CLINICAL VIGNETTE

Concomitant Graves' Disease and Papillary Thyroid Carcinoma

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Case Presentation

A 30-year-old male without significant past medical history presented to his primary care physician for evaluation of dysphagia associated with epigastric abdominal pain for three months. Initial evaluation found subclinical hyperthyroidism with thyroid stimulating hormone (TSH) level of 0.04 IU/mL (0.30 to 4.7). He was referred to endocrine and diagnosed with Graves' disease with positive thyroid stimulating immunoglobulin (TSI) 236% (< 140%). He was started on methimazole and was also noted to have left thyroid nodule.

Thyroid ultrasound confirmed a hypoechoic, solid partially calcified nodule measuring 1.1 cm in the left lower lobe. Thyroid fine-needle-aspiration biopsy showed cellular atypia of undetermined significance (AUS) with subsequent suspicious Afirma Genomic Sequencing Classifier and positive BRAF (V600) mutation. He underwent total thyroidectomy and central lymph node dissection which demonstrated multifocal papillary thyroid carcinoma with the largest focus in the left thyroid lobe measuring 1.2 cm, Warthin-like variant, and another focus in the right thyroid lobe measuring < 1 mm. Two paratracheal lymph nodes were negative for malignancy. Background thyroid parenchyma showed chronic lymphocytic thyroiditis.

Discussion

Previously, it was suggested that "thyrotoxicosis was insurance against cancer of the thyroid" due to lack of thyroid stimulation from a suppressed TSH.[1] However, in Graves' disease (GD), other factors support tumor growth and function, including chronic abnormal stimulation of the thyroid gland by circulating TSI.[2] Studies report incidence of thyroid neoplasm among patients with Graves' disease (GD) ranging from 1% to 9%.[3-7] Overall, thyroid cancer occurs in GD with a frequency of about 2% or less when these studies were combined.[8] Most cancers reported are papillary microcarcinomas with minimal clinical impact.[9]

Current guidelines for management of hyperthyroidism do not recommend routine ultrasound surveillance in GD.[10] Current management guidelines for differentiated thyroid cancer also do not provide specific recommendations for management of thyroid nodules in patients with GD.[11] A recent meta-analysis reported diffuse thyroid cancer associated with concurrent GD is associated with increased multifocality and distant metastasis, without increased mortality.[12]

Patients with hyperthyroidism and concurrent thyroid nodules should have careful evaluation to exclude the presence of associated malignancy. A palpable abnormality on physical examination should be further evaluated with imaging. Thyroid ultrasound is the best modality to characterize nodules and categorize the risk of malignancy associated with thyroid nodules. Radionuclide thyroid scanning may help determine whether a coexisting thyroid nodule is hyperfunctioning ("hot"), isofunctioning ("warm"), or nonfunctioning ("cold"). Current hyperthyroidism guidelines do not recommend cytologic evaluation of hyperfunctioning nodules due to low risk of malignancy.[10]

Conclusion

Our case report discusses the possibility of coexisting thyroid cancer in GD. Thyroid ultrasound showed a high sonographic pattern nodule and fine-needle-aspiration demonstrated suspicious molecular findings. A radionuclide thyroid scan was not performed, as biopsy was recommended regardless of the findings. We believe high suspicion thyroid nodules should have cytologic evaluation regardless of thyroid uptake results. Our patient's surgical pathology showed Warthin-like variant papillary thyroid carcinoma, which is a rare variant associated with chronic lymphocytic thyroiditis and has similar prognosis to classic papillary thyroid carcinoma.[13] Total thyroidectomy was curative; surgical pathology showing stage I disease (pT1bN0Mx) without evidence of local metastasis and radioactive iodine ablation was not recommended. She has done well without any evidence of cancer recurrence on follow up evaluations.

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