

## CASE REPORT

**BILATERAL BREAST METASTASIS FROM AN ADENOCARCINOMA OF LUNG: A CASE REPORT**Nasit Jitendra G<sup>1</sup>, Biren Parikh<sup>2</sup>, Manoj Shah<sup>3</sup><sup>1</sup>Assistant Professor, Department of Pathology, P.D.U. Medical College, Rajkot <sup>2</sup>Assistant Professor, <sup>3</sup>Professor and Head of the Department, Department of Pathology, Gujarat Cancer & Research Institute, Ahmadabad.**Correspondence:**

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**ABSTRACT**

Breast metastases from extramammary neoplasms are very rare. Breast metastasis is often confused with primary breast malignancy. Accurate differentiation of metastatic breast carcinoma from primary breast carcinoma is of crucial importance because the treatment and prognosis differs significantly. The pathologist has a key role in making the diagnosis of metastasis to the breast when histological appearance is similar to primary breast tumor. The clinical history is helpful to make the diagnosis. Metastasis to the breast usually indicates disseminated metastatic disease and poor prognosis. We report a case of 42-year-old female who developed bilateral breast metastasis 18 months after the diagnosis of primary adenocarcinoma of lung.

**Key words:** Breast metastasis, Adenocarcinoma, Lung, Bilateral**INTRODUCTION**

Breast cancer is a very common malignancy in women though metastases to the breast from extramammary malignancy are rare with incidence of 0.4 - 1.3%.<sup>1-6</sup> The most common primary tumors that metastasized to breast are haematological malignancies and malignant melanoma.<sup>1,4</sup> Few cases reported on non-small cell lung cancer (NSCLC) metastasizing to the breast.<sup>5,7,8</sup> Here, we report a case of 42-year-old woman with bilateral breast metastasis from an adenocarcinoma of lung with discussion on clinical, radiological and pathological findings with differentiation from primary breast carcinoma.

**CASE REPORT**

A 42-year-old woman presented with dyspnea and dry cough of 6 weeks duration. Chest examination revealed reduced breath sounds and percussion dullness at the right hemithorax. Chest roentgenogram revealed opacified shadow over the right lung field. Computed tomography of chest revealed 6.5 × 5.5 cm mass in the right lung with pleural effusion and few enlarged lymph nodes in paratracheal region (Figure 1). Transbronchial biopsy revealed high grade adenocarcinoma (Figure 2.A). On immunohistochemistry, tumor cells showed nuclear positivity for thyroid transcription factor-1 (TTF-1) (Figure 2.B). Tumor cells also positive for

cytokeratin 7 (CK7), monoclonal carcinoembryonic antigen (CEA), but negative for cytokeratin 20 (CK 20), CK5/6, estrogen receptors (ER), calretinin and thyroglobulin. She was treated with chemotherapy and remained asymptomatic for a period of 18 months.

Then she complained heaviness in both breast. Physical examination revealed painless, ill-defined mass in both breast. Mammography showed diffuse asymmetrical density in the subalveolar region and upper outer quadrant of the both breast without calcification (Figure 3). Fine-needle aspiration cytology showed highly pleomorphic cells, isolated or irregularly clustered. In view of previous malignancy, possibility of bilateral breast metastasis from an adenocarcinoma of lung was given. However, primary breast carcinoma should be excluded. Subsequent tru-cut biopsy from both breast revealed diffuse infiltration by nests of neoplastic epithelial cells around the benign mammary duct. Within the stroma, infiltrating high grade adenocarcinoma without desmoplastic stromal response was demonstrated. Lymphatic tumor embolus was evident (Figure 4). The tumor cells demonstrated immunoreactivity for TTF-1, CK 7 and monoclonal CEA. The tumor cells lacked expression of gross cystic disease fluid protein-15 (GCDFP-15), ER, progesterone receptor (PR), CK 5/6 and thyroglobulin (Figures 5). Tumor cells from breast revealed the same immunoprofile as the lung biopsy. Final diagnosis of

bilateral breast metastasis from an adenocarcinoma of lung was made. Patient received 4 course of chemotherapy but no clinical response and died after 6 months.

**Table 1:** Histological growth patterns of metastases to the breast

Growth pattern	Frequency and associated findings
Circumscribed nodule with surrounding normal breast tissue	Most common pattern
Infiltration around ducts and lobules	Second most common pattern; usually associated with lymphomas, leukemias and malignant melanoma
Lymphangitis	Less common pattern
Diffuse infiltration	Rare

**Table 2:** Histological features that may helpful in differentiation of breast metastasis from primary mammary neoplasm

Histological feature	Primary mammary carcinoma	Metastases to the breast
Margins	Usually infiltrating margins	Usually well circumscribed; rarely diffuse infiltration around duct and lobules
In situ carcinoma	Present and strongly supports primary mammary carcinoma. However, it is not present in all cases	Not seen
Desmoplastic stromal response / Elastosis	Commonly present	Rarely seen
Microcalcification	Usually present	Rarely seen with exception of serous papillary carcinoma of the ovary
Lymphatic or vascular tumor emboli	Common	Relatively much more common
Pigmentation and intranuclear inclusions	Not seen	Seen in malignant melanoma and hepatocellular carcinoma

**DISCUSSION**

The breast is an uncommon site for metastasis from extramammary tumors with incidence of 0.4 - 1.3%.<sup>1,2</sup> In about 25–40% of cases, metastasis to the breast is the initial manifestation of the disease.<sup>2</sup> The common sources of primary tumors are haematological malignancies, malignant melanoma, lung tumors, renal cell carcinoma, ovarian tumors, thyroid carcinomas and small bowel carcinoid.<sup>4,6</sup> Other tumors metastasized to breast are prostate, stomach, malignant mesothelioma and rhabdomyosarcoma.<sup>9</sup> Few cases reported on lung cancer metastasizing to the breast. NSCLC accounts for approximately 75% to 80% of all lung cancer.<sup>8</sup> Metastasis from NSCLC is commonly seen in the liver, adrenal glands, bone, brain, kidney and abdominal lymph nodes. The other unusual metastatic sites are the stomach, pancreas, small bowel, arteriovenous hemangioma, choroid plexus, muscle, umbilicus and penis.<sup>8</sup> However, to the best of our knowledge, bilateral breast metastasis from primary lung adenocarcinoma has been very rarely reported.

The majority of breast metastases present as well circumscribed, palpable, freely mobile, rapidly growing, painless firm masses in the upper outer quadrant of breast.<sup>4,5,9,10</sup> Multiple, bilateral and diffuse involvement of metastatic lesions is less common.<sup>10</sup> Occasionally breast metastasis is adherent to the skin.<sup>5</sup> The time interval from the diagnosis of primary extramammary neoplasm to breast metastasis varies between 1 month

and 15 years, with averages between 1 and 5 years.<sup>9</sup> Rarity of breast involvement by metastatic tumors is due to large areas of fibrous tissue, relatively poor blood supply and anatomically non-connected locations.<sup>11</sup> Female hormones may play role in cancer predisposition, based on the high occurrence of breast metastases in pubescent, lactating, and pregnant female.<sup>9</sup> Overall metastasis to the breast has been associated with poor prognosis with most patients dying within a year of diagnosis.<sup>4,8</sup>

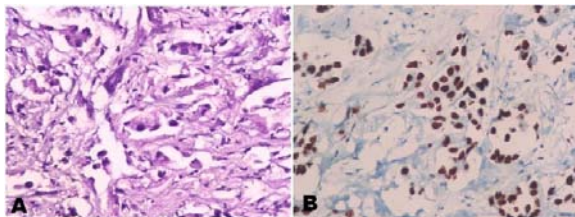
The mammographic findings of breast metastases are usually single, well-defined or slightly irregular margins without desmoplastic reaction and distortion of adjacent architecture. There is no spiculation or microcalcification. Rarely diffuse parenchymal and skin involvement is seen.<sup>6,10,11,12,13</sup> Ultrasound scan showed a hypoechoic mass, which is sometimes heterogeneous or poorly defined without architectural distortion.<sup>13</sup> Although radiology can provide some information to distinguish primary breast cancer from metastatic disease, excisional or core biopsy is usually needed for final diagnosis.

The histological diagnosis of breast metastasis is more difficult than primary breast neoplasms. Histologically four growth patterns of breast metastases are described in table 1.<sup>5</sup> Histological features that may helpful in differentiation of breast metastasis from primary breast neoplasms are given in table 2.<sup>1,2,5,9,11</sup> However, majority of the lesions do not show any specific histological

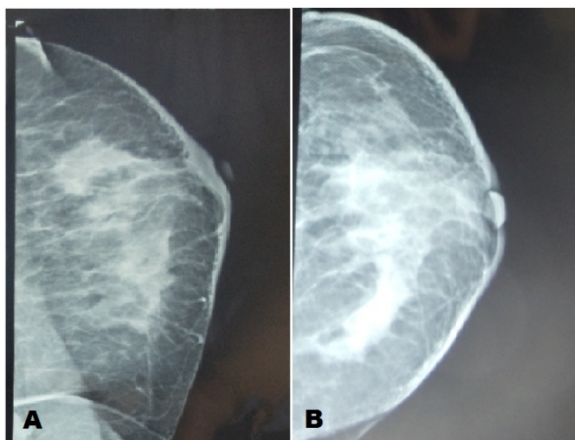
features like in our case. A history previous malignancy is helpful in approaching the diagnosis. The contribution of immunohistochemistry is very crucial to confirm the diagnosis. TTF-1 is expressed in the epithelial cells of the thyroid gland and lung. TTF-1 is expressed in 62% to 88% of all primary lung adenocarcinomas and less than 1% of adenocarcinomas of non-pulmonary origin.<sup>8</sup> TTF-1 is rarely positive in primary breast cancer except Klingen TA et al published a single case of TTF-1 positivity.<sup>14</sup>



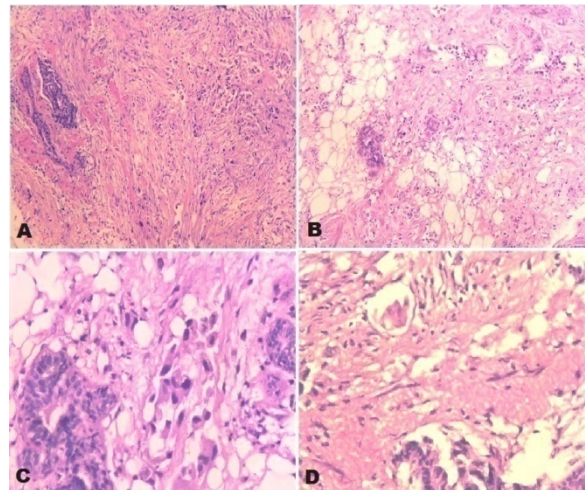
**Fig 1:** Computed tomography of chest revealed 6.5 × 5.5 cm mass in the right lung with pleural effusion and few enlarged lymph nodes in paratracheal region



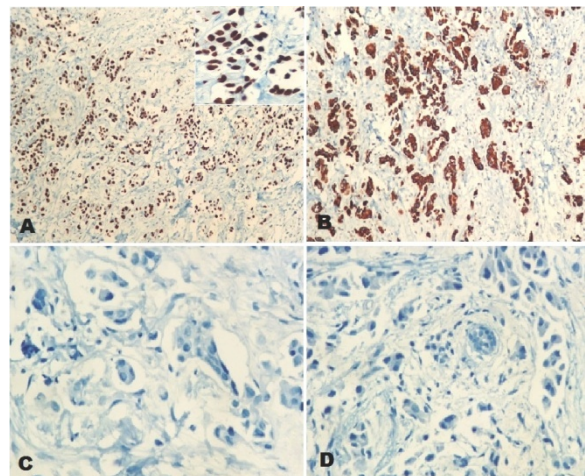
**Fig 2:** Lung biopsy: (A) Transbronchial biopsy revealed high grade adenocarcinoma (H & E stain, ×400). (B) On immunohistochemistry, tumor cells showed nuclear positivity for thyroid transcription factor-1 (TTF-1) (×400)



**Fig 3:** Mammography showed diffuse asymmetrical density in the subalveolar region and upper outer quadrant of the both breast without calcification



**Fig 4:** Breast biopsy: (A) Diffuse infiltration by nests of neoplastic epithelial cells around the benign mammary duct (H & E stain, ×100), (B) Infiltrating adenocarcinoma in the stroma without desmoplastic response (H & E stain, ×100), (C) High grade adenocarcinoma with adjacent benign mammary duct (H & E stain, ×400), (D) Lymphatic tumor embolus was evident (H & E stain, ×400)



**Fig 5:** Immunohistochemistry (IHC), Breast biopsy: (A) Positivity of TTF-1 in malignant cells (×100); inset figure showed strong nuclear positivity (×400), (B) Positivity of CK-7 in malignant cells (×100), (C) Estrogen receptor (ER) was negative in malignant cells (×400), (D) GCDFP-15 was negative in malignant cells (×400)

Negative expression of thyroglobulin excludes the diagnosis of papillary carcinoma of the thyroid.<sup>3</sup> Expression of ER, PR and GCDFP-15 favors primary breast carcinoma although occasionally convincing expression is seen in pulmonary adenocarcinoma.<sup>3</sup> Immunohistochemical panels for other tumors that metastasized to the breast, including leukemia-lymphoma (leukocyte common antigen, CD 20); malignant melanoma (S100, HMB45, melan-A); ovarian serous papillary carcinoma (CA 125, Wilms' tumour 1); prostatic carcinoma (Prostate specific antigen); stomach carcinoma (CDX2, CK 20); renal cell carcinoma (CD 10,

renal cell carcinoma marker, vimentin) are useful to differentiated from primary breast carcinoma.<sup>5</sup>

## CONCLUSIONS

Breast metastasis, although rare, should be considered in the differential diagnosis of primary breast carcinoma, particularly if there is a history of extramammary malignancy because the treatment and prognosis differ significantly. A history of a concurrent or previous malignancy combined with the clinico-radiological assessment and pathological evaluation is essential to diagnose breast metastasis. Immunohistochemistry is very crucial in approaching the diagnosis.

## REFERENCES

1. Klingen TA, Klaasen H, Aas H, Chen Y, Akslen LA. Secondary breast cancer: a 5-year population-based study with review of the literature. *APMIS* 2009;117:762-767.
2. Georgiannos SN, Aleong JC, Goode AW, Sheaff M. Secondary neoplasms of the breast: a survey of the 20th century. *Cancer* 2001; 92:2259-2266.
3. Maounis et al. Metastasis to the breast from an adenocarcinoma of the lung with extensive micropapillary component: a case report and review of the literature. *Diagnostic Pathology* 2010; 5:82.
4. Williams SA, Ehlers RA, Hunt KK, Yi M, Kuerer HM, Singletary SE, Ross MI, Feig BW, Symmans WF, Meric-Bernstam F. Metastases to the breast from nonbreast solid neoplasms: presentation and determinants of survival. *Cancer* 2007;110:731-737.
5. Andrew H S Lee. The histological diagnosis of metastases to the breast from extramammary malignancies. *J Clin Pathol* 2007;60:1333-1341.
6. Noguera JJ, Martínez-Miravete P, Idoate F, Diaz L, Pina L, Zornoza G, Martínez-Regueira F. Metastases to the breast: A review of 33 cases. *Australas Radiol* 2007;51:133-138.
7. Masmoudi A, Mathieu MC, Soria JC. Breast metastasis from lung adenocarcinoma: a case report. *Anticancer Res* 2003;23:1825-1826.
8. Min Yong Yoon, Chang Seok Song, Mi Hae Seo, Min Jae Kim, Tae Yun Oh, Un Ha Jang, Hyon Joo Kwag, Hee Sung Kim, Si Young Lim, Seong Yong Lim, Seung Sae Lee. A Case of Metachronous Metastasis to the Breast from Non-Small Cell Lung Carcinoma. *Cancer Res Treat.* 2010;42:172-175.
9. Vergier B, Trojani M, De Mascarel et al: Metastatic to the breast: differential diagnosis from primary breast carcinoma. *J Surg Oncol* 1991;48:112-116.
10. Mozaffari A, Rashidi I, Paziari F. Extra mammary tumors metastasis to the breast. *Pak J Med Sci* 2008;24:468-470.
11. Lee SK, Kim WW, Kim SH, Hur SM, Kim S, Choi JH, Cho EY, Han SY, Hahn BK, Choe JH, Kim JH, Kim JS, Lee JE, Nam SJ, Yang JH. Characteristics of metastasis in the breast from extramammary malignancies. *J Surg Oncol* 2010;101:137-140.
12. Bohman LG, Bassett LW, Gold RH, Voet R. Breast metastases from extramammary malignancies. *Radiology* 1982;144:309-312.
13. Lee SH, Park JM, Kook SH et al. Metastatic tumors to the breast: mammographic and ultrasonographic findings. *J Ultrasound Med* 2000;19:257-262.
14. Klingen TA, Chen Y, Gundersen MD, Aas H, Westre B, Sauer T: Thyroid transcription factor-1 positive primary breast cancer: a case report with review of the literature. *Diagn Pathol* 2010, 5:37.