Case Report

FOLLICULAR THYROID CANCER WITH PULMONARY METASTASIS PRESENTING AS TOXIC AUTONOMOUSLY FUNCTIONING THYROID NODULE

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ABSTRACT

Objective: We report the case of a patient in whom a toxic autonomously functioning thyroid nodule (AFTN) turned out to be an aggressive follicular carcinoma with pulmonary metastases and subclinical hyperthyroidism.

Methods: In this case study, we review the presentation, evaluation, diagnosis, and management of an aggressive follicular carcinoma presenting as an AFTN with hyperthyroidism. We also reviewed potential pitfalls in the diagnosis of this rare presentation of thyroid cancer when following the current standards of care in managing thyroid nodules.

Results: An 85-year-old female with atrial fibrillation was seen for an enlarging right thyroid nodule. Biochemical testing revealed subclinical hyperthyroidism. An enlarged, 4.2 × 3.4 × 4.1-cm right thyroid lobe nodule was noted on ultrasound and confirmed to be an AFTN by thyroid scintigraphy. Incidental pulmonary nodules were noted on computed tomography (CT) and found to be fluorodeoxyglucose (FDG)-avid on positron emission tomography (PET). She was treated with total thyroidectomy, and pathologic analysis confirmed the presence of a unifocal follicular thyroid carcinoma (FTC) with lymphovascular invasion. Postoperatively, she was also treated with radioactive iodine and levothyroxine suppressive therapy. Subsequent progression of metastasis ensued, and she died approximately 4 years after diagnosis.

Conclusion: Hyperthyroidism resulting from a functioning thyroid tumor is exceedingly rare. Flexibility in the approach to functioning thyroid nodules is essential. Our case demonstrates that thyroid malignancy in an AFTN should be suspected in elderly patients with rapidly growing nodules. **(AACE Clinical Case Rep. 2015;1:e00-e00)**

Abbreviations:
AFTN = autonomously functioning thyroid nodule; **CT** = computed tomography; **FDG** = fluorodeoxyglucose; **FNA** = fine needle aspiration; **FTC** = follicular thyroid carcinoma; **131-I** = radioactive iodine; **PET** = positron emission tomography; **Tg** = thyroglobulin; **TSH** = thyroid-stimulating hormone

INTRODUCTION

The incidence of thyroid cancers has risen throughout the years, with an estimated 62,980 new cases in 2014 (1). Diagnosis is often made by fine needle aspiration (FNA) and cytologic examination of thyroid nodules with sonographic features of malignancy. In iodine-sufficient regions, the work-up of a thyroid nodule starts with a serum measurement of thyroid-stimulating hormone (TSH). If the value is subnormal, further investigation with thyroid scintigraphy is warranted to rule out an autonomously functioning thyroid nodule (AFTN), which carries a low malignancy risk (2-4). We report a patient in whom an AFTN turned out to be an aggressive follicular thyroid carcinoma (FTC) with pulmonary metastases.

CASE REPORT

An 85-year-old female presented with a 4-month history of a progressively enlarging right-sided neck mass. Initially noted to be the size of her fingertip, this mass progressively grew into the size of a golf ball. She had

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associated hoarseness but no other compressive symptoms. She also complained of alternating diarrhea and constipation associated with weight loss and fatigue. There were no associated tremors, palpitations, or any other evidence of sympathetic hyperactivity. Her medical history was notable for atrial fibrillation and Alzheimer's dementia. There was no personal history of radiation exposure or any family history of thyroid malignancy.

On examination, a nontender, estimated 5.5 × 3 cm thyroid mass on the right with slight leftward tracheal deviation was noted. Thyroid function tests revealed subclinical hyperthyroidism with a low TSH of 0.34 μIU/mL (normal range, 0.5-5.0 μIU/mL) with a normal free thyroxine at 1.1 ng/dL (normal range, 0.6-1.6 ng/dL) and free triiodothyronine at 3.3 pg/dL (normal range, 2.5-3.9 pg/dL). Thyroid-stimulating immunoglobulin was normal at 125% (normal range, 0-129%). Ultrasonography showed an enlarged right thyroid lobe with a large heterogeneous 4.2 × 3.4 × 4.1-cm mass with an inferior curvilinear coarse calcification (Fig. 1). Because of subclinical hyperthyroidism, thyroid scintigraphy was performed and revealed a large dominant "hot" nodule on the inferior right lobe with relative suppression of the uninvolved gland. The 4- and 24-hour uptakes were 12% (normal range, 5-15%) and 19% (normal range, 15-35%), respectively (Fig. 2).

Given all these findings, a diagnosis of AFTN with hyperthyroidism was made, and the patient was started on methimazole. Incidental masses at the lung bases were noted on abdominal computed tomography (CT) done because of the patient's gastrointestinal symptoms. These were confirmed by chest CT and were noted to be fluorodeoxyglucose (FDG)-avid on positron emission tomography (PET) (Fig. 3). We proceeded with an FNA of the right thyroid nodule and found atypical cells highly suspicious for follicular neoplasm. The patient's pretreatment serum thyroglobulin (Tg) was 3,546.5 ng/mL (normal range, 1.3-31.8 ng/mL), and she underwent a total thyroidectomy. Pathology confirmed a 5.0 × 5.0 × 2.8-cm unifocal FTC with extensive capsular and lymphovascular invasion (Fig. 4). She was placed on levothyroxine suppressive therapy and was subsequently treated with 154 mCi of radioactive iodine (131-I). An additional 211 mCi of 131-I for persistent residual tumor was given 18 months after the first dose. A posttreatment whole-body scan showed numerous foci of various intensities of radiotracer uptake consistent with functioning lung metastases. She subsequently had progression of metastasis involving the liver. Her serum Tg initially decreased to 449.6 ng/mL at 7 months after her first 131-I treatment and subsequently to 47.3 ng/mL at 6 months after her second 131-I treatment.

The patient's dementia also progressed, and she was placed on palliative and comfort care. She died approximately 4 years after the FTC diagnosis. TSH suppression targets were never achieved during her disease course.

DISCUSSION

Thyroid nodules are prevalent in the population, particularly among females and the geriatric population, with approximately 3 to 7% found on palpation and 19 to 76% with ultrasonography (2-3). Thyroid cancers are identified in about 5 to 15% of these nodules, often diagnosed by FNA (5). On thyroid scintigraphy, about 85% of thyroid nodules are "cold," and 5% are"hot." These hot nodules are

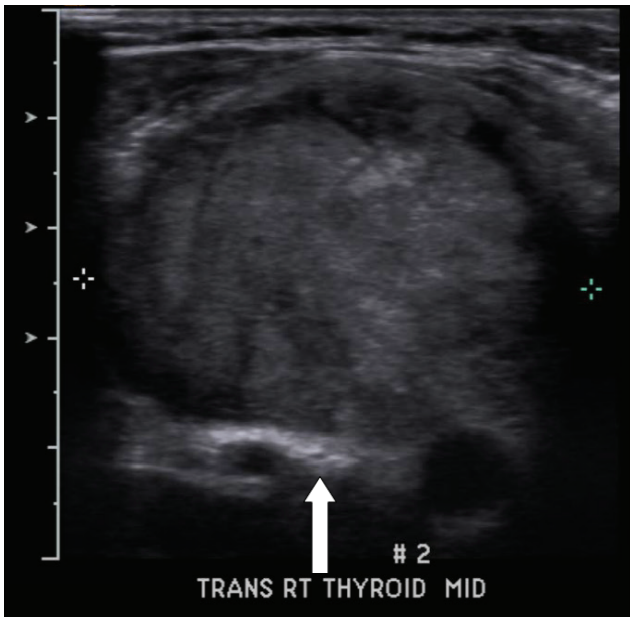

Fig 1. Transverse sonogram showing a large heterogeneous right thyroid nodule with an inferior curvilinear coarse calcification (*arrow*).

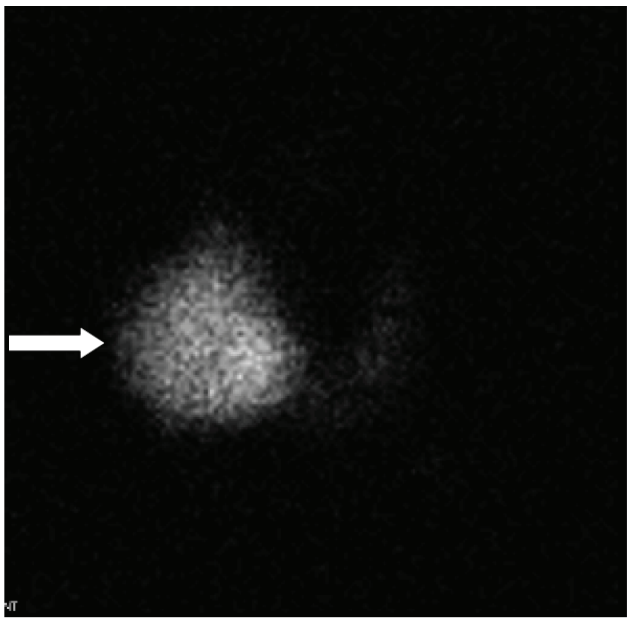

Fig. 2. Thyroid scintigraphy showing a dominant "hot" nodule on the inferior right lobe with relative suppression of the uninvolved gland.

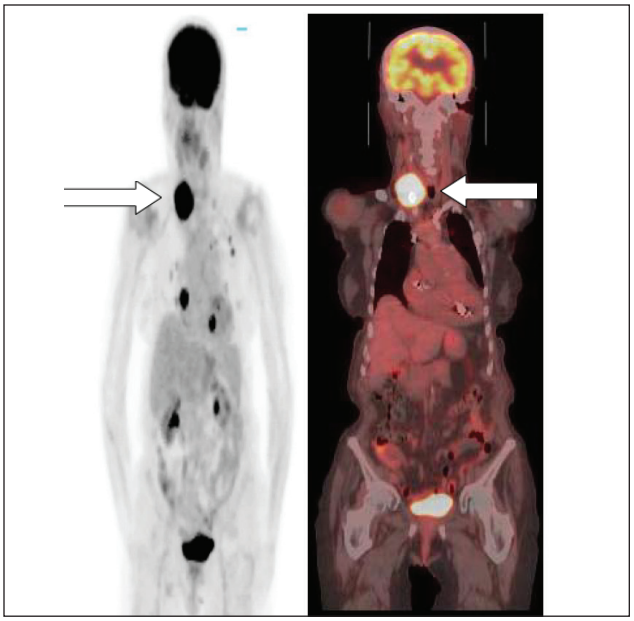

Fig 3. PET-CT scan shows the large intensely glucose avid right thyroid mass (*arrow*) with multiple pulmonary nodules bilaterally that were intensely glucose avid as well.

also known as AFTNs (6), which have a 2.7% prevalence rate (7). These nodules confer a lower malignancy risk (8) than "cold" nodules (9), which is why the aforementioned guideline was developed.

AFTNs harboring an intranodular thyroid cancer are seen in about 3.1% (0-12.5%) of AFTNs reported in the literature (10). This group of thyroid cancers was noted to be less aggressive compared with those associated with Graves disease, which were often multifocal with metastasis to the lymph nodes or distant sites (11). Over the past 2 decades, numerous reports have been published on hyperthyroidism caused by functioning metastatic thyroid cancers, such as the case we reported, with about 36 to 83% having distant metastasis at the time of hyperthyroidism diagnosis (12-14). This was often due to FTCs (12-13), with bone and the lungs as the most frequent sites of functional metastasis (12). The 10-year survival rate was 23 to 59% (12-13). Hyperthyroidism caused by metastatic thyroid carcinoma does not imply excess in the functional capacity of metastatic tissues; it is likely to be due to the increased mass of tumor cells with normal or less than normal functional activity (12).

Thyroid cancer can possibly masquerade as an AFTN, thus delaying its diagnosis and treatment. Among the incidental primary nonmetastatic differentiated thyroid cancer within an AFTN, thyroid surgery is often performed, with only about 30% of patients undergoing FNA (10). Mirfakhraee and colleagues reported that approximately 39% (9/23 cases) of FNA results were not concordant with the final pathologic diagnosis, and about 30.4% (7/23 cases) were noted to be benign on initial FNA (10). Although the study was retrospective with a small number of patients, the risk of malignancy was higher than the typical 0 to 3% potential malignancy risk of a benign cytologic finding in a thyroid nodule (15). In this type of presentation, papillary thyroid carcinoma was more common than FTC (57.1% vs. 36.4%), and the mean nodular diameter was 2.48 ± 1.70 cm, with some patients having compressive symptoms (10). The diagnosis may also be missed, particularly in microcarcinomas when 131-I is selected as the treatment option for AFTN.

FDG-PET may prove useful in the type of clinical presentation noted in our patient. Cohen and associates identified about 102 (2.3%) thyroid incidentalomas in 4,525 FDG-PET examinations (16). Among those who underwent FNA, 47% (7/15 cases) were noted to be malignant and 40% (6/15 cases) were nodular hyperplasia (16). Apart from the detection of primary and metastatic thyroid cancers, FDG-PET may prove useful in detecting these solid tumors in patients presenting with elevated Tg levels and negative whole body scintigraphy (17). In a study by Yoshio et al, FDG-avid PET/CT lesions were resistant to I-131 therapy with or without I-131 uptake (18), as occurred in our patient.

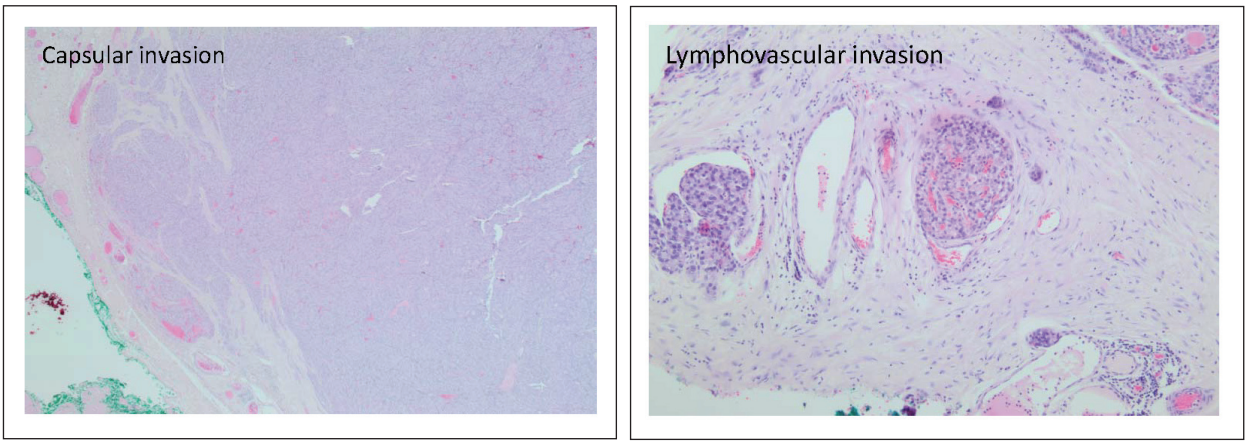

Fig. 4. Pathology confirmed unifocal follicular thyroid cancer with extensive capsular (*left*) and lymphovascular (*right*) invasion.

In recent years, activating mutations of the TSH receptor gene in AFTN harboring a thyroid malignancy have been reported (19). This may play a role in the management of this type of thyroid cancer presentation in the future.

CONCLUSION

Clinicians need to consider risk factors highly suspicious for thyroid malignancy such as sonographic findings (microcalcifications, size >2 cm, and an entirely solid composition) (20), extremes of ages, and compressive symptoms when evaluating thyroid nodules presenting as toxic AFTNs. Rapid tumor growth and symptoms of local invasion are suggestive of thyroid cancer. Maintaining a high index of suspicion in patients who have risk factors for thyroid malignancy may prevent diagnostic delays in this type of clinical presentation. Avoiding delays may prolong survival in this form of thyroid cancer presentation, which has a high mortality risk, particularly in patients with metastatic disease.

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DISCLOSURE

The authors have no multiplicity of interest to disclose.

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