



Case Report: Unusual Presentation Of Lung Adenocarcinoma Metastases To Breast

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Abstract

Introduction:

The most common site of primary malignancies in adult women is breast, but it is an uncommon site for metastases from extramammary malignancies. We hereby report a case with an unusual presentation of lung adenocarcinoma metastases to breast.

Case Presentation:

A 45 year old female presented to our hospital with exertional dyspnea, dragging pain in the back, decreased appetite for the past 3 weeks. CXR and CT of the chest showed a suspicious malignant mass in the right lung, which was later confirmed on histopathology. PET-CT revealed multiple skeletal metastases. After she passingly complained of hardening and thickening of her right breast, she was evaluated with mammography and ultrasound of breast. Mammography showed global asymmetry in the right breast with associated distortion, interstitial thickening and an ill defined mass in the central and upper quadrant of the right breast. Ultrasound right breast showed diffuse area of altered echogenicity with an ill-defined mass in right breast. As the findings were highly suspicious for breast malignancy, USG guided core biopsy was done from the right breast, which showed features consistent with poorly differentiated adenocarcinoma. As the patient was known to have a primary lung malignancy, IHC markers, GATA -3 and TTF -1 were done to differentiate primary breast malignancy from metastases of pulmonary origin. GATA 3 was negative and TTF 1 (Thyroid transcription factor) - was positive in tumour cells, confirming pulmonary origin of the tumor. Thus IHC profile was compatible with metastatic adenocarcinoma of pulmonary origin.

Conclusions:

Usually extra mammary malignancy metastases to breast present as rapidly growing, painless, firm, well circumscribed, and palpable bilateral masses with a predilection to the upper outer quadrants not associated with skin or nipple retraction. In our case, the findings were atypical as there was only involvement of the right breast with no discrete mass. The entire breast tissue was diffusely involved causing diagnostic dilemma. The contribution of clinical history and immunohistochemistry helped to arrive at a correct diagnosis to provide appropriate systemic treatment because the recommended therapy is different with considerably varying outcomes.

Keywords: Metastatic adenocarcinoma, IHC markers, GATA 3, TTF 1.

Introduction

Most common site of primary malignancies in adult women is breast, but it is an uncommon site for metastases from extramammary malignancies. Metastases to the breast often arise from primary cancer of the contralateral breast. The clinically observed rate of breast metastases from extramammary malignancies is rarer, ranging from 0.5 to 1.3. This rare occurrence of metastases to the breast is suggested to be due to the presence of large areas of fibrous tissue with a relatively poor blood supply and a small amount of lymphoid tissue content. [1,2,3]

The most common extra mammary sources are melanomas and lymphomas / leukemias. Other less common sources include carcinomas of the stomach, ovary, lung, and less frequently, carcinoid tumors, hepatocellular carcinoma, hypernephromas, carcinoma of tonsil, pleura, cervix, pancreas, perineum, endometrium and bladder. [1,4,5]. Predisposing factors correlating with the development of breast metastases have not been clearly identified [1,6]. However, endogenous and exogenous hormones are considered as one of the predisposing factors for several types of extramammary malignancies [1,5]. Estrogen may increase the stroma and vascularity of the breast, and may play a role in the development of metastases [1,5]. In male patients with prostatic carcinoma treated with estrogens, some rare cases of development of breast metastases have been reported. [1,7]

Metastases to breast from extramammary malignancies can have both hematogenous and lymphatic routes. There are some common identical radiological features of metastatic diseases of the breast. However, these features are not specific for metastatic disease and hence, it becomes difficult to differentiate breast metastases from primary breast cancers or benign lesions. In order to manage the disease appropriately and to avoid unnecessary surgery, it is important to be able to recognize the findings of metastatic lesions.

Case Presentation:

A 45 year old female presented to our hospital with exertional dyspnea and dragging pain in the back for the past 3 weeks. Patient complained of decreased appetite. There was no hemoptysis. CXR and CT scan of the chest were performed. A suspicious

malignant mass was seen in the right lung, which was later confirmed on histopathology. She was further evaluated with PET-CT which revealed multiple skeletal metastases. After 1 month of diagnosis, she was admitted for 1st cycle of chemotherapy. During her admission, she passingly complained of hardening and thickening of her right breast for which she was evaluated with mammography and ultrasound of breast.

Mammography showed global asymmetry in the right breast with associated distortion, interstitial thickening and an ill-defined mass with non-circumscribed margins in the central and upper quadrant of the right breast. There were no associated microcalcifications. There was associated retraction of the nipple. Ultrasound of right breast showed diffuse area of altered echogenicity with an ill-defined mass between 11-2 'o' clock positions in right breast. Based on mammography and ultrasound findings, category BIRADS 4C was assigned. As the findings were highly suspicious for breast malignancy, USG guided core biopsy was done from the right breast. Core biopsy showed features consistent with poorly differentiated adenocarcinoma.

As the patient was known to have a primary lung malignancy, IHC markers, GATA -3 and TTF -1 were done to differentiate primary breast malignancy from metastases of pulmonary origin. GATA 3 was negative and TTF 1 (Thyroid transcription factor) was positive in tumour cells, confirming pulmonary origin of the tumor. Thus IHC profile was compatible with metastatic adenocarcinoma of pulmonary origin.

Discussion:

The present case report describes a case of a 45 year old woman with a rare presentation of unilateral breast metastases from primary lung adenocarcinoma. We reported the clinical, radiological and pathological features of the breast metastases.

The incidence of breast metastases from an extramammary primary tumor is 0.5%-6.0%, if both solid tumors and hematologic malignancies are included. [8,9] In a study done on 6668 oncology patients, the incidence of breast metastases from solid malignancies was estimated to be about 0.76%; of which, 16% originated from primary pulmonary tumors, melanoma(31%), cervical, ovarian and

prostate tumors(18%), urologic tumors(12%), gastrointestinal tumors(7%), and 4% from sarcomas [10]. Another survey done on 6334 cases of breast masses identified 45 metastases from extramammary (0.56%); the most common primary tumors in this study being lung carcinoma (33.3%), lymphoma (20.0%), melanoma (6.7%), and adenocarcinomas of the stomach, colon, and ovaries (4.4%, 6.7%, and 6.7%) [11].

Although the observation of metastases to the breast from distant primary cancers is rare, inclusion of such metastases is necessary in the differential diagnosis of a breast abnormality in the presence of previously diagnosed extramammary or contralateral breast malignancy. Also, the assessment of appropriate histologic features is required to exclude the possibility of distant extra mammary metastases even in patients with no known history of malignancy, as in synchronous metastasis. The correct diagnosis of the breast mass helps in appropriate selection of chemotherapy, surgical intervention, and radiation therapy and is required for a decent quality of life for the patient.

Usually, patients with breast metastases from pulmonary adenocarcinoma present as rapidly growing, painless, firm, well circumscribed, and palpable bilateral masses with a predilection to the upper and outer quadrants[12,13,14,15]. Unlike primary tumors of breast, metastases from extramammary malignancies do not usually demonstrate skin or nipple retraction [15,16]. Differentiating breast metastases from primary breast adenocarcinoma based on only mammographic findings may be extremely difficult because of the large range of imaging manifestations of metastatic lesions. Thus, metastasis from extramammary malignancy to breast can mimic a primary breast malignancy or even a benign breast tumor [16,17,18]. Most commonly, mammography shows a well-circumscribed round mass, however, multiple well-circumscribed lesions with smooth margins may also be present [18,19,20]. Calcifications are rare in breast metastases, an exception being metastases from primary serous papillary carcinoma of the ovary [8,20,21].

But in our case, the findings were atypical with involvement of only the right breast with no distinct mass on mammography or ultrasound. On

mammography, there was diffuse interstitial thickening with architectural distortion and retraction of nipple of the right breast. On ultrasound, there was diffuse area of altered echogenicity with posterior acoustic shadowing. These findings are unusual for metastases, making the distinction between metastases from lung adenocarcinoma and primary mammary adenocarcinoma, particularly inflammatory carcinoma of breast, difficult. In such cases, the clinical history and the additional information given by immunohistochemistry to arrive at a diagnosis becomes extremely important. For example, TTF1 is a useful marker in detection of pulmonary adenocarcinoma with an estimated frequency of 68% to 80%. Except in a single case that was published by Klingenet al [22], no stains of TTF1 were positively detected in any primary breast carcinoma [25-27]. TTF-1 is a robust biomarker for detecting metastases from lung carcinoma. In the context of primary lung cancer, this biomarker is well characterized[23], suggesting that in the pathologic work-up of all the breast lesions, detected in patients with a history of lung cancer, the immunoreactivity of TTF-1 should definitely be done as a routine work up.

A combination of appropriate clinical history, imaging and pathological data help in better disease diagnosis rather than a single modality. A systematic and complete examination of the breast mass and specific immunohistochemical analysis are necessary to confidently differentiate a primary breast cancer from metastases to the breast to avoid unnecessary surgical procedures like mastectomy and provide necessary required systemic treatment, as the recommended therapies are possibly different for varying outcomes.

Conclusions:

Usually extra mammary malignancy metastases to breast present as rapidly growing, painless, firm, well circumscribed, and palpable bilateral masses with a predilection to the upper outer quadrants not associated with skin or nipple retraction. In our case, the findings were atypical as there was only involvement of the right breast with no discrete mass. The entire breast tissue was diffusely involved causing diagnostic dilemma. The contribution of clinical history and immunohistochemistry helped to arrive at a correct diagnosis to provide appropriate

systemic treatment because the recommended therapy is different with considerably varying outcomes

List of Abbreviations

1. CXR-Chest xr
2. IHC-Immuno histochemistry
3. GATA 3-GATA binding protein 3
4. TTF 1-Thyroid transcription factor 1

References:

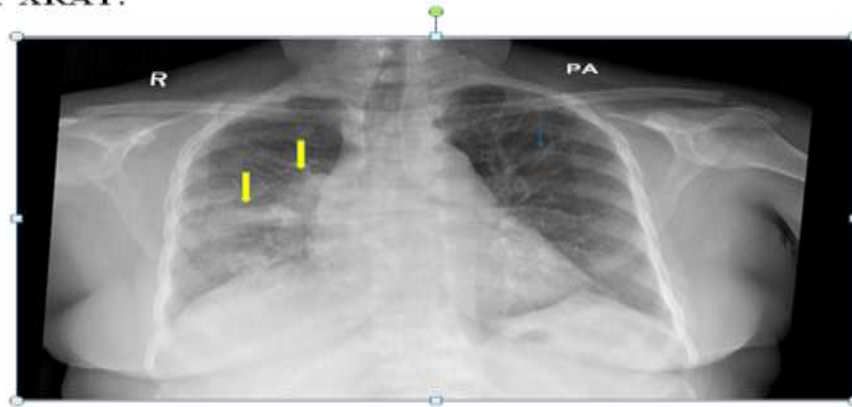
1. Lee SH, Park JM, Kook SH, Han BK, Moon WK. Metastatic tumors to the breast: mammographic and ultrasonographic findings. *J Ultrasound Med* 2000;19:257-262
2. Silverman JF, Feldman PS, Covell JL, Frable WJ. Fine needle aspiration cytology of neoplasms metastatic to the breast. *Acta Cytol* 1987;31:291-300.
3. Yeh CN, Lin CH, Chen MF. Clinical and ultrasonographic characteristics of breast metastases from extramammary malignancies. *Am Surg* 2004;70:287-290.
4. McCrea ES, Johnston C, Haney PJ. Metastases to the breast. *AJR Am J Roentgenol* 1983;141:685-690.
5. Vergier B, Trojani M, de Mascarel I, Coindre JM, Le Treut A. Metastases to the breast: differential diagnosis from primary breast carcinoma. *J Surg Oncol* 1991;48:112-116.
6. Amichetti M, Perani B, Boi S. Metastases to the breast from extramammary malignancies. *Oncology* 1990;47:257-260.
7. Nielsen M, Andersen JA, Henriksen FW, Kristensen PB, Lorentzen M, Ravn V, et al. Metastases to the breast from extramammary carcinomas. *Acta PatholMicrobiolScand A* 1981;89:251-256.
8. Toombs BD, Kalisher L. Metastatic disease to the breast: clinical, pathologic and radiographic features. *AJR Am J ROENTGENOL* 1977;129:673.
9. Yeh CN, Lin CH, Chen MF. Clinical and ultrasonographic characteristics of breast metastases from extramammary malignancies. *Am Surg* 2004;70:287.
10. Surov A, Fiedler E, Holzhausen HJ, et al. Metastases to the breast from non mammary malignancies; primary tumours, prevalence, clinical signs, and radiological features. *Acad RADIOL* 2011;18:565.pmid:21393030.
11. Sauer T. Fine needle aspiration cytology of extra mammary metastatic lesions in the breast: a retrospective study of 36 cases diagnosed during 18 years. *Cytojournal* 2010;7:10
12. Hajdu SI, Urban JA. Cancers metastatic to the breast. *Cancer* 1972;29:1691-1696.
13. Williams SA, Ehlers RA, Hunt KK, Yi M, Kuerer HM, Singletary SE, et al. Metastases to the breast from nonbreast solid neoplasms: presentation and determinants of survival. *Cancer* 2007;110:731-737.
14. Toombs BD, Kalisher L. Metastatic disease to the breast: clinical, pathologic, and radiographic features. *AJR Am J Roentgenol* 1977;129:673-676.
15. Yeh CN, Lin CH, Chen MF. Clinical and ultrasonographic characteristics of breast metastases from extramammary malignancies. *Am Surg* 2004;70:287-290.
16. 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.
17. Georgiannos SN, Chin J, Goode AW, Sheaff M. Secondary neoplasms of the breast: a survey of the 20th Century. *Cancer* 2001;92:2259-2266.
18. Noguera J, Martínez-Miravete P, Idoate F, Díaz L, Pina L, Zornoza G, et al. Metastases to the breast: a review of 33 cases. *Australas Radiol* 2007;51:133-138.
19. Vizcaíno I, Torregrosa A, Higuera V, Morote V, Cremades A, Torres V, et al. Metastasis to the breast from extramammary malignancies: a report of four cases and a review of literature. *Eur Radiol* 2001;11:1659-1665.
20. Lee SK, Kim WW, Kim SH, Hur SM, Kim S, Choi JH, et al. Characteristics of metastasis in the breast from extramammary malignancies. *J Surg Oncol* 2010;101:137-140.
21. Ko K, Ro JY, Hong EK, Lee S. Micropapillary lung cancer with breast metastasis simulating primary breast cancer due to architectural distortion on images. *Korean J Radiol* 2012;13:249-253.
22. 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.

24. Ordonez NG. Value of thyroid transcription factor 1 immunostaining in tumour diagnosis; a review and update. *Appl Immunohistochem Mol Morphol* 2012;20:429. Pubmed PMID:22531688.

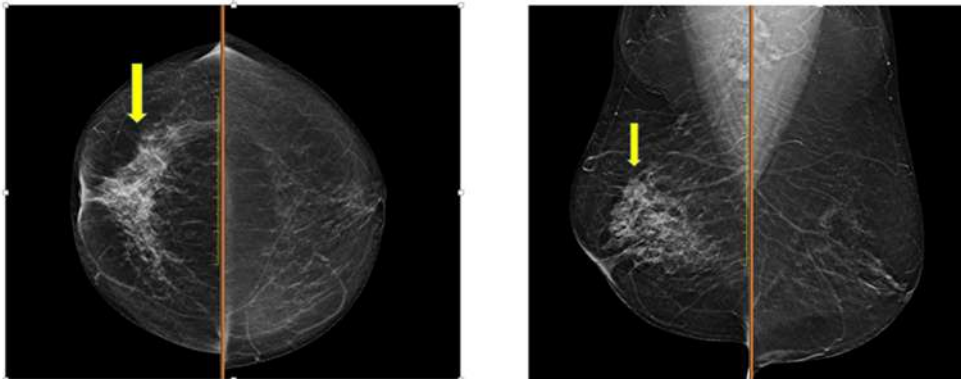
List of Figures

1. CHEST XRAY:



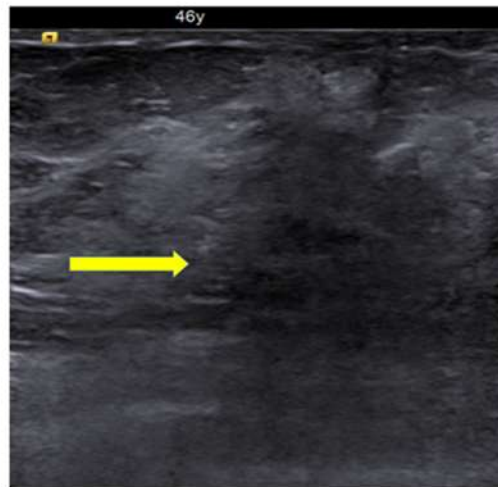
XRAY CHEST PA VIEW:
Ill defined radio opaque mass noted in the right mid zone and hilar region (yellow arrows) – pulmonary mass with hilar nodes. Diffuse interstitial thickening noted in bilateral lung fields. (blue arrow)-s/o lymphangitis carcinomatosa.

2. MAMMOGRAM:



MAMMOGRAM:
Global asymmetry noted in the right breast with associated distortion, interstitial thickening and a mass with indistinct margins in the central and upper quadrant of the right breast – BIRADS IV - C

3. TARGETED ULTRASOUND OF BREAST:



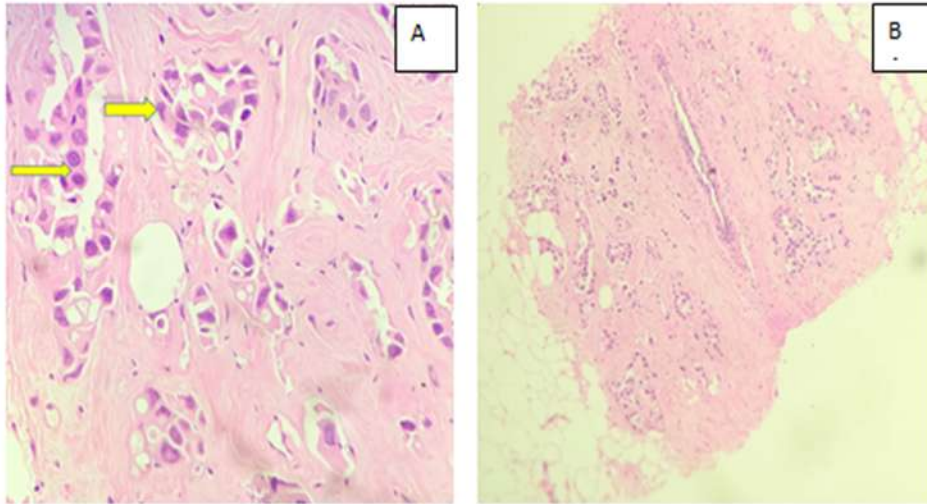
USG OF RIGHT BREAST:
Diffuse area of altered echogenicity with ill defined mass noted extending between 11-2 'o' clock position in right breast.

4. ULTRASOUND GUIDED BIOPSY:



USG guided core biopsy was done.

5. HISTOPATHOLOGY:



HPE (A and B): Cores of breast tissue infiltrated with neoplastic cells in cords, nests, showing high N/C ratio, pleomorphic nuclei and inconspicuous nucleoli.
- s/o poorly differentiated adenocarcinoma.

IHC(C and D) GATA 3 was negative and TTF 1 (Thyroid transcription factor) - was positive in tumour cells, confirming **pulmonary** origin .

