A Diagnosis of Thyroid Cancer Reveals a Triple Threat

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Introduction

The risk of secondary malignancies is increased in patients that have papillary thyroid cancer (PTC). It is not completely clear if this risk is due to radioactive iodine treatment or due to other causes. We present a case of a patient diagnosed with papillary thyroid cancer (PTC) found to have lung cancer and small lymphocytic lymphoma which appear to be unrelated to radioactive iodine treatment.

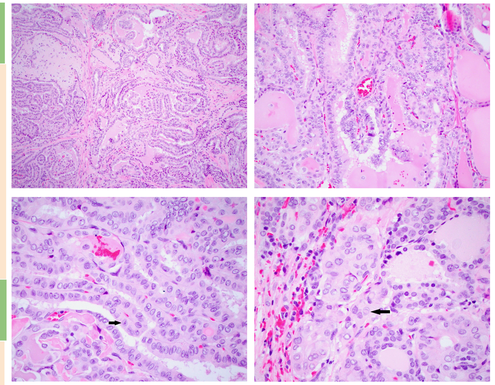
Case Presentation

A 72 yo woman with a history of Graves' disease, a-fib, and hyperparathyroidism initially presented to care for weight loss. She was found to have hyperthyroidism and was treated with methimazole. Thyroid ultrasound revealed multiple nodules including a 17mm right lower pole nodule with irregular borders for which she underwent FNA. Pathology demonstrated atypical-cells of undetermined significance (AUS), but thyroseq revealed a BRAF V600E mutation. She underwent total thyroidectomy with pathology showing multifocal thyroid cancer, 12mm and 0.8mm with 3/11 involved lymph nodes (LN) and right parathyroid adenoma.

Given a questionable lower left lung nodule on preop CXR, she underwent CT chest which revealed a 2 cm lung nodule. She had video assisted thoracoscopic (VATS) left lower lobe wedge resection with completion left lower lobectomy for a ***3 cm lung adenocarcinoma*** with negative margins and 33 negative LN.

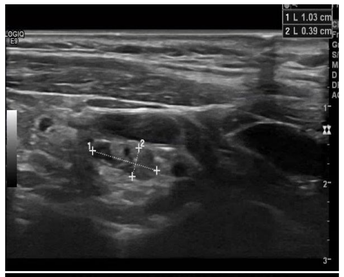
She was subsequently treated with RAI after recovery from VATS. Pretreatment thyroglobulin was 0.8 ng/ml with negative thyroglobulin antibodies. One month after RAI treatment, ultrasound of the neck revealed suspicious bilateral level IV LN which increased in size during short term follow up. Serum thyroglobulin was 0.3ng/ml with negative antibodies, also with TSH 0.29 mIU/L. Biopsy of right level IV LN was ***positive for PTC*** with thyroglobulin washout >5000.

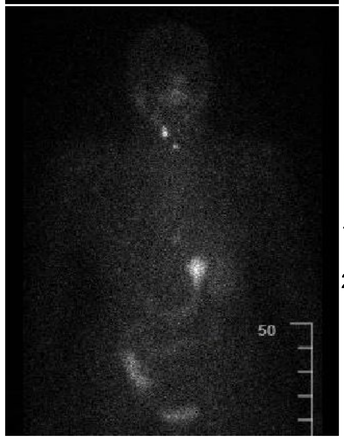
She subsequently underwent right-sided modified radical neck dissection, with lymph nodes revealing PTC ***also involved by small lymphocytic lymphoma***. She had repeat RAI ablation for thyroid cancer and is being actively monitored for her small lymphocytic lymphoma and lung adenocarcinoma.



Papillary Thyroid Carcinoma Histology, Classic (usual, conventional)
Figure 1. (top left) Papillary thyroid carcinoma. The tumor shows a papillary growth pattern with thin fibrovascular cores. There are interspersed follicles (H&E, X100).
Figure 2. (top right) Papillary thyroid carcinoma. There is nuclear enlargement, crowding and overlapping (H&E, X200).
Figure 3. (bottom left) Papillary thyroid carcinoma. Most nuclei have an optically clear appearance or fine evenly dispersed chromatin. There are irregular nuclear contours and longitudinal grooves (arrow) (H&E, X400).
Figure 4. (bottom right) Papillary thyroid carcinoma. Nuclear pseudoinclusions (arrow), when present are a very helpful diagnostic feature (H&E, X400).

Figure A (top)-
Post-thyroidectomy US suspicious R sided Level 4 LN, 1.03 cm in greatest dimension
Figure B (bottom)-
I-123 whole body scan shows R sided LN metastasis





Discussion

This case illustrates a rare presentation of PTC occurring concomitantly with 2 other primary malignancies. The case is especially intriguing as the other 2 primary cancers appear to have been present prior to completion of RAI remnant ablation of the thyroid cancer. It has long been known that there may be a risk of a second primary malignancy in patients treated with high dose radioactive iodine. However, in this novel case it appears the etiology of the other 2 cancers is unrelated to RAI ablation. Importantly, this pt harbors the BRAF V600E activating mutation found in 40-60% of all PTC, and especially common in the classic variant. While this mutation occurs early in tumorigenesis, it predisposes to loss of differentiation and promotes tumor invasion and progression. It has also been implicated to play a role in other malignancies as well, commonly of the breast and lung.

Additionally, the BRAF V600E mutation in thyroid malignancy may prove to be a valuable treatment target given the recent discovery of kinase inhibitors specifically targeting the mutated kinase isoform.

Conclusion

We present a patient with no known history of malignancy who presented with 3 de novo primary malignancies. This case may demonstrate an increased risk of malignancy in patients with thyroid cancer not necessarily related to radioactive iodine treatment.

References

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2. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer Haugen, Alexander, et al., Thyroid. Jan 2016, 26(1): 1-133.