Unusual Metastasis of Medullary Thyroid Carcinoma to the Breast: A Cytological and Histopathological Correlation

Parul Tanwar, Jatin S Gandhi, Anila Sharma, Manoj Gupta, Partha S Choudhary
Departments of Laboratory and Transfusion Services, Nuclear Medicine, Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India

Abstract

Breast metastases are a relatively rare condition and account for approximately 0.5–2% of all breast tumors. Recognition of metastatic tumors in the breast is important because it would prevent unnecessary mutilating surgery and would lead to appropriate treatment of the primary tumor. Breast metastases from medullary thyroid cancer (MTC) are very rare with only 21 reported cases in the literature. Some MTCs mimic primary invasive lobular carcinoma of the breast histopathologically and radiologically, making the distinction between the two diagnostically challenging. We present the case of a 45-year-old female presenting with a lump breast, which was later found out to be metastasis from medullary carcinoma thyroid.

Keywords: Breast; medullary thyroid cancer; metastasis

INTRODUCTION

Metastasis to breast is fairly uncommon, accounting for fewer than 2% of all breast tumors. Mammary metastases as the initial presentation are even more infrequent and can simulate a primary malignancy clinically and radiologically. However, it is essential to differentiate the two conditions because of the difference in their treatments; appropriate treatment of the primary tumor is the preferred course of action for metastatic disease whereas primary tumor is treated by surgery. Metastatic carcinoma from the opposite breast is the most common secondary tumor to the breast in females as opposed to hematopoietic tumors and prostate carcinoma, which are the most common metastatic tumors to the male breast. Other sites of metastatic disease include malignant melanoma, lung carcinoma (especially small cell carcinoma), renal cell carcinoma, gastrointestinal carcinoma, thyroid (papillary and follicular carcinomas), carcinoids, ovarian carcinoma, endometrial carcinoma, pancreatic carcinoma, and neuroblastoma. Medullary thyroid cancer (MTC) commonly metastasizes early to local lymph nodes, and later, distantly to the lungs and liver. Other sites of distant metastases are rare. However, MTC metastatic to the breast is extremely rare and only a few handful cases have been reported worldwide. There have been only 21 reported cases of MTC metastasizing to the breast.

We present the case of a 45-year-old female presenting with a lump in the breast, which was later diagnosed to be a metastasis from MTC.

Address for correspondence: Dr. Parul Tanwar, Department of Laboratory and Transfusion Services, Rajiv Gandhi Cancer Institute and Research Centre, Sector-5, Rohini - 110 085, New Delhi, India. E-mail: drparultanwar@gmail.com

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and E-cadherin was done [Table 1]. However, the tumor cells were negative for ER and PgR and showed no loss of expression of E-cadherin. A further inquiry about the detailed past history revealed that the patient was operated for a thyroid neoplasm 2 years ago, the details of which were unavailable at that time. Subsequently, an extended panel of IHC was used to determine the site of origin of the tumor. The tumor cells were positive for TTF1 [Figure 1d], calcitonin [Figure 1e], and carcinoembryonic antigen CEA [Figure 1f] whereas negative for thyroglobulin, GATA3 and napsin. Fluorodeoxyglucose (FDG) positron emission tomography (PET) showed FDG avid round soft tissue nodule measuring 15 × 13 mm, SUVmax 2.4, in the left breast [Figure 2]. Subsequently, a final diagnosis of metastatic MTC was conferred after discussion and feedback from nuclear medicine department based on the histomorphology and the PET avidity of the tumor.

**DISCUSSION**

Metastases in MTC are common and occur both by hematogenous and lymphatic spread. Regional lymph nodal involvement occurs early (affecting ~60% of patients) and later on distant metastases are found (~40% of patients). Breast metastases from MTC are very rare with only 21 reported cases in the literature [Table 2]. Importantly, some MTCs mimic primary invasive lobular carcinoma of the breast histopathologically and radiologically, making the distinction between the two diagnostically challenging.

Breast USG and mammography are useful diagnostic tools albeit the absence of pathognomonic criteria to establish the diagnosis of breast metastasis. On USG, metastatic nodule is mostly superficial, solitary, firm and adherent to the skin, and

![Figure 1: (a) Fine-needle aspiration cytology (FNAC) smears showed a population of singly dispersed (MGG stain x200). (b) FNAC smears shows plasmacytoid cells (Pap stain x200). (c) Tumor cells present in single file pattern, in a targetoid fashion around the mammary ducts (H and E stain x100). (d) Tumor cells showed positivity for TTF 1 (x40), (e) calcitonin (x200), and (f) carcinoembryonic antigen (x200)](image)

![Figure 2: Axial computed tomography (a) and fused fluorodeoxyglucose (FDG) positron emission tomography (b) images show FDG avid round soft tissue nodule (1.5 × 1.3 cm, SUVmax 2.4) in the left breast (White arrow)](image)

**Table 1: List of antibodies used in immunohistochemistry**

| Antibody                  | Clone                          | Dilution/RTU | Company          |
|---------------------------|--------------------------------|--------------|------------------|
| TTF1                      | Mouse monoclonal (8GTG3/1)     | 1:100        | Dako, Denmark    |
| Calcitonin                | Rabbit Polyclonal              | 1:50         | Dako, Denmark    |
| Carcinoembryonic antigen (CEA) | Mouse monoclonal (II-7)     | 1:25         | Dako, Denmark    |
| Thyroglobin               | Rabbit Polyclonal              | RTU          | Dako, Denmark    |
| GATA3                     | Mouse monoclonal (L-50-823)    | RTU          | Cell Marque, USA |
| Napsin                    | Rabbit monoclonal (MRQ-60)     | 1:100        | Cell Marque, USA |
| Estrogen receptor (ER)    | Mouse monoclonal (SP-1)        | RTU          | Ventana, USA     |
| Progesterone receptor (PgR) | Mouse monoclonal (1E-2)      | RTU          | Ventana, USA     |
| E-Cadherin                | Mouse monoclonal (NCH-38)     | 1:50         | Dako, Denmark    |
shows loss of tumor-associated acoustic shadowing. However, these features are not specific.[3]

The case reported here demonstrated metastatic MTC as a breast nodule diagnosed by FNAC. Primary MTC has characteristic cytological findings of poorly cohesive tumor cells with abundant granular cytoplasm and uniform, usually stippled nuclei, which are eccentrically placed. In addition, amyloid can also be observed. These cytologic features need to be differentiated from those of primary invasive lobular carcinoma and malignant lymphoma.[9] This necessitates the need of cell block preparation in every case so that further IHC workup can be done.

Although some metastatic tumors can be differentiated from primary breast cancers in the presence of histopathological features (i.e., the predominance of clear cells, melanin pigments), the histopathological features of metastatic tumors of the breast are frequently similar to those of primary breast cancers.[7] Consequently, the possibility of primary breast cancer should be kept in mind for differential diagnosis of breast nodules in patients who have a nodule in another organ.[3]

Histological features which may be suggestive of metastatic disease include a periductal or perilobular distribution in the absence of any in situ ductal or lobular component. There is minimal elastosis and desmoplasia associated with these lesions. Final confirmation usually requires IHC to establish the diagnosis of metastasis.[3]

Metastatic tumors to the breast present perplexing diagnostic problems both from the clinical as well as histological points of view. Accurate diagnosis of metastatic lesions is important to avoid unnecessary, radical surgical procedures and to assure appropriate adjunctive therapy. There are no reliable clinical criteria for distinguishing a primary tumor from a secondary tumor in the breast.[4]

Most of the metastatic tumors in the breast have been described in young or middle-aged women perhaps because the better blood supply in this age group encourages blood-borne metastasis, which is the most frequent mode of cancer spread to this organ. Overall prognosis of these cases is usually grave.[3]

**Conclusion**

Although MTC commonly metastasizes to local and distant sites, spread to the breast is very rare and should be considered a diagnostic possibility in patients with a past history of MTC presenting with an apparently primary breast lesion, especially in cases with unusual morphology, as seen in our case. Careful cytomorphological examination and appropriate ancillary studies such as IHC staining for calcitonin after FNAC may lead to a correct diagnosis and thus prevent unnecessary radical surgery.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

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**Table 2: Demographic and radiology characteristics, presence of metastases, and alive status of patients with metastatic medullary thyroid carcinoma to the breast (21 cases)**

| First author, year | Age | MEN 2 | Breast affected and number of metastatic nodules | Mammography-U/S | Metastases | Deceased/alive [D/A] |
|--------------------|-----|-------|-----------------------------------------------|-----------------|------------|---------------------|
| Stylianos Mandanas, 2015 | 67/M | No | R-1 | Yes-Yes | Cervical LN, Lung, bone | D |
| Martinez-Rodriguez, 2013 | 51/F | No | R-1 | No-No | Liver, bones, thoracic wall | A |
| Rodriguez-Gil, 2012 | 43/F | No | B/L-3 | Yes-No | Bone | D |
| Basu, 2010 | 32/F | NR | L-1 | NR-NR | NR | NR |
| Ricciato, 2010 | 54/F | No | L-1 | Yes-Yes | Cervical LN, liver, lungs, rib | A |
| Andreuilo, 2009 | 57/F | No | B/L-2 | Yes-Yes | NR | NR |
| Marcy, 2009 | 43/F | No | B/L-M | No-No | Cervical LN, tracheal wall | D |
| Nofech-Mozes, 2008 | 50/F | No | L-1 | Yes-Yes | Cervical LN, liver | A |
| Kim, 2008 | 39/F | No | R-2 | No-No | Cervical LN, liver | A |
| Kang, 2008 | 38/F | No | B/L-2 | Yes-Yes | Cervical LN | A |
| Vaughan, 2007 | 35/F | Yes | L-1 | Yes-Yes | Unknown distant mets | D |
| Vaughan, 2007 | 29/F | Yes | L-1 | Yes-No | Unknown distant mets | D |
| Vaughan, 2007 | 30/F | Yes | B/L-2 | Yes-Yes | Unknown distant mets | A |
| Lee, 2007 | 48/F | NR | NR-M | NR-NR | Cervical LN | NR |
| Ishitobi, 2004 | 54/F | No | B/L-M | Yes-Yes | NR | NR |
| Pritchett, 1998 | 42/F | No | R-1 | No-No | Cervical LN, lungs, brain | D |
| Kiely, 1995 | 64/F | No | L-1 | Yes-Yes | Cervical LN | A |
| Soo, 1995 | 40/F | Yes | L-2 | Yes-No | Cervical LN, liver | NR |
| Ali, 1994 | 28/F | Yes | NR-NR | NR-NR | NR | NR |
| Abuja, 1991 | 32/F | NR | NR-M | NR-NR | Cervical LN, lungs, bone | D |
| Ordenez, 1988 | 72/F | No | R-2 | No-No | Cervical LN, skin | D |

R = Right; L = Left; B/L = Bilateral; NR = Not reported; M = Multiple
Retinoblastoma in an Adult

Vasudha Garg, Ashumi Gupta, Sonam K. Pruthi, Pratima Khare

Department of Pathology, Dr B.S. Ambedkar Hospital, New Delhi, India

Abstract

Retinoblastoma is a rare malignant tumor of the retina usually seen in children before 5 years of age. The tumor is extremely rare in adults.

We report here an unusual case of retinoblastoma in a 55-year-old adult female who presented to us with an orbital mass at a late stage of the disease. Detailed laboratory investigations and imaging studies could not make a precise diagnosis. The treating ophthalmologist suspected primary intraocular tumor, metastatic carcinoma, malignant melanoma, or lymphoma and referred the patient for fine needle aspiration cytology (FNAC). Cytopathological examination of Giemsa-stained FNAC smear was consistent with that of retinoblastoma and established the diagnosis.

Keywords: Fine needle aspiration cytology, noncontrast computed tomography scan, retinoblastoma

Case Report

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Address for correspondence:
Dr. Pratima Khare, Department of Pathology, Dr B.S. Ambedkar Hospital, New Delhi - 110 085, India. E‑mail: drpratimakhare@gmail.com

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Conflicts of interest

There are no conflicts of interest.

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