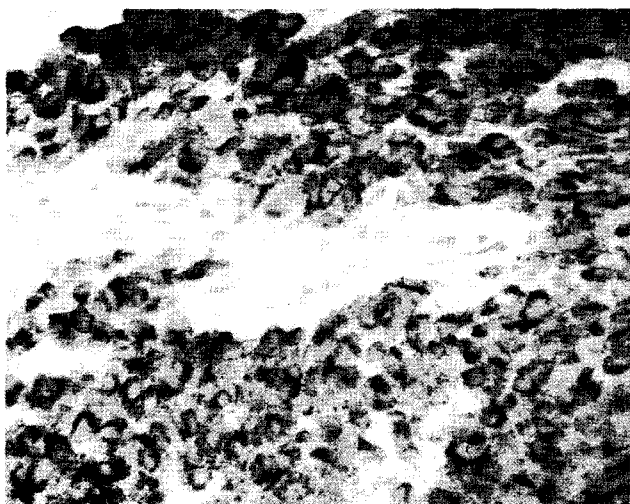


Fig. 3. Histology of tumor. The tumor cells are immunoreactive to antibody of HMB-45 (1:50, Dako).

that these tumor cells were diffusely and strongly immunopositive for S-100 protein (1:100, Zymed) and HMB-45 (1:50, Dako), and immunonegative for TTF-1 (1:200, Novocastra) (Fig. 3). These morphologic findings and immunophenotypic profiles indicated that this patient's thyroid lesion was a metastatic melanoma to the thyroid gland excluding a diagnosis of papillary thyroid carcinoma. The patient was not undergone surgical treatment because of multiple metastases at initial diagnosis. Four months later, she developed multiple lung metastases and died for multiple metastases.

## DISCUSSION

The incidence of metastasis to the thyroid gland in autopsy series varies from 1.25% to 24%.<sup>1</sup> Metastasis to the thyroid gland is usually considered as a terminal event with widespread malignant neoplasms.<sup>1</sup> Among the primary solid tumors found to metastasize to the thyroid are those of the kidney (32%), lung (28%), breast (20%), pleura (8%), uterine cervix (4%), skin (4%) and colon (4%).<sup>1-3</sup>

Malignant melanoma can metastasize to every organ. Thyroid involvement has been found on autopsy in 11% of patients who died of cutaneous melanoma, with metastasis to the thyroid usually occurring late in the course of disease.<sup>4-6</sup> Therefore, clinically significant metastatic malignant melanoma to the thyroid is a sign of disseminated disease and poor prognosis.<sup>7</sup>

It is extremely difficult to diagnose metastatic malignant melanoma to the thyroid using FNAB. For example, a recent case report described a patient with metastatic malignant melanoma to the thyroid gland diagnosed by FNAB.<sup>8</sup> Many cells had long, bipolar cytoplasmic processes. Moreover, the presence of papillary tumor cells, nuclear crowding and overlapping, and intranuclear grooves complicated the initial cytologic diagnosis, since malignant melanoma and papillary thyroid carcinoma have similar cytologic features.

The presence of melanin pigment, prominent nucle-

oli, lack of cell cohesion, and eccentric nuclei have been shown to be important cytologic features in the diagnosis of metastatic melanoma.<sup>9</sup> For example, melanin pigment has been detected in 66% of these tumors, but the patient described here, melanin-containing tumor cells were not observed.<sup>9</sup> In the absence of melanin pigment, a previous history of malignant melanoma or the presence of discohesive or isolated tumor cells with eccentric nuclei may have diagnostic value.<sup>10</sup>

Although high-resolution ultrasonography is highly sensitive in detecting small lesions of the thyroid gland and may improve the survival of patients with thyroid metastases, clinical assessment may be particularly difficult.<sup>11</sup> Therefore, morphologic diagnosis using FNAB is considered an important tool for establishing the nature of a thyroid tumor.<sup>11</sup> For example, although malignant melanoma and thymoma with a dominant epithelial component can mimic the cytologic features of papillary carcinoma,<sup>8,12</sup> immunohistochemical staining using antibodies to S-100 protein, HMB-45, and thyroglobulin can be helpful in differential diagnosis.

Although our patient had metastases of malignant melanoma, we could not identify the site of origin. This is not unusual, since analysis of 2446 patients with malignant melanoma found that 4% did not have a known primary site.<sup>13</sup> More than half were admitted with nodal disease only and one third were admitted with visceral metastases.

There is no clear consensus on the role of surgery in metastatic thyroid disease.<sup>6</sup> Even in advanced disease, however, surgery may have some benefits, including relief of symptoms and prolongation of life.<sup>7</sup> By Karakousis et al.,<sup>14</sup> patients treated with complete excision and chemotherapy showed a significantly increased survival rate compared to patients who underwent partial excision or those treated with chemotherapy alone.

In summary, we report here a patient with metastatic malignant melanoma to the thyroid mimicking a papillary carcinoma in FNAB. Findings in this patient indi-

cate that a complete clinical history, physical and radiologic examinations, and the appropriate use of immunohistochemistry are necessary to establish the nature of a thyroid tumor.

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