CASE REPORT

Medullary Thyroid Carcinoma Metastasis to the Breast and Axillary Lymph Nodes

Seung Pil Jung¹ · Hye Yoon Lee¹ · Jeoung Won Bae¹ · Hoon Yub Kim²

Received: 24 May 2014 / Accepted: 9 June 2015 / Published online: 25 June 2015
© Association of Surgeons of India 2015

Abstract Breast metastases of medullary thyroid carcinoma (MTC) are extremely rare, and only a few cases have been reported in the literature so far. Here, we report a case of metastatic MTC to the breast and axillary lymph nodes (LN). The case illustrates that (1) metastatic MTC of the breast could be clinically and pathologically misdiagnosed as primary breast cancer, such as invasive lobular carcinoma with axillary LN involvement; (2) unlike other metastatic breast cancer patients, who have very poor prognoses, our patient survived for more than 5 years after the breast and axillary surgery; and (3) metastasis of MTC to the breast is accompanied by axillary LN metastasis, which requires thorough axillary LN dissection, as in most primary breast cancers.

Keywords Carcinoma · Medullary · Thyroid · Neoplasm metastasis · Breast neoplasm

Introduction

Medullary thyroid carcinoma (MTC) is an uncommon thyroid cancer, comprising 5 to 8 % of thyroid neoplasms. In contrast to common thyroid tumors, this tumor originates from the calcitonin-producing parafollicular C cells. Regional metastases to cervical lymph nodes (LNs) occur early in the disease,

whereas distant metastases occur late. Breast metastases of MTC are very rare, and to our knowledge, less than 10 cases have been reported in the literature so far. Here, we present a case of metastatic MTC to the breast and axillary LNs misdiagnosed as primary invasive lobular carcinoma of the breast with axillary LN metastasis. The patient survived for more than 12 years after the initial diagnosis of MTC.

Case Report

Twelve years previously, a 49-year-old woman underwent total thyroidectomy and central and right lateral neck dissection for a 2-cm MTC in the right lobe, with metastases in all the 10 resected cervical lymph nodes. At 20 months postoperation, the patient underwent radiotherapy to the neck owing to elevated serum calcitonin (sCN) level. However, the sCN level increased again reaching 950.0 pg/mL at 6 years postoperation. As there was evidence of bilateral cervical nodal metastases in a cytologic examination of the aspirate, the patient underwent bilateral modified radical neck dissections. Pathologic examination revealed bilateral metastases in 19 of 44 resected lateral LNs. The sCN level dropped to 330.0 pg/mL postoperatively.

In the seventh year of follow-up after the initial operation, a palpable mass was identified in the left breast. Mammography revealed multiple well-circumscribed discrete nodules with suspicious microcalcifications in the left upper breast and ipsilateral axillary lymphadenopathy (Fig. 1). Histological examination of the biopsied tissues from the nodules indicated invasive lobular carcinoma (Fig. 2a). The patient underwent modified radical mastectomy, and pathologic examination finally revealed multifocal metastatic MTC, with cells diffusely positive for E-cadherin, calcitonin, and thyroid transcription factor-1 (TTF-1) on the immunohistochemistry (Fig. 2b–d). Metastases were present in 4 of 15 resected axillary LNs. The

✉ Hoon Yub Kim
hoonyubkim@korea.ac.kr

¹ Division of Breast and Endocrine Surgery, Department of Surgery, Korea University College of Medicine, Seoul, South Korea

² Department of Surgery, Korea University Thyroid Center, Korea University College of Medicine, Seoul, South Korea

Fig. 1 A craniocaudal mammogram (a) shows two well-circumscribed discrete nodules with suspicious microcalcifications in the left upper breast (arrows). A mediolateral oblique mammogram (b) shows multiple lymphadenopathies in the ipsilateral axilla (arrowheads)

patient is now in the fourth-year follow-up without evidence of recurrence after the last operation.

Discussion

Breast metastases comprise 0.5–2 % of all breast tumors [1, 2]. Diagnosis of a metastatic tumor should be considered in patients with known extramammary malignancies and when tumor morphology does not correspond to patterns typical for primary breast tumors. Secondary tumors on mammography appear as well-circumscribed masses without speculation [3],

and the lack of tumor-associated acoustic shadowing has been suggested as a characteristic ultrasonographic feature of metastatic tumors in the breast [2]. Multifocality, especially with an unusual histological pattern, should consider the possibility of the presence of a metastatic tumor. The presence of a carcinoma in situ component would support a primary breast lesion [4].

Immunohistochemistry plays an important role in the accurate identification of metastatic lesions. Primary breast carcinomas are positive for cytokeratin 7, and those of ductal origin express E-cadherin. However, E-cadherin expression is common to diverse neoplasm, including those of thyroid origin, as in this patient. The estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2/neu) are expressed in a subset of invasive breast carcinomas and in some other carcinoma. Thus, their presence or absence cannot determine whether a breast neoplasm is of metastatic origin. Data regarding ER, PR, and HER2/neu expression in MTCs, although based on a limited number of cases, suggest that MTCs are negative for ER and PR [5–7], at least on immunohistochemistry and that MTCs do not exhibit HER2/neu oncoprotein overexpression or gene amplification. Neuroendocrine markers may be expressed by primary breast carcinomas with neuroendocrine differentiation, MTCs, and various metastatic lesions, especially those of gastrointestinal origin [4].

Clinically, metastatic cancers to the breast have been associated with poor prognosis, with most patients dying within 1 year of diagnosis [2]. Compared to previous reports, our patient survived relatively long, for more than 12 years after the initial diagnosis. Therefore, we suggest that aggressive surgical treatment should be considered for such patients.

Fig. 2 In the core biopsy specimen (a), tumor cells are arranged in a nesting or trabecular pattern, separated by hyalinized stroma, and have centrally or eccentrically located small nuclei with a plasmacytoid appearance, similar to that observed in primary invasive lobular carcinoma of the breast ($\times 100$). Immunohistochemistry of the resected breast specimen reveals that tumor cells are positive for E-cadherin (b), calcitonin (c), and thyroid transcription factor-1 (TTF-1) (d) ($\times 100$)

Surgery may significantly improve the survival of a patient with a similar disease unlike for other metastatic breast cancer patients

Additionally, we can assume that MTC commonly spreads to the lymphatic system and subsequently progresses to distant sites. In this case, breast metastasis would be accompanied by axillary LN metastasis, possibly requiring complete axillary LN dissection for most advanced primary breast cancers.

References

1. Hajdu SI, Urban JA (1972) Cancers metastatic to the breast. *Cancer* 29(6):1691–1696
2. Yeh CN, Lin CH, Chen MF (2004) Clinical and ultrasonographic characteristics of breast metastases from extramammary malignancies. *Am Surg* 70(4):287–290
3. Bartella L, Kaye J, Perry NM, Malhotra A, Evans D, Ryan D, Wells C, Vinnicombe SJ (2003) Metastases to the breast revisited: radiological-histopathological correlation. *Clin Radiol* 58(7):524–531
4. Nofech-Mozes S, Mackenzie R, Kahn HJ, Ehrlich L, Raphael SJ (2008) Breast metastasis by medullary thyroid carcinoma detected by FDG positron emission tomography. *Ann Diagn Pathol* 12(1):67–71. doi:[10.1016/j.anndiagpath.2006.08.004](https://doi.org/10.1016/j.anndiagpath.2006.08.004)
5. Bur M, Shiraki W, Masood S (1993) Estrogen and progesterone receptor detection in neoplastic and non-neoplastic thyroid tissues. *Mod Pathol* 6(4):469–472
6. Colomer A, Martinez-Mas JV, Matias-Guiu X, Llorens A, Cabezas R, Prat J, Garcia-Ameijeiras A (1996) Sex-steroid hormone receptors in human medullary thyroid carcinoma. *Mod Pathol* 9(1):68–72
7. Arain SA, Shah MH, Meo SA, Jamal Q (2003) Estrogen receptors in human thyroid gland. An immunohistochemical study. *Saudi medical journal* 24(2):174–178