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Ectopic papillary thyroid carcinoma mimicking distant metastatic tissue

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Abstract

We report a case of a 50-year-old woman presenting with a solid nodule in each lung. She was previously suspected of having lung cancer and distant pulmonary metastasis on the basis of imaging findings. Surgical pathology revealed that the left lung nodule was adenocarcinoma, but the contralateral nodule was papillary thyroid carcinoma (PTC). We subsequently performed total thyroidectomy, and the histological findings of the resected specimen showed no suspicious tumor tissue. Overall, the results led to a diagnosis of ectopic intrapulmonary PTC with synchronous lung adenocarcinoma. Ectopic intrapulmonary PTC is a rare but true phenomenon that may be easily mistaken for pulmonary metastasis in daily practice. It is important to improve the recognition of ectopic intrapulmonary thyroid tumors to avoid misdiagnosis.

Keywords

Ectopic thyroid, papillary thyroid carcinoma, lung cancer, computed tomography, positron emission tomography/computed tomography, thyroidectomy, metastasis, multiple nodules, bilateral, single stage

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Background

Multiple solid pulmonary nodules are being detected with increasing frequency on multidetector computed tomography (CT).[16] Most of these nodules are benign; however, malignancy is still an important consideration in the differential diagnosis.[16] Typical or atypical nodules may develop as a result of synchronous multiple primary malignant neoplasms or metastases, or they may arise from ectopic extrathoracic tissues. Ectopic thyroid tissue is rare. Ninety percent of ectopic thyroid tissue occurs along the pathway of thyroid embryological migration (especially on the midline or laterally in the neck). However, in a few cases (10%) this tissue is found in the esophagus, heart, lung, aorta, mediastinum, duodenum, or gallbladder.[1] Although the presence of malignant change in ectopic thyroid tissue remains controversial, ectopic thyroid cancer without identifiable primary tumors in the thyroid gland does occur.[1,8] We herein present a case of ectopic intrapulmonary papillary thyroid carcinoma (PTC) mimicking distant metastasis.

Case presentation

A 50-year-old woman came to our clinic for evaluation because of a complaint of nonspecific abdominal pain. She had no cough, fever, or hemoptysis, and there was no remarkable medical history. On CT, two solid nodules were incidentally detected; one in each lung (Figure 1). On chest enhanced CT, both nodules were markedly enhanced. The attenuation values (nonenhanced and enhanced, respectively) of the right pulmonary nodule were 35 HU and 105 HU, and the attenuation values of the left pulmonary nodule were 27 HU and 53 HU (Figure 2); the values for the ectopic thyroid tissue ranged from 83 HU to 183 HU. The concentrations of tumor markers associated with lung cancer were within normal limits. To determine whether the pulmonary nodules were malignant tumors, we performed whole-body ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/CT (PET/CT). The left lung nodule was hypermetabolic, and we did not detect other abnormal FDG uptake (Figure 3). However, the preoperative diagnosis of the right lung nodule remained uncertain regarding whether the nodule was malignant or benign, and whether this was a metastatic tumor or whether the nodules indicated multiple primary tumors. Considering the chest enhanced CT findings, we gave a possible diagnosis of metastatic tumor. Video-assisted thoracic surgery (VATS) with lobectomy for the left lung nodule and wedge resection for the right lung nodule were performed. Histopathology of the left lung nodule indicated adenocarcinoma

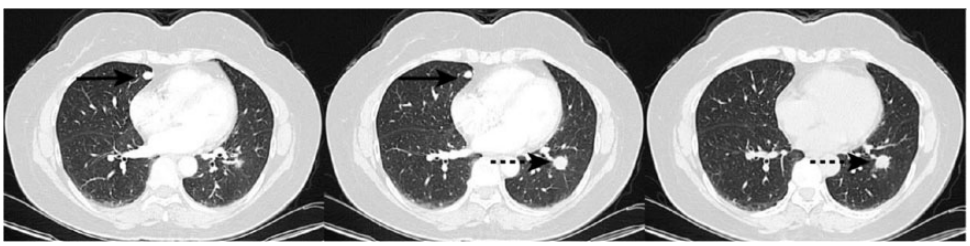

Figure 1. Chest CT lung window images. An 18-mm, spiculated nodule with surface umbilication is visible in the left lower lung lobe (dotted arrows). A 10-mm, well-defined, round nodule is visible in the right lower lung lobe (solid arrows).
CT, computed tomography.

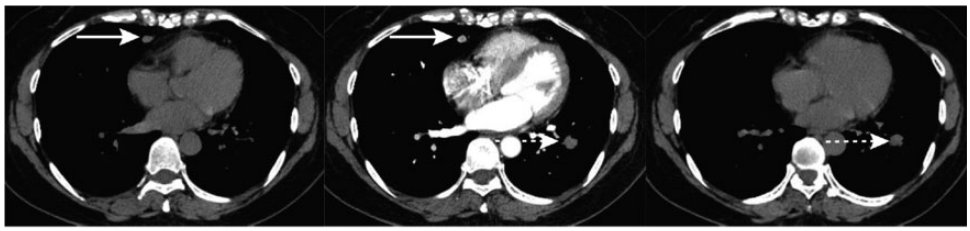

Figure 2. Mediastinal chest nonenhanced and enhanced CT images. The attenuation values (nonenhanced and enhanced, respectively) of the right pulmonary nodule were 35 HU and 105 HU (solid arrows), and the attenuation values of the left pulmonary nodule were 27 HU and 53 HU (dotted arrows).
CT, computed tomography.

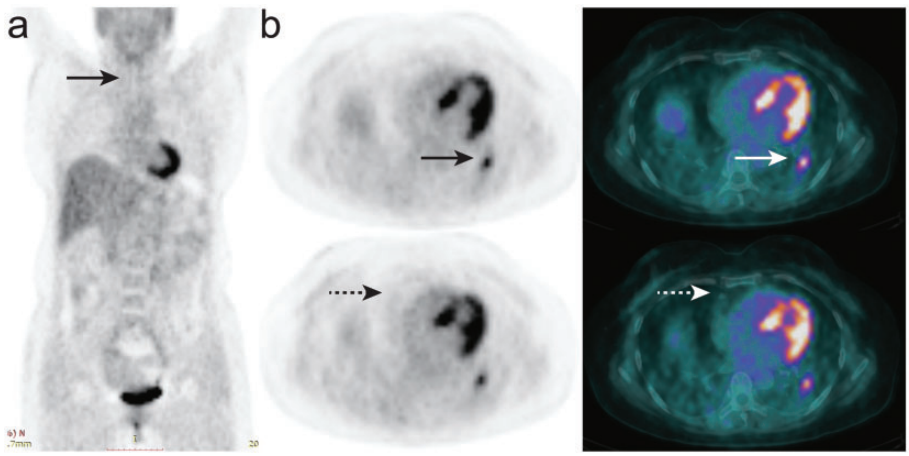

Figure 3. 18F-FDG-PET images of the lung nodules (a and b). The pulmonary nodule detected in the left lung is hypermetabolic (b, solid arrows). No other abnormal 18F-FDG uptake was noted, including in the contralateral pulmonary nodule (b, dotted arrows) and in both lobes of the thyroid gland (a, solid arrow)
18F-FDG-PET, 18F-flurodeoxyglucose positron emission tomography.

infiltrating the lung tissue, and immunohistochemical stains were positive for cytokeratin (CK) 7, thyroid transcription factor-1 (TTF-1), and napsin A (Figure 4a). Contrary to our expectations, histopathological examination of the right lung nodule revealed papillary carcinoma. Immunohistochemical staining of the tumor cells was positive for CK 19, TTF-1, and thyroglobulin (Figure 4b).

To confirm whether the intrapulmonary PTC was metastatic, thyroid ultrasonography was performed, and three thyroid nodules (ranging in size from 8 mm to 10 mm) were detected and involved both thyroid lobes. The sonographic characteristics of the thyroid nodules were consistent with thyroid cancer, namely solid composition, hypoechogenicity, microcalcifications, and irregular margins. Laboratory tests revealed that the concentrations of thyrotropin, thyroid hormones, and thyroglobulin were within the respective normal ranges. Thyroid nodules smaller than 1 cm are not contraindicated for fine needle aspiration (FNA).[(new)] However, after multidisciplinary consultation, we considered that total thyroidectomy was the best option in this

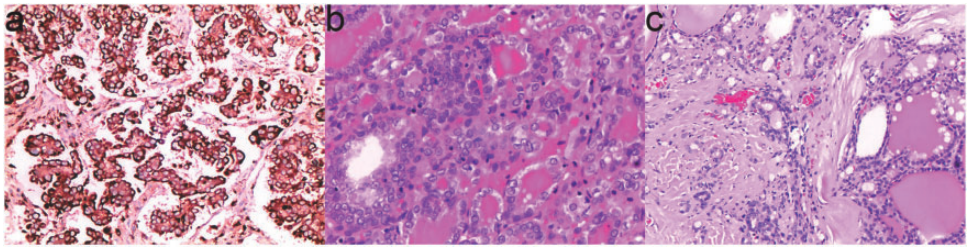

Figure 4. Histopathology of the excised tissues. Histopathological images indicating micropapillary adenocarcinoma (immunohistochemical staining, 400 × magnification) (a). Tumor tissue is present in papillary and adenoid arrangements, and the cytological and nuclear features are consistent with papillary carcinoma (hematoxylin and eosin, 200 × magnification) (b) and No carcinoma was found in the thyroid tissue (hematoxylin and eosin, 400 × magnification) (c).

case. Therefore, we performed thyroidectomy with central compartment neck dissection. The histology results showed that all three thyroid nodules were benign, and we found no other suspicious tumor tissue in the thyroid (Figure 4c) or the surrounding lymph nodes. Whole body iodine-131 screening after surgery was advised; however, the patient refused. After careful multidisciplinary consultation, ectopic intrapulmonary PTC was finally diagnosed. During the 4-year follow-up, which comprised re-evaluation every 3 to 6 months, serum thyroglobulin levels remained normal, while imaging studies suggested enlarged lymph nodes in regions IV and V of the left neck. Biopsy was performed, and the pathological report suggested metastasis of lung adenocarcinoma.

Discussion

The middle-aged woman in this case was euthyroid, asymptomatic, and incidentally found to have intrapulmonary PTC. Wang et al.[2] reported that the most common concomitant malignancies with lung cancer in women in China were breast cancer, cervical cancer, and thyroid cancer. We mistook the intrapulmonary PTC for distant metastasis by considering certain features, such as the peripheral location of the nodule in the left lower lung lobe, enhancement with contrast imaging, and malignant sonographic characteristics of the thyroid nodules. However, we did not find a detectable primary tumor despite the histopathological examination of the entire thyroid gland. It was a critical issue in this case to determine whether the intrapulmonary PTC was metastatic or ectopic. Previous studies reported that malignant changes in ectopic thyroid tissue were found in the esophagus, thyroglossal duct cyst, adrenal gland, lingual thyroid, and mediastinum.[3–7] However, Xu et al.[8] considered that metastasis from PTC without identifiable primary tumors in the thyroid gland was a true phenomenon. There are two underlying hypotheses to explain this rare phenomenon. First, if the microcarcinoma measures less than 3 mm in size, it might not be detected with routine pathological examination. Second, Xu et al.[8] considered that complete or partial tumor regression in thyroid carcinoma did exist, as with Merkel cell carcinoma, hepatocellular carcinoma, and renal cell carcinoma. In the current case, whole-body iodine-131 screening after surgery was advised; however, the patient refused. After careful multidisciplinary consultation, ectopic intrapulmonary PTC was finally diagnosed.

Pulmonary adenocarcinoma is a malignant epithelial tumor that stains positively

for CK, CK 7, TTF-1, and napsin A. The tumor may show variable morphological features, including acinar, papillary, micropapillary, or solid growth patterns. Any tumor with 20% or more of a high-grade pattern, such as solid, micropapillary, and/or complex glandular patterns, is considered poorly differentiated and associated with a poor prognosis.[9] In our case, the predominant morphological feature of the pulmonary adenocarcinoma was a micropapillary pattern. Subsequently, the enlarged lymph nodes in the left neck revealed metastasis of lung adenocarcinoma. Genetic testing suggested epidermal growth factor (EGFR) receptor mutations (exon 19 deletions), which have shown a good clinical response to EGFR tyrosine kinase inhibitors.

With the wide used of CT, an increasing number of patients without clinical symptoms are found to have multiple pulmonary nodules.[16] It has been reported that surgical intervention is beneficial in patients with synchronous multiple pulmonary malignant lesions.[10,11] Yao et al.[12] showed that some patients with synchronous bilateral multiple pulmonary nodules benefitted from single-stage bilateral surgery; however, the authors did not recommend single-stage bilateral lobectomy. Through performing single-stage lobectomy plus contralateral wedge resection, we achieved the goal of radical treatment of the tumors in our patient. In similar cases, single-stage bilateral surgical resection is an acceptable approach for correct treatment and diagnosis.

CT is a conventional method for detecting and characterizing pulmonary nodules as well as predicting resectability. Owing to the high concentration of iodine, ectopic thyroid tissues have a high density (range: 40–130 HU) on CT.[13,14] Although the density was less than that of the ectopic tissue, the intrapulmonary PTC in this case also had a high density (35 HU; nonenhanced). A multi-institutional trial demonstrated the usefulness of contrast-enhanced CT in further differentiating benign from malignant pulmonary nodules.[15] If the intensity of nodule enhancement is >15 HU, we favor a malignant etiology.[16] However, other studies have reported that ectopic intrapulmonary thyroid tissue showed strong enhancement,[13] and the ectopic thyroid tissue could be easily recognized on contrast-enhanced CT.[17] In this case, we found that the enhanced chest CT attenuation value (105 HU) of the intrapulmonary PTC was similar to that of the ectopic thyroid tissue (range: 83–183 HU).[14] Contrast-enhanced CT is an acceptable approach to obtain a correct diagnosis when solid pulmonary nodules (especially those with a diameter of $\leq$10 mm) show high density on CT and do not show accumulation of FDG on FDG-PET. However, histological confirmation remains necessary.

Conclusion

Intrapulmonary PTC measuring approximately 10 mm in diameter without a primary tumor in the thyroid gland has not been reported in the previous literature. When intrapulmonary PTC is present with lung cancer, PTC can be easily mistaken for distant metastasis. As proven in this case, ectopic intrapulmonary thyroid tumors should not be overlooked clinically.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions

JWL and YSQ made the diagnosis and wrote the manuscript. YL assisted with revising the manuscript. ZHS created the pathological sections and performed the immunohistochemical staining. NH participated in the data collection and followed-up the patient. All authors have read and approved the final version of this manuscript.

Declaration of conflicting interest

The authors declare that there are no competing interests.

Ethics statement

The Ethics Committee of Chengde Central Hospital approved this study. The patient agreed to participate in this study and provided written informed consent to publish this case report and her relevant data.

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