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# Delayed Thyroid Metastasis of Lung Adenocarcinoma Mimicking Primary Thyroid Carcinoma: A Case Report

## Authors' Contribution:

Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

AD 1 **Yen Thi Le**   
ADF 2-4 **Hau Xuan Nguyen**  
BCE 1 **Thai Hong Le**  
BCEF 2 **Anh Tuan Doan Van**  
BCE 3 **Duong Thai Pham**   
BCE 3 **Tuan Minh Vu**  
BCE 2 **Hoang Van Nguyen** 

1 Department of Quan Su Medical Oncology, Vietnam National Cancer Hospital, Hanoi, Vietnam  
2 Department of Oncology, Hanoi Medical University, Hanoi, Vietnam  
3 Department of Quan Su 2 Surgery, Vietnam National Cancer Hospital, Hanoi, Vietnam  
4 Oncology Center, Hanoi Medical University Hospital, Hanoi, Vietnam

**Corresponding Author:** Hau Xuan Nguyen, e-mail: [nguyenxuanhau@hmu.edu.vn](mailto:nguyenxuanhau@hmu.edu.vn)

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**Patient:** Female, 69-year-old  
**Final Diagnosis:** Delayed thyroid metastasis of lung adenocarcinoma  
**Symptoms:** A progressively enlarging anterior neck mass  
**Clinical Procedure:** —  
**Specialty:** Oncology

**Objective:** Rare coexistence of disease or pathology

**Background:** Thyroid metastasis from lung cancer is uncommon, accounting for approximately 8.3% of all thyroid metastases, which themselves occur in only about 1.4% to 3% of patients undergoing thyroid surgery; it poses significant diagnostic challenges due to its clinical and cytological resemblance to primary thyroid neoplasms.





**Case Report:** We report the case of a 69-year-old woman with a history of non-small cell lung carcinoma (NSCLC) that had remained stable for 9 years, who presented with a progressively enlarging anterior neck mass. Ultrasound and fine-needle aspiration (FNA) initially suggested a benign thyroid lesion. However, given the marked interval growth of the nodule and the patient's oncologic history, a right thyroid lobectomy was performed for diagnostic and therapeutic purposes. Histopathology supported by immunohistochemical analysis was consistent with the diagnosis of metastatic adenocarcinoma of pulmonary origin involving the thyroid. Imaging studies did not demonstrate additional metastatic sites, although a small pulmonary nodule of uncertain importance was noted. She was subsequently referred for systemic therapy. We analyze the diagnostic challenges, histopathologic characteristics, limitations of FNA, and the critical role of immunohistochemistry in differentiating metastatic lesions from primary thyroid carcinoma.

**Conclusions:** This case highlights the potential for misdiagnosis of metastatic thyroid lesions, particularly when cytological findings suggest a benign nodule, and underscores the importance of integrating clinical history, imaging, and immunohistochemistry to achieve an accurate diagnosis. Long-term surveillance remains essential in cancer survivors, as metastatic disease can occur after a prolonged disease-free interval.

**Keywords:** Immunohistochemistry • Thyroid Nodule • Carcinoma, Non-Small-Cell Lung

**Abbreviations:** FNA, fine-needle aspiration; NSCLC, non-small cell lung carcinoma; IHC, immunohistochemistry

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## Introduction

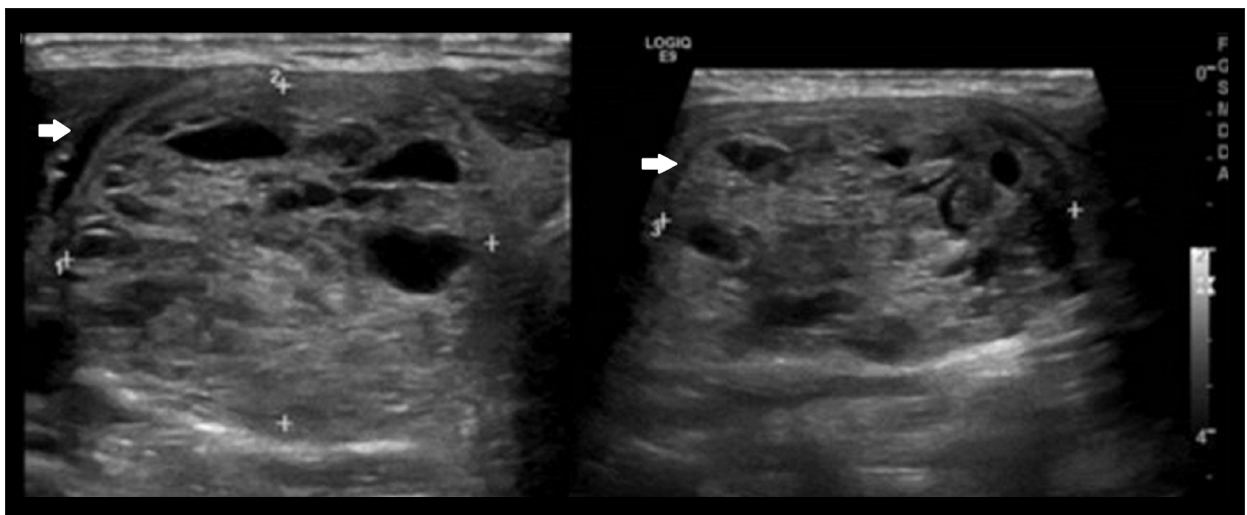
Although the thyroid gland is highly vascularized, it remains an uncommon site for metastasis, with a reported incidence of approximately 1.4% to 3% in clinical series. A systematic review of the English-language literature from 2000 to 2010 found 372 cases of thyroid metastases from non-thyroid malignancies, underscoring their rarity [1]. Similarly, a retrospective analysis conducted at the University of Massachusetts Medical Center from 1993 to 2013, including surgical and autopsy specimens, identified only 10 cases of metastatic involvement of the thyroid [2]. The most common primary cancer metastasizing to the thyroid is renal cell carcinoma (34%-48%), followed by colorectal and breast carcinomas. Metastasis from lung cancer is relatively uncommon, accounting for approximately 8.3% of cases, most frequently arising from adenocarcinoma [1,2]. Distinguishing metastatic lesions from primary thyroid neoplasms remains a significant diagnostic challenge. Thyroid metastases often present as solitary nodules and can closely mimic primary thyroid carcinoma on imaging and cytology, particularly in the absence of synchronous metastatic disease or following a prolonged disease-free interval after treatment of the primary tumor. This overlap can lead to misdiagnosis and suboptimal management. Furthermore, given its rarity and heterogeneous presentation, no standardized diagnostic or therapeutic guidelines have been established. We report a rare case of thyroid metastasis from lung adenocarcinoma occurring 9 years after initial treatment, emphasizing the importance of considering metastatic disease in patients presenting with thyroid nodules and a history of malignancy, even after a long disease-free interval.

## Case Report

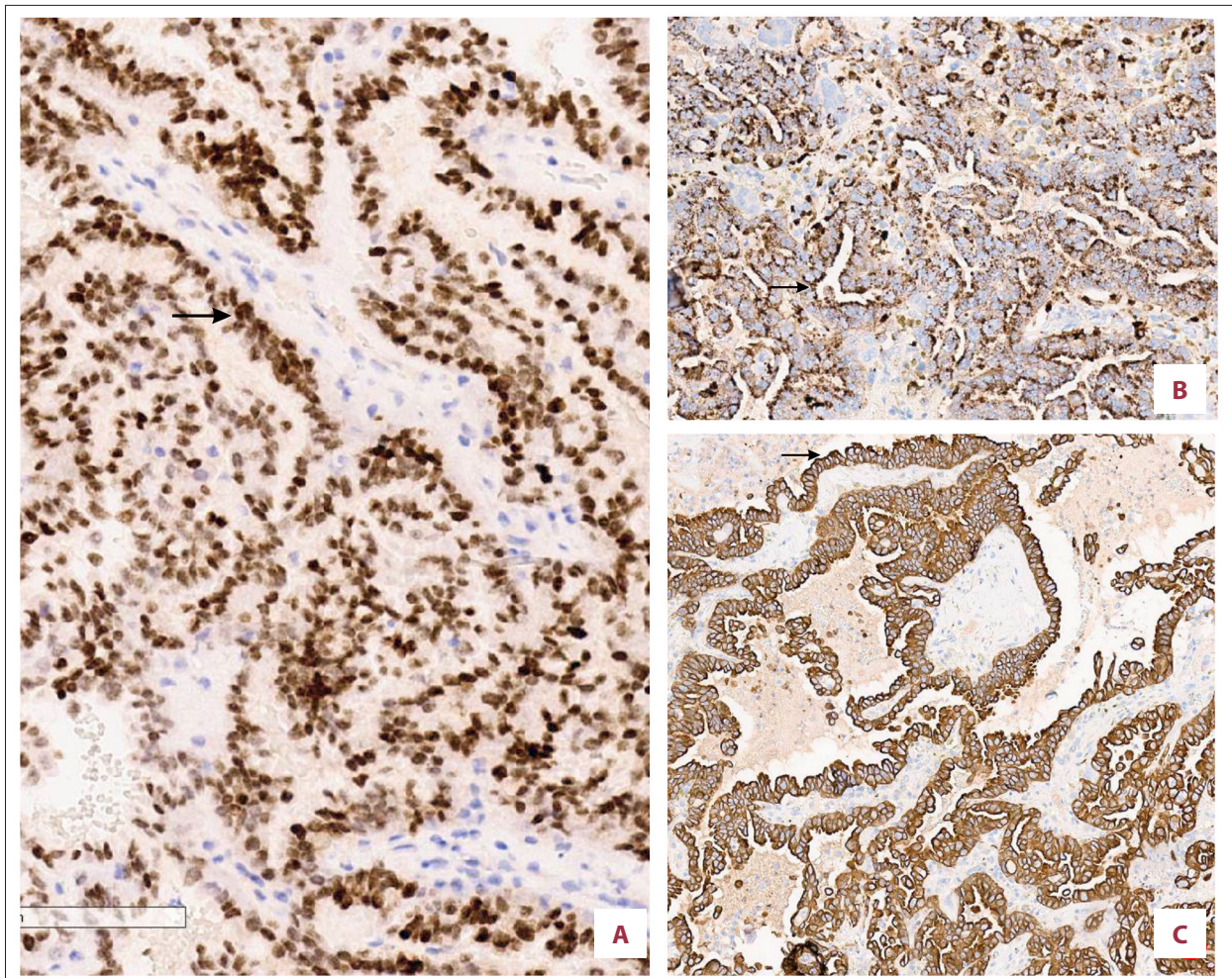
A 69-year-old female patient was diagnosed with left lung cancer (cT2N1M0) in October 2016, with histopathological examination confirming adenocarcinoma. Although surgical resection was indicated, she declined surgery. She subsequently underwent concurrent chemoradiotherapy with a total radiation dose of 60 Gy combined with a weekly Paclitaxel-Carboplatin regimen at a regional hospital. Following completion of chemoradiotherapy, she achieved a partial response according to the available medical records. However, pre- and post-treatment computed tomography (CT) images and histopathological records were unavailable for review. Despite extensive attempts to retrieve them, these materials could not be obtained due to the long interval since treatment and changes in archival systems. The patient was discharged and scheduled for regular follow-up every 3 to 6 months at the provincial hospital.

In June 2025, she presented with a progressively enlarging anterior neck mass that had been noticeable for 1 year. On clinical examination, she was alert. A large mass was palpated in the anterior thyroid region, which moved with deglutition. No symptoms of airway compression or dysphagia were reported.

Ultrasonography and fine-needle aspiration (FNA) were performed as the initial diagnostic evaluation. Ultrasound of the right thyroid lobe revealed a 35×30 mm well-defined, heterogeneous mixed-echoic nodule without calcifications or increased vascularity, classified as TIRADS 3, with no evidence of abnormal cervical lymphadenopathy bilaterally (Figure 1). A prior ultrasound performed 1 year earlier demonstrated a smaller thyroid nodule measuring 13×15 mm, also classified



**Figure 1.** Ultrasound images of the right thyroid lobe demonstrating a well-defined, mixed-echoic nodule measuring 35×30 mm. The lesion shows smooth margins, no internal calcifications, and no evidence of increased vascularity, consistent with TIRADS 3. (White arrows highlight the lesion boundaries).

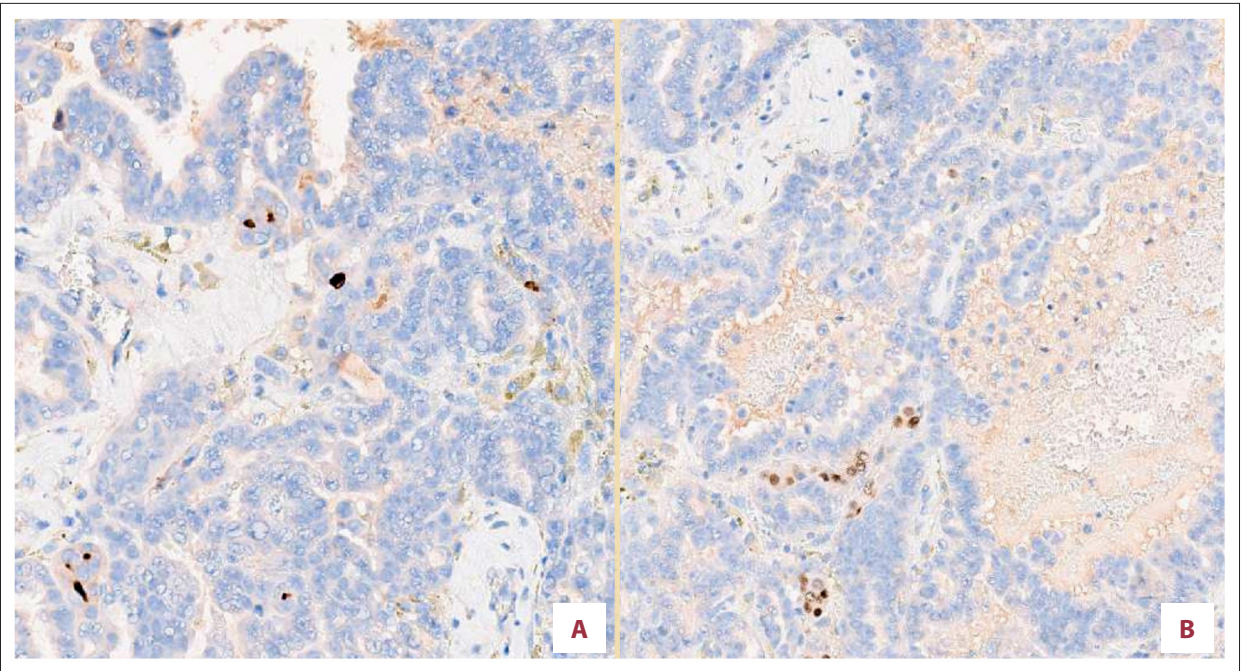


**Figure 2.** Immunohistochemical analysis demonstrated strong nuclear positivity for Thyroid Transcription Factor-1 (TTF-1, clone SPT24, Dako) (A), diffuse cytoplasmic positivity for Napsin A (clone IP64, Cell Marque) (B), and positivity for Cytokeratin 19 (CK19, clone RCK108, Dako) (C) in tumor cells (original magnification  $\times 200$ ). Positive tumor cells exhibiting brown immunoreactivity are indicated (black arrows).

as TIRADS 3. No additional thyroid nodules with suspicious ultrasonographic features were identified.

Cytology suggested a benign thyroid follicular lesion (Bethesda II). Cytological examination revealed follicular epithelial cells with relatively uniform nuclei and no definitive features of malignancy, which may have contributed to a benign interpretation. Thyroid function tests (TSH – thyroid stimulating hormone, FT4 – free thyroxine) were within normal limits. Chest CT demonstrated a 6-mm solid lesion in the left lower lobe of the lung, with adjacent fibrotic changes, which remained stable on serial imaging. No additional metastatic lesions were detected on available imaging studies. Positron emission tomography–computed tomography (PET-CT) was not performed due to financial constraints. Given the small size and radiological stability of the pulmonary nodule, invasive biopsy was not pursued; therefore, its nature remains uncertain.

Despite the benign cytological findings, surgical intervention was recommended because of the marked interval growth of the thyroid nodule, its relatively large size, and the patient's history of lung adenocarcinoma, raising concern for a possible secondary malignancy. The patient subsequently underwent right thyroid lobectomy. Gross analysis revealed a well-circumscribed, soft, brown-red tumor measuring approximately 3 cm in greatest dimension. Histopathological examination demonstrated mucin-producing glandular structures with papillary and micropapillary architecture. These findings suggested papillary adenocarcinoma and raised the suspicion of a metastatic origin. Immunohistochemistry was positive for TTF-1, Napsin A, and CK19 (Figure 2), but negative for thyroglobulin and PAX8 (Figure 3), consistent with the diagnosis of metastatic pulmonary adenocarcinoma to the thyroid. Molecular testing for driver mutations and PD-L1 expression was not performed because of financial limitations. The patient was subsequently



**Figure 3.** Immunohistochemical staining for Thyroglobulin (clone EP250, Cell Marque) (A) and PAX8 (clone MRQ-50, Cell Marque) (B) was negative in tumor cells (original magnification  $\times 200$ ). These findings supported the diagnosis of metastatic pulmonary adenocarcinoma involving the thyroid gland.

referred for oncologic management and was started on chemotherapy with a pemetrexed-carboplatin regimen, with treatment response assessed after every 3 cycles.

## Discussion

Lung cancer remains the leading cause of cancer-related death worldwide, with approximately 1.8 million deaths annually [3]. The most common metastatic sites include the brain, bones, liver, adrenal glands and contralateral lung, whereas metastatic involvement of the thyroid gland is rare, with a reported incidence of 1.4% to 3% among patients undergoing surgery for suspected thyroid malignancy [1]. Metastatic spread to the thyroid occurs predominantly via hematogenous or lymphatic routes, while direct invasion is less frequent [1]. Despite its abundant vascularization, the thyroid appears relatively resistant to metastatic seeding, a phenomenon that has been attributed to rapid blood flow, high oxygen tension, and elevated iodine concentration within the gland [1,4]. In this case, the absence of cervical lymphadenopathy and lack of adjacent tumor involvement made lymphatic spread and direct invasion unlikely. Moreover, the prolonged disease-free interval of 9 years supports a delayed hematogenous dissemination from the primary lung adenocarcinoma.

Among extrathyroidal malignancies, renal cell carcinoma, lung carcinoma, gastrointestinal tumors, and breast carcinoma are

the most frequent primary sources of thyroid metastases [1,3]. Within lung cancer subtypes, adenocarcinoma is the histological variant most commonly associated with thyroid metastasis [2,5]. Clinically, metastatic lesions often present as solitary thyroid nodules and can closely mimic primary thyroid neoplasms on imaging and cytology, particularly in the absence of synchronous metastatic disease. Diagnostic difficulty is further compounded when the primary tumor is clinically occult or when a long disease-free interval has elapsed.

FNA is a first-line diagnostic tool for thyroid nodules due to its high sensitivity and specificity for primary thyroid carcinoma. A prior history of lung carcinoma is therefore a critical clue in the evaluation of newly detected thyroid nodules. Thyroid metastases can occur years or even decades after treatment of the primary malignancy [2]. The longest reported interval is 21 years between primary foregut neuroendocrine carcinoma and thyroid metastasis [6]. In lung cancer, most thyroid metastases are detected within 12 to 24 months of the primary tumor diagnosis [7]. The present case is notable for the unusually long interval of 9 years between primary lung adenocarcinoma and thyroid metastasis, underscoring the importance of long-term surveillance of thyroid carcinoma. However, its diagnostic accuracy is substantially lower for metastatic lesions, particularly in cystic or necrotic lesions. Papi et al (2007) reported false-negative rates up to 25% to 30% for thyroid metastases, largely due to atypical cell morphology and inadequate sampling [8-10]. In patients with a history of malignancy, the presence of

atypical cytology or a follicular-patterned lesion on FNA—especially when the features are not consistent with primary thyroid neoplasms—should prompt consideration of metastatic disease. Pulmonary papillary adenocarcinoma can even mimic papillary thyroid carcinoma histologically. In our case, the follicular-patterned cytology without overt malignant features likely contributed to a false-negative FNA result, underscoring the limitations of cytology alone in this clinical context.

Immunohistochemistry (IHC) plays a pivotal role in determining metastatic lung adenocarcinoma from primary thyroid malignancies, particularly when the histomorphological features are inconclusive. Thyroid transcription factor-1 (TTF-1) is expressed in both pulmonary adenocarcinoma and follicular-derived thyroid neoplasms and therefore lacks specificity when used in isolation [11]. However, its co-expression with Napsin A, a highly sensitive and specific marker for pulmonary adenocarcinoma, strongly favors a pulmonary origin [12]. In contrast, thyroglobulin is a highly specific marker for thyroid-derived neoplasms, and its absence effectively excludes primary thyroid carcinoma [13-15]. Similarly, PAX8 expression is characteristic of thyroid and renal tumors but is not observed in pulmonary carcinomas, further supporting a metastatic pulmonary origin when negative [16]. Additional cytokeratin markers such as Cytokeratin 7 (CK7) or Cytokeratin 19 (CK19) can also be positive in pulmonary adenocarcinoma, although they are not specific. Nevertheless, no single immunohistochemical marker is entirely specific, and accurate diagnosis requires interpretation of a panel of markers in conjunction with clinical and histopathological findings.

In addition to immunohistochemical profiling, molecular analysis can provide further diagnostic support in selected cases. Rearrangements involving RET, as well as RAS and BRAF mutations, are commonly observed in papillary thyroid carcinoma, whereas EGFR mutations and ALK rearrangements are characteristic of pulmonary adenocarcinoma [15,17]. However, given the potential overlap of molecular alterations, these findings should be interpreted with caution and are insufficient to reliably determine tumor origin in isolation. A recent case report described thyroid metastasis from lung cancer harboring a BRAF V600E mutation, which demonstrated a favorable response to targeted therapy with dabrafenib and trametinib, emphasizing the emerging role of molecular profiling in establishing tumor origin [18].

Management of thyroid metastasis should be individualized based on disease extent, metastatic pattern, patient performance status, and the biological characteristics of the primary tumor. In case of thyroid metastases from lung adenocarcinoma, which can represent an oligometastatic state, surgical resection can be considered, followed by systemic therapy including targeted therapy or immunotherapy depending on the

tumor's molecular characteristics and PD-L1 expression [19,20]. Several studies have suggested that surgical excision can provide symptomatic relief, local disease control, and, in selected patients, prolonged survival, with reported median post-surgical survival of 2 to 4 years [1,19,20]. Nevertheless, some authors advise against routine surgical resection because of the aggressive nature and poor prognosis of lung cancer, except when the thyroid metastasis causes significant symptoms [21]. The optimal extent of surgery for thyroid metastases, whether lobectomy or total thyroidectomy, remains controversial and has not yet been standardized [22,23]. In our patient, who was initially evaluated during follow-up for a presumed benign thyroid nodule, right thyroid lobectomy was performed for the isolated lesion, providing local disease control and preventing potential airway or esophageal compression. When thyroid metastasis from lung cancer is suspected preoperatively, repeat FNA with immunocytochemistry or core-needle biopsy should be considered to confirm the diagnosis and guide appropriate management.

The overall prognosis of thyroid metastasis from lung cancer remains poor, with a reported median survival of less than 12 months in disseminated disease [24,25]. The prognosis largely depends on the biological behavior of the primary tumor and the extent of systemic disease. Favorable prognostic factors reported in the literature include a prolonged disease-free interval, solitary metastatic involvement, and the feasibility of complete surgical resection, whereas disseminated metastases and aggressive tumor biology are associated with poorer survival [1,24]. In the present case, a prolonged disease-free interval of 9 years was documented and no additional metastatic sites were identified on available imaging studies. Nevertheless, as prognosis is primarily driven by systemic disease progression, close and long-term surveillance remains essential.

This case report has several limitations. First, the original histopathological slides and detailed pathological data from the primary lung adenocarcinoma were unavailable for re-evaluation. Despite efforts to retrieve these materials, they could not be obtained, likely due to the prolonged and archival constraints. This limits the ability to perform a direct pathological comparison between the primary tumor and the current lesion. Second, as a single case report, the findings are inherently limited in generalizability and do not allow for definitive clinical recommendations. Furthermore, completeness of clinical data is constrained by the long interval between the initial diagnosis and the current presentation, which may have limited a comprehensive assessment of disease progression.

Although case reports have inherent limitations, they provide valuable clinical insights, particularly for rare conditions such as thyroid metastasis from lung adenocarcinoma. This case highlights the importance of considering metastatic disease in

patients presenting with thyroid nodules and a history of malignancy, even after a prolonged disease-free interval. Accurate diagnosis requires careful integration of clinical history, imaging findings, histopathological evaluation, and immunohistochemical analysis. In particular, the use of an appropriate immunohistochemical panel, including markers such as Thyroid Transcription Factor-1 and Napsin A in combination with thyroid-specific markers such as Thyroglobulin and PAX8, is essential for distinguishing metastatic pulmonary adenocarcinoma from primary thyroid malignancies. Increased awareness of this rare metastatic pattern may help clinicians avoid misdiagnosis and guide appropriate management strategies.

Given the rarity of thyroid metastasis from lung adenocarcinoma, further studies are needed to better characterize its clinical features, diagnostic challenges, and optimal management strategies. Large case series or multicenter studies may help clarify the incidence, patterns of metastasis, and long-term outcomes of patients with this condition. In addition, future research focusing on the role of advanced imaging techniques and molecular profiling may provide further insights into the mechanisms underlying thyroid metastasis and improve diagnostic accuracy. A better understanding of these factors may ultimately contribute to earlier detection and optimal treatment strategies for patients with metastatic disease involving the thyroid gland.

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## Conclusions

Thyroid metastasis should be considered in patients with a history of malignancy presenting with thyroid nodules. This case illustrates a rare presentation of delayed thyroid metastasis from lung adenocarcinoma occurring after a prolonged disease-free interval. It highlights the potential for diagnostic misinterpretation, particularly when imaging and cytology suggest a benign process, and underscores the critical role of immunohistochemistry in establishing the correct diagnosis. Sustained clinical vigilance and long-term surveillance remain essential, as late metastatic events can occur even after years of apparent disease stability. Further studies are needed to refine diagnostic approaches and inform evidence-based management strategies for this uncommon clinical entity.

## Department and Institution Where Work Was Done

Vietnam National Cancer Hospital, Hanoi, Vietnam.

## Patient Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

## Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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