—Case Reports—

Use of Ultrasonographic Shear Wave Measurements to Diagnose Thyroid Metastasis from Breast Carcinoma

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A metastatic thyroid tumor (MTT) arising from breast carcinoma (BC) is rare and sometimes difficult to diagnose. We present a case of MTT from BC; we suspected anaplastic thyroid carcinoma at initial presentation. The patient was a 58-year-old female with a hard nodule in the right anterior neck and a history of breast cancer. Computed tomography indicated tumors on both thyroid lobes, and ultrasonography (US) with shear wave measurement (SWM) showed malignant features. We performed fine needle aspiration cytology (FNAC), the results of which led us to strongly suspect MTT from BC. The surgically resected specimen was evaluated histopathologically, including by immunohistochemistry (IHC), and the diagnosis was confirmed. In addition to FNAC and IHC, SWM is useful to diagnose MTT from BC. (J Nippon Med Sch 2023; 90: 398–403)

Key words: metastatic thyroid tumor (MTT), breast carcinoma (BC), shear wave measurement (SWM), fine needle aspiration cytology (FNAC), immunohistochemistry (IHC)

Introduction

Metastatic thyroid tumor (MTT) from an extrathyroidal malignancy accounts for only 1-3% of surgically resected thyroid malignancies[1,2]. The most frequent primary lesion is renal cell carcinoma, which accounts for nearly half of all cases, followed by colorectal, lung, and breast carcinoma (BC)[1,2]. Preoperative diagnosis of MTT is usually difficult and the treatment outcomes are generally dismal.

Shear wave measurement (SWM) is a new elastographic modality originally used for evaluating liver disease. However, some reports indicated that SWM could be used to detect thyroid diseases such as chronic thyroiditis[3–6], malignant and benign nodules[7–10] and lymph node (LN) metastasis from thyroid carcinoma[11].

Herein, we present an unusual case of MTT from BC, where anaplastic thyroid carcinoma (ATC) was suspected at the time of initial presentation. Diffuse masses in both lobes of the thyroid, and swelling of the bilateral LNs, were detected by imaging studies, and SWM indicated malignancy. The patient had a history of BC. We performed fine needle aspiration cytology (FNAC) and strongly suspected MTT from BC. Further, the surgically resected specimen was evaluated by histopathological examination, including immunohistochemistry, and the diagnosis was confirmed.

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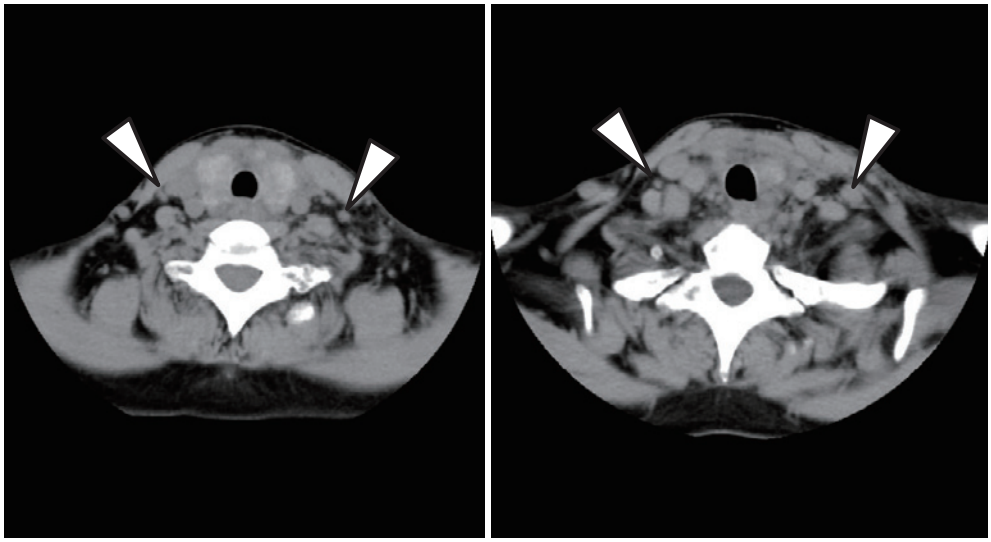

Fig. 1 Computed tomography of the thyroid and lateral neck.
Computed tomography scan of the thyroid and lateral neck revealed a heterogeneous thyroid gland and lateral lymph node swelling (white-headed arrows).

Case Presentation

A 58-year-old Japanese female was referred to our hospital, which specializes in thyroid diseases, with an anterior neck swelling. She had suffered from hoarseness and neck swelling for 3 months. Physical examination revealed a hard nodule in the anterior neck. Computed tomography and ultrasonography (US) revealed diffuse, irregularly shaped tumors on both thyroid lobes and swelling of the bilateral neck LNs (**Fig. 1, 2**). Color Doppler US and elastography indicated hypoechoic, avascular and hard thyroid tumors (**Fig. 2C, D**). SWM also revealed hard heterogeneous masses (**Fig. 2E**). Shear wave velocity (Vs) provides quantitative information on tissue hardness; the net volume of Vs (VsN) is an indicator in quantitative evaluations of the reliability of Vs measurements[12]. In this case, the Vs and VsN were 2.57 m/s and 27.0% for the right lobe, and 2.66 m/s and 27.2% for the left lobe, respectively. The patient had undergone left nipple-sparing mastectomy and sentinel LN resection 13 years ago. The pathological diagnosis was invasive ductal carcinoma (solid type, T2N0M0, stage IIA). The estrogen receptor (ER) was expressed by 90% of the tumor cells, and the progesterone receptor (PR) by 30%, but the cells were human epidermal growth factor receptor 2 (HER2)-negative (score 0). Two years after initial surgery, subcutaneous local recurrence developed and tumor resection was performed. Eight years later, recurrence involving the axillary and supraclavicular LNs was observed. Anti-cancer drugs, Faslodex (an anti-estrogen drug), anastrozole (an aromatase inhibitor), and ethinylestradiol (an ER agonist) were continued. The pathological state of cancer was sufficiently controlled by the drugs and she did not require another surgery. On her visit to our hospital 13 years later, the preoperative diagnosis was thyroid metastasis from BC.

We performed FNAC of both thyroid lobes using a 22-gauge needle under US guidance. We found mutually cohesive, atypical cell clusters with chromatin-rich nuclei, but without intranuclear cytoplasmic inclusions or nuclear grooves. Some atypical cells exhibited intracytoplasmic lumina (ICL) (**Fig. 3**). The cytological interpretation was metastasis of an adenocarcinoma, rather than a poorly differentiated thyroid carcinoma or anaplastic thyroid carcinoma (ATC). Given the history of BC, MTT from BC was strongly suspected.

We planned total thyroidectomy with bilateral neck LN dissection. However, only non-curative resection was possible (such that part of the mass thus remained), because the tumors had replaced the thyroid gland and extended into the anterior cervical muscles and tracheal wall. Pathological examination revealed that the malignant cells had spread widely to adipose tissue, fibrous connective tissue, the perineural region, and skeletal muscle around the thyroid gland. Overall, the morphological appearance of the tumor was compatible with adenocarcinoma (**Fig. 4A, B**). Immunohistochemical analysis revealed that the tumor cells were negative for thyroglobulin (Tg) (**Fig. 4C**), thyroid transcription factor-1 (TTF-1) (**Fig. 4D**) and the ER, but positive for HER2 (**Fig. 4E**) and mammaglobin (focally weak) (**Fig. 4F**). The

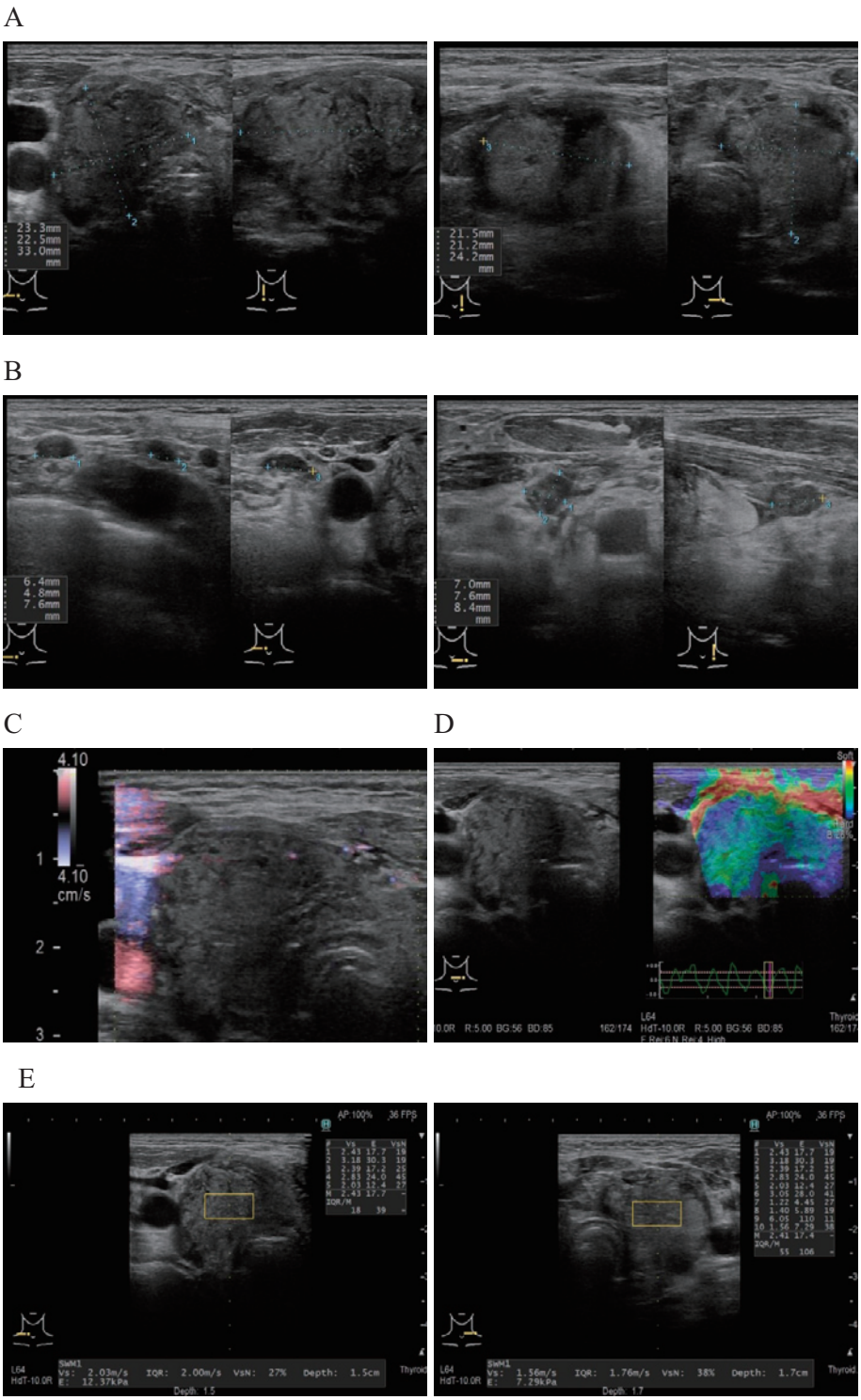

Fig. 2 Ultrasonography of the thyroid.
Ultrasonography revealed irregularly shaped, heterogeneous and hypoechoic lesions on both lobes of the thyroid (A; B mode). Swelling of the bilateral neck lymph nodes was also apparent (B; B mode). Color Doppler ultrasonography (C) and elastography (D) revealed avascular heterogeneous tumors. Shear wave measurements were performed five times on each lobe (E; nos. 1–5: right lobe, nos. 6–10: left lobe). All images were obtained using an Aloka Arietta 850 instrument (Hitachi, Tokyo, Japan) fitted with an L64 linear probe (5–18 MHz).

pathological diagnosis was MTT of mammary adenocarcinoma.

Discussion

MTT is a rare disease that is difficult to diagnose by im-

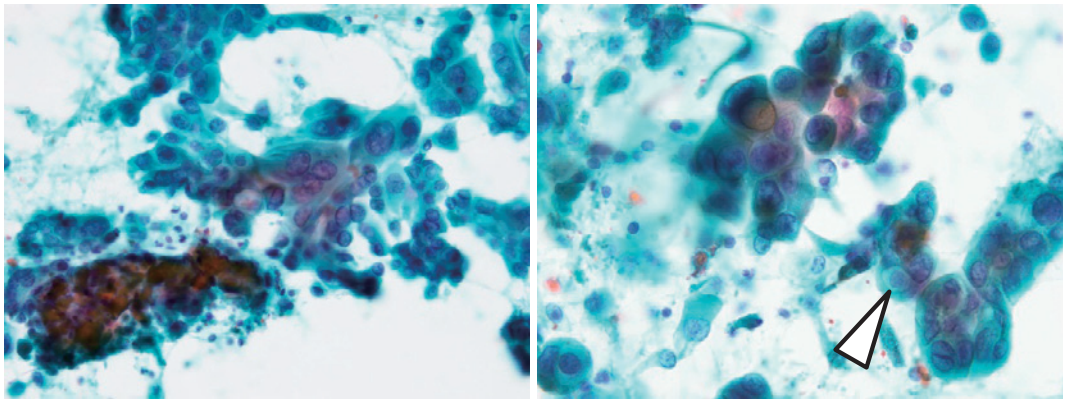

Fig. 3 Fine needle aspiration cytology findings.
The tumor cells were mutually cohesive with intracytoplasmic lumina (ICL). No apparent nuclear grooves or intranuclear cytoplasmic inclusions (typically observed in papillary thyroid carcinomas) were apparent. Intraluminal deposits in the ICL were evident (white arrowhead) (Papanicolaou stain).

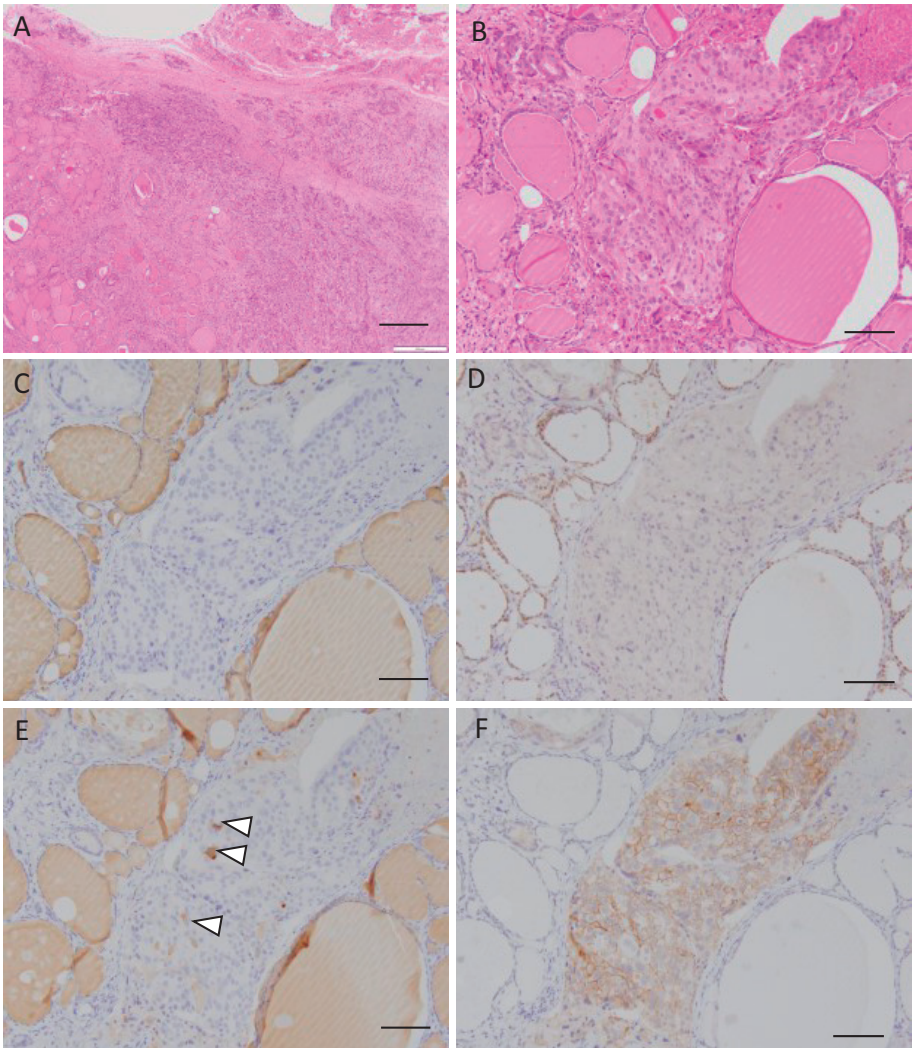

Fig. 4 Pathological examination.
Tumor cells were noted among intact thyroid follicles (hematoxylin-and-eosin stain, A, B). The tumor cells were negative for thyroglobulin (Tg) (C) and thyroid transcription factor-1 (TTF-1) (D), and focally positive for mammaglobin (arrowheads) (E) and human epidermal growth factor receptor 2 (HER2) (F). Bars: 500 μm (A), 100 μm (B–F).

aging studies. Based on US findings, Saito *et al*.[13] diagnosed 29 patients with MTT, including 10 from BC. Based on the US pattern, they classified MTT into two categories: diffuse and nodular types. In the diffuse type, the entire thyroid gland is replaced by a diffuse hypoechoic mass. In the nodular type, uni- or multinodular hypoechoic lesions are seen, along with ill-defined margins. All diffuse tumors (n = 9) were accompanied by subclavian LN metastases; this was the case for only 6 of 18 nodular tumors. It was speculated that diffuse MTTs were lymphogenous metastases, while the most nodular MTTs were hematogenous metastases. Our case appeared to be of the nodular type on US, but the clinical course suggested that it was lymphogenous, while the pathological finding of LN swelling indicated that the tumor was diffuse-type.

SWM can be used to differentially diagnose malignant and benign thyroid nodules[8–11]. In the present case, the Vs values of the tumors in both lobes were high, indicating malignancy. Previously, we reported that the preoperative SWM Vs was significantly higher (cutoff = 1.97 m/s), and the VsN (cutoff = 64.2%) significantly lower, in thyroid carcinomas compared to benign nodules[14]. That report was based on data from primary thyroid carcinomas rather than metastases. However, for malignant tumors, the VS value was high, and the VsN low ("malignant pattern"). In the present case (the VS value was well over 1.97 m/s in both lobes (2.57 and 2.66 m/s, respectively), while and the VsN was below 64.2% (27.0 and 27.2%). SWM may be useful for differentiating MTT of BC and benign thyroid nodules, but not for differentiating MTT of BC and ATC.

It is necessary to distinguish a poorly differentiated thyroid carcinoma or ATC from BC-orientated MTT. Although FNAC is useful for diagnosing MTT, Zhang *et al*.[15] found that MTT from BC required a wide differential diagnosis even when biopsy and IHC data were available. Of the various MMTs, that from BC is most accurately diagnosed (94.7% accuracy rate) by thyroid FNAC[16]. ICL does not always indicate malignancy, but ICL is a useful marker of breast adenocarcinoma[17]. ICL was found in 71-100% of BC cases on histopathological examination and 9.4-55.6% on FNAC[17–19]. ICL with intraluminal deposits are referred to as type A ICL (**Fig. 3**).

To confirm the primary tumor responsible for MTT, IHC using specific markers is very helpful. Tg and TTF-1 are highly specific for differentiated thyroid carcinomas. For BCs, ER and mammaglobin are useful. Mammaglobin is a 93-kDa glycoprotein of the uteroglobin family. Bhargava *et al*.[20] reported that mammaglobin was more sensitively detected in tissue blocks compared to other IHC markers. Mammaglobin is overexpressed in BC, and plays an important role in the diagnosis of metastatic BC[21,22]. In our case, the IHC results differed between primary and metastatic BC. The ER and PR were positive, while the HER2 test was negative, in the primary BT, whereas the ER was negative and HER2 focally positive in the MTT. Such "tumor marker conversion" or "receptor conversion"[23,24] can occur during cancer progression. Hoefnagel *et al*.[24] studied receptor conversion of ER, PR, and HER2 in 233 BC patients with distant metastases (76 skin, 63 liver, 43 lung, 44 brain and 7 gastro-intestinal) by re-staining all samples. ER and PR conversion (at a 10% threshold) occurred in 10.3 and 30.0% of patients, respectively. In 10.7% of patients, conversion from ER+ or PR+ to ER−/PR− was noted, while conversion from ER−/PR− to ER+ or PR+ was seen in 3.4% of cases. HER2 conversion occurred in 5.2% of patients. In our case, the malignancy may have become more severe, as reflected by the difference in HER2 status between the primary BC and MTT.

Conclusion

MTT from BC is a rare malignancy. In addition to FNAC and IHC, SWM is useful for diagnosis.

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Conflict of Interest: The authors have no conflicts of interest.

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