Clinical Case Report

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Contrast-enhanced ultrasound diagnosis of hepatic metastasis of concurrent medullary-papillary thyroid carcinoma

A case report

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Abstract

Rationale: Co-occurrence of medullary thyroid carcinoma (MTC) and papillary thyroid carcinoma (PTC) in the same thyroid gland with liver metastasis is a rare condition. To our knowledge, the utility of contrast-enhanced ultrasound (CEUS) to diagnose it is much less.

Patient concerns: A 33-year-old female was referred to our hospital due to the increase in plasma calcitonin concentration and carcino-embryonic antigen 12 months after her total thyroidectomy. To find metastasis, she received laboratory tests, gray-scale US, and CEUS. In our paper, ethical approval was not necessary, as this article is a case report, which is based on the clinical information of the patient. Because our case does not refer to the patient's privacy, informed consent is not necessary.

Diagnoses: Gray-scale abdominal ultrasound image demonstrated a mildly hyperechoic nodule in the liver. In CEUS, the nodules were hyperenhanced in the arterial phase. In the late arterial phase, the enhancement was washed out quickly. The nodules presented hypoenhancement in the portal and parenchymal phase, which conformed to the hepatic metastasis.

Interventions: The patient received thyroid and liver surgery.

Outcomes: She was free of disease for 10 months at the time of this report.

Lessons: In this case, liver metastases from MTC can be detected and characterized reliably as hypoenhancing lesions during the portal venous and late phases of CEUS, washing out starts early, and is marked. We suspect MTC is a kind of tumor that tends to have rich blood supply and consider contrast-enhanced ultrasound as a suitable method for the follow-up of patients with MTC.

Abbreviations: CEA = carcino-embryonic antigen, CEUS = contrast-enhanced ultrasound, CT = calcitonin, FNAC = fine-needle aspiration cytology, MTC = medullary thyroid carcinoma, PTC = papillary thyroid carcinoma.

Keywords: contrast-enhanced ultrasound, liver metastasis, medullary thyroid carcinoma, papillary thyroid carcinoma

1. Introduction

The incidence of distant metastases in medullary thyroid carcinoma is high, mainly to the lung and liver. Local neck lymph node metastasis of papillary thyroid carcinoma (PTC) occurs early. Co-occurrence of medullary thyroid carcinoma (MTC) and PTC in the same thyroid gland with hepatic metastatic is rare, which caused a major limitation of the present study with the small number of patients. Herein, we report a case of coexistence of medullary-papillary thyroid carcinoma with hepatic metastasis.

2. Case report

A 33-year-old female's thyroid nodules and cervical lymphadenopathy were found incidentally during a physical examination. Gray-scale ultrasound image demonstrated 2 solitary nodules in the bilateral thyroid lobes (Fig. 1). And her cervical lymphadenopathy was found too.

Ultrasonography-guided fine-needle aspiration cytology (FNAC) showed medullary carcinoma metastases in the right cervical lymph nodes. Hence, a total thyroidectomy and cervical lymph nodes dissection was performed and revealed a nodule in the right lobe of thyroid (nodule 1, measured 0.7 cm in diameter), and a smaller nodule (nodule 2, measured 0.3 cm in diameter) in the left lobe. Pathologically, the nodule 1 was diagnosed as MTC and that in the left lobe as PTC. Operation was followed by 131I treatment. By the way, no family members had MTC, PTC, or multiple endocrine neoplasms, and Ret mutation analyses have not been performed in the patient or any family members.

Preoperative serum studies revealed calcitonin (CT) was 585.5 pg/mL and carcino-embryonic antigen (CEA) was 16.44 ng/mL. After the operation, the CT and CEA level merely decreased

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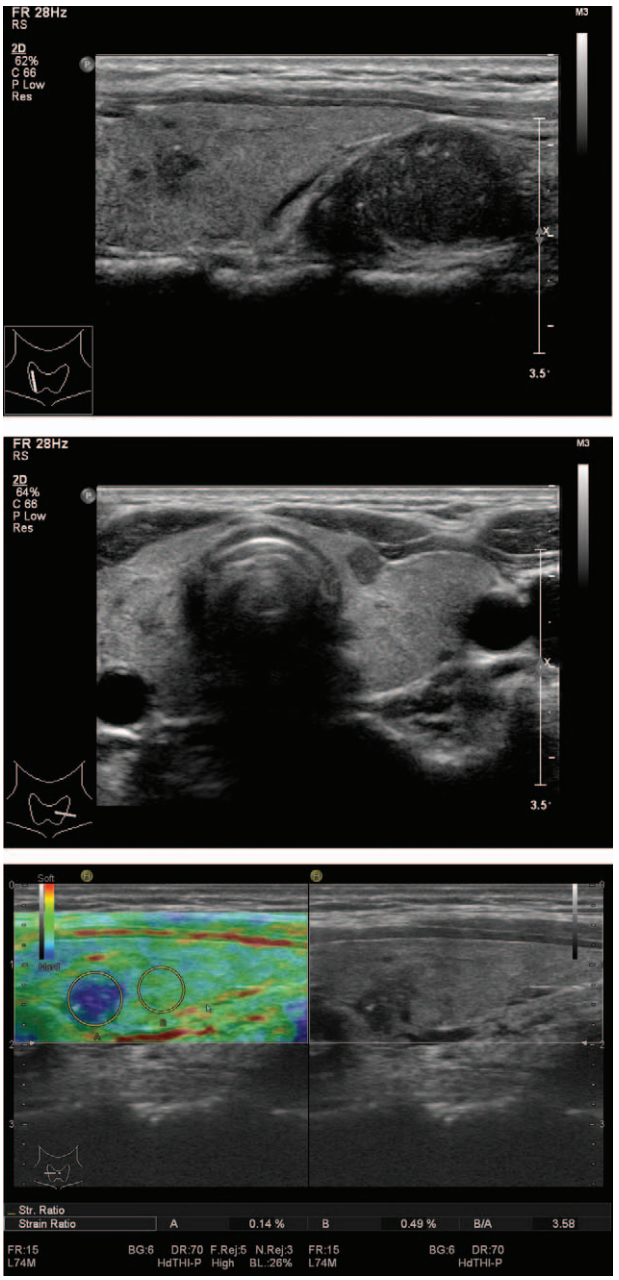

Figure 1. Gray-scale ultrasound image findings: 2 nodules at the bilateral thyroid lobes. A, It was an $8 \times 6 \times 8$ mm size hypoechoic nodule with an irregular shape in the middle lobe of right thyroid. B, This showed other nodules were about $4 \times 3 \times 4$ mm in size, which was hypoechoic, with an mildly irregular shape, a clear margin. C, Figure was an elasticity imaging, which showed the different strain ratios of nodule in the right lobe when compared with normal thyroid parenchyma nearby. The strain ratio of the nodule and the parenchyma was 0.14% and 0.49% respectively, the B/A was 3.58.

slightly to 375.0 pg/mL and 11.0 ng/mL respectively. However increased CT (441.2 pg/mL) and CEA (8.41 ng/mL) have occurred since her hepatectomy.

In view of her persistently high level of serum CT and CEA, in admission, the patient's doctor suggested contrast-enhanced ultrasound (CEUS) examination with patient's consent. First, the gray-scale abdominal ultrasound image demonstrated a mildly hyperechoic nodule at the junction of posterior and anterior segments of the right liver lobe. The nodule was about 1.4×1.3 cm in size with a relatively clear margin and regular shape (Fig. 2A).

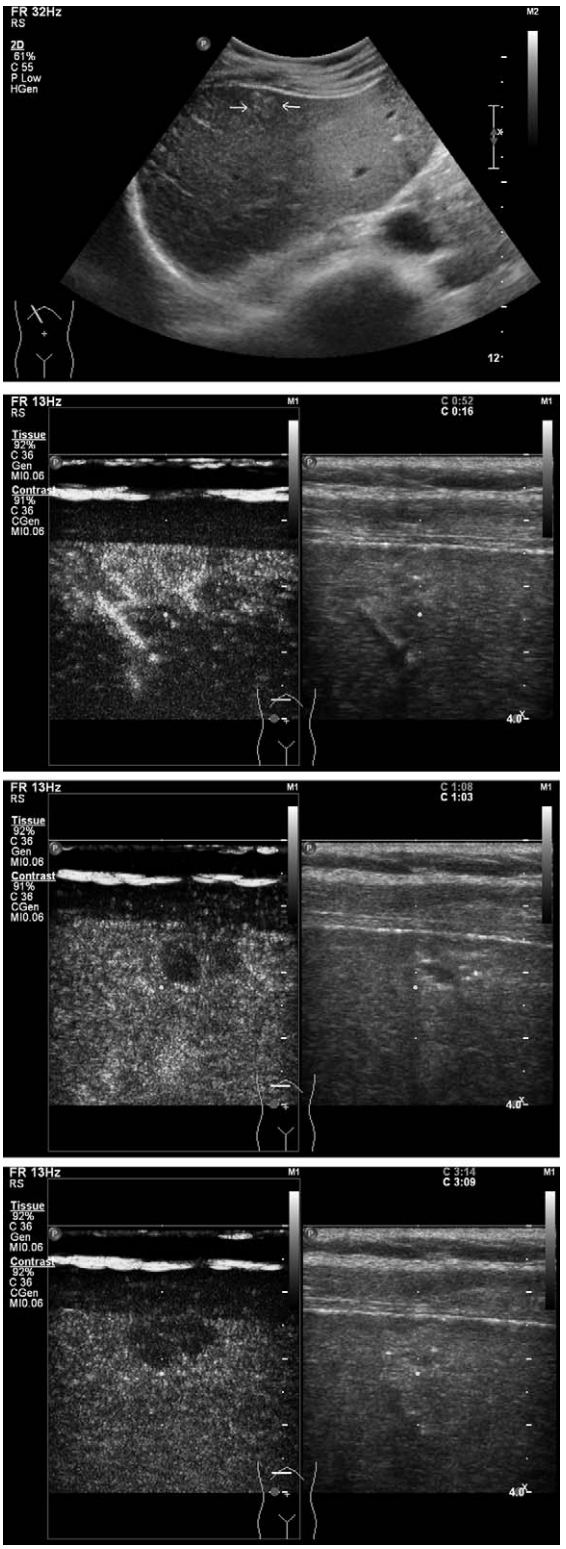

Figure 2. A, This showed a mildly hyperechoic nodule at the junction of posterior and anterior segments of right liver lobe. The nodule was about 1.4×1.3 cm in size with a relatively clear margin and regular shape. The inside echo was net-like and with a few hyperechoic foci without acoustic shadowing. B, This exhibited in the arterial phase, the nodules were hyperenhanced. The nodules presented hypoenhancement in the portal (C) and parenchymal (D) phase.

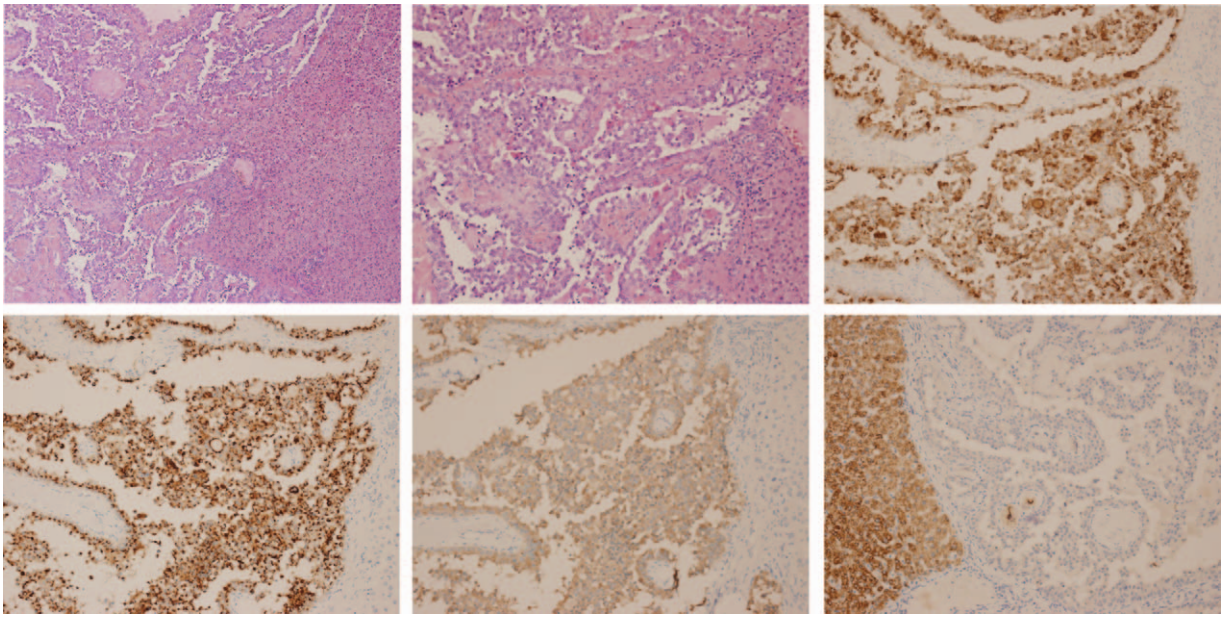

Figure 3. A and B, This showed numbers of medium-size tumor cells were arranged in plates, palisade, and cord-like structure in microscopically. Within neoplasmic stromal, angiopoiesis was present. C–F, This showed immunophenotyping findings: (C) showed calcitonin was positive, (D) showed CgA was positive, (E) showed Syn was positive, (F) showed negative for HCC. CgA = chromogranin A; HCC = hepatocellular carcinoma; Syn = synaptophysin.

For further CEUS examination, a 1.2 mL contrast agent (SonoVue) suspension was injected through the right cubital vein, then 5 mL saline flushing. An iU22 ultrasound system (Royal Philips, Amsterdam, The Netherlands) equipped with a C5-1 (1–5 MHz) and C9-3 (3–9 MHz) transducer was used for examination. The mechanical index setting was 0.06 for CEUS. Compared with normal liver parenchyma, in the arterial phase, the nodules were hyperenhanced (Fig. 2B), in the late arterial phase, the enhancement washed out quickly. The nodules presented hypoenhancement in the portal (Fig. 2C) and parenchymal (Fig. 2D) phase. As a result, referring to the patient history, a diagnosis of metastasis of thyroid carcinoma was made after CEUS.

Soon afterward, the patient underwent laparoscopic resection of the liver mass. Paraffin sections of the liver tissues were stained with hematoxylin and eosin and Congo red. Microscopically, liver tissue can be seen, numbers of medium-size tumor cells were arranged in trabecular, cord-like. Relative uniform medium-size epithelioid neoplasm cell had abundant cytoplasm and round nuclei. Amyloid was easy to be found and necrosis was absent (Fig. 3A and B). Immunohistochemistry results showed all of the tumor cells expressed synaptophysin, chromogranin A, CEA, Calcitonin, erythroleukemia TF-1 cells, Pan Cytokeratin, and one monoclonal antibody (<1%). The tumor cells were negative for Hepatocellular carcinoma, thyroidglobulin (Fig. 3C–F). Therefore, the patient was diagnosed with hepatic metastasis of thyroid medullary carcinoma rather than papillary carcinoma. She was free of disease for 10 months with low CT and CEA level at the time of this report.

3. Result and discussion

Medullary thyroid carcinoma (MTC) is a rare, neuroendocrine malignancy, developing in C cells that produce CT, which accounts for 5% to 8% of all thyroid malignancies.[1,2] Seventy percent of patients suspected of MTC have neck lymph nodes metastases and 10% distant metastases when physical palpation discovered thyroid neoplasms.[3] PTC is a distinctly different type of thyroid carcinoma from MTC, with totally different types of cellular origin. PTC is the most common thyroid carcinoma, accounting for approximately 75% to 80% of thyroid malignancies.[4] Co-occurrence of MTC and PTC in the same thyroid gland with hepatic metastasis is rare, which caused a major limitation of the present study with the small number of patients.

All pathological types of thyroid carcinoma can transfer to liver through blood vessels. Hepatic metastases usually happen to MTC, but it is not uncommon to PTC. One out of 3 of medullary thyroid cancer cases shows lymph node metastases at the time of diagnosis, approximately 10% to 15% in distant metastases and 25% develop metastases during the course of the disease.[5] Distant metastases from MTC occur initially in about 14% of patients.[6]

It is not rare that after years of excision of primary MTC lesions, distant metastases appear. Marieke reported a female who was diagnosed with MTC at the age of 22, metastases were found in her liver and iliac bone in her 50 seconds.[5] Nikolaou et al[7] reported a patient who had been diagnosed with thyroid carcinoma 19 years before she had liver metastatic disease. The prognosis is usually poor when distant metastases appeared.

Given that distant metastases are mostly carrying a negative impact on disease prognosis, a long-term routine follow-up for MTC patients is suggested. The continuous follow-up of MTC patients requires an easily available, safe, reliable, and cost-effective diagnostic method. Data regarding using CEUS to diagnose progressive liver metastases in the rare patients with MTC are scarce and limited to case reports.

Sonography is a widely used method for detecting liver metastases. Generally, unenhanced US may be of limited value for identifying metastases, CEUS increased significantly the number of liver lesions detected than unenhanced sonography. Accuracy of detection of metastatic disease of CEUS (81.4%) was similar to that of triple-phase spiral CT (89.2%),[8] suggesting that we consider whether the CEUS is a suitable method for the follow-up of patients with MTC.

Sonographic features of hepatic metastases are various, but mostly are similar to its primary lesions and are dependent on blood supply. Liver metastases can be detected and characterized reliably as hypoenhancing lesions during the portal venous and late phases, with very few exceptions. Wash-out starts early, usually in the portal venous phase, and is marked.[9] In this case, the nodules were hyperenhanced in the arterial phase, and in the late arterial phase, the enhancement washed out quickly. The nodules presented hypoenhancement in the portal and parenchymal phase. After CEUS, the features of 3 phases conform to the hepatic metastasis. Esik et al[10] mentioned that MTC belongs to the group of neuroendocrine tumors, the natural history of neuroendocrine tumors includes a pronounced early lymphatic spreading and hepatic dissemination of typical hypervascular lesion. In pathology, MTC histological slices show more or less angiogenesis. Lai et al[11] reported that hypervascularity is more frequent in MTC when compared with PTC. In this case within the neoplasmic stromal, angiopoiesis was present. As a result, we suspect MTC is a kind of tumor that tends to have rich blood supply.

Synchronous occurrence of MTC and PTC in the same thyroid gland is a rare condition. MTC and PTC have 2 types of prevalence, clinical manifestation, laboratory tests, histopathological appearance, and therapeutic measures. Machens and Dralle[12] reported the incidence of papillary carcinoma in thyroids with medullary carcinoma to be 3.6%. When distant metastases appeared, it is significant to make an accurate diagnosis during treatment planning.

In summary, hepatic metastatic from medullary thyroid carcinoma is a rare condition; although a major limitation of the present study is the small number of patients involved, our case is important as it is the first to highlight the utility of contrast-enhanced ultrasound for diagnosing and follow-up in patients with thyroid carcinoma.

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