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An Uncommon Presentation of FDG-PET Avid Papillary Thyroid Carcinoma Adrenal Metastasis

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Background	We present a rare case of a 61-year-old male presenting with pharyngitis and dysphagia who was found to have papillary thyroid cancer of the tall cell variant with spread to cervical and mediastinal lymph nodes, pulmonary metastases, and most interestingly, an adrenal metastasis.
Summary	This patient with tall cell papillary thyroid cancer presented with unremitting pharyngitis and dysphagia in the setting of a palpable neck mass and underwent total thyroidectomy with extensive neck dissection revealing initially pT3N1b disease. Following hormone withdrawal and 170 millicuries (mCi) Iodine-131 (I-131) treatment, he was observed to have ongoing disease in the cervical lymph nodes and enlarging pulmonary nodules. The patient was found to have a suspicious adrenal mass on surveillance imaging. In the setting of a negative Iodine-123 (I-123) whole body scan and increasing thyroglobulin levels, poorly differentiated metastatic disease was suspected. Fluorodeoxyglucose-positron emission tomography (FDG-PET) was performed and confirmed uptake in the neck and mediastinum, thyroid bed, and the right adrenal gland. In addition to further neck dissection, the patient underwent laparoscopic right adrenalectomy revealing metastatic papillary thyroid cancer.
Conclusion	Papillary thyroid cancer is generally an indolent cancer with a low mortality rate and infrequent metastases on presentation, however certain variants, such as the tall cell variant, have been observed to act more aggressively. In the setting of suspected metastases with unrevealing thyroid-tissue targeted imaging modalities, FDG-PET can be used for further investigation and localization. This report highlights the use of FDG-PET for identification of a rare metastasis of papillary thyroid cancer to the adrenal gland leading to subsequent surgical excision.

Keywords	Thyroid, papillary thyroid carcinoma, tall cell variant, FDG-PET, metastasis, adrenal gland

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Case Description

Papillary thyroid cancers have a reputation of being a relatively indolent, slow growing cancer, however certain variants may behave rather aggressively. While papillary thyroid cancer is frequently observed to metastasize to the bone and lungs, few cases of adrenal metastases and their management exist in the literature. This is the case of a 61-year-old otherwise quite healthy male who presented with unremitting pharyngitis and dysphagia and was found to have papillary thyroid cancer of the tall cell variant, which metastasized to cervical lymph nodes, mediastinal lymph nodes, the lungs, and lastly the adrenal gland.

Our patient was initially evaluated at an outside hospital for two months of pharyngitis in the setting of a wildfire exposure. Following negative throat cultures and treatment with a course of antibiotics, he was found to have a palpable neck mass on reevaluation for persistent symptoms. Further investigation with ultrasound followed suggesting prominent thyroid nodular disease and abnormal appearing central and right lateral lymph nodes. Fine needle aspiration (FNA) of the nodules confirmed papillary thyroid cancer. A preoperative-planning CT confirmed findings suspicious for locally advanced thyroid malignancy. The patient was therefore taken for a total thyroidectomy with extended paratracheal, paraesophageal, and upper mediastinal lymph node resection, and a right modified radical neck dissection. Intraoperatively, the tumor was unexpectedly found to be invading a portion of the trachea necessitating cervical tracheal resection with primary tracheoplasty. Surgical pathology revealed a multifocal papillary thyroid carcinoma of the tall cell variant with a right lobe and isthmus tumor measuring up to 2.7 cm with a separate 0.5 cm of involvement within the left lobe. Tumor was focally present at the surgical margins and in 6 of 29 lymph nodes consistent with pT3 N1b stage disease.

Eight weeks following surgery, he underwent adjuvant treatment with 170mCi I-131 following hormone withdrawal. Posttreatment, a whole-body radioactive iodine scan showed a focal increase in the right lower quadrant of the abdomen with unclear localization. Computed tomography (CT) revealed an indeterminate left pulmonary nodule for which surveillance was initiated with repeat CT in nine months showing progression in size and number of several sub-centimeter pulmonary nodules.

Over a year after his initial surgery, ultrasound suggested bilateral cervical lymph node recurrence in the setting of a negative I-123 scan with high thyroglobulin levels and undetectable thyroglobulin antibodies. Following a positive FNA, he underwent a left modified neck dissection confirming ongoing cervical disease. A follow up chest CT revealed further growth of his presumed pulmonary metastases and a suspicious, enlarging 2.6cm right adrenal nodule. Again, a cervical ultrasound showed bilateral enlarged lymph nodes. A negative I-123 whole body scan in the setting of increasing thyroglobulin levels suggested ongoing poorly differentiated metastatic disease. As has become more common over the last several years, FDG PET scan was then used for further characterization of his presumed metastases. Indeed, FDG revealed abnormal uptake within cervical and mediastinal lymph nodes, within the thyroid bed, and most interestingly, in the right adrenal gland with an SUV uptake of 10.6 (Figure 1).

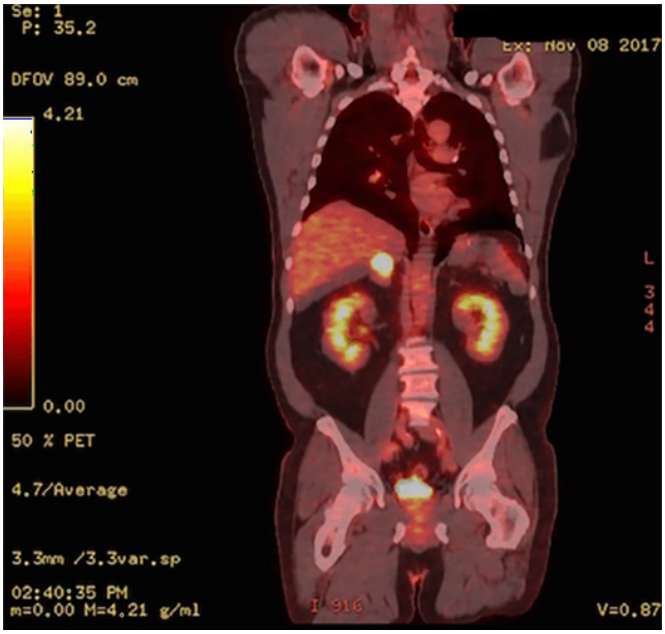

Figure 1. FDG PET demonstrating a hypermetabolic mass in the right adrenal gland.

A follow-up adrenal protocol CT portrayed a right adrenal nodule measuring 3.4 x 2.8 cm with 32 Hounsfield units (HU) on noncontrast images, 74 HU on portal phase images, and 44 HU at 10 minutes. An absolute washout of 71% and a relative washout of 40% were observed, suggestive of an adrenal adenoma.

Prior to surgical excision of the adrenal mass, laboratory investigation revealed no sign of a functional adrenal tumor. Therefore, the patient underwent an uneventful, laparoscopic right adrenalectomy revealing metastatic papillary thyroid carcinoma (Figure 2).

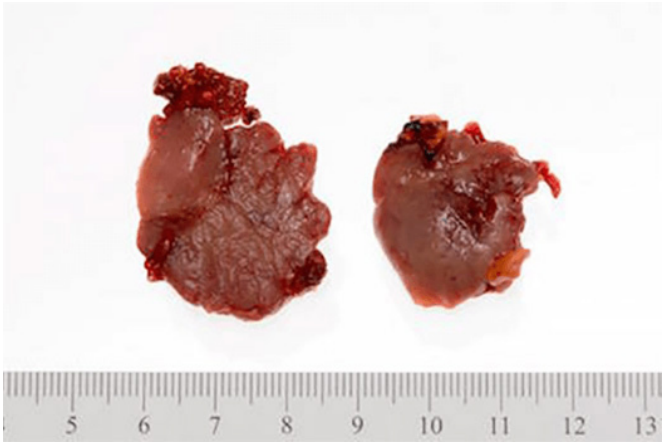

Figure 2. Right adrenal gland with 3.7 x 3.5 x 3.0 cm nodule with pathology suggestive of metastatic papillary thyroid carcinoma

In regard to the ongoing disease in the neck, the patient later underwent a third neck and mediastinal dissection for metastatic disease in his cervical lymph nodes and a mediastinal lymph node. Subsequent treatment plans for this patient will likely be adjuvant external beam radiation therapy to the neck for palliation followed by another dose of radioactive iodine treatment at 200mCi after thyroid hormone withdrawal to slow the progression of his cervical disease.

Discussion

All type thyroid cancer incidence in the United States is on the rise.[1] In papillary thyroid cancer in particular, a recent study cited an incidence increase of 3.5% annually since 1981.[2] It is important to note that the papillary type is thought to account for nearly 80% of thyroid neoplasms.[3] Papillary carcinoma tumors are classified as having a mixture of both follicular and papillary structures, including overlapping nuclei, longitudinal grooves, and invaginations of cytoplasm in the nuclei.[4] This increase in incidence cannot be explained by over diagnosis alone as there has been a significant, yet less hasty incidence of advanced stage and larger primary tumor size papillary thyroid cancers with associated increased mortality rates.[2]

These neoplasms are often indolent, yielding a 10-year mortality rate of less than 7%.[5] Common localized metastases occur through spread to the lymphatics of the thyroid and to regional lymph nodes as well. The mortality rate of distant metastases of papillary thyroid carcinoma is reported as roughly 50%.[6] These distant metastases are known to routinely present in the bone or lungs but are rare and only occur in about 2% of patients with papillary thyroid carcinoma.[7] Metastasis to tissues other than the bones or lungs is extremely rare. The prognosis of patients with distant metastases is determined by a number of factors, including patient age, tumor grade, size, metastatic site, ability to concentrate, and appearance on chest X ray.[8,9] The histologic type of papillary carcinoma is also of utmost importance as certain variants are notably more aggressive. The tall cell variant is observed to more frequently present with lymphovascular invasion, extrathyroidal extension, and distant metastases.[10,11] It has a disease-free survival rate that is at least 10% less than classic papillary thyroid carcinoma.[12]

Thyroid carcinoma metastasis to the adrenal gland is very uncommon and few cases are reported in the literature for patients diagnosed with papillary thyroid carcinoma.[13-15] Following thyroidectomy, patients have opted for both adrenalectomy with radioiodine therapy, or radioiodine therapy alone. Patients with easily resectable and/or isolated adrenal metastases are good candidates for adrenalectomy. This patient met the criteria for an adrenalectomy with an isolated adrenal metastasis in the setting of presumed lung disease. 18F-fluorodeoxy glucose positron emission tomography/ computed tomography (18F-FDG PET/CT) has become a more common imaging modality in the setting of negative radioiodine scans and elevated thyroglobulin levels.[16] FDG PET in our case indicated a right adrenal enhancement and multiple pulmonary nodules, indicative of adrenal malignancy and pulmonary metastases, respectively. Prior to the patient's right adrenalectomy, thyroglobulin levels were elevated to 149 pmol*L-1, far greater than the 20 pmol*L-1 level which is significantly associated with the presence of residual disease.[17] Papillary thyroid carcinoma metastases are generally recommended to be treated with surgical resection as deemed appropriate for the patient's wellbeing. Previously, resectability has been performed only in isolated metastases. If resection can be performed successfully, patients can experience prolonged survival, increasing five-year survival from roughly 10 to 24%.[18]

Conclusion

A 61-year-old male who presented initially with unremitting pharyngitis, dysphagia, and a palpable neck mass who was found to have papillary thyroid cancer of the tall cell variant which metastasized to cervical lymph nodes, medi-

astinal lymph nodes, the lungs, and lastly the right adrenal gland confirmed on FDG-PET imaging. The patient underwent total thyroidectomy, several neck dissections, a mediastinal dissection, and lastly laparoscopic right adrenalectomy in addition to radioactive iodine treatment and planned external beam radiation therapy.

Lessons Learned

While most classic papillary thyroid cancer presentations are rather indolent, certain variants such as the tall cell variant, can present in an aggressive fashion with locally advanced disease and more frequent occurrence of distant metastases. There is not yet clear evidence to determine the effect on mortality resection of distant metastases, and more specifically adrenal metastases, will have on survival, as it is a relatively rare occurrence described in few case reports to date. When common imaging modalities are nondiagnostic, FDG-PET imaging is helpful in localizing distant thyroid cancer metastases to uncommon locations, such as the adrenal gland, particularly in the setting of poorly differentiated cancers.

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