

## CLINICAL VIGNETTE

# Papillary Thyroid Carcinoma with an Isolated Adrenal Metastasis

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### **Keywords**

Adrenal Metastasis, Tall Cell Variant, Papillary Thyroid Carcinoma, Adrenalectomy, Whole Body Scan, PET-CT

### **Introduction**

An estimated 56,460 new cases of thyroid cancer will be diagnosed in 2012, a 1.03% lifetime risk of developing thyroid cancer in the general population<sup>1</sup>. Of these thyroid cancers, nearly 90% are papillary thyroid carcinomas (PTC) with less than 5% metastatic at the time of diagnosis and an additional 7 - 23% developing metastases over long-term of follow-up<sup>2</sup>. PTC spreads via the lymphatic system from the thyroid tissue to regional lymph nodes. Distant metastases are rare and portend a worse prognosis<sup>3</sup>. When they occur, they are most commonly seen in the lung or bone. Case reports have reported PTC metastases to the pancreas and breast<sup>4</sup>, brain<sup>5-7</sup>, skin<sup>8</sup>, extremity muscles<sup>9</sup>, orbit<sup>10</sup> and liver<sup>11</sup>. To our knowledge, there are only three previously reported cases of isolated metastases to the adrenal gland<sup>6,12,13</sup>. An additional case with concomitant pulmonary and bone metastases has been reported<sup>14</sup>.

We report a fourth case of pathologically confirmed adrenal metastasis, in the absence of other distant metastases, from tall cell variant PTC and review the diagnosis and management of adrenal metastases.

### **Case Summary**

A 72-year-old male initially presented with right thyroid enlargement. The patient was clinically and biochemically euthyroid and without family history of thyroid disease, malignancy or personal history of radiation exposure. Past medical history included CABG and esophageal diverticulum. Ultrasound revealed a 1.5 cm right thyroid nodule. Fine needle aspiration was suspicious for papillary thyroid

carcinoma with hypercellular sheets and papillary arrangements of cells with occasional nuclear grooves. The patient was referred for surgical excision.

Extensive metastatic and locally invasive disease was found at surgery. The patient underwent total thyroidectomy, central neck dissection, right modified radical neck dissection, tracheal resection of three rings and reconstruction with cricotracheal anastomosis. Final surgical pathology demonstrated multifocal tall cell variant papillary thyroid carcinoma with the largest focus measuring 2.1 cm in the right thyroid lobe, a smaller 1.3 cm focus in the left lobe and metastases to level 3 and 6 lymph nodes (22 positive lymph nodes, in total). The inferior tracheal margin was also positive. Post-operative thyroglobulin, in the setting of thyroid hormone withdrawal stimulated TSH (96 mcIU/mL) remained elevated at 2,162 ng/mL, falling to 470 ng/mL one month later (TSH 86.2 mcIU/mL) with a negative thyroglobulin antibody.

The patient was unable to undergo adjuvant radioactive iodine therapy due to postoperative dysphagia, and ultimately required gastrostomy tube placement. I-123 surveillance whole body scan, performed 6 months post-operatively, documented two foci of uptake in the neck and one in the anterior mediastinum, consistent with nodal disease. No distant metastases were noted. Recurrent papillary thyroid carcinoma in the neck was confirmed on fine needle aspiration biopsy.

Ten months after initial surgery, the patient returned to the operating room for right posterior triangle neck dissection and left modified radical neck dissection. One month later, the patient was placed on a low-iodine diet and thyroid hormone was withdrawn in preparation for radioactive iodine ablation with 200 millicuries. Thyroglobulin increased from 1,460 ng/mL to 3220 ng/mL with TSH 183 mcIU/mL.

Post-therapy whole body scan and SPECT-CT images demonstrated two foci of intense tracer activity noted in the neck as well as a 3.4 x 2.4 cm nodule in the left adrenal gland. Computed tomography (CT) of the abdomen and pelvis confirmed a left adrenal mass measuring 3.5 x 2.5 cm, measuring 36 Hounsfield units on a noncontrast image, 151 HU on enhancement image and 77 HU on delayed imaging. Biochemical evaluation was unremarkable. Left laparoscopic adrenalectomy was performed without complication. Pathology confirmed metastatic tall cell variant papillary thyroid carcinoma. Morphologic features of the original cancer and the adrenal metastasis were similar with both staining positive for TTF-1 and thyroglobulin. Post-operative thyroglobulin, in the setting of suppressed TSH of 0.11 mIU/mL fell to 4.6 ng/mL with a negative thyroglobulin antibody.

### ***Discussion and Review of the Literature***

Well-differentiated papillary thyroid cancer is a relatively common malignancy associated with a high cure rate<sup>15</sup>. Unfortunately, metastatic disease develops in 7 – 23% of patients. Morbidity and mortality are increased in patients with distant metastases, but prognosis depends on patient age, tumor grade, tumor size, site of metastases, ability of metastases to concentrate I-131 and complete resection<sup>16</sup>.

The reported long-term survival rates of patients diagnosed with metastatic PTC range from 13 – 100% (17). The wide variation is attributed to the heterogeneity of the patient groups with regard to timing of development of metastatic disease, disease burden, and treatment. Of note, none of the previous reviews of metastatic disease and outcome cited here included patients with adrenal metastases.

Review of the literature demonstrated four cases of differentiated papillary thyroid carcinoma metastatic to the adrenal glands. Hurthle cell carcinoma, follicular, medullary, and anaplastic carcinoma metastases to the adrenal glands have also been reported. However, isolated metastasis to adrenal glands remains a rare occurrence for thyroid carcinomas of all types.

Adrenal metastases are often asymptomatic and occur in conjunction with other distant metastases<sup>18</sup>. Lung, kidney, gastrointestinal (stomach, esophagus, liver/bile duct) and breast cancers are the most common primary tumor sites<sup>19</sup>. Metastases to the

adrenal gland, in the absence of other distant metastases remain a rare occurrence for all types of malignancies. The pathophysiology of this pattern of metastases has not been well delineated.

The four published cases of isolated adrenal metastases from differentiated PTC reported a mean patient age of  $66.8 \pm 8.2$  years. The mean size of the primary PTC lesion was  $4.1 \pm 2.9$  cm and no distant metastases were present at the time of initial evaluation. The mean time to detection of adrenal metastasis was  $18.7 \pm 27.5$  months. I-123 or I-131 whole body scan detected the lesions in three of four cases with<sup>18</sup> F-FDG-PET-CT scan and CT scan confirmation. Adrenalectomy in conjunction with radioiodine therapy was performed in three of the cases while one case was treated with radioiodine therapy alone. Only one report documented long term follow up with a survival of 13 years after diagnosis and initial treatment of adrenal metastasis<sup>14</sup>. The case presented here differs somewhat from previously reported cases in that the lesion was detected within 2 years of initial presentation.

The utility of post-therapy scans (PTS) for the detection of metastases from PTC has been investigated in several studies. Sherman et al<sup>20</sup> found previously unidentified metastases in 10% of patients on PTS and Fatourechi et al<sup>21</sup> identified abnormal foci of uptake in 13% of patients on PTS. The studies document discordance between pre- and post-therapy scan, emphasizing the importance of posttherapy scans in patients with elevated thyroglobulin levels or other indication of metastatic disease. In addition, while whole body scans detected adrenal metastases in the above-noted studies, more aggressive or dedifferentiated tumors may lose the ability to concentrate iodine, especially after several course of radioactive iodine. In these cases<sup>18</sup>, F-FDG-PET-CT is a preferred method of imaging<sup>22</sup>.

Management of distant metastatic lesions often involves surgical and non-surgical treatment. When possible, definitive surgical excision of the metastatic focus is performed<sup>23</sup>. Given the paucity of cases of isolated adrenal metastases, case series investigating the management of these lesions are small and have not focused specifically on the care of patients with PTC and adrenal metastases. Previous studies including multiple cancer types with metastases to the adrenal gland, predictors of improved survival included disease-free interval greater than six months, complete resection and pathologic diagnosis of adenocarcinoma<sup>24,25</sup>. In one study of 41 patients

(56% with non-small cell lung cancer), not including any patients with PTC, only the disease-free interval greater than 6 months correlated with improved survival<sup>26</sup>. This effect may be attributed to the more indolent course of cancers that remain stable over a prolonged period of time. Regardless, available data suggest benefit of adrenalectomy without disadvantages beyond surgical risk.

Despite the improved outcome with surgery for adrenal metastasis, ongoing monitoring of thyroglobulin, thyroglobulin antibody and imaging is essential in the long-term management of patients with PTC and distant metastases. Fortunately, our patient demonstrated a significant decrease in thyroglobulin levels following adrenalectomy from 3,220 to 4.7 ng/mL. However, the persistent detectable Tg value indicates persistent low-volume locoregional disease<sup>27</sup>.

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