OncoTargets and Therapy Dovepress

Open Access Full Text Article

CASE REPORT

Thyroid Gland as a Metastatic Site for Hepatocellular Carcinoma: A Rare Case Report

Yang-Lu Ge[1,2], Shui-Quan Jin[2], Lv-Zhou Han[2], Xiang Zhang[3,4]

[1]School of Medicine, Ningbo University, Ningbo, Zhejiang, 315211, People's Republic of China; [2]Yuyao Hospital of Traditional Chinese Medicine, Ningbo, Zhejiang, People's Republic of China; [3]School of Medicine, Shanghai University, Shanghai, People's Republic of China; [4]UCL Centre for Kidney and Bladder Health, Royal Free Hospital, London, UK

Correspondence: Lv-Zhou Han, Yuyao Hospital of Traditional Chinese Medicine, Ningbo, Zhejiang, People's Republic of China, Email hanlvzhou1023@163.com; Xiang Zhang, School of Medicine, Shanghai University, Shanghai, People's Republic of China, Email rmhaxz1@ucl.ac.uk

Background: Thyroid gland metastasis from distant primary tumors is uncommon, with liver cancer being a particularly rare source. This case report describes the clinical challenges and diagnostic journey of a thyroid mass in a patient with chronic hepatitis B, liver cirrhosis, and hepatocellular carcinoma, underscoring the rarity and complexity of such metastatic relationships.

Case Presentation: A 63-year-old male with a long-standing history of hepatitis B-related liver cirrhosis and a recent diagnosis of hepatocellular carcinoma presented with a rapidly enlarging painful right-sided thyroid mass associated with swelling but no systemic symptoms such as fever or dysphonia. This prompted a thorough diagnostic workup. Enhanced neck scans indicated a mass potentially originating from the thyroid with tracheal compression, yet crucially, there was no evidence of lung involvement based on the chest CT. Despite the rarity of liver-to-thyroid metastasis, the patient's multifaceted medical history warranted a broad differential diagnosis.

Intervention and Outcome: Surgical intervention included a right-sided thyroidectomy and partial left thyroidectomy under general anesthesia. Histopathological examination unexpectedly confirmed the presence of metastatic thyroid cancer originating from the primary liver tumor. This led to further extensive surgical management, including lymph node dissection in the central neck area. The postoperative regimen was adapted to include thyroid hormone replacement and ongoing treatment for hepatocellular carcinoma. The patient's postoperative recovery was closely monitored, reflecting stable disease with no immediate complications.

Conclusion: This case highlights the clinical rarity and diagnostic challenges of liver cancer metastasizing to the thyroid. It emphasizes the need for vigilance in patients with known primary malignancies, especially hepatocellular carcinoma, presenting with new thyroid abnormalities. This advocates for a comprehensive diagnostic approach in such atypical presentations.

Keywords: hepatocellular carcinoma, thyroid metastasis, liver cancer, metastatic cancer, case report

Introduction

Hepatocellular carcinoma (HCC) is one of the most prevalent and lethal malignancies worldwide, particularly in regions with high incidences of hepatitis B and C infections.[1,2] Chronic liver diseases, such as hepatitis and cirrhosis, are well-established precursors to the development of HCC, underscoring the link between viral liver pathology and oncogenesis.[3,4] As the fifth most common cancer globally and the third leading cause of cancer-related deaths, HCC presents significant challenges in both diagnosis and management.[5,6]

The metastatic behavior of HCC is predominantly characterized by its spread to the lungs, bones, adrenal glands, and, less frequently, the brain.[7,8] Such dissemination patterns are driven by the vascular nature of the liver and the venous drainage systems that directly connect to these organs.[9] However, metastasis to the thyroid gland remains exceedingly rare, with few documented cases in medical literature. This rarity poses unique clinical challenges and often leads to a delayed or complicated diagnostic process because it deviates from the typical clinical expectations and presentations seen in HCC metastases.

The presence of HCC metastasis in the thyroid gland is not only a diagnostic anomaly but also an indicator of advanced and aggressive disease. This underscores the importance of a thorough approach in the clinical assessment of

Received: 19 July 2024
Accepted: 26 October 2024
Published: 14 November 2024

thyroid masses in patients with known primary liver cancer, particularly those with a background of chronic viral hepatitis and cirrhosis. This case report aims to shed light on such a rare occurrence, discussing both the diagnostic journey, and thereby contributing to the sparse literature on atypical metastatic presentations of HCC.

Case Presentation

A 63-year-old male patient with a notable medical history of chronic hepatitis B and liver cirrhosis presented with an enlarging, painful, and firm mass on the right side of his thyroid. This mass had been noticed on April 6, 2021, two weeks prior to presentation, and had rapidly grown to a significant size. His medical history included multiple interventions for hepatocellular carcinoma (HCC), including targeted therapy with sorafenib, which was modified due to progressive disease noted on follow-up imaging.

The patient has a history of chronic hepatitis B and liver cirrhosis for over 30 years, treated with entecavir 1 tablet daily. In July 2020, the patient was diagnosed with liver malignancy and underwent hepatic arterial chemoembolization in August and November 2020 at Shanghai Eastern Hepatobiliary Surgery Hospital (Figure 1). Further hepatic arterial chemoembolization was performed in February and August 2021 at Ningbo Lihuili Hospital. In November 2021, the patient received immune therapy with 200 mg intravenous toripalimab at Ningbo Second Hospital, which he tolerated without significant adverse reactions. Concurrently, he was on targeted therapy with lenvatinib and continued antiviral treatment with entecavir.

The patient denies a history of hypertension, diabetes, or significant cardiovascular, cerebrovascular, pulmonary, or renal diseases. He has no known drug or food allergies but experiences seasonal pollen allergies. There is no known family history of thyroid disease or hepatocellular carcinoma, nor any reported genetic disorders, psychiatric illnesses, or similar conditions within three generations.

The patient worked as a farmer. He is a former smoker, having smoked for over 20 years before quitting one year ago, and he consumes alcohol occasionally. The patient lives with his spouse and has two adult daughters who visit regularly and provide emotional support. He reports significant anxiety and concern regarding the impact of his cancer diagnosis on his quality of life and daily activities.

Computed tomography (CT) scanning of the neck region in April 2021 revealed a considerable nodule in the right thyroid lobe, raising concerns of a neoplastic origin (Figure 2). Importantly, CT scans confirmed the absence of lung involvement, which is typically expected in metastatic cases of HCC (Figure 3), thus indicating a rare pattern of metastatic disease progression. Conversely, ultrasound examinations in April 2021 depicted a nodule in the right thyroid

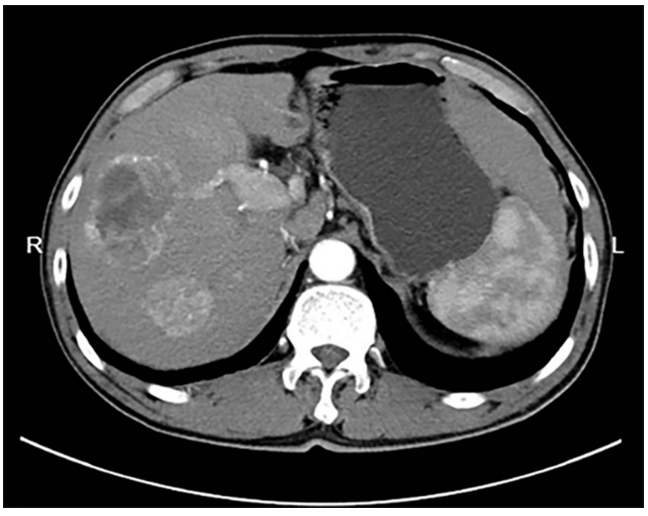

Figure 1 Abdominal CT Scan Showing Hepatocellular Carcinoma. This contrast-enhanced computed tomography (CT) scan of the abdomen demonstrates multiple hypervascular lesions characteristic of hepatocellular carcinoma (HCC) within the liver. The largest lesion is seen occupying the right lobe with significant mass effect and heterogeneous enhancement. The scan provides a clear visualization of the tumor burden and its anatomical relationship with surrounding hepatic structures.

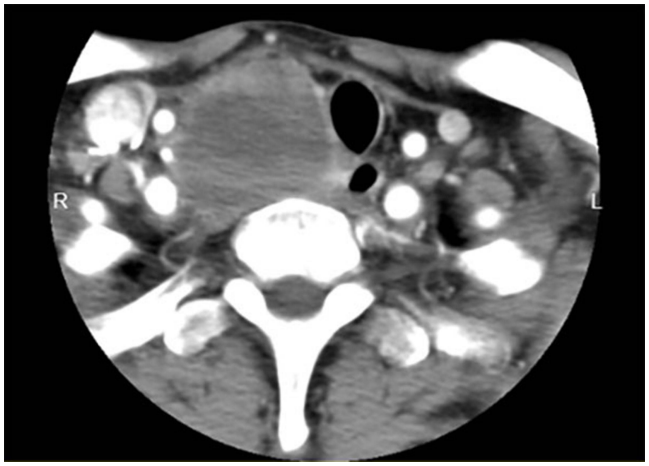

Figure 2 Neck CT Scan Showing Thyroid and Surrounding Structures. This axial slice from a contrast-enhanced computed tomography (CT) scan of the neck displays the thyroid gland with a notable mass in the right lobe. The mass appears as a well-defined area with increased density compared to the surrounding thyroid tissue, suggesting the presence of a neoplastic lesion. No significant or invasion into adjacent structures is visible.

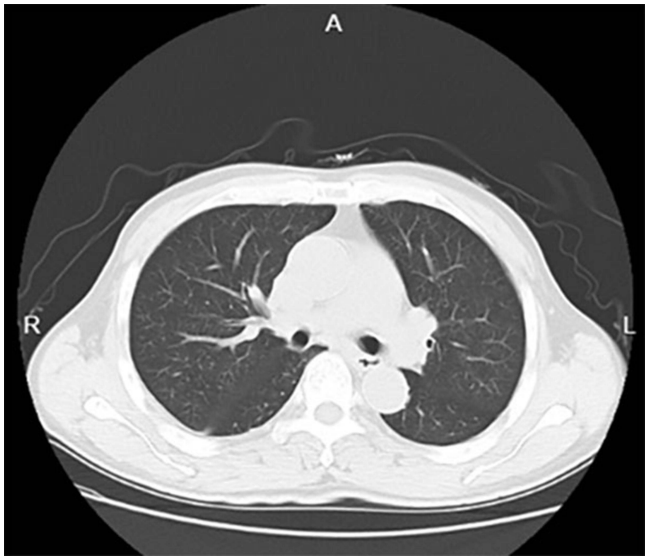

Figure 3 Chest CT Scan Demonstrating Clear Lungs. This axial computed tomography (CT) scan of the chest shows clear lung fields without evidence of nodules, masses, or metastatic disease.

lobe that, despite its size, exhibited characteristics more typical of a benign lesion, such as well-defined margins and uniform echotexture (Figure 4).

Immunohistochemistry (IHC) was pivotal in confirming the origin of the thyroid nodule, demonstrating that the cellular composition was consistent with metastatic HCC rather than primary thyroid cancer or another form of metastatic disease (Figure 5). The absence of thyroid-specific markers, TTF-1 and Tg, which are generally present in thyroid-origin tumors, played a crucial role in ruling out primary thyroid malignancies. Furthermore, the tumor cells exhibited specific liver markers such as HepPar-1(+) and Arginase-1(+), confirming the liver as the primary source. Additional IHC findings included Ki-67 at 10%, indicating moderate proliferative activity, which suggests a significant, but not extreme, rate of tumor growth.

Before surgical intervention, the patient underwent a comprehensive evaluation of thyroid function. These results indicated that the thyroid function was within normal limits at the time of testing, suggesting that the thyroid gland's functional capacity was maintained despite the presence of a significant neoplastic mass (Table 1).

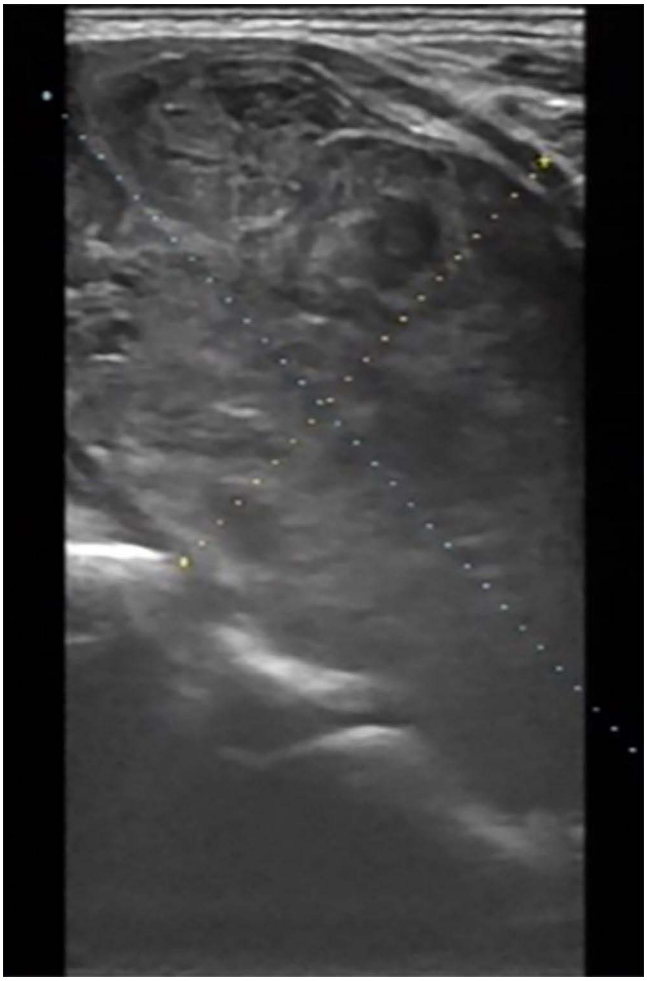

Figure 4 Ultrasound Imaging of the Thyroid Gland. This ultrasound image provides a detailed view of the thyroid gland, highlighting a significant mass in the right lobe. The mass measures approximately 65.7 mm x 38.2 mm. Despite its size, the mass displays well-defined margins and a uniform echotexture, characteristics typically indicative of a benign lesion, rather than a neoplastic origin.

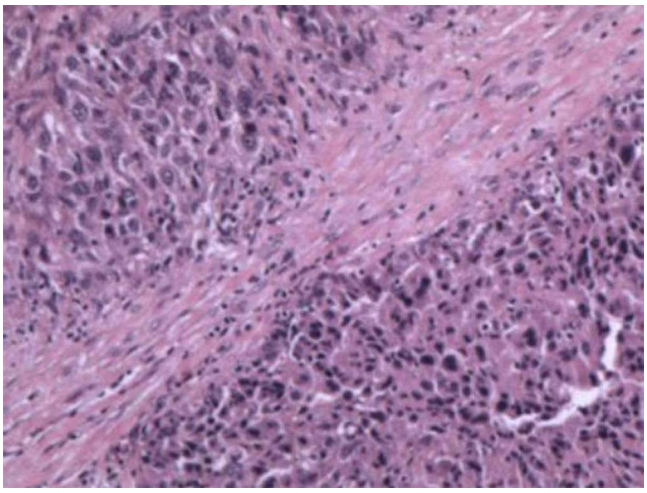

Figure 5 Histopathological Examination of Thyroid Mass. This histopathology slide, stained with hematoxylin and eosin (H&E), shows a high-power microscopic view of the thyroid tissue obtained from the patient. The image demonstrates a dense infiltration of atypical cells with hyperchromatic nuclei and prominent nucleoli, typical features of neoplastic tissue. The irregular arrangement and increased cellular density suggest aggressive tumor behavior, consistent with the histological characteristics of hepatocellular carcinoma metastasis in the thyroid gland. Immunohistochemical staining results further validate the diagnosis: TTF-1(-), Tg(-), Ki-67(10%), HepPar-1(+), Arginase-1(+).

Table 1 Thyroid Hormone Levels

Hormone	Normal Range	Result
Total Triiodothyronine (T3)	1.2–3.1 nmol/L	1.63 nmol/L
Total Thyroxine (T4)	66–181 nmol/L	142.1 nmol/L
Free Triiodothyronine (FT3)	3.1–6.8 pmol/L	4.13 pmol/L
Free Thyroxine (FT4)	12.0–22.0 pmol/L	14.0 pmol/L
Thyroid Stimulating Hormone (TSH)	0.27–4.2 mIU/L	2.65 mIU/L

Notes: This table presents the thyroid hormone levels for the patient, indicating all values are within the normal range. The measurements include Total Triiodothyronine (T3), Total Thyroxine (T4), Free Triiodothyronine (FT3), Free Thyroxine (FT4), and Thyroid Stimulating Hormone (TSH).

Due to the aggressive nature of the detected metastasis and the patient's complex medical history, several therapeutic interventions were necessary. The initial treatment for HCC involved hepatic arterial chemoembolization and targeted therapy with lenvatinib, alongside ongoing antiviral treatment with entecavir. Despite these measures, the disease progressed, leading to the discovery of the thyroid mass.

Given the significant size and symptoms of the thyroid mass, surgical intervention was warranted. In April 2021, the patient underwent a right-sided thyroidectomy and partial left thyroidectomy, followed by lymph node dissection in the central neck area. Postoperatively, the patient was started on levothyroxine 75 mcg daily to manage hypothyroidism resulting from the thyroidectomy. The dosage was later adjusted to 100 mcg daily based on follow-up thyroid function tests indicating suboptimal hormone levels.

Following the surgical intervention, immune therapy with 200 mg intravenous toripalimab was added to the treatment regimen to address the progressive disease. This combination aimed to manage the metastatic cancer more effectively.

The patient experienced no adverse reactions post-thyroidectomy, including hypocalcemia, electrolyte imbalance, hoarseness, or incision infection. Regular monitoring showed no significant adverse effects from adjusted systemic therapy with lenvatinib.

The patient expressed initial fear and anxiety about the cancer diagnosis and the need for multiple surgeries. Post-treatment, he reported relief from the discomfort caused by the thyroid mass and an improved ability to breathe and swallow. He appreciated the thorough follow-up care and felt reassured by the regular monitoring and clear communication from the healthcare team. Despite the ongoing challenges of managing a complex medical condition, the patient felt hopeful due to the multidisciplinary approach to his treatment. He described a sense of gratitude towards the medical staff and highlighted the importance of emotional support from family and friends during his treatment journey.

Discussion

This case report presents a rare instance of thyroid metastasis originating from primary hepatocellular carcinoma (HCC) in a 63-year-old male with a background of chronic hepatitis B and liver cirrhosis. The unusual occurrence of liver cancer metastasizing to the thyroid provides significant insight into the complex interplay of oncological pathology and challenges conventional understanding of cancer dissemination.

Metastasis to the thyroid from non-thyroidal primary tumors is exceedingly rare, with the thyroid gland being an infrequent site for distant metastases. This is despite the gland's extensive blood supply, which theoretically should increase its susceptibility to metastatic deposits.[10–12] Liver cancer, particularly hepatocellular carcinoma, metastasizing to the thyroid is an exceptional event, documented in only a handful of case reports worldwide.[13] This rarity can be partly attributed to the unique physiological and biochemical environment of the thyroid gland. It is hypothesized that the high iodine content and rapid iodine turnover in the thyroid may create a hostile environment for the survival and proliferation of metastatic cancer cells.[14,15] Additionally, the organ's intrinsic ability to secrete thyroid hormones, which have systemic metabolic effects, might also play a role in inhibiting tumor growth or establishment.[16–18]

In the case discussed, notably, there was no evidence of lung involvement, a common metastatic site for liver cancer, at the time of the thyroid cancer diagnosis. Typically, liver cancer would be expected to metastasize to adjacent organs such as the lungs before reaching the thyroid,[19,20] making this case particularly rare where the cancer seems to have "jumped" directly to the thyroid, bypassing the lungs entirely.

The diagnosis of thyroid metastasis in the context of known primary malignancies like HCC requires a high degree of clinical suspicion.[21,22] In patients with a history of liver cancer, the sudden appearance or rapid growth of a thyroid mass must prompt an investigation into potential metastatic disease. This case required an integrated diagnostic approach, utilizing both enhanced imaging techniques and confirmatory histopathological analysis post-surgery. The presentation of thyroid metastasis can mimic benign thyroid nodules or primary thyroid cancers, making it critical to differentiate these conditions through careful pathological examination.

Given the rarity of such cases, there are no established guidelines for the treatment of thyroid metastasis from liver cancer. The primary goal is often palliative, focusing on symptom relief and maintaining quality of life. In this patient, the decision to proceed with thyroidectomy was driven by the need to alleviate compressive symptoms and prevent potential airway obstruction, underscoring the personalized nature of treatment in such rare occurrences.[23,24] The role of surgery in managing thyroid metastases remains debated, largely due to the varied prognosis and the often advanced stage of primary disease at diagnosis.

The prognosis for patients with thyroid metastasis from hepatocellular carcinoma is generally considered poor, reflecting the aggressive nature of the primary tumor and its propensity for widespread dissemination.[25] Early detection and tailored management strategies are critical for potentially improving outcomes,[26] although the overall impact may be limited by the advanced stage of the underlying hepatocellular carcinoma.

Conclusion

This exceptional case of thyroid metastasis from primary hepatocellular carcinoma significantly broadens our current medical perspective and underscores the necessity for ongoing investigations into the dynamics of cancer metastasis. It highlights the critical need to suspect a metastatic origin for new thyroid masses in patients with a history of significant malignancies, especially those involving hepatocellular carcinoma.

Ethics Approval and Consent to Participate

The study, including the publication of case details and any accompanying images, received approval from the ethics committee of Yuyao Hospital of Traditional Chinese Medicine.

Written informed consent was obtained from the participant.

Consent for Publication

All authors and the patient have agreed to publish, including the accompanying images.

Disclosure

The authors declare that they have no conflicts of interest.

References

1. Kumar V, Shukla SK. Identification and characterization of molecular targets in hepatocellular carcinoma. *Front Mol Biosci*. 2023;10: 1202614.
2. Jain D, Janmeda P. Exposure, formation, and various available treatments to combat hepatocellular carcinoma: a comprehensive review. *Appl Biol Chem J*. 2023;4:69–83. doi:10.52679/tabcj.2023.0007
3. Syyam A, Akbar HR, Jilkova ZM, Afzal S. Role of genetic and epigenetic modifications in the progression of hepatocellular carcinoma in chronic HCV patients. *Livers*. 2023;3(1):82–92. doi:10.3390/livers3010008
4. Stella L, Santopaolo F, Gasbarrini A, Pompili M, Ponziani FR. Viral hepatitis and hepatocellular carcinoma: from molecular pathways to the role of clinical surveillance and antiviral treatment. *World J Gastroenterol*. 2022;28(21):2251. doi:10.3748/wjg.v28.i21.2251
5. Parra NS, Ross HM, Khan A, et al. Advancements in the diagnosis of hepatocellular carcinoma. *Int J Transl Med*. 2023;3(1):51–65. doi:10.3390/ijtm3010005
6. McMahon B, et al. Opportunities to address gaps in early detection and improve outcomes of liver cancer. *JNCI Cancer Spectrum*. 2023;7:kad034.

7. Han S, Xue L, Wei Y, et al. Bone Lesion-Derived Extracellular Vesicles Fuel Prometastatic Cascades in Hepatocellular Carcinoma by Transferring ALKBH5-Targeting miR-3190-5p. *Adv Sci*. 2023;10(17):2207080. doi:10.1002/advs.202207080
8. Shao G, Zhi Y, Fan Z, Qiu W, Lv G. Development and validation of a diagnostic and prognostic model for lung metastasis of hepatocellular carcinoma: a study based on the SEER database. *Front Med*. 2023;10. doi:10.3389/fmed.2023.1171023
9. Mielgo A, Schmid MC. Liver tropism in cancer: the hepatic metastatic niche. *Cold Spring Harbor Perspect Med*. 2020;10(3):a037259. doi:10.1101/cshperspect.a037259
10. Hussain SMA, Cole S, Hussain I. Colorectal cancer metastases in thyroid: case report and literature review. *Thyroid Res*. 2023;16(8). doi:10.1186/s13044-023-00150-y
11. Saini T, et al. Fine needle aspiration cytology of metastatic tumours to the thyroid. *Cytopathology*. 2023;34:239–249. doi:10.1111/cyt.13220
12. Balta H, Kocaman N, Ucer O. A rare but very serious disease: tumors metastasizing to the thyroid in the light of cases. *Tissue Cell*. 2022;79:101958. doi:10.1016/j.tice.2022.101958
13. Zhong H-C, et al. Metastasis of liver cancer to the thyroid after surgery: a case report. *World Journal of Clinical Cases*. 2022;10(15):5036–5041. doi:10.12998/wjcc.v10.i15.5036
14. Cazarin J, Dupuy C, Pires de Carvalho D. Redox Homeostasis in Thyroid Cancer: implications in Na+/I− Symporter (NIS) Regulation. *Int J Mol Sci*. 2022;23(11):6129. doi:10.3390/ijms23116129
15. Tkachenko R, Kuryk O, Golovko A, Rudnytska O, DISTANT METASTASIS TO THE THYROID GLAND: CLINICAL REVIEW. *Clin Preventive Med*. 2020;4:105–113. doi:10.31612/2616-4868.4(14).2020.10
16. Aranda A, Martínez-Iglesias O, Ruiz-Llorente L, García-Carpizo V, Zambrano A. Thyroid receptor: roles in cancer. *Trends Endocrinol Metab*. 2009;20(7):318–324. doi:10.1016/j.tem.2009.03.011
17. Lin HY, et al. Thyroid hormone, cancer, and apoptosis. *Compr Physiol*. 2011;6:1221–1237.
18. Vonderhaar BK. Effect of thyroid hormones on mammary tumor induction and growth. *Hormonal Regulation Mammary Tumors*. 1982;1982:138–154.
19. Ostrovsky V, Bar-Zakai B, Miller R, et al. Single liver metastasis of a follicular variant of papillary thyroid carcinoma: a rare pattern of organ spread. *Endocrinol Diabetes Metab Case Rep*. 2020;2020. doi:10.1530/EDM-20-0074
20. Ozaki K, Higuchi S, Kimura H, Gabata T. Liver metastases: correlation between imaging features and pathomolecular environments. *Radiographics*. 2022;42(7):1994–2013. doi:10.1148/rg.220056
21. Park JY, Yi SY, Kwon T, et al. Sonographic diagnosis of thyroid metastasis from hepatocellular carcinoma. *Clin Ultrasound*. 2019;47(1):44–46. doi:10.1002/jcu.22652
22. Stergianos S, Juhlin CC, Zedenius J, Calissendorff J, Falhammar H. Metastasis to the thyroid gland: characterization and survival of an institutional series spanning 28 years. *Eur J Surg Oncol*. 2021;47(6):1364–1369. doi:10.1016/j.ejso.2021.02.018
23. Nervo A, Ragni A, Retta F, et al. Interventional radiology approaches for liver metastases from thyroid cancer: a case series and overview of the literature. *J Gastrointestinal Cancer*. 2021;52(3):823–832. doi:10.1007/s12029-021-00646-6
24. Kim YH, Kim H-C, Lee YB, et al. Transarterial Radioembolization as an Effective Local Treatment Modality for Liver Metastasis of Thyroid Cancer. *Endocrinol Metab*. 2022;37(2):383. doi:10.3803/EnM.2022.1437
25. Liang HH, Wu C-H, Tam K-W, et al. Thyroid metastasis in a patient with hepatocellular carcinoma: case report and review of literature. *World J Surg Oncol*. 2007;5(1):1–4. doi:10.1186/1477-7819-5-144
26. Farina E, Monari F, Tallini G, et al. Unusual thyroid carcinoma metastases: a case series and literature review. *Endocrine Pathol*. 2016;27(1):55–64. doi:10.1007/s12022-015-9410-7