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Case report

Thyroid metastasis revealing a lung adenocarcinoma: A case report and review of the literature

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ABSTRACT

Introduction: Metastatic lung adenocarcinoma in the thyroid is very rare. The clinical presentation and the radiological findings for metastasis carcinoma are nonspecific and do not allow the distinction between metastatic lung carcinoma and primary thyroid tumor.
Case presentation: We report the case of a pulmonary papillary adenocarcinoma revealed by a thyroid metastasis in a 62-year-old and non-smoker patient with no history of cancer.
Discussion: Thyroid metastasis revealing a primary adenocarcinoma of lung is extremely rare. In the absence of a history of lung cancer, the histological appearance of a papillary adenocarcinoma localized in the thyroid can be misdiagnosed as a primary thyroid cancer given the non-specificity of the clinical, radiological and histological presentations. Immunohistochemical analysis and molecular studies are the gold standards for establishing the diagnosis of the primary site.
Conclusion: In this report we aim to discuss the histological and immunohistochemical features of lung adenocarcinoma metastazing in thyroid gland through a literature review. We are also targeting to highlight the essential role of immunohistochemistry and molecular study for the confirmation of the primary pulmonary origin and to discuss therapy for patients with lung cancer metastatic in the thyroid [17].

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1. Introduction

Thyroid metastases are rare malignancies with poor prognoses. The most common primary neoplasm metastasizing to the thyroid gland are renal cell carcinoma, breast carcinomas and lung carcinomas. Pulmonary adenocarcinoma with metastasis to thyroid represents an extremely rare condition and only a few cases have been reported in the literature.

We report a case of a thyroid metastasis revealing an unknown papillary adenocarcinoma of the lung.

2. Case presentation

A 62-year-old patient presented to the Department of General Surgery for a cervical nodule increasing in size over 3 months with no respiratory symptoms. The patient did not have any medico-surgical or smoking history. Physical examination revealed a palpable thyroid nodule.

Blood investigations including thyroid-stimulating hormone (TSH) and free thyroxine were normal. Neck ultrasonography revealed a solid hypoechoic nodule of the left thyroid lobe measuring 16 × 13 × 9 mm and classified as EU-TIRADS 5. The anatomopathological study of the fine-needle aspiration cytology (FNAC) of the thyroid nodule revealed cells showing distinct malignant features, so the lesion was classified as Bethesda category VI (malignant), hence the indication of total thyroidectomy. The specimen was sent to the pathology department.

Seen the suspicious lung images of fortuitous discovery on the chest X-ray performed as part of the preoperative assessment, the patient underwent a Contrast-enhanced Computed Tomography (CT) scan of the thorax after thyroid surgery (and not before it for lack of financial means of the patient and for fear of her loss of sight since she refused any treatment and additional investigation at the beginning). It showed an

Abbreviations: CK7, Cytokeratin 7; TTF1, Thyroid transcription factor 1.

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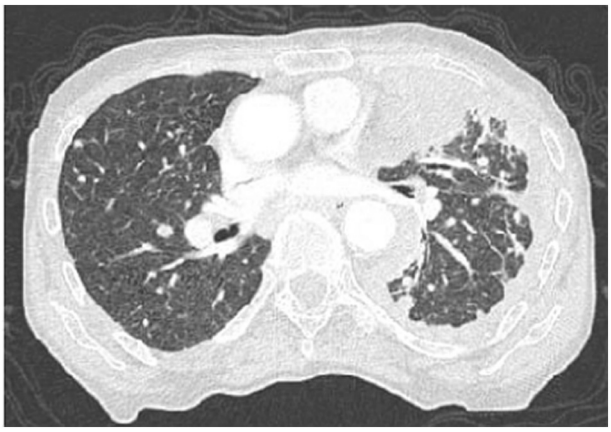

Fig. 1. Computed Tomography (CT) scan of the thorax showing a large heterogeneous mass of the left lung.

82x54x39 mm left mass with ipsilateral and contralateral pleural and pulmonary localizations (Fig. 1). A biopsy of this lung mass was performed.

The histological examination of the 2 samples shows a tumoral proliferation of the same histological aspect, it's about carcinomatous proliferation composed of papillary structures with fibrovascular cores, and lined by cuboidal to columnar neoplastic cells.

The immunohistochemical stains of neoplastic cells in lung biopsy and thyroid nodule were positive for CK7, TTF-1 and napsin- A but negative for thyroglobulin (Figs. 2 and 3). These anatomopathological results were in favor of pulmonary papillary adenocarcinoma with thyroid metastases.

The patient was referred to Respiratory Medicine and oncology departments for treatment of the metastatic cancer of pulmonary origin.

3. Discussion

The metastatic thyroid gland is extremely rare despite its rich vascular supply. It is found mainly in autopsy cases, and represents less

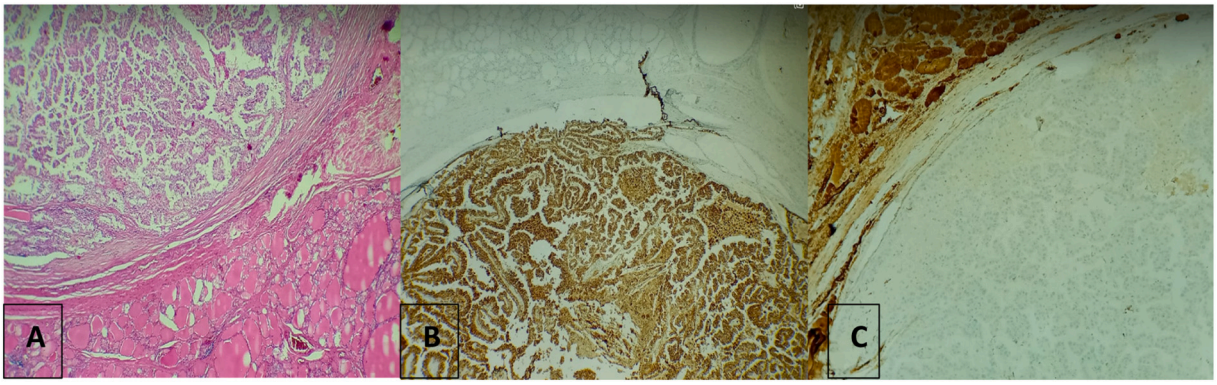

Fig. 2. *Microscopic view of the thyroid tumor:* A) Thyroid tissue is massively infiltrated by papillary carcinomatous proliferation (Hex40). B) Tumor cells are positive for Napsin A ×40. C) but negative for thyroglobulin ×100.

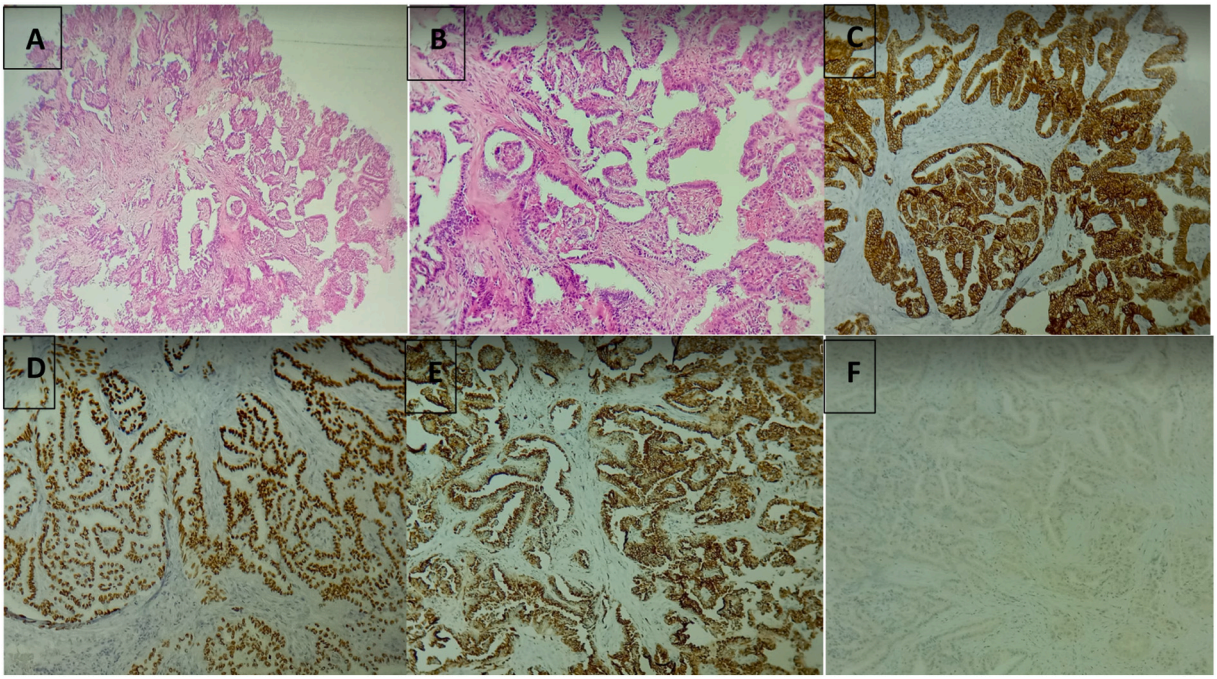

Fig. 3. Pathological examination of the lung biopsy showing a papillary adenocarcinoma with fibrovascular cores. (A: hematoxylin and eosin [H&E], _40 and B: H&E, _100). The cells are strongly positive for CK.7(C), TTF1 (D) and Napsin A (E) But negative for thyroglobulin (F), (all, _100).

Table 1
Summary of published reports of thyroid metastasis from lung adenocarcinoma.

N	Author	Year and country	Patient age	sex	Location of thyroid metastasis	Clinical presentation	Evolution
1	Elliott RH et al.	1959 USA	67	Female	Hard nodular thyroid and fixed left supraclavicular nodes	Enlarging goiter, dyspnea, sternal pain and cough	Died 9th postoperative day.
2	Megumi Miyakawa. et al.	2001 Japan.	50	Female	Not mentioned	Right shoulder pain	Died of respiratory failure
3	Costantine Albany	2011 USA	68	Male	Left thyroid lobe	Fatigue, shortness of breath, cough and weight loss	Free of disease 8 mounths later
4	Tariq Namad et al.	2015 USA	48	Female	Multiple thyroid nodules	Progressive fatigue, dyspnea, and dysphagia	Free of disease 3 mounths later
5	Wey SL et al.	2015 Taiwan	71	Female	Right thyroid lobe	Not mentionned	Not mentionned
6	J. Khalil	2015 Morocco	37	Female	Right thyroid lobe	Nodular goiter	Free of disease one year later
7	Hironori Kawamoto	2016 Japan	42	Female	The right thyroid lobe	Left inguinal pain	Not mentionned
8	A. Dao	2017 Burkina Faso	59	Male	Right thyroid nodule.	Dyspnea, dry cough, and a chest pain	Died 2 months later after brain radiotherapy.
9	Diana Simoniene	2018 Lithuania	58	Male	Not mentionned	Increasing volume of the neck, shortness of breath, and changes in voice and swallowing disorder	Died
10	Jun Cao, Yan-Er	2019 China	54	Male	Right thyroid lobe	Slight cough and expectoration	Regular and free of disease
11	Ahmed Ben Saad	2020 Tunisia	50	Male	Left thyroid lobe	Cervical nodules	Died
12	Hye Mi Ko and Je-Ryong Kim	2020 Korea	76	Female	Right thyroid nodule	Increasing volume of thyroid nodule	Not mentionned
13	Enes ERUL	2021 Turkey	67	Female	Diffusely enlarged thyroid gland	Painless lump in her neck	Still alive after 15th month of crizotinib treatment.

than 3 % of thyroid cancers among the living [1]. Breast, kidney, lung, and gastrointestinal tract have been reported to be the most common primary sites that metastasize to the thyroid gland [2]. Lung is the second common site [3]. Direct invasion, hematogenous spread and lymphatic metastasis are the most common routes of metastasis [1]. The histological types of the different reported cases of lung cancer metastasizing to the thyroid were small cell carcinoma, squamous cell carcinomas, adenocarcinoma and anaplastic small cell carcinoma [2]. Only a few cases of primary lung adenocarcinoma were reported. Research of English language reports using the keywords "lung adenocarcinoma and thyroid metastasis" revealed only 13 cases of thyroid metastasis from pulmonary adenocarcinoma (Table 1) [4–13].

The interval between the diagnosis of the primary lung carcinoma and the discovery of a thyroid metastasis varies between one month and twenty-six years [7]. In our case report, the thyroid metastasis was the revealing sign of lung adenocarcinoma; This condition has been exceptionally reported in the literature.

Clinically, patients with thyroid metastasis present non-specific symptoms such as thyroid nodule or goiter, cervical discomfort, dyspnea, dysphagia, or dysphonia [14].

.Biologically, the balance of thyroid hormones is generally unaffected. However, dysfunction of the thyroid gland has been reported in some cases due to the destruction of thyroid follicles by tumor cells [15].

Medical imaging including ultrasound, a cervical scanner with and without injection CT and PET scan show no specific signs to confirm the thyroid or lung origin of the tumor [7].

Histological examination and especially immunohistochemical studies are crucial for the diagnosis of metastatic lung carcinoma. It can be performed on different types of samples namely fine needle aspiration (FNA), biopsy and thyroidectomy specimens. FNA is a minimally invasive, rapid, and inexpensive technique allowing to make cell blocks used for immunostains. However, it might be non-contributory if insufficient cells are available. Biopsy and surgical specimens are more precise [13]. Several immunohistochemical markers, including CK7, TTF1, thyroglobulin, and Napsin A are essential for diagnosis. CK7 and TTF-1 have been reported to be positive in primary lung adenocarcinoma and thyroid cancers; Positive labeling of tumor cells with anti-thyroglobulin antibody confirms their thyroid origin. However, negative labeling does not eliminate a thyroid origin since some primary thyroid tumors may show negative immunostaining [7]. Napsin A has been proven sensitive and specific immunomarker for identifying a lesion of lung origin, hence its capital interest [16].

Molecular studies are also helpful in the distinction between thyroid papillary carcinoma and lung carcinomas. *RET/PTC* rearrangements, *RAS* mutations and *BRAF* mutations are frequently found in thyroid papillary carcinoma, while *EGFR* mutations, and *ALK* rearrangements are usually identified in lung carcinoma [3].

Surgery is indicated in patients with isolated thyroid lesions with no evidence metastasis in other sites and for relieving compressive symptoms in patients with disseminated disease [3]. Systemic treatment with chemotherapy or targeted therapy is used in the case of polymetastatic cancer. Radiotherapy is used as a palliative treatment for symptoms due to thyroid metastases [7] Radioiodine treatment is not indicated for thyroid metastases [12].

4. Conclusion

Diagnosis of papillary carcinoma in the thyroid gland as a primary or metastatic neoplasm is a significant challenge. In the absence of specific clinical or radiological signs, immunohistochemical and molecular studies remain the gold standard for diagnosis.

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Ethical approval

Not applicable.

Consent for publication

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Availability of data and materials

Not applicable.

Registration of research studies

Not applicable.

Guarantor

Elouarith Ihssan

CRediT authorship contribution statement

IE and OA analyzed and interpreted the patient data and wrote the manuscript. IE and LB made the figs. IE performed the histological examination. KZ and OM proposed the study, supervised IE and revised the manuscript. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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