



ORIGINAL RESEARCH PAPER	Oncology
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METASTATIC LUNG ADENOCARCINOMA PRESENTING AS A CONTRALATERAL BREAST LUMP: A DIAGNOSTIC CHALLENGE.

KEY WORDS: carcinoma lungs, carcinoma breast, immunohistochemistry, Metastatic adenocarcinoma

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ABSTRACT	A 52-year-old Retroviral positive female presented with a painful lump in the right breast that had persisted for 2 months. She reported no pulmonary or abdominal symptoms. On physical examination, a small, well-defined, tender lump was noted in the upper outer quadrant of the right breast, which was fixed to the skin. Comprehensive investigations were conducted, including Fine Needle Aspiration Cytology (FNAC), excision biopsy, immunohistochemistry, and a PET scan. These investigations led to the diagnosis of primary lung adenocarcinoma with metastases to the breast and bone.
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BACKGROUND:

Although breast cancer is prevalent among adult females, metastasis to breast tissue from an extramammary malignancy is quite rare [1, 2]. Sitzentfrey, in 1907, was the first to publish a case of ovarian carcinoma metastatic to the breast [3]. Since then, a wide variety of malignancies have been reported to metastasize to the breast. According to the literature, the most common primary tumors are melanomas, leukemias, lymphomas, and renal adenocarcinomas [4]. For symmetrically paired organs, such as breasts, it is expected that metastases from any given malignancy via hematogenous spread would affect either breast equally. On the contrary, if metastasis occurs predominantly in one of the paired organs, it may imply that hematogenous spread is not the predominant route for metastasis. Despite the fact that the lung is the most common cancer site in terms of incidence and mortality, there are just a handful of published cases on pulmonary carcinomas metastasizing to the breast. The incidence has been reported to be 0.5–3% [1, 2], affecting patients with an average age of 57.4 years and showing a female predominance [5]. As rare as it is to see secondary metastasis to the breast, it is even rarer to see metastasis to the contralateral breast. Metastatic disease to the breast is an important diagnostic clinical dilemma because its treatment differs greatly from that of primary breast cancer.

ray revealed a homogenous radio-opacity in the left lung which was reported as consolidation changes in left lung (Fig 1). An excision biopsy with frozen section for clear margins was then performed, and the histopathological report (HPR) indicated an impression of invasive carcinoma of the breast or metastatic adenocarcinoma (Fig 2). Immunohistochemistry (IHC) was subsequently performed, which revealed immunopositivity for CK7, TTF1, Napsin A, and CEA, leading to a diagnosis of metastatic adenocarcinoma, consistent with metastasis from a primary lung tumor. A pulmonary core 12-gene panel identified an EGFR mutation (Exon 19 deletion), confirming the IHC diagnosis. Positron emission tomography (PET) scan showed an irregular heterogeneous mass lesion in the upper lobe of the left lung, measuring approximately 5.7 x 5.1 cm, with increased FDG uptake, likely representing the primary malignancy site (Fig 3). Additionally, extensive metabolically active sclerotic osseous metastasis was noted (Fig 4). A diagnosis of metastatic Adenocarcinoma was made. Patient was planned for 3 weekly/ 21 day cycle of PEM-CARBO (Inj Pemetrexed + Inj Carboplatin) with plan to repeat PET Scan after 6 cycles.

Case Report:

A 52-year Retroviral positive female presented with a lump in the right breast for 2 months and associated pain for the past 15 days. The patient had no history of trauma, fever with chills, weight loss, breathlessness, chest pain, hemoptysis, or abdominal pain/mass. General physical examination and vital signs were within normal limits. On inspection, a bluish spot measuring 0.5x0.5 cm was noted in the upper outer quadrant of the right breast, adjacent to the nipple. On palpation, a solitary lump approximately 1x1 cm was detected in the upper outer aspect of the right breast. It had a smooth surface with regular margins, was firm to hard in consistency, and was fixed to the skin but not to the underlying breast tissue. No axillary or supraclavicular lymph nodes were palpable. Systemic examination was normal. The breast ultrasound (USG) revealed features consistent with fibroadenoma. However, fine-needle aspiration cytology (FNAC) of the lump showed characteristics of poorly differentiated carcinoma or high-grade sarcoma. A chest X-

Fig 1: Chest Xray



Fig 2: Excision Biopsy



Fig 3: PET Scan

DISCUSSION:

Worldwide, lung cancer is the most common cancer in terms of both incidence and mortality, with 1.6 million new cases and 1.378 million deaths annually [9]. Approximately one-fifth of newly diagnosed lung adenocarcinomas present with distant metastases. The most common sites of metastasis are the brain, bone, liver, and adrenal glands, in decreasing order of frequency. Breast metastases from extramammary malignancies are rare. Patients with breast metastasis usually have widespread disease and a poor prognosis. In Surov's study [8], breast metastasis typically appeared as a solitary nodule rather than multiple lesions. Sixty percent of patients with metastatic breast cancer were diagnosed incidentally during staging for the primary cancer, with subsequent biopsy confirming the diagnosis in 70% of cases. Only 31% of the patients had a painful solitary nodule or multiple nodules, with or without axillary lymphadenopathy [5].

Thyroid transcription factor-1 (TTF-1) is expressed in 68-80% of lung adenocarcinomas and, with the exception of a single case reported by Klingen TA et al., has never been reported to stain positive in breast adenocarcinoma [7]. Napsin A is expressed in 80-90% of lung adenocarcinomas but is usually negative in breast cancer, making it a reliable biomarker for diagnosing lung adenocarcinoma. Cytokeratin 7 (CK7) can be identified in metastatic lung and thyroid cancers and is used to determine the origin of metastatic lesions. Estrogen receptor (ER) is expressed in 80% and progesterone receptor (PR) in 60% of breast cancers, whereas gross cystic disease fluid protein 15 (GCDFP-15) is expressed in 45-53% of breast cancers. GATA3 is positive in most metastatic breast cancers and urinary tract carcinomas. No single marker provides

100% specificity or sensitivity in identifying the origin of a metastatic tumor, so a comprehensive analysis using several markers is necessary. TTF-1, Napsin A, and CK7 are useful markers for lung adenocarcinoma, whereas ER, PR, HER2, and GATA3 are commonly used to identify breast cancer.

In the present case, the patient presented with a single painful lump, consistent with findings in Surov's study. Histopathology was not always conclusive; thus, immunohistochemistry (IHC) markers, especially TTF-1, Napsin A, CK7, and molecular studies such as EGFR mutations, were crucial in diagnosing and determining the tissue of origin [6,7]. The PET scan helped identify metastases and confirm the disease stage. Chemotherapy is the standard treatment for patients with metastatic lung adenocarcinoma, and the 5-year survival rate for advanced stages of lung adenocarcinoma is approximately 37%.

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