

Metastatic Melanoma Presenting as a Thyroid Nodule in a 38-Year-Old Woman

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Thyroid nodules are common and are often found incidentally by palpation or by radiographic imaging. The prevalence of thyroid nodules varies according to diagnostic modality and has been reported at approximately 4% by palpation,^{1,2} 13% to 67% by ultrasonography,³ and 50% by autopsy in individuals with no previous thyroid disease.⁴ Although most thyroid nodules are benign and require only monitoring,⁵ 5% to 10% are malignant,^{6,7} with a small proportion due to metastatic lesions from other primary tumors. Currently, fine-needle aspiration (FNA) is a standard diagnostic procedure to differentiate between benign and malignant thyroid nodules, but this procedure is associated with a 15% to 30% rate of an indeterminate/suspicious cytologic interpretation and a 5% false-negative rate.⁵ As such, consideration of clinical risk factors for malignancy and use of additional immunochemistry markers may be important adjuncts to diagnosis. This article presents the case of a woman who presented with neck enlargement and was subsequently diagnosed with metastatic melanoma after evaluation of a mass in the left lobe of the thyroid.

CASE PRESENTATION

Initial Presentation and History

A 38-year-old woman was referred to the endocrinologist by her oncologist for evaluation of neck enlargement. The patient's past medical history was significant for melanoma, which was removed in 1993 from her right shoulder and interpreted as a Spitz nevus by pathologic examination. No further evaluation or treatment was done at that time. Subsequently, she had been in good health until early 2006, when she noticed a 7-cm axillary mass while pregnant. Core needle biopsy findings were compatible with malignant melanoma. In February 2006, the melanoma was locally excised and no extranodal extension was detected. Pathologic evaluation of the surgical specimen revealed a 5-cm tumor with 1 of 6 positive lymph nodes. Computed tomography (CT) of the chest and abdomen did not reveal any evidence of metastasis. After the delivery of her child

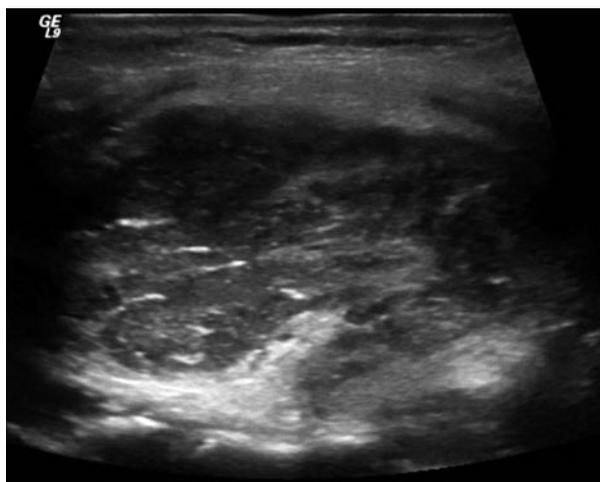


Figure 1. Ultrasound image of the thyroid nodule showing a heterogeneous mass replacing nearly the entire left lobe of the thyroid.

in June 2006, the patient began interferon therapy. Four months postpartum, the patient noticed a neck mass. She denied neck pain, hoarseness, dysphagia, or dyspnea. There was no previous exposure to radiation or any personal or family history of thyroid disease. She reported no medication use. She was euthyroid with normal thyroid function tests.

Physical Examination and Diagnostic Studies

On physical examination, the patient had thyroid enlargement of the left lobe. Ultrasound of the thyroid revealed a solid heterogeneous mass measuring $3.0 \times 2.8 \times 5.5$ cm and replacing nearly the entire left lobe of the thyroid (**Figure 1**). FNA of left thyroid nodule was performed in September 2006. Pathologic evaluation of the aspirate revealed several single and loosely clustered large spindle-to-oval cells with large pleomorphic

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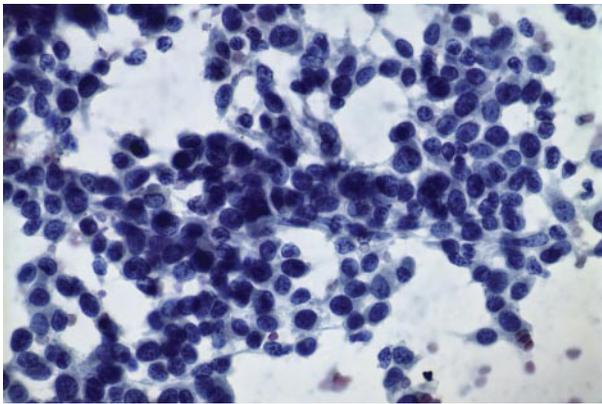


Figure 2. Cytology of aspirate of the thyroid nodule showing malignant tumor cells, which are spindle cells with large nuclei and prominent nucleoli in a solid pattern (Papanicolaou's stain, 400x magnification).

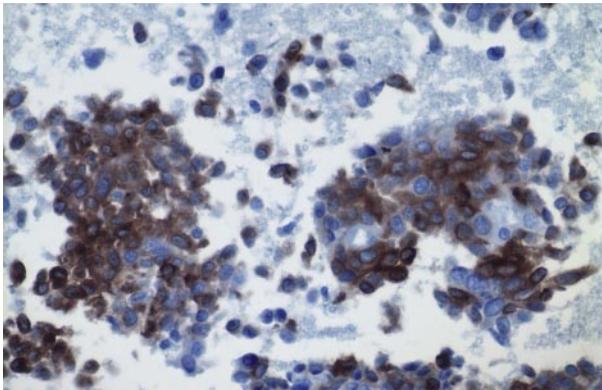


Figure 3. Immunohistochemistry on cell block from the aspirate of the thyroid nodule demonstrating immunoreactivity of tumor cells to the stains specific to melanoma detection (HMB-45, Melan-A, and tyrosinase monoclonal antibodies, 400x magnification).

nuclei with irregular contours, conspicuous nucleoli, and abundant granular cytoplasm, suggestive of a malignant tumor (**Figure 2**). Immunohistochemistry staining with thyroglobulin antibodies and staining specific to melanoma (HMB-45, Melan-A, and tyrosinase monoclonal antibodies) was performed on a cell block from the thyroid aspirate. The tumor cell cytoplasm reacted negatively with the thyroglobulin antibodies and positively with the melanoma staining, also consistent with melanoma (**Figure 3**). One month later, the patient underwent a left thyroid lobectomy. Pathologic findings of the left thyroid mass were consistent with metastatic melanoma (**Figure 4** and **Figure 5**).

At a follow-up visit 3 months later with the oncologist, recurrence of the melanoma was found in a right cervical lymph node. Subsequent CT scans of the neck, chest, and abdomen revealed additional involvement

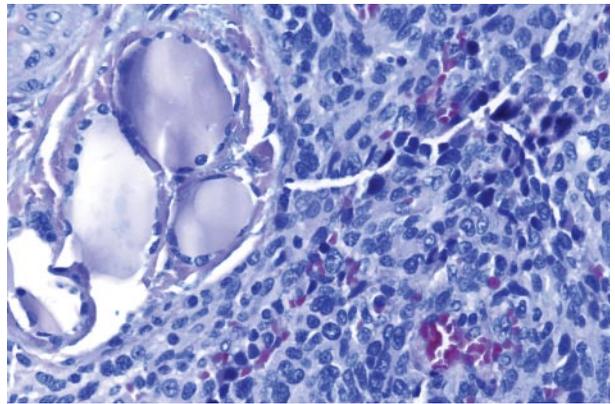


Figure 4. Histology of metastatic melanoma to the thyroid gland (hematoxylin and eosin stain, high power).

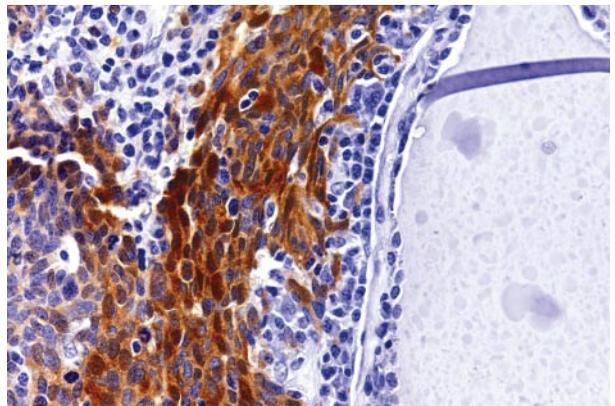


Figure 5. Immunocytochemistry of the thyroid surgical specimen showing immunoreactivity of tumor to monoclonal antibodies to S-100, a marker of melanoma (high power).

of lymph nodes in the mediastinum, pericardium, and pelvic area. Chemobiotherapy consisting of cisplatin, vinblastine, dacarbazine, and interferon was initiated.

THYROID METASTASIS

Despite the high relative vascular perfusion to the thyroid, metastasis to the thyroid is uncommon, occurring in less than 2% of clinically detected thyroid cancers;^{8,9} however, the prevalence at autopsy appears to be higher, up to 24% depending on the population studied.¹⁰ Metastasis to the thyroid gland has been associated with several primary malignancies, including renal cell carcinoma, breast cancer, lung cancer, gastrointestinal malignancies, melanoma, sarcoma, hematologic malignancies, and other genitourinary cancers. Renal cell carcinoma and breast and lung cancers are the most common primary sources.^{8,9,11,12} Metastasis to the thyroid may occur concomitantly with metastases to other sites or many years after the original diagnosis of the primary

tumor.¹¹ While factors that predict thyroid metastases are not well defined, two 10-year retrospective reviews of thyroid pathology records found that only older age (> 60 yr) was more frequently associated with thyroid metastases, an observation that simply may reflect the increased risk for malignancy with age.^{10,13}

The first case of thyroid metastases secondary to melanoma is believed to have been reported by Sheppard and Moseley,¹⁴ who described metastases to the thyroid and lungs in a 48-year-old man with a history of primary melanoma. When metastases of the thyroid are associated with melanoma or any other primary malignancy, thyroid function tests tend to be normal, even when involvement of the gland is extensive.¹⁵ Moreover, melanoma-related metastases to the thyroid may occur several years after initial diagnosis. For instance, Bozbora et al¹⁶ reported a case of malignant melanoma in a thyroid nodule 5 years after excision of a 2-mm skin melanoma.

The most common clinical presentation of metastatic lesions to the thyroid is a solitary nodule or multinodular goiter, identified incidentally or by palpation.¹⁰ In most cases, the diagnosis can be made with FNA.^{10,13} However, immunohistochemistry may be a helpful adjunct in the evaluation of thyroid nodules in patients with a past history of malignancy,¹⁷ particularly when delineation between metastases and primary thyroid cancer is difficult. For melanoma, immunohistochemistry with antibodies to melanocyte differentiation antigens (ie, HMB-45, tyrosinase, melanoma cell adhesion molecule) can differentiate between metastasis and thyroid pathology.¹⁸ In 1 report, immunostaining confirmed the diagnosis in 2 cases in which melanoma mimicked papillary carcinoma.¹⁹

Although most reports have suggested a poor prognosis associated with thyroid metastases,¹¹ others have questioned this generalization,¹³ particularly among patients with renal cell carcinoma as the primary tumor.²⁰ The management of thyroid metastases is primarily surgical, but no clear consensus exists with regard to the extent of surgery. Some recommend lobectomy for solitary thyroid metastasis and total thyroidectomy for bilateral metastases.^{21,22} However, thyroidectomy may not prolong survival,¹³ and clinical judgment and patient preference should be considered in light of the palliative, survival, and prognostic benefits, which largely depends on the characteristics of the primary tumor.⁹

SUMMARY

Although thyroid nodules are extremely common and are generally benign, the appearance of a new thyroid nodule or goiter should prompt an evaluation for metastatic disease in a patient with a history of ma-

lignancy. FNA is the diagnostic standard, but immunohistochemistry staining can aid in making a definitive diagnosis. **HP**

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REFERENCES

1. Tunbridge WM, Evered DC, Hall R, et al. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol (Oxf)* 1977;7:481-93.
2. Vander JB, Gaston EA, Dawber TR. The significance of nontoxic thyroid nodules. Final report of a 15-year study of the incidence of thyroid malignancy. *Ann Intern Med* 1968;69:537-40.
3. Tan GH, Gharib H. Thyroid incidentalomas: management approaches to nonpalpable nodules discovered incidentally on thyroid imaging. *Ann Intern Med* 1997;126:226-31.
4. Mortensen JD, Woolner LB, Bennett WA. Gross and microscopic findings in clinically normal thyroid glands. *J Clin Endocrinol Metab* 1955;15:1270-80.
5. Cooper DS, Doherty GM, Haugen BR, et al; The American Thyroid Association Guidelines Taskforce. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2006;16:109-42.
6. Werk EE Jr, Vernon BM, Gonzalez JJ, et al. Cancer in thyroid nodules. A community hospital survey. *Arch Intern Med* 1984;144:474-6.
7. Belfiore A, Giuffrida D, La Rosa GL, et al. High frequency of cancer in cold thyroid nodules occurring at young age. *Acta Endocrinol (Copenh)* 1989;121:197-202.
8. Lin JD, Weng HF, Ho YS. Clinical and pathological characteristics of secondary thyroid cancer. *Thyroid* 1998;8:149-53.
9. Wood K, Vini L, Harmer C. Metastases to the thyroid gland: the Royal Marsden experience. *Eur J Surg Oncol* 2004;30:583-8.
10. Nakhjavani MK, Gharib H, Goellner JR, van Heerden JA. Metastasis to the thyroid gland. A report of 43 cases. *Cancer* 1997;79:574-8.
11. Kim TY, Kim WB, Gong G, et al. Metastasis to the thyroid diagnosed by fine-needle aspiration biopsy. *Clin Endocrinol (Oxf)* 2005;62:236-41.
12. Mirallie E, Rigaud J, Mathonnet M, et al. Management and prognosis of metastases to the thyroid gland. *J Am Coll Surg* 2005;200:203-7.
13. Papi G, Fadda G, Corsello SM, et al. Metastases to the thyroid gland: prevalence, clinicopathological aspects and prognosis: a 10-year experience. *Clin Endocrinol (Oxf)* 2007;66:565-71.
14. Sheppard BC, Moseley HS. Malignant melanoma metastatic to the thyroid as initial evidence of disseminated disease. *J Surg Oncol* 1990;43:196-8.
15. Stavrianos SD, McLean NR, Wadhera V, Chippendale AJ. Metastatic melanoma of the thyroid. *Br J Oral Maxillofac Surg* 1998;36:242.
16. Bozbora A, Barbaros U, Kaya H, et al. Thyroid metastasis of malignant melanoma. *Am J Clin Oncol* 2005;28:642-3.
17. Porcell AI, Hitchcock CL, Keyhani-Rofagha S. Use of immunohistochemistry in fine needle aspiration of thyroid nodules in patients with a history of malignancy. A report of two cases. *Acta Cytol* 2000;44:393-8.
18. Carlson JA, Ross JS, Slominski A, et al. Molecular diagnostics in melanoma. *J Am Acad Dermatol* 2005;52:743-75.
19. Miji LO, Nguyen GK. Metastatic melanoma of the thyroid mimicking a papillary carcinoma in fine-needle aspiration. *Diagn Cytopathol* 2005;32:374-6.
20. Giuffrida D, Ferrau F, Pappalardo A, et al. Metastasis to the thyroid gland: a case report and review of the literature. *J Endocrinol Invest* 2003;26:560-3.
21. Rosen IB, Walfish PG, Bain J, Bedard YC. Secondary malignancy of the thyroid gland and its management. *Ann Surg Oncol* 1995;2:252-6.
22. Chen H, Nicol TL, Udelsman R. Clinically significant, isolated metastatic disease to the thyroid gland. *World J Surg* 1999;23:177-80.