Clinical vignette

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Radioiodine scan revealing a primary lung adenocarcinoma in a patient with differentiated thyroid carcinoma

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Abstract

The radioiodine scan is a non-invasive imaging modality that allows for the visualization of functional thyroid tissue, as well as the detection of thyroid cancer remnants and metastases. However, it is important to note that radioiodine uptake is not exclusive to thyroid tissue and can lead to false-positive results if unexpected uptake occurs in non-thyroidal tissue. Herein, we present a case of a patient diagnosed with thyroid carcinoma, whose radioiodine scan demonstrated increased uptake in the thorax, corresponding to a lung carcinoma.

KEYwords: false positive; radioiodine; lung cancer; thyroid carcinoma; multiple primary malignant neoplasms

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Introduction

Despite the high accuracy of radioiodine (RAI) scans in detecting persistent or recurrent differentiated thyroid cancer (DTC), they have limitations due to extrathyroidal radioiodine uptake observed in both benign and malignant conditions [1]. This can be particularly challenging when uptake occurs in regions where DTC commonly spreads. The lung is the most frequent site of distant metastasis in papillary and follicular thyroid cancer [2]. However, it can also be affected by secondary primary malignancies, which have become more prevalent in recent years [3, 4]. Misdiagnosing a secondary primary malignancy as a recurrence or metastasis of the initial cancer can lead to inappropriate treatment and a poor prognosis. In this case report, we describe a patient with synchronous papillary thyroid carcinoma and uncommon RAI-avid lung adenocarcinoma, for whom there was a diagnostic challenge in differentiating primary lung cancer from metastatic DTC based on RAI scan results.

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Case presentation

A 42-year-old female, with non-smoking history, had multinodular goiter and EU-TIRADS V nodule in the left thyroid lobe. She underwent total thyroidectomy with cervical lymph node dissection, and histopathology revealed bilateral papillary thyroid carcinoma (PTC) with lymph node metastases. She received thyroid hormone suppression therapy and a dose of 3.7 GBq of radioactive iodine therapy (RAIT). The post-RAIT whole-body scan showed increased uptake in the anterior cervical region and posterior uptake on the left hemithorax (Fig. 1A, B). Follow-up RAI whole-body scan indicated the disappearance of cervical uptake and persistence of left thoracic uptake. Stimulated serum sTg level was 4.11 ng/mL, Unstimulated Tg level was 0.2 ng/mL and anti-Tg level was 2.33 IU/mL (normal range $<$ 4.11 IU/mL). There were no parietal abnormalities or RAI contamination. Thoracic CT demonstrated a 45 $\times$ 37 mm lung mass of the lower left lobe with spiculated borders, bilateral nodules, and micronodules (Fig. 1C). Bronchoscopy showed subsegmental stenosis of the Nelson's and the paracardiac bronchi. Histopathology with immunohistochemistry revealed a carcinomatous proliferation of large cells with positive anti-thyroid transcription factor-1 staining (anti-TTF1) and negative anti-thyroglobulin (anti-TG) and anti-P40 staining, molecular testing showed mutation of the epidermal growth factor receptor gene

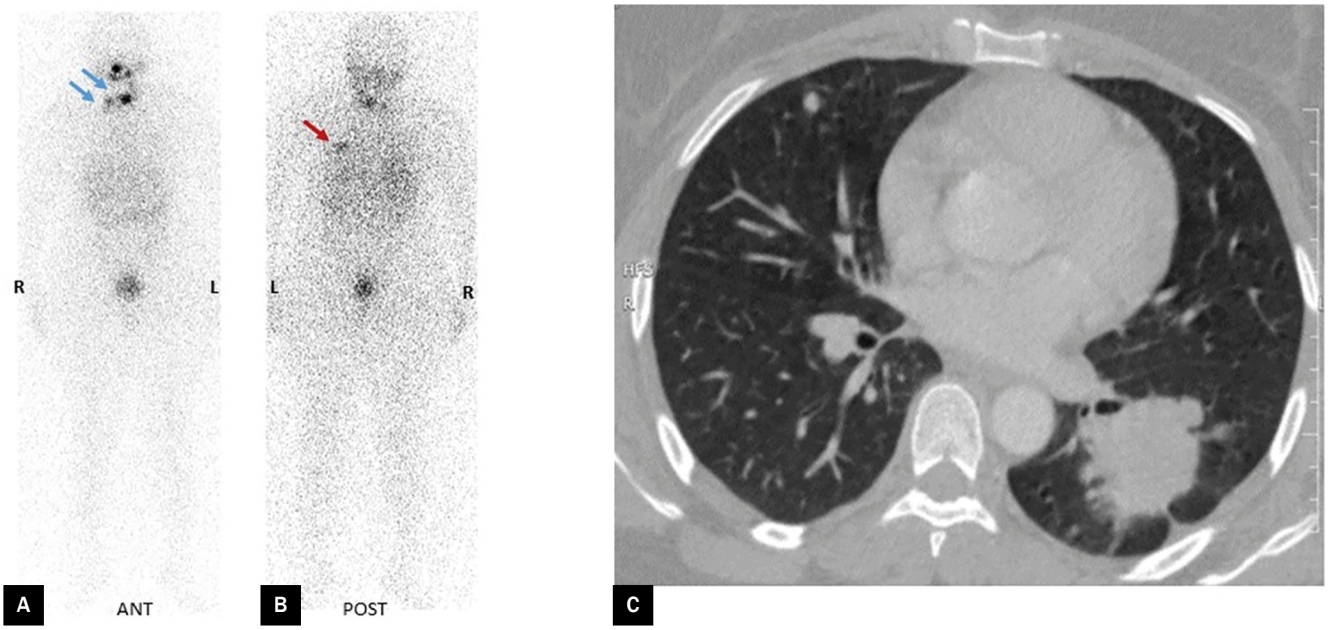

Figure 1. (**A**) Anterior view of post-radioiodine therapy whole body scan: increased uptake in the cervical region corresponding to thyroid remnants (blue arrows); (**B**) posterior view: increased uptake in the left side of the thorax (red arrow); (**C**) axial CT

(EGFR) (Fig. 2). All were compatible with the diagnosis of primary lung adenocarcinoma. The patient was addressed to the oncology department as the lung adenocarcinoma was urgent to treat, she underwent both chemotherapy and anti-EGFR therapy, and evolution was marked by a regression of the lung mass, nodules, and micronodules. Further thyroid follow-up revealed an unstimulated Tg level of 0.2 ng/mL with no abnormality on cervical echography.

Discussion

Our patient was diagnosed with two distinct malignancies, papillary thyroid carcinoma, and lung adenocarcinoma, which was a presentation of synchronous multiple primary malignant neoplasms (MPMTs).

MPMTs are becoming more common, which can be attributed to improved diagnostic tests, improved screening, and surveillance of cancer patients, as well as factors related to cancer treatments (radiotherapy, chemotherapeutics such as alkylating agents and topoisomerase II inhibitors), genetic and environmental factors [4, 5]. Data from cancer registries show that MPMTs have a global prevalence ranging from 0.4% to 21% [6, 7]. According to Babacan et al. [5], the most common malignancy pair in men (13%) is head and neck cancer-lung cancer [4]. Breast cancer is the most commonly associated malignancy in women, accounting for 36% of all second cancers [8, 9]. A review of the literature revealed no consensus on the incidence of synchronous lung and thyroid cancers, but Ronckers et al. [9] discovered a lower number of observed cases than expected cases of lung carcinoma with concurrent differentiated papillary thyroid carcinoma in the US surveillance, epidemiology, and end result (SEER) database. Smaller single-center studies, such as the one conducted by Omur et al. [8], found that lung carcinoma was the second most common malignancy, occurring in 3 of 15 cases of synchronous thyroid carcinoma.

Extrathyroidal RAI uptake has been observed in normal tissues (salivary gland, breast, thymus, liver, gastric, and colon mucosa), cystic structures (bronchogenic cyst, breast cyst, renal cyst, and hepatic cyst), inflamed tissues (acute respiratory infection, granuloma, cholecystitis, and trauma), benign tumors (meningioma, breast fibroadenoma, hepatic angioma, uterine myoma, and struma ovarii), and malignant non-thyroid tumors (lung, breast, gastric, and ovary cancers) [10, 11]. As a result, RAI scans are susceptible to interpretation error, which may contribute to incorrect DTC staging, unnecessary RAI treatment, and misdiagnosis of diseases other than DTC. Although the underlying physiopathology of non-thyroidal RAI uptake is not fully understood, this mechanism was classified as follows in a review by Oh and Anh [10]: 1) functional NIS expression in normal tissues or in various benign and malignant tumors, 2) thyroid hormone metabolism, 3) retention of radioiodinated body fluids associated with or without structural change, 4) retention and uptake of radioiodine in inflamed tissues, 5) contamination by physiologic secretions, and 6) unknown.

SLC5A5, which encodes NIS, has been found to be expressed in lung cancers according to the Human Protein Atlas [11]. Furthermore, a previous study found NIS expression in significant proportions of different types of lung cancer, including 76.6% in adenocarcinoma, 36.1% in squamous cell carcinoma, and 20.0% in small cell carcinoma [12]. Tumoral inflammatory response may play a role in some aspects of radioiodine uptake in malignant tumors, as inflammation is linked to cancer [13]. In our case, one or both of these mechanisms could explain the RAI uptake in the lung carcinoma. Although its expression has not been shown to have prognostic value in lung cancer [11], NIS expression in lung

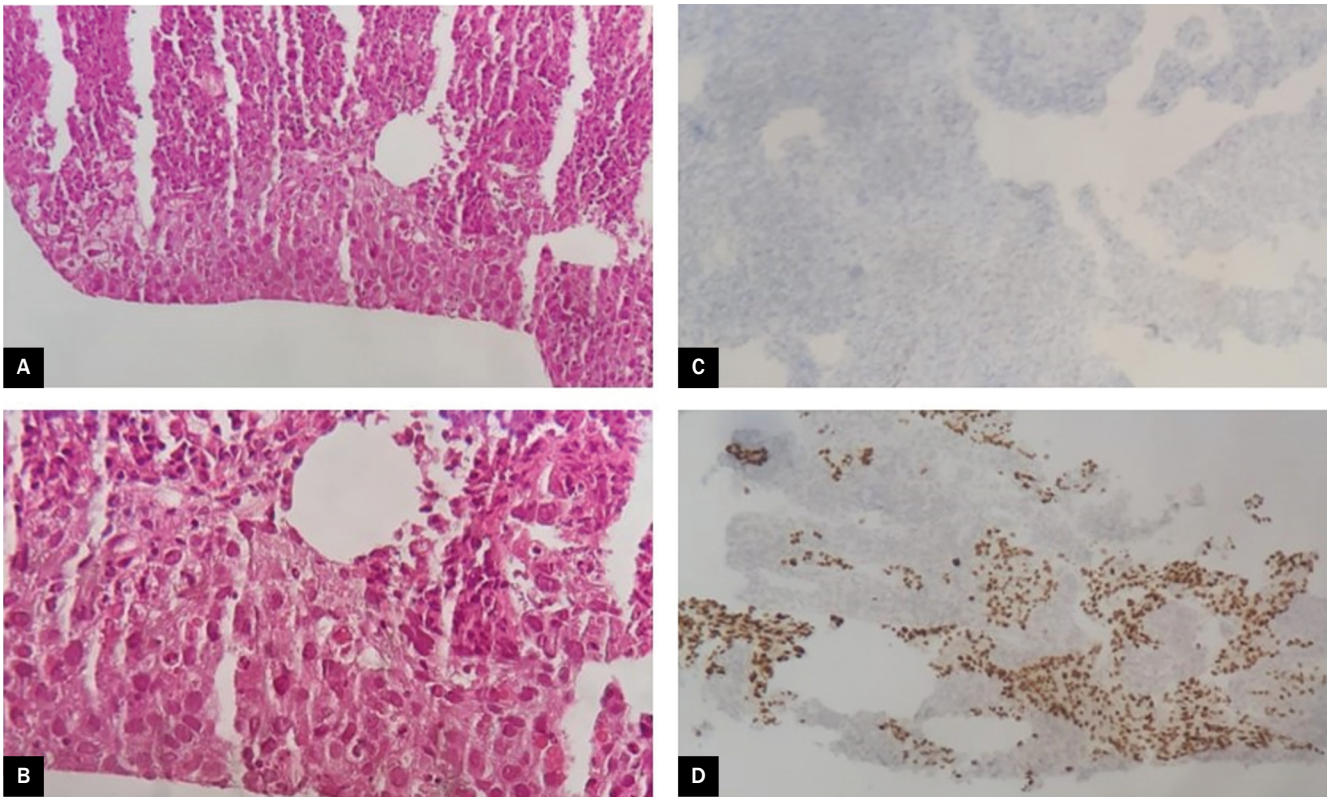

Figure 2. Morphologic and immunohistochemical findings in microscopic view of lung adenocarcinoma; (**A**) morphological findings under medium magnification; (**B**) morphological findings under high magnification; (**C**) negative anti-TG staining; (**D**) positive anti-TTF1

cancer is of particular interest because it may offer potential applications in the surveillance and treatment of lung cancer using RAI [14].

Conclusions

Multiple primary malignant tumors are frequently misdiagnosed as recurrence or metastasis of the original malignancy, resulting in ineffective treatment and a negative impact on the patient's prognosis. Physicians should be aware of the possibility of primary malignancies developing in patients with a history of DTC, particularly in the lungs, which is a common site of metastases and may have a high level of sodium iodide symporter expression and radioiodine avidity, making the distinction between primary lung cancer and metastatic DTC difficult. Therefore, it is critical to use appropriate diagnostic evaluations to make the correct diagnosis and select the best therapeutic option.

Article information and declarations

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None.

Author contributions

MB — contributed to writing the manuscript and to reviewing the literature; SD and JR — contributed to collecting data; OB — contributed to the literature review; AM, HG, and IG — participated in its design and coordination; NB — corrected the manuscript before submission.

Conflict of interest

The authors declare that they have no competing interests.

Ethics statement

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

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Supplementary material

None.

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