Metastasis of Merkel Cell Carcinoma to the Thyroid Gland: a Case Report

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ABSTRACT

Merkel cell carcinoma (MCC) is an uncommon neuroendocrine cutaneous malignancy. The thyroid gland is an exceptionally rare site of metastasis for MCC. Thus, metastasis to the thyroid gland may entail diagnostic difficulties. An 82-year-old man presented with a palpable neck tumor in the right anterior neck. Computed tomography scan revealed a 3.4 cm, enhancing tumor in the right thyroid gland. The patient underwent fine needle aspiration, and cytologic and immunohistochemical findings revealed metastasis of MCC to thyroid gland. We decided to perform surgical excision of the right thyroid gland. The patient was discharged 2 days after surgery without any complications. Various immunohistochemical studies were performed with the surgical specimen. The tumor cells were positive for CK 20 and CD 56, but negative for thyroid transcription factor-1. Finally, the histopathologic diagnosis confirmed as metastasis of MCC to the thyroid gland. Here, we present an exceedingly rare metastasis of MCC to the thyroid gland and discuss its diagnosis and treatment. In patients with a known history of a primary malignancy, the differential diagnosis of any abnormal findings in the thyroid gland should always include possibility of potential metastasis.

Keywords: Thyroid gland; Merkel cell carcinoma; Metastasis

INTRODUCTION

Merkel cell carcinoma (MCC) is a highly aggressive and rare neuroendocrine malignancy arising from the skin. The tumor was first described in 1972 by Cyril Toker (1) as a variant of sweat gland carcinoma called trabecular cell carcinoma of the skin. MCC is an uncommon tumor, with its reported incidence of 0.6 per 100,000 person-years (2). It is predominantly seen in the elderly on the sun-exposed areas of the body (3,4). Some reports suggest ultraviolet radiation as a risk factor, as most MCCs occur on sun-damaged skin (5,6). Another risk factor related to the pathogenesis of MCC is immune suppression. MCC is found to be more common among patients with human immunodeficiency virus, lymphoma, or leukemia (7-9).

MCC commonly presents with a nonspecific erythematous or violaceous firm nodule. The most common clinical features of MCC have been summarized by the acronym AEIOU: 1) A for asymptomatic tenderness; 2) E for expanding rapidly (<3 months); 3) I for

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immunosuppression; 4) O for older than age 50; and 5) U for ultraviolet-exposed sites. Up to 89% of patients with MCC met 3 or more of the AEIOU criteria (6).

The treatment modalities for MCC remains inconsistent and recommendations are not uniform. Mainstay of treatment is multidisciplinary management with local excision, postoperative radiotherapy and adjuvant chemotherapy depending on the stage of the disease (10).

The head and neck are the most common site of occurrence, accounting for about 50% (11). Majority of patients present with a localized skin tumor and clinically negative lymph nodes. At the time of diagnosis, 30% have metastatic disease in the skin, liver, bone, lung, brain or distant lymph nodes (12,13). However, the thyroid gland is a rare site of metastasis for MCC with only few cases published to date. Here, we report a case of metastatic MCC to the thyroid gland.

**CASE REPORT**

An 82-year-old man was referred to the division of thyroid and endocrine surgery with palpable neck tumor in the right anterior neck. The tumor had been detected 7 months before. Computed tomography (CT) scan revealed a 3.4 cm heterogenous enhancing tumor with calcification in right thyroid gland (Fig. 1), which indicated metastasis from MCC.

The patient initially presented with a 5 cm left axillary lesion for 2 months. Within the past month, the lesion rapidly grew to 10 cm. A needle biopsy was performed, and the tumor was diagnosed as MCC. This patient underwent wide excision of the left axillary region with axillary lymph node dissection due to MCC’s high rate of metastasis to lymph nodes.

Afterwards, the patient was admitted to our department for further clinical evaluation and treatment. At initial sonographic examination, the tumor in his right anterior neck was microlobulated with microcalcification. Findings showed high suspicion for malignancy, such as anaplastic thyroid carcinoma. The patient underwent fine needle aspiration (FNA) of the largest tumor located in the right thyroid gland. Cytology features on FNA revealed irregular clusters of small to intermediate sized cells which showed monomorphous tumor cells with scant cytoplasm and round hyperchromatic nuclei with finely granular chromatin (Fig. 2A). Numerous mitosis and karyorrhectic nuclei were present. Immunohistochemical study was performed, and results were positive for CK 20 and CD 56. Immunostaining for CK
20 on cell block showed a paranuclear dotlike pattern (Fig. 2B). The patient was subsequently diagnosed as metastasis of MCC to the thyroid gland.

We decided to perform right hemithyroidectomy to resolve patient’s symptoms. Intraoperative findings showed apparent extrathyroidal extension to the recurrent laryngeal nerve and strap muscles, but no enlarged lymph nodes. The patient had the recurrent laryngeal nerve cut off during operation, but was discharged the next day without any specific symptoms.

Histopathologic examination showed infiltration of the thyroid gland by MCC. The tumor consisted of small to intermediated sized cells with round nucleus, inconspicuous nucleoli and scant cytoplasm infiltrating the thyroid gland (Fig. 3A). Numerous mitoses and areas with necrosis were observed. Immunohistochemical studies were performed for synaptophysin, CD 56 (Fig. 3C), CK 20 (Fig. 3D), and thyroid transcription factor-1. The tumor cells were positive for synaptophysin (Fig. 3B), CD 56 (Fig. 3C) and CK 20 (Fig. 3D), but negative for thyroid transcription factor-1 (Fig. 3E) and calcitonin (Fig. 3F). These results finally confirmed the diagnosis of metastasis of MCC to the thyroid gland.

Adrenal metastasis was confirmed on abdominal CT 3 months after right hemithyroidectomy, and adrenalectomy was performed. The patient was referred to the department of hematology and oncology for additional systemic treatment. However, the patient refused further treatment due to economic burden and old age.

**DISCUSSION**

Primary thyroid cancer is the most common endocrine malignancy, and its incidence accounts for 1%–1.5% of all cancers (14,15). Despite rich vascular supply of the thyroid gland, metastatic thyroid cancers are an exceptionally rare. Possible reason for such a low incidence of metastatic thyroid cancers, is abundant arterial supply which is associated high oxygen saturation and iodine content in the thyroid gland. This inhibits the growth of malignant cells in the thyroid gland (16,17). Clinical metastasis to the thyroid gland occurs less than 3%, but this number may increase in the future due to greater use of high-resolution ultrasonography and FNA (18,19). The most common cancers metastasizing to the thyroid gland are renal cell, lung, colorectal, breast, stomach, and melanoma (20,21). However, MCC is rare type of cancer to metastasize to the thyroid gland.

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MCC is a highly rare neuroendocrine malignancy of the skin, accounting for less than 1% of skin cancers. It is a fast-growing tumor and commonly metastasizes to bone and lymph nodes (22). The protocol of treatment for MCC should be based on a multidisciplinary approach, including wide local excision, chemotherapy and radiotherapy (23). Surgical removal of the primary tumor is most important due to its aggressiveness. Postoperative radiation therapy is generally recommended for locoregional control (24). The role of chemotherapy remains controversial in patients with no metastatic disease, and although many chemotherapeutic regimens show positive results, survival benefit has not been conclusively demonstrated (24). MCC shows an aggressive clinical course and local recurrence and distant metastasis are common. Overall survival at 5 years is approximately 51% for local disease, 35% for nodal disease, and 14% for distant disease (25).

Metastasis of MCC to the thyroid gland is an exceptionally rare clinical finding. Only 3 other cases have been described in literature (4,26). Primary diagnostic method for metastatic thyroid cancers is FNA cytology (27). Classic cytologic features of MCC are small to intermediate cells with scant cytoplasm, large round-to-oval nuclei with homogenous chromatic pattern, no nuclear infoldings or indentations, and several mitoses (4). For further evaluation of thyroid lesions, magnetic resonance imaging, CT, or positron emission tomography/CT can be used to distinguish malignancy from benign tumors (24).

Immunohistochemistry is essential to differentiate MCC from other malignancies (28). The tumor expresses CK 30, neuroendocrine markers (chromogranin A, CD 56), neurofilament, and thyroid transcription factor-1. Staining results for MCC is positive for CK 20 and neurofilament and negative for thyroid transcription factor-1. Small cell lung carcinoma must be differentiated from MCC, and using a panel of immunohistochemistry markers can be helpful. Especially, immunohistochemical stains for CK 20, neurofilament, and

Fig. 3. Metastatic Merkel cell carcinoma in the thyroid gland. (A) Low-power view of hematoxylin-eosin stained showing features of small round tumor infiltrating the thyroid gland (×100). Tumor cells are positive for (B) synaptophysin, (C) CD 56, and (D) CK 20, and negative for (E) thyroid transcription factor-1 and (F) calcitonin (×100).
thyroid transcription factor-1 are useful markers for differentiation of MCC from lung small cell carcinoma (29). MCC is positive for CK 20 and neurofilament and negative for thyroid transcription factor-1, while lung small cell carcinoma is positive for thyroid transcription factor-1 and negative for CK 20 and neurofilament.

Most patients with metastatic thyroid cancer were asymptomatic at presentation. However, some patients with metastatic thyroid cancer had symptoms such as palpable neck tumor, dysphagia, or hoarseness (30). In this case, the patient initially presented with palpable neck tumor.

Although surgical removal of metastatic thyroid cancer is performed to prevent potential morbidity related to recurrence in the neck. However, prognosis is poor in most patients. For metastatic thyroid cancer, systemic therapy with chemotherapy is the treatment of choice. Radioactive iodine therapy is not indicated for metastatic thyroid cancer.

In conclusion, we present a highly rare case of a patient with metastasis of MCC to thyroid gland. In this case, thyroidectomy did not appear to affect the patient’s prognosis, but our patient had some symptoms and we decided to undergo thyroid lobectomy. The clinical significance of this case is that any abnormal findings in the thyroid gland in patients with MCC, the possibility of metastasis from the primary malignancy should always be evaluated. Early and prompt diagnosis can facilitate appropriate treatment and may improve prognosis.

REFERENCES