CASE REPORT

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Colorectal Cancer Metastasizing to the Thyroid Gland: A Rare and Interesting Case

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ABSTRACT

Thyroid cancers are rare, accounting for 2-3% of all malignancies. They are usually asymptomatic and incidentally detected. Histopathologic evaluation should be performed for definitive diagnosis. A 60-year-old woman with rectal cancer was found to have a 3 cm thyroid nodule on positron emission tomography/computed tomography. While the first biopsy was benign, a second biopsy showed a follicular lesion of uncertain significance. Despite lung lesion regression, the thyroid lesion progressed, leading to a left lobectomy. Pathology revealed the thyroid lesion as metastatic intestinal-type adenocarcinoma, which is related to poorly differentiated thyroid carcinoma. This changed her treatment plan for metastatic rectal cancer. The case underscores the importance of considering metastasis in thyroid nodules, especially in patients with other cancers like colorectal cancer. It highlights the need for thorough differential diagnosis, recognize the potential for thyroid malignancy, and the role of thyroidectomy in cases where biopsy results are inconclusive. This case is remarkable for representing a tumor-to-tumor metastasis, where colorectal adenocarcinoma metastasized into a primary poorly differentiated thyroid carcinoma-an exceedingly rare phenomenon. The diagnostic complexity, including inconclusive fine needle aspiration biopsies and delayed progression despite systemic treatment, underscores the importance of maintaining a high index of suspicion when evaluating thyroid nodules in patients with known malignancies.

Keywords: Colorectal cancer; thyroid metastasis; tumor-to-tumor metastasis; immunohistochemistry; secondary malignancy

INTRODUCTION

Colorectal cancer rarely metastasizes to the thyroid gland. Even more uncommon is the phenomenon of tumor-to-tumor metastasis, in which one malignant tumor spreads into another distinct tumor. Although the thyroid gland is highly vascularized and theoretically a potential site for metastasis, its unique metabolic environment is believed to inhibit such occurrences. This case report presents a colorectal adenocarcinoma metastasizing to a primary poorly differentiated thyroid carcinoma-an extremely rare instance of tumor-to-tumor metastasis.[1-4] The incidence of metastasis to thyroid cancer is rare and accounts for only 2-3%. Also, tumor-to-tumor metastasis is even more unusual. In recent years, due to the increasing use of imaging studies in oncological follow-ups, especially positron emission tomography/computed tomography (PET/CT), rare metastases or secondary primary tumors are being detected more frequently. Brindle et al.[5] In their study of 7221 PET/CT scanned patients, thyroid malignancy was detected in 25% of patients with thyroid incidentoloma. In a case report published by Loree et al.[6], synchronous papillary thyroid cancer was detected after PET/CT scanning in a patient diagnosed with rectal cancer. This case report aims to present a case of rectal adenocarcinoma metastasizing to a primary poorly differentiated thyroid carcinoma. Such metastases are exceptionally uncommon, and tumor-to-tumor metastasis adds another layer of rarity. In addition, knowledge about metastasis of rectal cancer to another primary thyroid neoplasm is limited to sparsely

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reported case reports in the literature.[7-10] Our case not only highlights the unusual presentation of thyroid metastases but also contributes valuable insights into the mechanisms underlying tumor-to-tumor metastasis, making it a significant addition to the literature.

CASE REPORT

A 60-year-old female patient was followed up with neoadjuvant chemoradiation (no surgery was performed at patient request), for locally advanced rectal cancer. Abdominoperineal resection was performed, due to the development of local recurrence approximately 1 year after the end of treatment. During imaging performed for preoperative staging, a 2 cm nodule with FDG uptake in the left lobe of the thyroid gland was detected. The nodule was evaluated as benign by a fine needle aspiration biopsy. Apart from this, the patient had no signs of distant metastasis and was operated on. Informed consent was obtained from the patient.

Histopathological evaluation reported poorly differentiated rectum adenocarcinoma at stage III and immunohistochemical examination revealed no *MMR* gene loss. Afterwards, chemotherapy was given as adjuvant chemotherapy. The patient had no signs of recurrence or metastatic disease in the imaging performed after this treatment. Control imaging was planned at 3-month intervals. Unfortunately, the patient did not come for approximately 1 year for oncology follow-ups due to the Coronavirus disease 2019 pandemic. In the PET/CT scan taken, an approximately 3 cm lesion with intense FDG uptake was detected in the left lobe of the thyroid gland. In addition to that, metastatic lesions, the largest of which was 2.5 cm in size, were detected in both lungs (Figure 1). Thereupon, due to the detection of K-RAS mutation, 6 cycles of FOLFOX + bevacizumab treatment were administered in the first-line treatment. During the treatment, the lesion in the left lobe of the thyroid was resampled, and it was reported as category III (follicular lesion of undetermined significance) according to the Bathesda classification. Since lung metastases responded to the treatment the lesion in the thyroid gland progressed, left thyroid lobectomy was performed. In pathological evaluation, the tumor was reported as an intestinal type adenocarcinoma metastasis within a primary poorly differentiated thyroid carcinoma (Figure 2). Immunohistochemical evaluation was performed for thyroglobulin, TTF-1, SATB2, CEA and CDX-2 expression. In subsequent follow-ups of the patient, while the majority of the nodules observed in both lungs had a similar appearance, some nodules in the right upper lobe posterior segment showed increased size and metabolic activity on PET/CT. Right lung upper lobectomy was performed, and the pathological examination was reported as colon adenocarcinoma (Figure 3). CK7 and TTF-1 negativity, but CK20, CDX-2, and SATB2 positivity, are observed in immunohistochemical studies. Metastatic nodules in the thyroid gland can often be mistaken for benign thyroid nodules or primary thyroid malignancies. Fine needle aspiration biopsy, immunohistochemistry, (e.g., CK20 positivity, CK7 negativity) and genetic analysis have played a critical role in the diagnosis. Figures 2, 3 illustrate the progression of disease and the pathological distinction between the thyroid primary and the colorectal metastasis. Immunohistochemical staining, including CDX2 and SATB2 positivity and CK7/TTF-1 negativity, confirmed the metastatic colorectal origin within the thyroid carcinoma. Due to the K-RAS mutation in the patient, the chemotherapy regimen was switched to FOLFIRI and aflibercept as second-line treatment. After 3 months, PET/CT showed progression of lesions in the lung, and regorafenib treatment was started. While the patient's treatment continued, he was hospitalized in the intensive care unit due to general condition disorder, pneumonia, and sepsis. Unfortunately, she died.

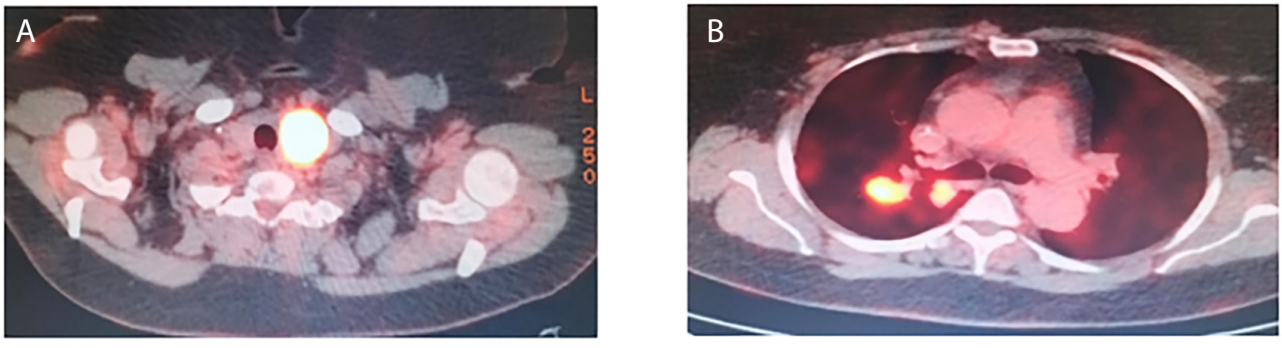

FIGURE 1: A-B Thyroid and lung metastasis at PET/CT imaging.

PET/CT: Positron emission tomography/computed tomography

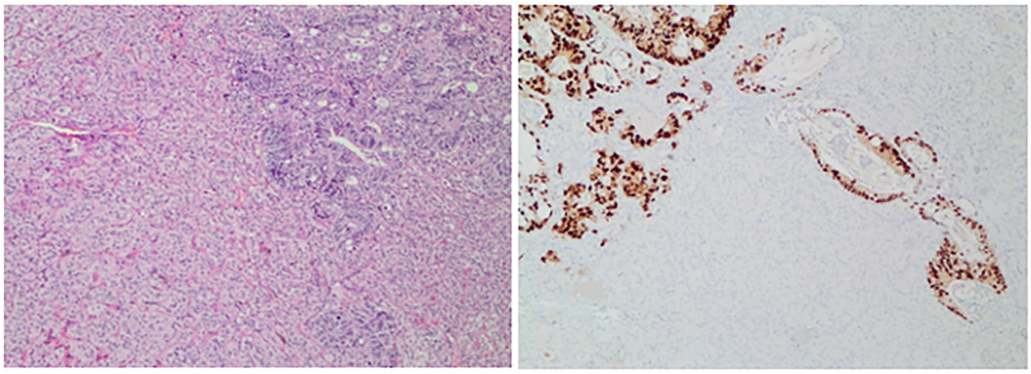

FIGURE 2: Metastasis of intestinal type adenocarcinoma (stained with CDX2 diffusely and strongly) inside primer poorly differentiated thyroid carcinoma.

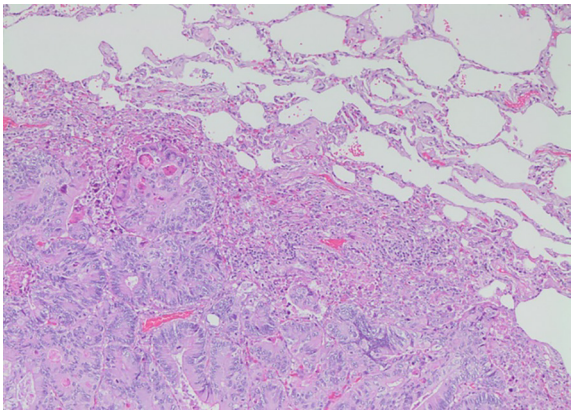

FIGURE 3: Lung metastasis of intestinal type adenocarcinoma at histopathologic examination.

DISCUSSION

The purpose of discussing this case is to highlight that rectal cancer rarely metastasizes to the thyroid, and there is limited information on this subject in the literature. Therefore, sometimes the nodule in the thyroid may be considered benign and neglected. However, every nodule in the thyroid gland should be considered important, and additional investigations should be performed. Thyroid metastases are extremely rare and only account for approximately 1-3% of all thyroid malignancies. Although metastatic disease is thought to be frequent due to the well vascularized nature of the thyroid gland, factors such as the high oxygen content, iodine concentration, and peroxidase activity of the thyroid gland are thought to inhibit metastasis formation. The most common primary tumors that metastasize are: renal cell carcinoma, lung cancer, breast cancer, melanoma, gastrointestinal cancers (rarely) In a study by Lee et al.[11], thyroid, ovarian, prostate, and hematologic malignancies were more likely to be detected as secondary primary malignancies in patients with colon tumors, and bone and soft tissue malignancies in patients with rectal tumors. The average duration of secondary primary cancer detection is around 4.7 (2.7-7.5) years.

Tumor-to-tumor metastasis is an extremely rare phenomenon, particularly involving colorectal adenocarcinoma metastasizing into a primary thyroid malignancy. The diagnostic challenge arises from overlapping cytological features and the possibility of misinterpreting metastatic lesions as primary thyroid tumors. In our case, histopathologic and immunohistochemical analyses were essential for identifying the dual origin. Recognition of such rare metastatic patterns is crucial as it influences both treatment planning and prognosis. Thyroid metastasis of colorectal cancer is rare and coexistence of primary thyroid neoplasm with thyroid metastasis is even less frequently observed. When a thyroid nodule is detected in every patient with known malignancy, a differential diagnosis should be made by fine needle aspiration biopsy. The sensitivity and specificity of fine needle aspiration biopsy in detecting metastases are above 90%. There are very few documented cases of colorectal cancer metastasizing to the thyroid gland. Hussain et al.[7] and Chen et al.[8] reported solitary thyroid metastases mimicking primary thyroid carcinoma, while Luo et al.[9] described a rare case of metastasis into a synchronous papillary carcinoma. Similar to our case, these reports emphasized the diagnostic challenge and the pivotal role of immunohistochemical markers in distinguishing tumor origin. Our case adds further novelty by demonstrating tumor-to-tumor metastasis into a poorly differentiated thyroid carcinoma, a scenario scarcely reported in the literature.[10] Treatment should be planned according to the stage and extent of the primary tumor. A radical surgical approach is unnecessary in thyroid gland metastases of aggressive and extensive metastatic tumors. If the expected survival is long and the metastasis is isolated, thyroidectomy may be effective in long-term disease control. In recent years, the addition of targeted biological agents to combination chemotherapy regimens in colorectal cancers has resulted

in an improvement in both disease-free survival and overall survival. It should be kept in mind that thyroid lesions detected during the staging of colorectal cancers could be metastases. In the workup of such cases, distinguishing thyroid neoplasm from thyroid metastases by use of histopathologic sampling and performing thyroidectomy in symptomatic cases could be an appropriate approach. Thyroid metastasis from rectal cancer has been reported rarely in the literature. This increases the scientific value of our case. Tumor-to-tumor metastasis is not only rare but diagnostically challenging, especially when both tumors coexist within the same gland. Recognizing such a phenomenon is critical as it can significantly alter staging, prognosis, and treatment strategy. In our patient, surgical resection of the thyroid lesion enabled accurate histopathologic classification, ultimately redirecting systemic therapy.

CONCLUSION

The possibility of metastatic disease should be kept in mind when evaluating masses in the thyroid, especially in patients with a history of malignancy. Further research is needed to better understand the mechanisms and diagnostic modalities of such rare metastases.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.M., P.B., O.K., Concept: N.M., Ö.C.E., Design: N.M., A.Y., M.F.K., Data Collection or Processing: N.S., E.K., P.E., Analysis or Interpretation: Y.A., A.K.G., A.Ç., Literature Search: İ.V.B., Writing: N.M., Critical Review: R.A., S.I., References and Fundings: Ö.E., M.S.

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