Case Report: Coexistence of Papillary Thyroid Cancer and Thyroid Lymphoma
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ABSTRACT
We describe a case of a 75-year-old female found to have concurrent papillary thyroid cancer and diffuse large B cell lymphoma of the thyroid.

CASE PRESENTATION
A 75-year-old female presented to the hospital with weakness and a 35-lb weight loss over a 6-month period. She was found to have a new diagnosis of Type 2 diabetes and was evaluated by endocrinology. Physical exam was notable for a palpable right sided thyroid nodule. Thyroid stimulating hormone (TSH) was normal. Thyroid ultrasound confirmed a 4 x 4.8 cm nodule in the right lobe. Fine needle aspiration (FNA) of the nodule revealed atypia of undetermined significance, but the sample tested positive for BRAF and NRAS mutations, concerning for papillary thyroid cancer. She underwent total thyroidectomy. Pathology revealed a combination of multifocal papillary carcinoma, diffuse large B-cell lymphoma (DLBCL) of the thyroid, and chronic lymphocytic thyroiditis. Post-thyroidectomy, she was started on oral levothyroxine to maintain a euthyroid state.

Follow-up positron emission tomography/computed tomography (PET/CT) scan showed no fluorodeoxyglucose (FDG) uptake in the neck, chest, abdomen, and pelvis. Several 2-3 mm nodules were found in both upper lobes of the lung, some of which demonstrated minimal cavitation which were nonspecific and likely infectious or inflammatory in origin. Metastatic disease in the lung was considered unlikely given the upper lobe predominance. Her DLBCL was characterized as stage IIE.

She followed up with medical oncology for management of her DLBCL. She was initiated on standard of care for her disease, including a combination of chemotherapy with 3 cycles of R-CHOP and local radiation, which reportedly has a 90-95% 5-year overall survival rate for stage I extra-nodal DLBCL.1 She is following with endocrinology for her stage I papillary thyroid cancer, now status-post total thyroidectomy, and continues to take levothyroxine for thyroid replacement. After her treatment for lymphoma is complete, the need for radioactive iodine (RAI) treatment would be discussed further between oncology and endocrinology.

DISCUSSION
Papillary thyroid cancer is the most common thyroid cancer, making up 70-80% of diagnosed thyroid cancers.2 The BRAF V600E mutation, which activates the mitogen-activated protein kinase (MAPK) signaling pathway, is found in 40-45% of papillary thyroid cancers.3 BRAF mutation screening is typically performed with FNA biopsies of thyroid nodules to aid in the diagnosis of papillary thyroid cancer. However, this mutation is found in other thyroid malignancies as well, including thyroid lymphomas. In one study reviewing 33 thyroid lymphomas of various types, 8 of the 33 lymphomas were positive for a BRAF mutation, including the V600E mutation, D594G mutation, and K601N mutations.3 Of note, the presence or absence of the BRAF mutation did not change outcomes. These patients were treated with a combination of surgery, radiation, and/or chemotherapy with an overall 33% mortality from their respective thyroid lymphoma.

In comparison to papillary thyroid cancer, primary thyroid lymphomas are rarer, accounting for less than 5% of all thyroid cancers or 2 cases per million.2,4 Primary thyroid lymphomas are typically B-cell in origin and affect middle-aged to older individuals, primarily women. They usually present as rapidly growing neck masses and less commonly present with compression symptoms or B type symptoms. Patients usually present with Stage I disease. Diffuse large B-cell lymphoma is the most common subtype of thyroid lymphoma; mucosa-associated lymphoid tissue (MALT) lymphomas are the second most common.4 Of thyroid lymphomas, MALT lymphomas tend to be more indolent in nature with a favorable prognosis. MALT lymphomas localized to the thyroid gland tend to respond well to total thyroidectomy and radiation but about 40% of diffuse B-cell lymphomas evolve from MALT lymphomas.5 The 5-year survival of diffuse B-cell lymphoma is less than 50% with treatment, including chemotherapy and radiation.6 This increases the importance of early diagnosis of thyroid lymphoma.

There is an association between papillary thyroid cancer and MALT lymphoma in the setting of Hashimoto’s thyroiditis.2 MALT lymphomas in particular are difficult to distinguish from Hashimoto’s thyroiditis on FNA biopsy as they are histologically similar. Hashimoto’s thyroiditis has been associated with 10-58% of cases of papillary thyroid
cancer and more than 90% of cases of thyroid lymphoma.\textsuperscript{2} However, the co-occurrence of papillary thyroid cancer and thyroid lymphoma is very rare.\textsuperscript{2} This case demonstrates that as a clinician, one must be aware of the possibility of multiple concurrent thyroid malignancies.

Of note, our patient was never diagnosed with thyroiditis prior to her presentation, but had evidence of chronic thyroiditis on final pathology. Because of the association of thyroid malignancy in patients with Hashimoto’s thyroiditis, there should be adequate surveillance in patients with a history of Hashimoto’s thyroiditis for papillary thyroid cancer as well as thyroid lymphoma. Some studies suggest performing a thyroid ultrasound at the initial visit for patients diagnosed with Hashimoto’s thyroiditis to screen for thyroid malignancy.\textsuperscript{5} Although, the risks and benefits of this type of surveillance would likely need to be studied further. In addition, testing for BRAF, NRAS and a growing list of other genetic mutations, particularly in patients with atypia of undetermined significance on FNA biopsy, is becoming more prominent in the identification of thyroid malignancies.\textsuperscript{6} These mutations are frequently present in papillary thyroid cancer, but are also seen in thyroid lymphoma, making it important to consider thyroid lymphoma in the differential diagnosis when these mutations are detected in thyroid FNA samples.\textsuperscript{7}

REFERENCES