PATHOLOGICA 2023;115:186-191;
DOI: 10.32074/1591-951X-780

Case Report

Intratumoural metastasis of primary lung adenocarcinoma to non-invasive follicular thyroid neoplasm with papillary-like nuclear features

Subhash Yadav[1], Suman Kumar Ankathi[2], Asawari Patil[1], Rajiv Kaushal[1]

[1] Department of Surgical Pathology, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India;
[2] Department of Radiodiagnosis, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India

Summary
Metastasis to the thyroid gland is very uncommon with an incidence of 2-3% of all thyroid malignancies. A higher incidence is noted in autopsy studies indicating incidental detection. However, tumour-to-tumour metastasis is extremely uncommon with a handful of cases published in the literature to date. Also, non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFT-P) is a rare neoplasm; diagnosis requires meticulous sampling of the entire capsule and fulfilment of other diagnostic criteria. We report a case of primary adenocarcinoma of lung in a 57-year-old female who additionally had a left thyroid nodule which appeared suspicious on ultrasonography. Histology of lung tumour was conventional papillary adenocarcinoma while aspiration cytology from the thyroid raised suspicion of metastatic adenocarcinoma. On hemithyroidectomy, the thyroid nodule showed metastatic adenocarcinoma in the centre of the nodule, while the peripheral portion showed non-invasive follicular thyroid neoplasm with papillary-like nuclear features; the diagnosis of which was confirmed with complete sampling of the thyroid capsule. The immunoprofile also supported the above dual histology. This is an extremely uncommon occurrence and metastasis within a NIFT-P has not been reported to the best of our knowledge.

Key words: intratumoural metastasis, NIFT-P, pulmonary adenocarcinoma, immunohistochemistry

Received: May 22, 2022
Accepted: January 3, 2023

Correspondence
Subhash Yadav
Department of Pathology Tata Memorial Centre Homi Bhabha National Institute, Mumbai, India
E-mail: drsubhashyadav23@gmail.com

How to cite this article: Yadav S, Ankathi SK, Pati, A et al. Intratumoural metastasis of primary lung adenocarcinoma to non-invasive follicular thyroid neoplasm with papillary-like nuclear features. Pathologica 2023;115:186-191. https://doi.org/10.32074/1591-951X-780

Introduction

Metastasis to the thyroid gland is uncommon with an incidence of 2-3% of all thyroid malignancies. This rate is higher in autopsy studies ranging from 5-to 24%. Most of the tumours that metastasize to the thyroid are from the breast, lung, kidney, and gastrointestinal tract [1-4]. Multiple tumours in a single individual are known, although tumour-to-tumour (TtoT) metastasis is extremely uncommon. Berent in 1902 was the first to describe metastasis of primary squamous carcinoma of the jaw to renal cell carcinoma [5]. Since then, approximately 100 cases of TtoT metastasis have been reported in literature wherein the donor neoplasm is usually from the lung and breast. Less than 30 cases have been described in the literature where the recipient tumour was primary thyroid neoplasm and only 10 cases of ToT have been described from lung cancer to thyroid cancer [2,6-8]. We also report a similar rare case of TtoT metastasis from lung adenocarcinoma to noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFT-P) review of the literature.

Case history

A 57-year-old woman with no comorbidities complained of coughing on and off for the last five months and one episode of hemoptysis. She was treated symptomatically without much relief at another hospital. A computed tomography (CT) scan of the thorax including the neck showed a 4.5 x 4 x 3.7 cm lesion in the right upper lobe of the lung, few satellite nodules in the apical segment and an enlarged right hilar lymph node appearing suspicious for metastasis. Ultrasonography of the left thyroid gland showed multiple nodules of varying size, the largest being 13 x 12 mm. The largest nodule was solid, well-defined, and hypodense and hence suspicious for neoplasm on imaging. The remaining thyroid nodules were small and microcystic, possibly representing goitre (Fig. 1a). Positron emission tomography (PET) scan revealed uptake in lung and in the left thyroid nodule with a maximum standardised uptake value (SUVmax) of 10.1 and 5.8 respectively. No other sites of metastasis were detected on imaging. The lung tumour was clinically staged as T2bN1M1b. Subsequently, the lung lesion was biopsied and the thyroid lesion was subjected to fine-needle aspiration cytology (FNAC).

Histology of the lung mass revealed a tumour with a papillary architecture having a large nuclei and nucleoli resembling an adenocarcinoma with a papillary pattern. On immunohistochemistry, the tumour was positive for thyroid transcription factor-1 (TTF-1) and napsin-A while being negative for thyroglobulin and Pax-8. FNAC from the thyroid lesion showed sheets of high-grade carcinoma cells with papillary architecture. The tumour cells were large, polygonal with a large nuclei and prominent nucleoli as described in the histology. Intranuclear grooves or inclusions were not seen in these papillary clusters. Also, the background thyroid follicular cells showed a prominent Hurthle cell change. Nuclear features of papillary thyroid carcinoma were not seen in the thyroid follicular cells. Immunocytochemistry showed positivity for thyroid transcription factor-1 (TTF-1) and negative staining for paired box gene-8 (Pax-8) in tumour cells. Thus, the diagnosis of primary lung adenocarcinoma with

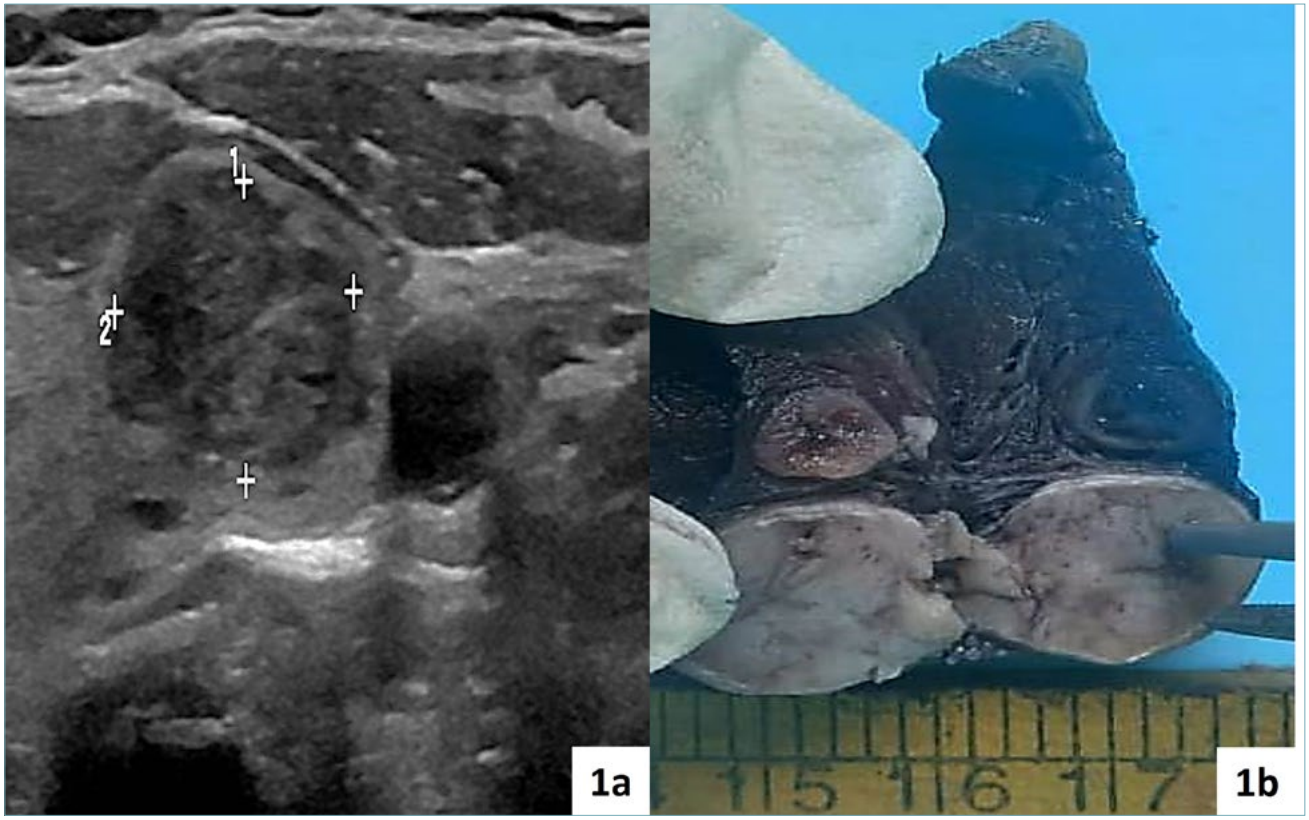

Figure 1. (a) Ultrasonography of the left thyroid shows a solid nodule measuring approximately 1.5 cm with few areas of breakdown. Background thyroid showed few nodules of goitre. (b) The gross image of the left thyroid gland shows a well-defined capsulated solid whitish nodule with few areas of breakdown/cystic change. Background thyroid shows spongiform nodules of goitre.

metastasis to the thyroid was offered. The patient underwent left hemithyroidectomy given the isolated metastasis and for confirmation of cytological diagnosis.
Gross examination of the thyroid showed a well-circumscribed well-encapsulated whitish firm thyroid nodule measuring 1.5 cm with a central area of breakdown. The nodule was completely submitted for histological examination. The rest of the thyroid showed a few small spongiform nodules resembling goitre (Fig. 1b).
Histology showed a completely encapsulated nodule composed of two morphologically different tumours. The central part of the nodule showed a papillary tumour with enlarged hyperchromatic nuclei, moderate eosinophilic cytoplasm, and prominent nucleoli. Focal hob-nailing of tumour cells was also seen. In contrast, the periphery of the nodule showed histologically a different tumour arranged in a micro-follicular pattern. The cells lining these follicles showed mild nucleomegaly, vesicular nuclei and occasional nuclear grooves. Vascular or lymphatic invasion were not identified. Extrathyroid extension was not seen. The entire capsule was submitted for review and did not show any capsular invasion. Background thyroid gland revealed goitre. Morphologically, the peripheral tumour resembled NIFT-P as per the criteria (Figs. 2, 3) This difference in histology was supported by the respective immunohistochemical stains. The central papillary tumour was strongly positive for cytokeratin-7 (CK7) and napsin-A; it was negative for thyroglobulin and Pax-8 while the peripheral follicular tumour was positive for thyroglobulin and Pax-8 and negative for napsin-A. (Fig. 4) Although TTF-1 can be positive in both thyroid and lung tumours, positive staining for napsin-A in the central component; and thyroglobulin in the peripheral component supported pulmonary and thyroid origin respectively. Hence, a diagnosis of metastatic papillary adenocarcinoma, consistent with primary in the lung to non-invasive follicular thyroid neoplasm with papillary like nuclear features (NIFT-P) was offered. Due to poor general condition and metastatic disease, the patient was offered palliative chemotherapy of cisplatin and etoposide in low doses. However, the patient was not keen on treatment and after the initial cycle was lost to follow-up.

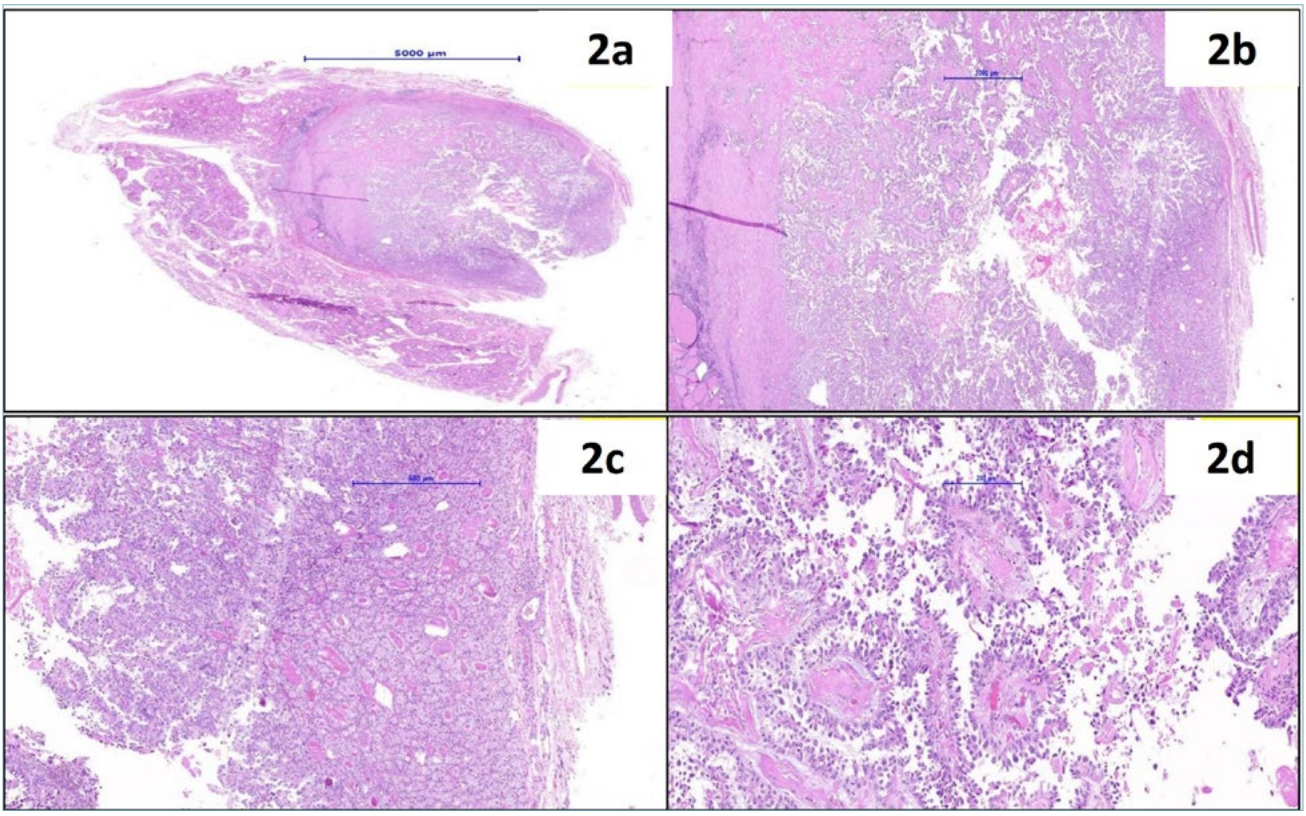

Figure 2. (a) Scanner view of the thyroid nodule showing complete capsule of the nodule (HE40x); (b) Histology shows a well-encapsulated tumour composed of central papillary architecture and peripheral follicular architecture (HE100x); (c) interphase of the papillary and follicular architecture of the tumour (HE100x); (d) papillary adenocarcinoma morphology representing the lung tumour (HE200x).

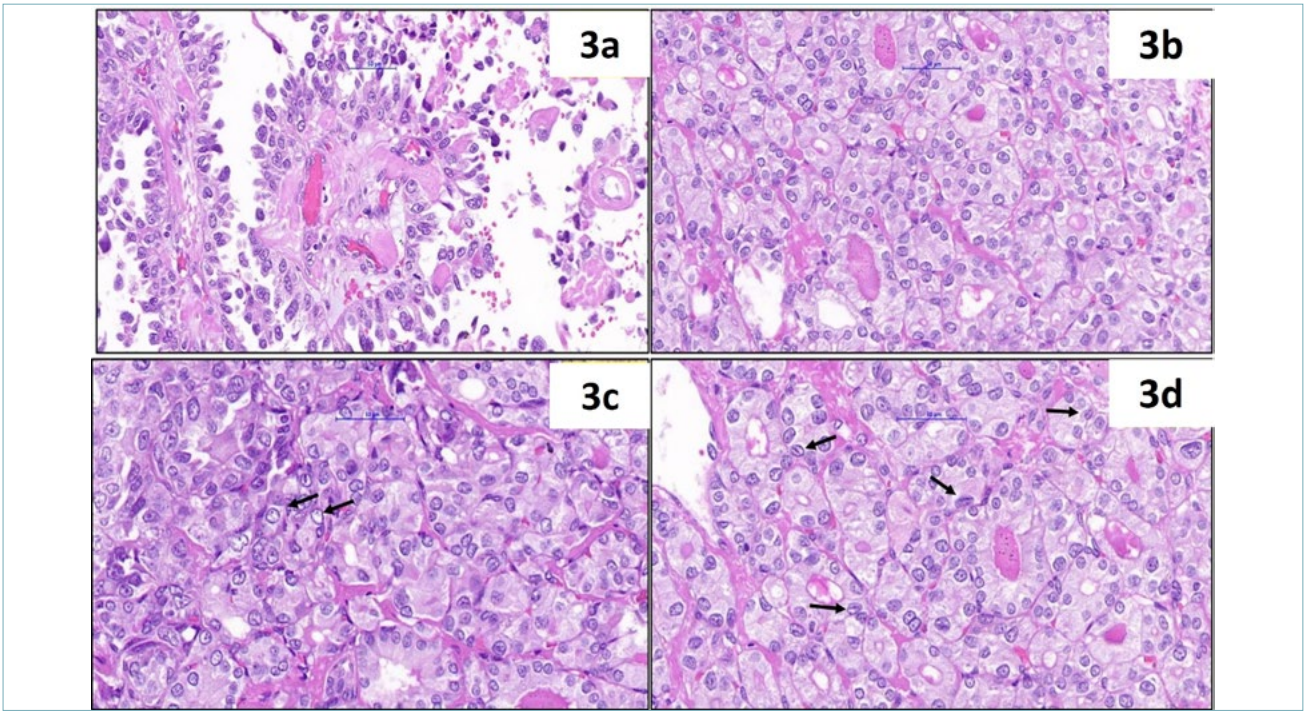

Figure 3. (a) Well-formed papillae lined by tumour cells with high nuclear grade and moderate cytoplasm (HE400x); (b-d) follicular pattern of the tumour at the periphery showing mild nuclear enlargement and pale nuclei/ nuclear clearing seen in (c) (black arrow) along with nuclear grooves in (d) (black arrows) (HE400x).

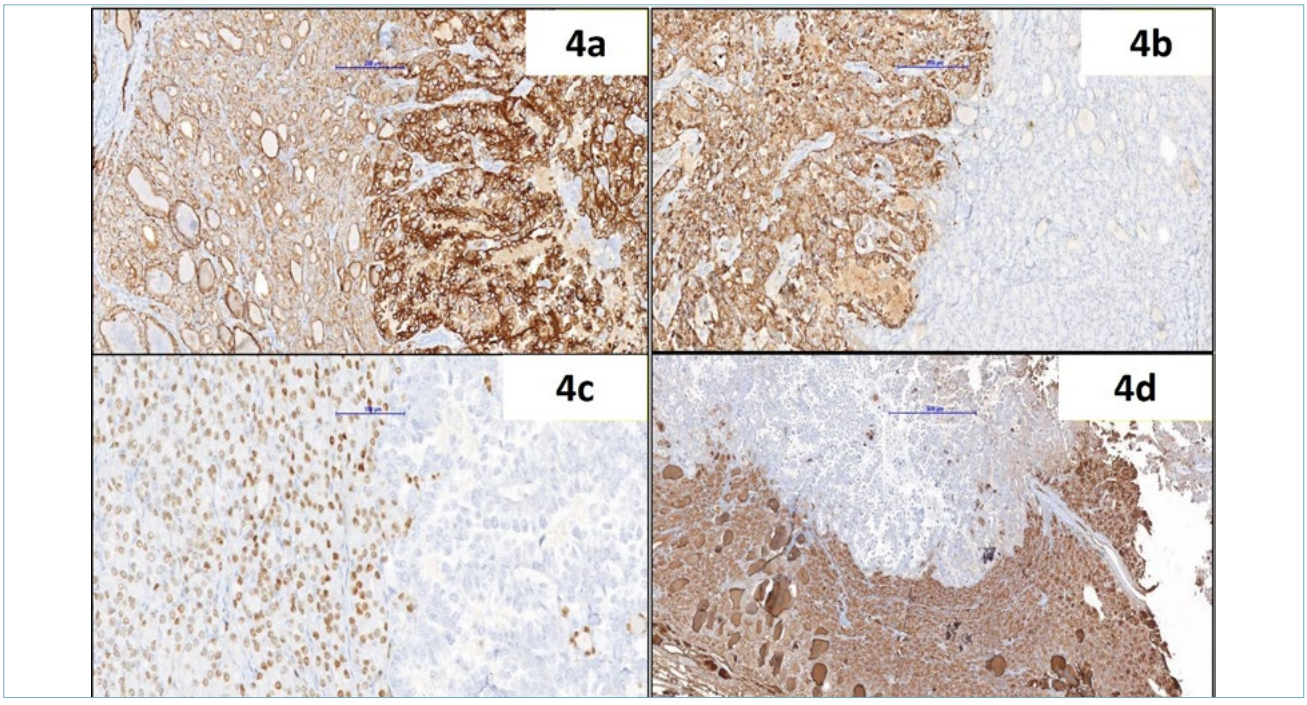

Figure 4. (a) CK7 showing strong positivity in the papillary areas and moderate-intensity positivity in the follicular areas; (b) Napsin-A is positive in the adenocarcinoma component indicating primary pulmonary origin while being negative in the follicular component; (c) and (d) pax-8 and thyroglobulin highlight the peripheral follicular tumour indicating thyroid origin while the central adenocarcinoma component is negative.

Discussion

Cancer metastasis involves attack by the immune system, lack of oxygen and necessary nutrients, large amounts of lactic acid production by glycolysis and increased cell death [9]. Metastasis to the thyroid gland is uncommon despite having a rich vascular supply and mostly occurs as secondary involvement in cases of advanced metastatic disease [10,11]. Renal cell carcinoma is the most common donor for metastasis to the thyroid neoplasm followed by lung and breast tumours [4]. Ghossein et al. published the largest single-centre series of 30 cases of metastasis to thyroid over a period of 16-years with the most common primary donor site being the kidney followed by the lung. They had three cases of TtoT metastasis in their series; one case was of clear cell renal cell carcinoma metastasising to NIFT-P. The other two cases were from primary colorectum and oesophagus metastasising to papillary thyroid carcinoma and follicular adenoma, respectively [12] (Tab. I).

As per Steven et al. the criteria used in diagnosing tumour-to-tumour metastasis is that the recipient tumour is a true neoplasm and that the donor neoplasm is a true metastasis, that is, invasion into the substance of recipient neoplasm is proven, with the caveat that the presence of only tumour emboli within a recipient neoplasm does not qualify as a true TtoT metastasis [4]. Collision tumour, contiguous growth of one neoplasm into another adjacent neoplasm, and metastasis to a lymph node already involved by lymphoreticular malignancy are all excluded [13,14].

NIFTP is the new terminology proposed for encapsulated follicular variants of papillary thyroid carcinoma (EFVPTC) without evidence of capsular and/or lymphovascular invasion. A team of endocrine experts coined this new term “NIFT-P” at ‘The Endocrine Pathology Society’ meeting in March 2015 [15]. A distinction of this entity was necessary as no patient from the non-invasive group developed any adverse event (no recurrence, no lymph node metastasis, no distant metastasis) compared to the invasive encapsulated follicular variant of papillary thyroid carcinoma who developed some adverse events in 12% of the cases including distant metastasis [16,17]. In our case, the complete nodule with its capsule was sampled and did not show any capsular and/or vascular invasion. In the review paper by Steven et al. of the 28 thyroid neoplasms serving as a recipient, follicular adenoma was the most common benign thyroid neoplasm (16/28) and papillary thyroid carcinoma is the most common malignant recipient thyroid neoplasm (9/28) [4]. To the best of our knowledge, this would be the first case of adenocarcinoma of lung metastasising to NIFT-P.

Conclusion

NIFT-P is an unusual and rare tumour with a defined gross appearance and reporting protocol. Hence, meticulous gross appearance and reporting is necessary to diagnose these unusual entities and every tumour can be a possible bed for other metastases of another tumour. Thus, one should be aware of them and should use ancillary methods to diagnose them.

Conflicts of interest

The authors declare no conflict of interest.

Funding

No funding was obtained for this study.

Ethical consideration

No procedures were performed on the participants as a part of this study. This is a retrospective observational study done in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No ethical clearance was needed as this is a retrospective observational isolated case report.

Author contributions

SY, RK, AP: concept, design, final approval, draft writing; SY, RK: analysis, interpretation, draft writing; SY , SA, AP, RK: critical revisions, final approval.

References

1 Bohn OL, De las Casas LE, Leon ME. Tumor-to-tumor metastasis: Renal cell carcinoma metastatic to papillary carcinoma of thyroid-report of a case and review of the literature. Head Neck Pathol 2009 3:327-330. https://doi.org/10.1007/s12105-009-0147-9

2 Wey SL, Chang KM. Tumor-to-Tumor Metastasis: Lung Carcinoma Metastasizing to Thyroid Neoplasms. Case Rep Pathol 2015;153932. https://doi.org/10.1155/2015/153932

3 Kameyama K, Kamio N, Okita H, Hata J. Metastatic carcinoma in follicular adenoma of the thyroid gland. Pathol Res Pract 2000;196:333-336; discussion 337-8. https://doi.org/10.1016/s0344-0338(00)80065-5

4 Stevens TM, Richards AT, Bewtra C, et al. Tumors metastatic to thyroid neoplasms: a case report and review of the literature. Patholog Res Int 2011;2011:238693. https://doi.org/10.4061/2011/238693

5 Berent W. Seltene metatasenbildung. Zentralbl Allg Pathol 1902;13:406-410.

6 Baloch ZW, LiVolsi VA. Tumor-to-tumor metastasis to follicular variant of papillary carcinoma of thyroid. Arch Pathol Lab Med. 1999;123:703-706. https://doi.org/10.5858/1999-123-0703-TTTMTF

7 Moody P, Murtagh K, Piduru S, et al. Tumor-to-tumor metastasis: pathology and neuroimaging considerations. Int J Clin Exp Pathol 2012;5:367-373.

8 Gowda KK, Bal A, Agrawal P, et al. Tumor-to-tumor metastasis: small cell carcinoma lung metastasising into a follicular adenoma

of the thyroid. Indian J Pathol Microbiol 2017;60:133-335. https://doi.org/10.4103/0377-4929.200037

[9] Wang RA, Lu YY, Fan DM. Reasons for cancer metastasis: a holistic perspective. Mol Clin Oncol 2015;3:1199-1202. https://doi.org/10.3892/mco.2015.623

[10] Nixon IJ, Coca-Pelaz A, Kaleva AI, et al. Metastasis to the thyroid gland: a critical review. Ann Surg Oncol 2017;24:1533-1539. https://doi.org/10.1245/s10434-016-5683-4

[11] Wang X, Huang Y, Zheng Z, et al. Metastases to the thyroid gland: a retrospective analysis of 21 patients. J Cancer Res Ther 2018;14:1515-1518. https://doi.org/10.4103/jcrt.JCRT_435_16

[12] Ghossein CA, Khimraj A, Dogan S, Xu B. Metastasis to the thyroid gland: a single-institution 16-year experience. Histopathology 2021;78:508-519.

[13] Fadare O, Parkash V, Fiedler PN, et al. Tumor-to-tumor metastasis to a thyroid follicular adenoma as the initial presentation of a colonic adenocarcinoma. Pathol Int 2005;55:574-579. https://doi.org/10.1111/j.1440-1827.2005.01871.x

[14] Campbell LV Jr, Gilbert E, Chamberlain CR Jr, et al. Metastases of cancer to cancer. Cancer 1968;22:635-643. https://doi.org/10.1002/1097-0142(196809)22:3<635::aid cncr2820220320 > 3.0.co;2-o

[15] Alves VAF, Kakudo K, LiVolsi V, et al. Noninvasive Follicular Thyroid Neoplasm With Papillary-Like Nuclear Features (NIFTP): Achieving Better Agreement By Refining Diagnostic Criteria. Clinics (Sao Paulo) 201821;73:e576. https://doi.org/10.6061/clinics/2018/e576.

[16] Jug R, Jiang X. Noninvasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features: An Evidence-Based Nomenclature Change. Patholog Res Int 2017;1057252. https://doi.org/10.1155/2017/1057252

[17] Amendoeira I, Maia T, Sobrinho-Simões M. Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): impact on the reclassification of thyroid nodules. Endocr Relat Cancer 2018;25:R247-R258. https://doi.org/10.1530/ERC-17-0513