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Malignant melanoma metastatic to the thyroid gland: a case report and review of the literature.

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**MALIGNANT MELANOMA METASTASIZING TO THE THYROID
GLAND**

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INTRODUCTION

Metastatic disease in the thyroid gland accounts for less than 1% of cases of thyroid cancer^{1,2}. The most common sources of metastases are renal cell carcinoma, breast carcinoma, and lung carcinoma³⁻⁶. Clinically apparent metastatic melanoma to the thyroid gland is rare, accounting for less than 5% of metastatic tumors to the thyroid⁶.

We present a case of a patient with malignant melanoma metastatic to the thyroid gland as the first manifestation of distant metastatic disease.

CASE

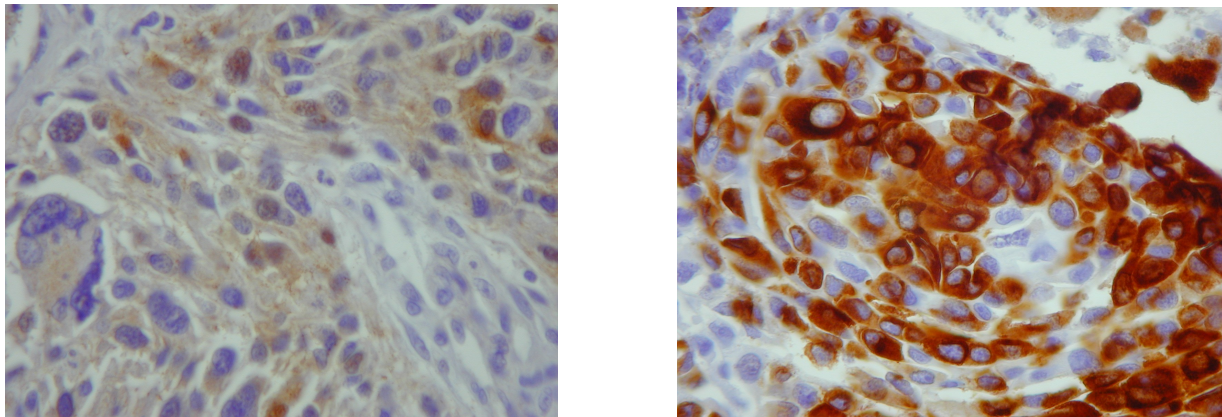


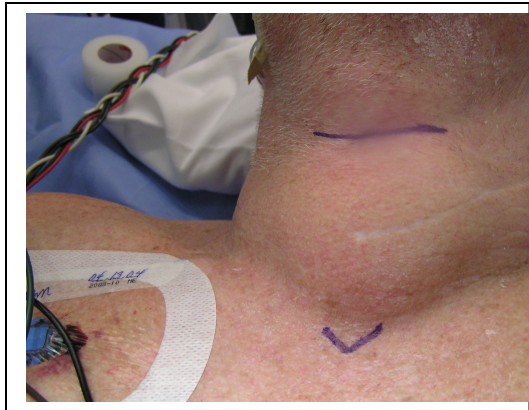
Figure 1: a) S-100 stain of melanoma cells from FNA specimen, b) Melan-A stain from FNA specimen

A 68-year-old male with a 30 pack year tobacco history presented with a left posterior triangle neck mass measuring 1.5 cm. Physical exam and radiographic studies performed at the time failed to reveal a primary tumor—just the posterior triangle mass. An FNA of the mass at the time revealed a poorly differentiated squamous cell carcinoma. The patient was taken to the

operating room for direct laryngoscopy with biopsy, left tonsillectomy, esophagoscopy and bronchoscopy with bronchoalveolar lavage, as well as repeat FNA of the neck mass. Again, there was no evidence of a primary lesion. However, FNA at this time was suggestive of melanoma, and this diagnosis was confirmed via immunophenotyping, which showed the cells staining positive for Melan-A and S-100 (Figure 1). Biopsies of the left tonsil, nasopharynx and left tongue base were all negative. The patient then underwent a left modified radical neck dissection. The posterior triangle neck mass was discovered to be a lymph node which tested positive for malignant melanoma. All other nodes were negative. No primary site for the malignant melanoma was found, and the patient was scheduled for postoperative radiation therapy and chemotherapy. However, the patient was reluctant to receive these treatments and subsequently was not further treated.

Eighteen months later, the patient presented with a midline neck mass representing a diffusely enlarged thyroid gland. The gland measured 10cm in diameter (Figure 2). An FNA of the mass was performed which revealed malignant cells consistent with a melanoma and

confirmed by positive Melan-A and S-100 stains.
Figure 2: Patient's neck mass presenting as enlarged thyroid gland.



The patient underwent an MRI of the neck, revealing a diffusely enlarged cystic thyroid gland without associated cervical adenopathy (Figure 3).

Approximately two weeks later, the patient began having seizures, and an MRI of the brain revealed a 1.7cm mass in the region of the anterior superior vermis, with associated mass effect and mild hydrocephalus (Figure 4). This was suspicious for metastatic melanoma. At this time, a CT scan of the

chest, abdomen, and pelvis was obtained, showing a soft tissue lesion in the suprapubic region consistent with metastatic melanoma.

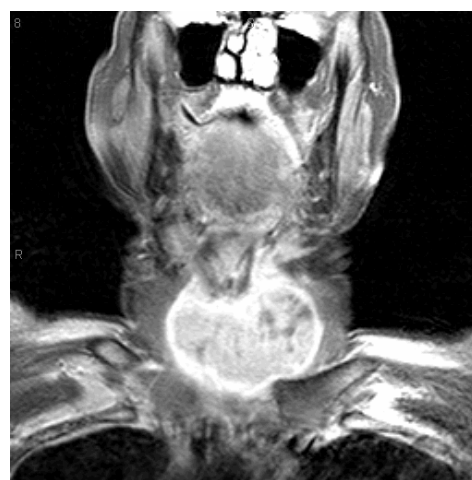
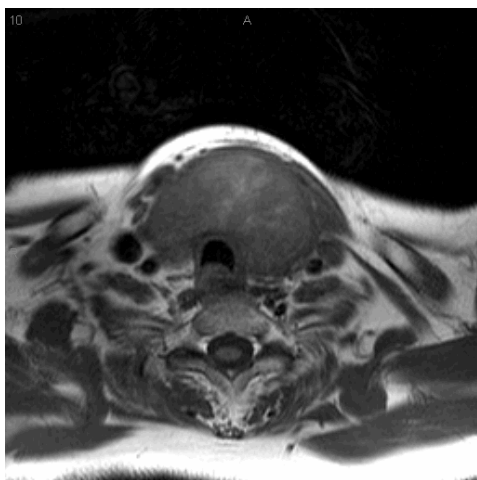


Figure 3: a) Axial T1W MRI showing enlarged thyroid gland, b) Coronal T2W MRI showing similar findings.

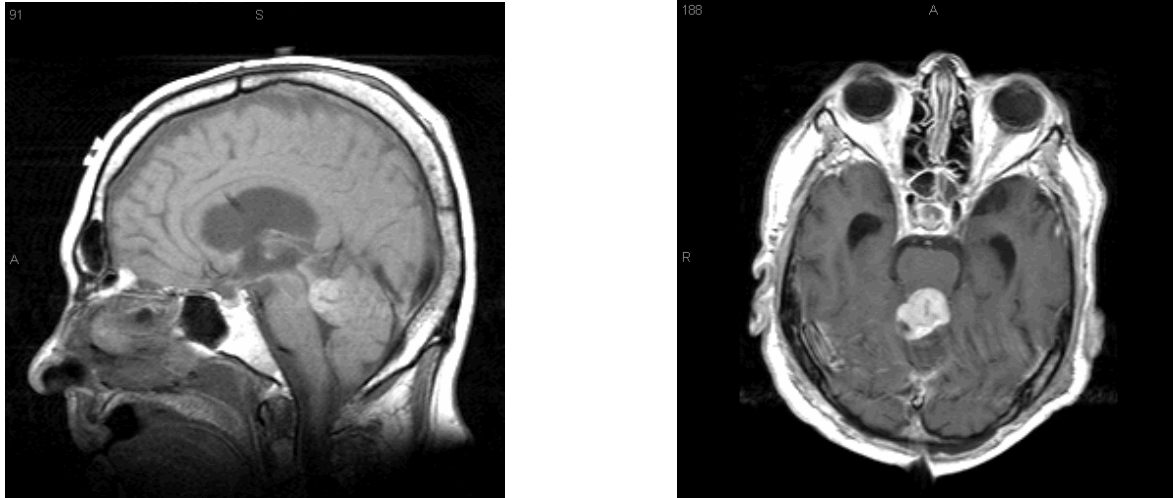


Figure 4: a) Sagittal T1W MRI showing enhancing lesion of anterior vermis with associated hydrocephalus, b) axial T1W MRI showing similar findings.

The patient soon developed ventilator dependent respiratory failure, and he was taken to the operating room for a subtotal thyroidectomy for establishment of a tracheostomy (Figure 5).

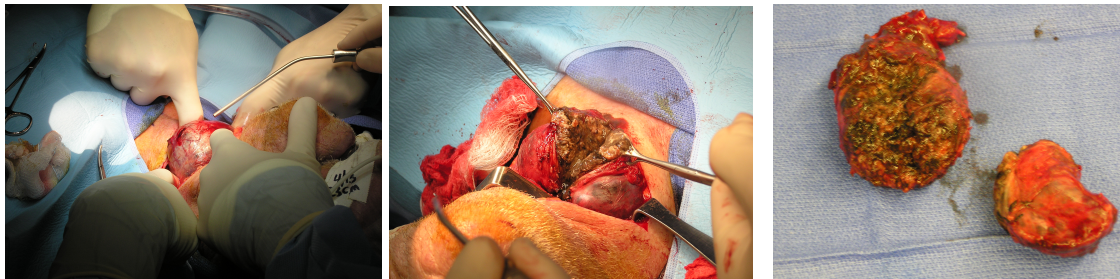


Figure 5: a) Intraoperative view of enlarged thyroid gland; b) division of thyroid gland to facilitate removal prior to tracheostomy; c) gross subtotal thyroid specimen removed. Note the extensively pigmented thyroid parenchyma.

Histologic specimens showed the thyroid largely being replaced by metastatic melanoma with extensive necrosis (Figure 6). The patient subsequently required placement of a ventriculoperitoneal shunt to treat the hydrocephalus secondary to the metastatic lesion in his posterior fossa.

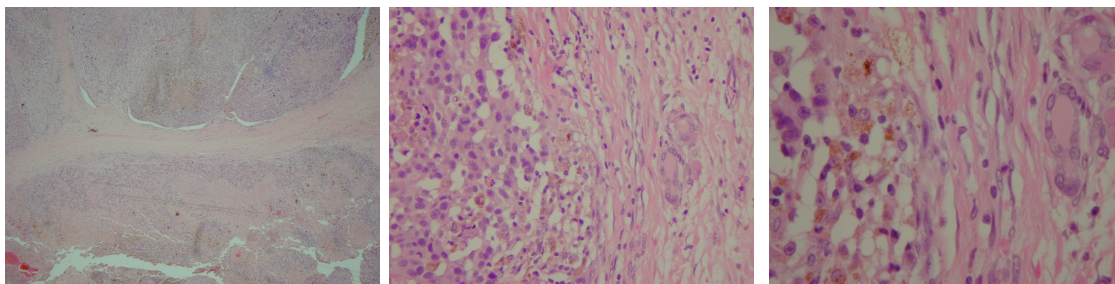


Figure 6: a) H&E stain, 2x view showing extensive replacement of thyroid parenchyma by nests of melanoma and considerable necrosis; b) 20x view showing melanoma on the left and thyroid on the right—two thyroid follicles are seen; c) the 40x view best shows the pigment and hemosiderin among the melanoma tubes.

DISCUSSION

The case presented above is similar to the few other case reports detailing metastatic melanoma to the thyroid gland. Our patient's presenting symptom was a lump in the neck, and studies have shown this to be the most common complaint among patients with metastatic disease to the thyroid gland^{7,8}. Other authors have found that the pathology of the thyroid shows total replacement of the gland by metastatic melanoma, yet with preservation of thyroid function⁹⁻¹¹. Our patient, too, had no clinical evidence of hypothyroidism. His laboratory thyroid abnormalities (slightly decreased TSH, normal free T4) more likely represent the slight variation in thyroid function tests seen in euthyroid sick syndrome. Shimaoka et al describe a likely explanation for this phenomenon—it takes weeks to months for total ablation of thyroid function to manifest as hypothyroidism, and most patients do not survive long enough with metastatic tumor for hypothyroidism to become apparent¹². Additionally, although it has been suggested that pre-existing abnormalities of the thyroid, such as nodules or adenomas, predisposes it to metastatic lesions^{13,14}, our patient, like that of Mitra's⁹, did not have any such abnormalities upon pathological examination of the gland or upon clinical history.

Various autopsy studies have revealed the incidence of malignant melanoma metastasizing to the thyroid gland to be high. Although Nakhjavani et al⁶ found melanoma to account for less than 5% of clinically apparent metastatic thyroid tumors, autopsy studies have shown the number to be much higher – as high as 35% of all metastatic lesions to the thyroid¹³. The disparity can be explained by the fact that in autopsy studies, metastatic lesions are discovered only upon microscopic examination of small, careful cuts of the gland. Small foci of metastases may not present clinically as a thyroid nodule or goiter. In autopsy studies focused only on patients with melanoma, Patel et al found the incidence of thyroid metastases to be 26% in the 261 autopsies performed¹⁵. In a similar study of 41 patients with melanoma, Shimaoka et al found thyroid metastases in 39%¹². It is not surprising that melanoma has such a high propensity for the thyroid gland given that the thyroid is a highly vascular organ and melanoma spreads via the hematogenous route. In fact, melanoma has the ability to metastasize to almost every organ given its aggressive nature. The most common sites of metastases for melanoma are lymph node, lungs, liver and brain¹⁵. Thus, although patients with melanoma may commonly have thyroid metastases without clinical consequence, it is rare that a mass in the thyroid would be their only clinically apparent sign of metastatic melanoma. Although our patient was discovered to have additional inguinal lymph node and brain metastases during his hospital course, it was his thyroid nodule that was the first indication of metastatic disease.

Metastases of any malignancies to the thyroid are much more common than one would expect. The incidence of metastatic growths in the thyroid gland when patients are known to have metastatic tumors is fairly high. In a large autopsy study in Malmo of 7332 patients with known malignancy, 2.8% were found to have thyroid metastases¹⁸. Other studies have found the incidence as high as 9.5%¹². Combining various autopsy studies, a more representative figure is 5-6%. These surprising numbers have prompted some to state that metastatic thyroid neoplasms may be 10 times as numerous as primary thyroid cancers¹². Watts reports that FNA of six patients presenting with a thyroid nodule who had a past history of malignancy, four had cytologic evidence of malignancy, representing 66%¹⁶. This led him to conclude, along with Shimaoka et al, that in a patient with a history of cancer, a malignant thyroid nodule is much more likely than a primary^{12,16}.

Our case allows for discussion of the diagnosis and management of thyroid metastases. FNA has been reported to be the initial procedure of choice in diagnosis of metastatic lesions to the thyroid, and it carries low morbidity^{16,17}. In our patient, although the initial FNA of his left neck mass misrepresented melanoma as poorly differentiated squamous cell carcinoma, his subsequent two FNAs of the left neck mass and the thyroid mass confirmed melanoma with the help of immunohistochemical stains. The FNA in this patient was useful in guiding management of the patient. Clearly a metastatic lesion to the thyroid must be managed very differently than a lymphoma or a primary thyroid tumor. In general, secondary neoplasm to the thyroid is usually an indicator of poor prognosis. Metastatic cancer to the thyroid predominates in the sixth, seventh and eighth decade of life, and these patients in general have a worse prognosis secondary to advanced age^{5,8}. More importantly, thyroid metastases are usually part of a widely disseminating malignancy. In most case series of metastases to the thyroid gland, other metastatic deposits are identified at or soon after the discovery of the lesion. With the exception of metastases from renal cell carcinoma, Rosen et al showed patient survival less than 2 years after discovery of thyroid metastases¹⁷. McCabe et al had an average survival of 12 months in their 17 patients with metastases to the thyroid⁸. In discussing melanoma specifically, patients with metastatic melanoma have a median survival of 24 months, irrespective of site of metastasis¹⁵. Less than 1% of melanoma patients have single organ metastasis, and when combined with other poor prognostic indicators, surgical management of metastatic melanoma is most often limited to palliative measures¹⁵. Thyroidectomy is an accepted procedure for palliation from dyspnea or dysphagia, or as in our patient, placement of tracheostomy tube. In the rare case that the thyroid is the only site of metastatic deposits, thyroidectomy can be curative⁷.

Any patient with a history of malignancy and a thyroid nodule presents a diagnostic dilemma. Is this a benign nodule, a new primary, or a metastasis? The FNA can be very helpful in distinguishing these entities. If it represents metastatic disease, is this a “new” metastases suggesting a neoplastic recurrence, or is this merely the growth of microscopic deposits from a much earlier neoplasm? Others have authored similar dilemmas - Ivy describes melanoma in the thyroid gland years before and years after the primary is ever discovered⁵. Nakhjavani et al report months between detection of primary malignancy and metastases to the thyroid⁶. In our patient, the thyroid metastasis presented 18 months after initial diagnosis of metastatic melanoma. Did his thyroid metastases represent a new primary, or was it the remnant deposits from an inadequately treated initial melanoma? In our case, it is especially difficult as a primary neither for the initial lesion, nor for the thyroid and brain metastases was ever found. However, given the high incidence of thyroid metastases in malignancy, and given the long time period between initial neoplasm and discovery of thyroid metastases, we must agree with Nakhjavani et al that any patient with a previous history of malignancy with a thyroid mass should be considered as having metastases until proven otherwise⁶.

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