

# Breast Metastasis from Lung Adenocarcinoma Diagnosed with Fine Needle Aspiration Cytology: A Case Report

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## ABSTRACT

*Metastases to the breast from extramammary neoplasms are very rare. Correct diagnosis of breast malignancy is important for establishing appropriate management and for avoiding unnecessary radical surgery. Metastasized breast malignancies from non-small cell lung carcinoma are extremely rare. Here we report a 55-year old female patient with breast metastasis from lung adenocarcinoma which was diagnosed with fine needle aspiration cytology and confirmed by immunocytochemistry.*

**Key words:** breast metastasis, lung adenocarcinoma, fine needle aspiration cytology

## Introduction

Breast cancer is the commonest malignancy in women and accounts for 18% of all female cancers<sup>1</sup>. Metastases to the breast are unusual and make up approximately 2% of all malignant mammary neoplasms<sup>2</sup>. Metastases to the male breast are encountered even less frequently<sup>3</sup>. The commonest cause is spread from a contralateral breast carcinoma. Patients with unilateral breast carcinoma have 5-15% risk of developing cancer in the contralateral breast which may be either synchronous or metachronous. The majority of lesions are second primary growths rather than metastases<sup>1</sup>.

Reported primary tumors metastasizing to the breast include melanoma<sup>4</sup>, hematopoietic malignancies<sup>5</sup> and carcinoma from the lung, genitourinary or gastrointestinal tract<sup>5-10</sup>. A clinical and radiological presentation of metastases may mimic both benign and malignant primary neoplasms. Fine-needle aspiration cytology (FNAC) or open biopsy of the breast masses is generally performed for diagnosis<sup>11-13</sup>. The importance of FNAC diagnosis is especially stressed, as this can make it possible to differentiate between a metastasis and a second primary tumor and thus to avoid unnecessary mastectomy and

ensure that appropriate chemotherapy and radiotherapy are implemented<sup>1</sup>. In most cases FNAC permits the correct diagnosis of a metastatic neoplasm but it is necessary to know the patient's clinical history and to perform immunocytochemistry stains on the smears, to arrive at a definitive diagnosis.

## Case Report

A 55-year old female, smoker (50 pack/years) suffered of a strong pain in her right shoulder and arm and lost 10 kg of weight for four months. Patient came with chest roentgenogram, CT and bronchoscopy findings done in another hospital. Chest radiograph followed by a computerized tomographic scan of the chest identified two suspected nodules in the left upper pulmonary lobe: first in the core of the lobe, beside pulmonary artery which infiltrate the mediastinum (in aorticopulmonary window) and second in the apex, on the border of anterior and apicoposterior segment of the lobe, 18 mm in its largest diameter. CT revealed also enlarged mediastinal and pretracheal lymph nodes and two well marginated lumps

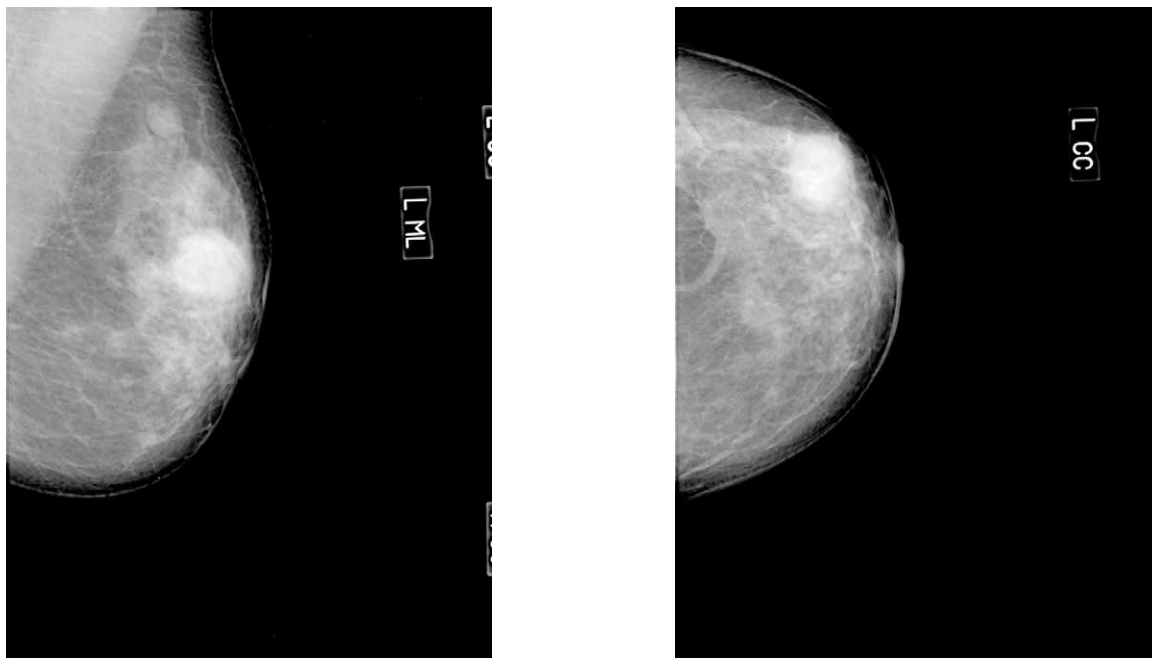


Fig. 1. and Fig. 2. Two breast masses with 27 and 15 mm in diameter in the upper outer quadrant of the left breast noted on mammography examination (in mediolateral and craniokaudal projection).

in the upper lateral quadrant of her left breast of 27 and 15 mm in its largest diameter which were not identified on five months old mammographic findings. Bronchoscopic examination was done but endobronchial cytology revealed no evidence of malignancy. Patient came to our hospital for further examination.

She had a firm mobile palpable lesion in the upper outer quadrant of her left breast, about 30 mm in its largest diameter which patient notice two weeks ago like

small mass with very rapid growth. Bronchoscopy was repeated and proved subsegmental orifice mucosa of anterior bronchi of the upper left pulmonary lobe, infiltrated with tumor. Bronchial washings and brushings specimens obtained by bronchoscopy revealed medium to large malignant cells isolated and in loosely cohesive groups, variable in size with dense, abundant and vacuolated cytoplasm and round to oval, usually eccentric nuclei, with finely granular chromatin and nucleoli. The cy-

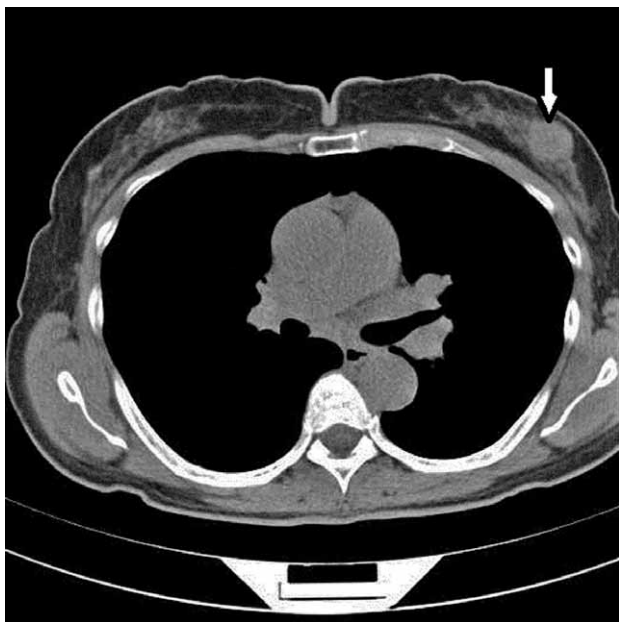


Fig. 3. and Fig. 4. The same two breast masses on CT examination.

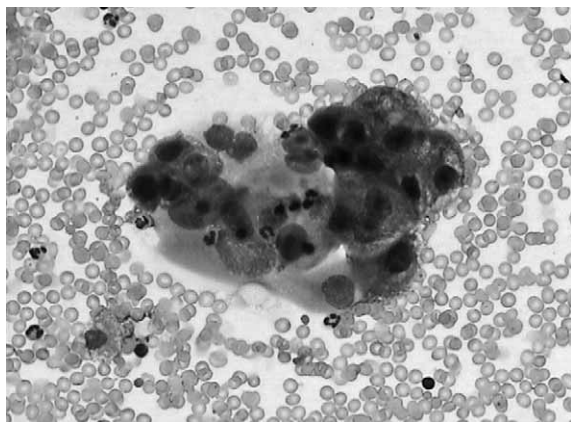


Fig. 5. One papillary group of adenocarcinoma cells, in bronchial washing specimen, variable in size with abundant and vacuolated cytoplasm and round to oval, usually eccentric nuclei, finely granular chromatin and prominent nucleoli. Some carcinoma cells containing neutrophils in their cytoplasm – emperipolesys phenomenon. (May-Grünwald-Giemsa stain, x200).

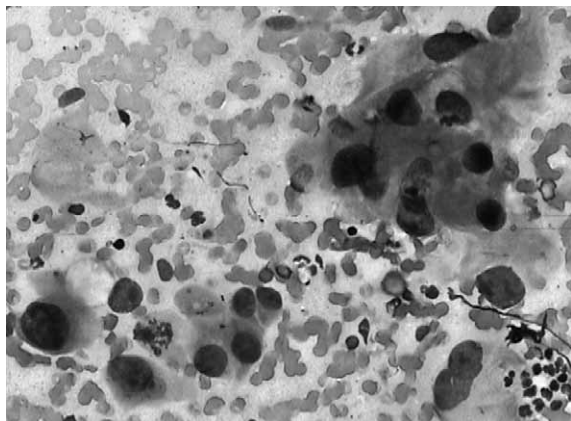


Fig. 6. Adenocarcinoma cells, in bronchial brushing specimen, isolated and in loosely cohesive groups, one carcinoma cell is in mitosis. Erythrocytes and some small lymphocytes and neutrophils in the background (May-Grünwald-Giemsa stain, x200).

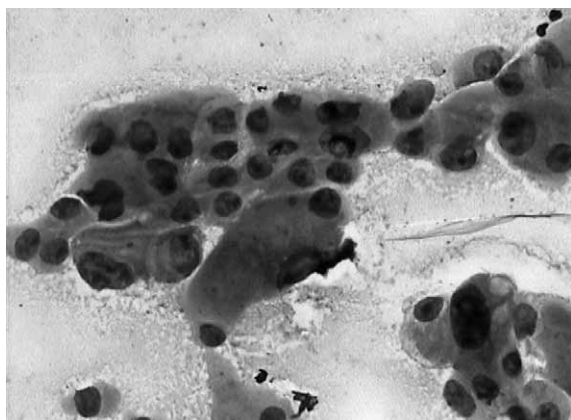


Fig. 7. Adenocarcinoma cells in FNAC specimens of the left breast show the same cytomorphology as in bronchial washing and brushing specimens (May-Grünwald-Giemsa stain, x200).

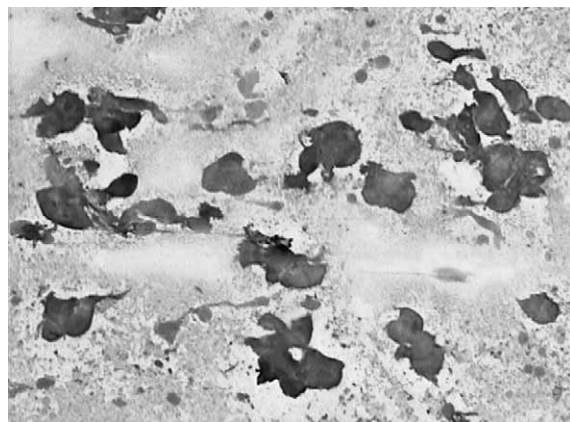


Fig. 8. Adenocarcinoma cells in FNAC specimen positive for cytokeratin 7 (Immunocytochemistry, x100).

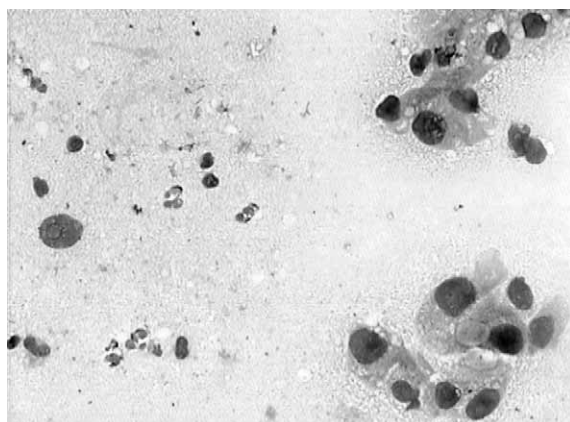


Fig. 9. Adenocarcinoma cells in FNAC specimen negative for cytokeratin 20 (Immunocytochemistry, x200).

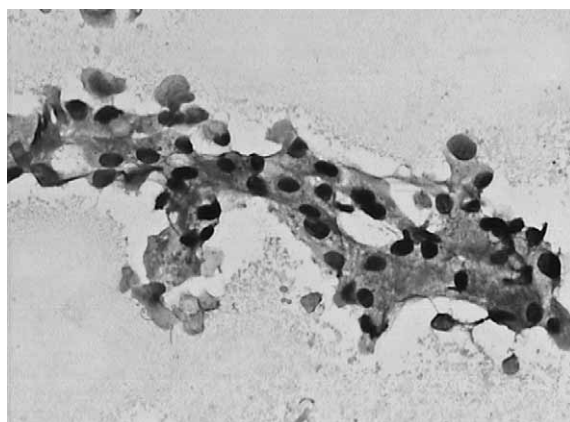


Fig. 10. Adenocarcinoma cells in FNAC specimen positive for thyroid transcription factor 1 (Immunocytochemistry, x200).

tological diagnosis was adenocarcinoma. Repeated mammography examination of her left breast showed two nodules in the upper outer quadrant of 20 and 30 mm in its largest diameter. Ultrasound examination was per-

formed with fine needle aspiration cytology of the biggest, 30 mm lesion of her left breast. FNAC was performed using 22-gauge needle. Slides were air-dried and stained using the May-Grünwald-Giemsa method. An FNAC procedure yielded abundant material consisting of a population of slightly cohesive groups as well as isolated malignant cells with abundant and vacuolated cytoplasm, round to oval eccentric nuclei and nucleoli. Adenocarcinoma was diagnosed. In our case, primary lung malignancy was known, so metastatic lesion was considered in the differential diagnosis of tumor of the breast. The cytological slides of the primary lung tumor were reviewed and compared with the fine needle aspiration cytological slides of the left breast. Immunocytochemistry was performed on the smear to corroborate the diagnosis and showed malignant cells positive for cytokeratin 7 and thyroid transcription factor 1 (TTF-1) and negative for cytokeratin 20. Metastatic lung adenocarcinoma was diagnosed. Patient started with therapy treatment in another hospital.

## Discussion

Metastasis to the breast from extramammary carcinoma is extremely rare<sup>14,15</sup>. In previously reported clinical series ranges from 0.5-2% of all breast malignancies<sup>16-18</sup> and in autopsy series, the range of the incidence is from 1,7-6,6%<sup>18,19</sup>. Metastatic lesions are not distinguishable from primary tumors clinically, radiologically and sometimes even cytopathologically. Besides leukemia or lymphoma, breast metastases have been reported to be most commonly from melanoma, rhabdomyosarcoma and the lung<sup>20</sup>. Metastases from solid organs, such as the lung, skin, kidney and stomach were more frequently in the earlier part of the last century and in the latter part of the last century involvement of the breast by hematologic malignancies is becoming relatively more common<sup>3</sup>.

Clinically, metastatic lesions are not distinguishable from primary tumors. Presentation with pain, tenderness and discharge is distinctly unusual<sup>11,21</sup>. A solitary lesion is the most common clinical presentation, while well-defined nodules have been seen in 11% of cases and diffuse involvement in 4%<sup>22</sup>. 26% of cases had bilateral lesions. The lesion tends to be superficially located in the upper outer quadrant. 25% of cases had adherence to the skin and nipple retraction never has been reported. Axillary lymph node involvement is frequently encountered<sup>1</sup>. Metastatic lesions may grow rapidly but the majority of cases present with a firm freely mobile lump mimicking benign disease. Rarely a large rapidly growing lesion may be confused with inflammatory breast carcinoma<sup>14</sup>.

Radiology may be more successful in differentiating the metastatic from primary tumor. Radiographic distinction is extremely difficult because of the wide spectrum of presentation of the metastatic nodules. They may mimic a primary breast carcinoma or even a benign abnormality radiographically. This includes presentation with single or multiple lesions with or without dermal involvement and almost always without microcalcifications

which occurs mainly in patients with metastatic ovarian carcinoma containing psammoma bodies<sup>23,24</sup>. Metastases are more likely to be multiple and frequently bilateral: perhaps owing to their centripetal growth, they form a nidus of tumor cells that are usually round with fairly well-defined margins<sup>21,25,26</sup>. In our presented case, the patient has multiple, well-circumscribed metastases. Lesions, that metastasize to the breast, presented on ultrasound examination like usually round or ovoid, with some degree of lobulation, with variable internal echoes ranging from scattered low-amplitude signals to heterogeneous fairly prominent reflections. The posterior echoes are usually preserved, and as with all round solid breast masses, relative enhancement may occur<sup>26</sup>. Most types of metastatic tumors in the breast can be accurately diagnosed by needle aspiration cytology or excisional biopsy if the patient has previously diagnosed non-mammary malignant neoplasms, but clinical correlation with previous specimens, special stains and immunocytochemistry are necessary for an accurate diagnosis<sup>27</sup>

Pathologically, it can be also difficult to recognize tumor as metastatic<sup>3</sup>. The distinction of primary breast malignancy from metastases on cytohistology is based on features not usually seen in primary tumors of breast, such as intracytoplasmic pigment melanin in melanoma, small undifferentiated cells in small cell lung carcinoma and hematopoietic cells. Difficulty arises in tumors with similar morphologic pattern as primary carcinoma of the breast<sup>28</sup>. Particularly in patients with metastatic adenocarcinoma diagnosis with recourse to immunocyto/histochemistry is difficult or impossible<sup>29</sup>. On the other hand, some primary breast tumors have unexpected morphologic appearances that can be mistaken for tumors usually encountered outside the breast. Examples of such tumors include primary signet ring carcinoma and pure squamous cell carcinoma of the breast<sup>3</sup>. There are some histologic indicators that may aid in recognition of secondary tumors. Azzopardi has commented that elastosis is a consistent indicator of primary neoplasms but is rarely seen in secondary tumors<sup>30</sup>. Lee et al. claimed that carcinoma in situ were seen only in primary mammary cancers<sup>31</sup>. Other factors for metastatic rather than primary origin include a sharp transition at the border of the lesion and the presence in the subcutaneous, rather than parenchymal breast tissue. Vergier and al. identified a number of characteristics typical of metastases, namely atypical histologic features for a primary breast carcinoma, a well-circumscribed tumor with multiple satellite foci, the absence of an intraductal component and the presence of many lymphatic emboli<sup>32</sup>.

In our case, after cytomorphological correlation of primary lung adenocarcinoma and fine-needle aspiration cytology specimens of the left breast, the possibility of metastases was considered first. Immunocytochemistry techniques are undoubtedly proved metastases of pulmonary origin. Adenocarcinoma of both, breast and lung show the same immunochemical pattern for cytokeratin 7 and 20, so we also used thyroid transcription factor 1

which nuclear reactivity serve as a marker of pulmonary origin. It is important to keep in mind that thyroid carcinoma may express this marker, so metastatic thyroid carcinoma to the lung is a potential diagnostic trap. In our case cytomorphological features eliminated thyroid origin of carcinoma. The treatment of secondary malignancy of the breast should be directed of the primary disease. Surgical therapy should be as conservative as possible and usually entails wide local excision.

In summary, in the evaluation of a patient presenting with a breast mass metastatic disease of the breast must be considered in the differential diagnosis. Aspiration cytology plays a major role in differentiating metastases from a primary breast tumor, but with complete knowledge of the clinical history of the patient. Unusual cytology pattern should raise the possibility of metastases and then immunocytochemistry staining can be very useful.

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## METASTAZA PLUĆNOG ADENOKARCINOMA U DOJCI DIJAGNOSTICIRANA CITOLOŠKOM PUNKCIJOM: PRIKAZ SLUČAJ

### SAŽETAK

Metastaze u dojku od strane primarnih malignih neoplazmi izvan dojke su vrlo rijetke. Točna dijagnoza maligne bolesti dojke je važna, kako za određivanje pravilnog terapijskog tretmana, tako i zbog izbjegavanja nepotrebnog radikalnog kirurškog zahvata. Metastaze plućnih karcinoma ne-malih stanica u dojku su ekstremno rijetke. Prikazujemo slučaj 55-godišnje žene sa metastazom adenokarcinoma pluća u dojku što je dokazano citološkom punkcijom i potvrđeno imunocitokemijskom obradom.