Metastatic Adenocarcinoma of the Lung Mimicking Papillary Thyroid Carcinoma

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ABSTRACT

Objective: To report cases of metastatic lung adenocarcinoma mimicking papillary thyroid carcinoma and the potential for lung adenocarcinoma with papillary features and papillary thyroid carcinoma to be confused based on fine needle aspiration biopsy alone.

Study design: Retrospective case series.

Methods: Patients who had lung adenocarcinoma with metastases to the thyroid gland that were initially diagnosed as papillary thyroid carcinoma were identified. Their charts were reviewed, including the history, physical findings, imaging studies and pathology.

Results: We present two cases of patients who had synchronous thyroid and lung masses. The initial work-up in both cases—including FNA biopsy—was suspicious for papillary thyroid carcinoma; however, further tissue studies confirmed lung adenocarcinoma as the primary tumor. The confounding clinical features and pathologic considerations, including the importance of immunohistochemical markers, are discussed.

Conclusion: Lung adenocarcinoma metastatic to the thyroid gland can be confused with papillary thyroid carcinoma. Although rare, it should be in the differential diagnosis for patients with synchronous thyroid and lung masses. Given the challenges in making a correct diagnosis based on FNA biopsy alone, consideration should be made to obtain a tissue biopsy with immunohistochemical analysis to make a definitive diagnosis.

REFERENCES


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INTRODUCTION

- Metastases to the thyroid gland are rare; the most common origins are the lungs, along with the colon and rectum.
- Authors comment specifically on the utility of fine needle aspiration (FNA) biopsy in distinguishing these entities from primary thyroid malignancies.
- Because of the significant overlap in cytologic appearance between thyroid and lung carcinomas, making a definitive diagnosis can be challenging.

CASE REPORT 1

- A 76-year-old woman presented with several months history of a right neck mass; she had a 15 pack-year history of tobacco use.
- CT scan revealed a 4-cm mass adjacent to the thyroid gland (Figure 1A) and a mass in the right lung with a large pleural effusion.
- An FNA biopsy demonstrated metastatic papillary thyroid carcinoma (PTC), but immunohistochemical (IHC) staining revealed overlapping profiles between pulmonary and thyroid primary sources with positivity for AE1/AE3, CK7, TTF-1, synaptophysin A, p53 and thyroglobulin.
- Pathology from the primary confirmed a well-differentiated adenocarcinoma with focal squamous differentiation exhibiting variable positivity for CK7, CAM 5.2, vimentin, EMA and p53.
- PET-CT showed a large, irregularly shaped hypermetabolic neck mass (SUV 56) in continuity with the right thyroid lobe (Figure 1B). No hypermetabolic lung nodules were noted, but a 6-mm right lower lobe nodule was identified along with a small right pleural effusion with faint FDG uptake.
- An I-123 scan with right thyroid lobe uptake, read in conjunction with the PET-CT was highly suspicious for a primary thyroid malignancy.
- An open biopsy of an enlarged perithyroid lymph node was performed to clarify the diagnosis.
- Pathology revealed adenocarcinoma with papillary features favoring non-thyroid origin (Figure 2A). Follow-up IHC staining was positive for CK7, CAM 5.2 and TTF-1 (Figure 2B) and negative for D4-24, GCDFP-15, CEA, WT-1 and calcitinin, supporting a final diagnosis of metastatic pulmonary adenocarcinoma.
- The patient has subsequently been followed closely by the medical oncology and palliative care teams.

CASE REPORT 2

- A 59-year-old female with pulmonary tuberculosis presented with fatigue and progressively enlarging bilateral cervical lymphadenopathy.
- CT scans revealed diffuse thyroid enlargement and irregularity, multiple enlarged supraclavicular, mediastinal, hilar, retrocervical and cervical lymph nodes, as well as a 2.5-cm irregular mass in the right upper lobe (Figure 3A & B).
- FNA of a cervical lymph node revealed poorly differentiated carcinoma.
- The patient subsequently developed dyspnea and a pericardial effusion; cytology of the pericardiocentesis fluid was consistent with carcinoma with neuroendocrine features.
- A core biopsy of the left thyroid lobe was positive for poorly differentiated carcinoma and areas of adenocarcinoma with papillary features; IHC staining was TTF-1 positive and thyroglobulin and calcitinin negative.
- A lung biopsy also showed carcinoma with neuroendocrine features.
- The clinical picture and immunostaining were consistent with T2N3M1b (stage IV) lung adenocarcinoma metastatic to the thyroid.
- The patient has since undergone 2 cycles of chemotherapy with resolution of her cervical lymphadenopathy.
- Follow-up CT scans of the neck and chest 3 months after initial diagnosis and treatment have shown a reduction in the size and number of cervical and hilar lymphadenopathy.

DISCUSSION

- Although FNA biopsy is commonly performed to evaluate lesions of the thyroid, misleading diagnoses can be made due to: 1) sampling error and 2) an unknown primary site of malignancy.
- Metastatic lesions to the thyroid gland portend poor prognosis, with most patients succumbing to their disease shortly after diagnosis.
- Cases described in the literature involve a lengthy history between development of the primary carcinoma and subsequent presentation of metastatic disease to the thyroid gland.
- Other authors have reported similar cases initially diagnosed as primary PTC, based on FNA cytology, but later confirmed to be metastases.
- IHC plays an important role in FNA cytology in differentiating the origin of primary cancers. Fleerzet and Kirbis assessed the diagnostic potential of TTF-1—specific marker for tumors of pulmonary or thyroid origin—which, when utilized in conjunction with FNA, was able to aid in the diagnosis of primary pulmonary malignancy in 1/3 of cases where the primary site was unknown. Thyroglobulin positivity also helped in distinguishing metastatic thyroid carcinoma from those originating from the lung. However, as illustrated by the present case and other reports, the use of IHC markers such as TTF-1 and thyroglobulin with FNA cytology may still cause some diagnostic confusion.
- One of the other potential confounding features of the first case was the subtle pulmonary findings on CT scan, which may have played a role in the study interpretation to be most suggestive of a thyroid malignancy with lateral neck metastases. Thus, despite the advancement of imaging modalities in the diagnosis and management of multiple types of malignancies is becoming more prevalent, we must also recognize the potential limitations of these powerful tools.

CONCLUSIONS

- Although rare, a diagnosis of metastatic lung adenocarcinoma should be considered in patients presenting with possible metastatic PTC.
- An increased index of suspicion may be especially warranted when historical risk factors for lung cancer are present and there is clinical or radiological evidence for an underlying primary pulmonary process.
- In these cases, FNA cytology may not be able to effectively distinguish metastatic PTC from primary lung adenocarcinoma with papillary features.
- IHC analysis may be helpful, but is also subject to diagnostic inaccuracy because these entities may demonstrate positivity for similar tumor markers.
- In cases where significant diagnostic uncertainty is present, open surgical biopsy may be indicated with formal histopathologic analysis prior to definitive treatment.

Figure 1. A) Axial CT demonstrating a large mass adjacent to the right thyroid gland with inhomogeneous attenuation, central necrosis and effacement of surrounding fascial planes; B) PET showing corresponding irregular area of hypermetabolic activity (SUV 56).

Figure 2. Histopathologic specimens showing A) papillary projections intermixed with glandular structures (H&E, original magnification 10x) and B) IHC staining with TTF-1 positivity (original magnification 40x).

Figure 3. Axial CT demonstrating A) thyroid enlargement with multiple bilateral nodules and B) a 2.5-cm irregular mass in the posterior segment of the right upper lobe (arrow).