

# Pulmonary Small Cell Carcinoma with Thyroid and Cerebellum Metastases



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## ABSTRACT

Pulmonary small cell carcinoma typically metastasizes to lymph nodes, liver, adrenal glands, brain, and pleura; thyroid involvement is exceptionally rare. A 57-year-old woman presented with an eight-month history of progressive dyspnea. Clinical examination revealed an enlarged thyroid gland with palpable nodules in both lobes. Contrast-enhanced chest CT demonstrated a lobulated right hilar mass extending into the posterior mediastinum. CT-guided biopsy of the hilar lesion confirmed small cell lung carcinoma on histopathology. Fine needle aspiration of the thyroid nodules yielded hypercellular smears containing medium-sized round cells with hyperchromatic nuclei. To exclude primary medullary thyroid carcinoma with pulmonary metastasis, serum calcitonin and carcinoembryonic antigen (CEA) were measured, revealing levels of 20 pg/mL and 49.91 ng/mL, respectively. Integrating these findings, the diagnosis of pulmonary small cell carcinoma with thyroid metastasis was established. This case underscores that, although rare, the thyroid gland can serve as a metastatic site for small cell lung carcinoma. Therefore, in patients with a known primary malignancy, the appearance of a new thyroid nodule warrants prompt evaluation for possible metastatic disease.

## Introduction

Lung cancer is the second most prevalent malignancy worldwide. Among its various histologic subtypes, pulmonary small cell carcinoma accounts for approximately 13% of all lung cancers and is characterized by rapid progression and poor prognosis [1]. Typical sites of metastasis include the lymph nodes, liver, adrenal glands, brain, and pleura [2].

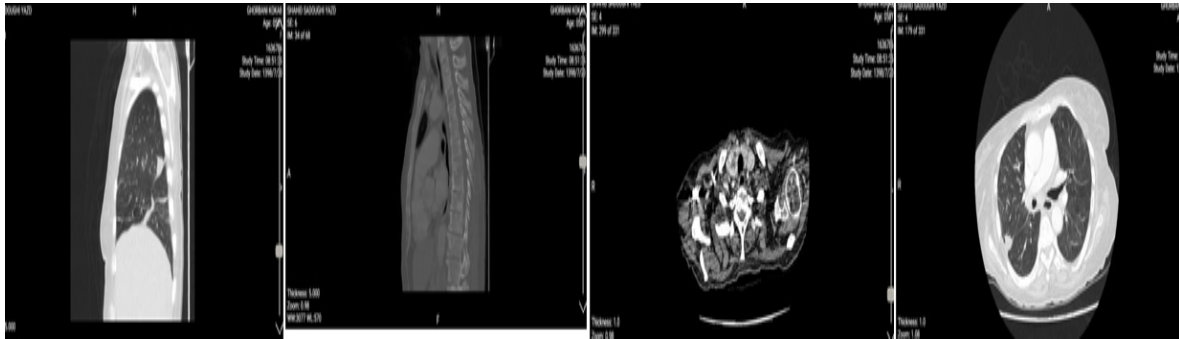
Thyroid malignancies are categorized as either primary or secondary. Primary thyroid tumors generally exhibit indolent growth with local extension and are associated with a favorable prognosis [3]. Interestingly, despite the thyroid gland's rich vascular supply, metastatic involvement from extra-thyroidal primaries is relatively uncommon [4]. Proposed explanations for this rarity include the gland's high intraglandular iodine concentration and accelerated blood flow, which may hinder tumor cell implantation

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**Fig. 1.** Spiral CT scan of the thorax with contrast revealed a lobulated right hilar mass with extension to posterior mediastinum. The mentioned mass encased right pulmonary artery and vein and their main branches. Evidence of mild to moderate right pleural effusion was seen.

[5]. The reported prevalence of clinically detected thyroid metastases is approximately 0.16–0.48% of all thyroid fine-needle aspiration biopsies, with metastatic lesions constituting approximately 1.4–3% of all malignant thyroid neoplasms [6]. Distinguishing primary from secondary thyroid tumors can be challenging, yet it is clinically crucial given the distinct therapeutic approaches required for each [7]. The most frequent primary sites for thyroid metastasis, in descending order, are the kidney, colorectum, lung, breast, melanoma, and sarcoma [8]. Lung cancer accounts for about 3.8% of all thyroid metastases, with adenocarcinoma being the most common histologic subtype to spread to the gland [9]. In contrast, small cell carcinoma rarely metastasizes to the thyroid [10].

Herein, we present a rare case of thyroid metastasis originating from pulmonary small cell carcinoma, a clinically significant presentation that underscores the importance of considering metastatic disease in patients with thyroid nodules and a history of lung malignancy.

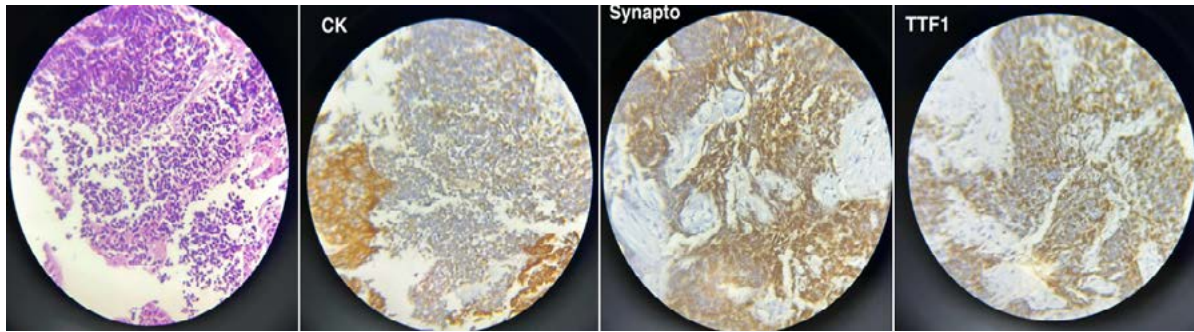
### Case presentation

A 57-year-old woman presented with an eight-month history of progressive dyspnea. During the preceding month, she had developed a productive cough and hemoptysis. She also reported a weight loss of approximately 5 kg, intermittent fever, chills, and radiating pain in the right upper extremity. Past medical history was unremarkable, while social history revealed opium use without cigarette smoking. On general examination, she was alert and oriented. No cyanosis, clubbing, peripheral edema, or lymphadenopathy was observed. The thyroid gland was enlarged and firm, with two palpable nodules in both lobes. Pulmonary auscultation demonstrated diminished breath sounds at the right lung base accompanied by diffuse wheezing.

Laboratory investigations were notable for elevated LDH (1090 IU). Chest radiography revealed mild mediastinal widening and right pleural effusion. Contrast-enhanced spiral CT of the thorax showed a lobulated right hilar mass extending into the posterior mediastinum, encasing the right pulmonary artery and vein and their major branches, with associated mild to moderate pleural effusion (Figure 1).

Pleural fluid analysis demonstrated LDH of 585 IU, protein 39 mg/dL, albumin 2.9 g/dL (serum albumin 4.0 g/dL), WBC count of 5000/ $\mu$ L, and RBC count of 11,000/ $\mu$ L. CT-guided biopsy of the hilar mass revealed tumor tissue composed of small to medium-sized cells with increased nuclear-to-cytoplasmic ratio, hyperchromatic nuclei, fine chromatin, inconspicuous nucleoli, and crush artifact. Immunohistochemistry showed positivity for pan-CK, chromogranin A, synaptophysin, and CD56, while CK7 and calcitonin were negative. The Ki-67 labeling index was 85% (Figure 2). These findings confirmed the diagnosis of small cell carcinoma. Thyroid ultrasonography revealed a 19  $\times$  15 mm isoechoic nodule with a hypoechoic halo in the left lobe, as well as a 15  $\times$  37 mm heterogeneous nodule in the right lobe. Multiple reactive cervical lymph nodes were also identified. Fine-needle aspiration (FNA) of both nodules demonstrated hypercellular smears composed of medium-sized round cells with hyperchromatic nuclei arranged in nests or singly. Following endocrine consultation, serum calcitonin and carcinoembryonic antigen (CEA) levels were measured to exclude medullary thyroid carcinoma with pulmonary metastasis. Calcitonin was 20 pg/mL (reference  $\leq$ 10 pg/mL), while CEA was 49.91 ng/mL.

Abdominal CT imaging was unremarkable; however, brain MRI revealed a high-signal lesion in the left cerebellum (Figure 3). Integrating these findings, the diagnosis of small cell carcinoma with thyroid and



**Fig. 2.** Section revealed tumor tissue composed of small to medium sized cells with increased nuclear to cytoplasmic ratio, hyperchromatic nuclei, fine chromatin, inconspicuous nucleoli, and crush artifact (H&E X10). Immunohistochemistry showed positivity for pan CK, synaptophysin, and TTF1. Ki67 labeling index was 85%.



**Fig. 3.** Brain MRI revealed an abnormal high signal focus in left cerebellum

cerebellar metastases was established. The patient was subsequently admitted to the oncology ward, where systemic chemotherapy was initiated, followed by cranial irradiation.

## Discussion

Lung cancer remains one of the most lethal malignancies, with hematogenous and lymphatic dissemination serving as critical determinants of prognosis [11]. Although the precise mechanisms of metastatic spread are not fully elucidated, it is well established that distinct histological subtypes of lung cancer exhibit characteristic dissemination patterns. While the liver and adrenal glands represent the most frequent sites of hematogenous metastasis, recognition of less common metastatic distributions is equally essential for guiding accurate staging and therapeutic strategies [12].

Metastatic involvement of the thyroid gland from non-thyroid primaries is rare, though autopsy series have documented such occurrences [10]. Some studies suggest that metastases preferentially develop in thyroids with pre-existing pathology, such as thyroiditis or multinodular goiter [13]. Patients with thyroid metastases may remain asymptomatic or present with compressive symptoms affecting adjacent structures; thyroid function tests are typically normal,

as observed in our case [14]. Sonographic findings may include hypoechoic nodules, with calcification considered the most specific ultrasonographic indicator of malignancy (sensitivity: 85.8–95%) [15]. In our patient, ultrasonography revealed a 19 × 15 mm isoechoic nodule with a hypoechoic halo in the left lobe and a 15 × 37 mm heterogeneous nodule in the right lobe.

Fine-needle aspiration cytology (FNAC) is regarded as the initial diagnostic modality, with one study reporting diagnostic accuracy of 73.7% [16]. When FNAC results are inconclusive, core biopsy with immunohistochemical (IHC) staining is recommended. Differentiating primary from secondary thyroid tumors is crucial, as therapeutic approaches and prognostic outcomes differ substantially. IHC plays a pivotal role in this distinction [17]. Primary small cell carcinoma of the thyroid is exceedingly rare; many cases initially diagnosed as such have subsequently been reclassified as primary lymphomas, poorly differentiated insular carcinomas, or small cell variants of medullary carcinoma following comprehensive IHC evaluation [18].

The interval between lung cancer diagnosis and detection of thyroid metastasis is typically short, averaging 4.8 months in one study [19]. Rare presentations include the coexistence of toxic

multinodular goiter and thyroid metastasis from small cell lung carcinoma in patients with thyrotoxicosis [20]. In our case, surgical intervention was not appropriate due to concomitant cerebellar metastasis; moreover, surgery is generally not recommended in the management of small cell pulmonary carcinoma. Previous reports describe patients treated with cisplatin and etoposide followed by cranial irradiation, as in the case reported by Osawa et al. Overall, thyroid metastasis from small cell lung carcinoma portends a poor prognosis, with survival often limited to approximately two months after diagnosis [21].

## Conclusion

We therefore emphasize that the emergence of a thyroid nodule in patients with a known malignancy—particularly one as aggressive as small cell lung carcinoma—should prompt immediate evaluation with FNAC to exclude metastatic disease. Although uncommon, the thyroid may represent a site of metastasis from pulmonary small cell carcinoma, as demonstrated in our patient. Heightened clinical awareness of this possibility is essential for timely diagnosis and appropriate palliation.

## Ethical Considerations

### Compliance with ethical guidelines

The present case report was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran, and was prepared in accordance with applicable local laws and institutional ethical requirements. Written informed consent was obtained from the patient for inclusion in the report, as well as for the publication of any potentially identifiable images or clinical data.

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### Conflict of Interests

The authors have no conflict of interest to declare.

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