Medical and Research Publications
International Open Access

Case Report **Journal of MAR Oncology (Volume 5 Issue 6)**

Primary Lung Cancer masquerading as Breast Lump after Intercostal Drainage Tract Metastasis: A Case Report

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Received Date: May 02, 2023

Published Date: May 20, 2023

A 68-year-old, never-smoker female, developed cough with expectoration and shortness of breath in October 2021. She was evaluated and found to have Right sided pleural effusion. Fluid Microscopy, Malignant Cytology, and Acid-Fast Bacilli staining did not reveal any positive findings. The effusion recurred and Intercostal Drainage (ICD) tube was inserted in the Right pleural space in December 2021. She was empirically started on Anti-tubercular therapy from January 2022 and in February 2022 ICD tube was removed. In March 2022, she noticed a right breast lump which was painless in nature. Mammography corroborated a 1x0.4cm Right breast lesion at 9 o'clock position. She underwent a Right Breast Lumpectomy in April 2022. Histopathology of the lumpectomy was suggestive of an Invasive Papillary Carcinoma, Grade 2, Tumor size 1x0.9x0.3cm. Formal lymph node dissection had not been performed. Immunohistochemistry (IHC) staining on the Lumpectomy specimen was negative for Estrogen Receptor (ER), Progesterone Receptor (PgR), and Her2neu. She did not receive any oncologic treatment thereafter.

She presented to our centre in July 2022, with persistent cough, and right sided chest pain. Her ECOG performance status was 2 and had right sided basal crepts. Other systemic examination was unremarkable. Contrast Enhanced Computed Tomography (CECT) of the Chest, Abdomen, and Pelvis showed post operative changes in the right breast, loss of right lung volume with mediastinal shift to the right, multiple right sided pleural based nodules with loculated right pleural effusion, multiple left lung nodules, mediastinal and hilar lymphadenopathy. Fine Needle Aspiration Cytology of the pleural nodule was suggestive of Adenocarcinoma. The patient and her family were counselled regarding the mismatch of the histology of Papillary Carcinoma and its ER and PgR negativity and that further IHC was warranted to confirm its primary nature. However, the family were unwilling, at that point, to undergo further testing.

A working diagnosis of metastatic breast cancer was made but a differential diagnosis of primary lung cancer was considered. Chemotherapy was initiated with Nabpaclitaxel 100mg/m2 + Carboplatin Area-Under-the Curve 2 (AUC2) on D1, D8, D15 q28 day cycles. Post 3 cycles, there was partial response as per RECIST 1.1 on CECT scans. At this time point, in October 2022, the family consented for further evaluation. Histopathology review of formalin-fixed and paraffin-embedded blocks from lumpectomy was suggestive of Adenocarcinoma (Fig 1A). IHC revealed CK7+, CK20+, TTF1+, Napsin A+ (Fig 1B) and negativity for GATA3, ER, SOX10 suggesting a primary lung adenocarcinoma.

It was clinically correlated that the ICD tube had been placed at a similar position to where the patient first noticed her breast lump. This likely indicated that a pleural deposit tracked its way into the breast parenchyma through the ICD tract. Next Generation Sequencing was performed on the tumour sample

which detected an EGFR L858R pathogenic variant and TP53 likely pathogenic variant. She had completed 4 cycles of chemotherapy by then. Targeted therapy options were discussed with the family, and they opted for Afatinib 40mg/day. Further chemotherapy was withheld and Afatinib initiated in November 2022. At 3 months follow up, in Feb 2023, the patients' disease is in Partial remission as per RECIST 1.1 and required dose reduction to 30 mg/day for skin and gastrointestinal toxicity. She is currently on the same dose as of 1st May 2023.

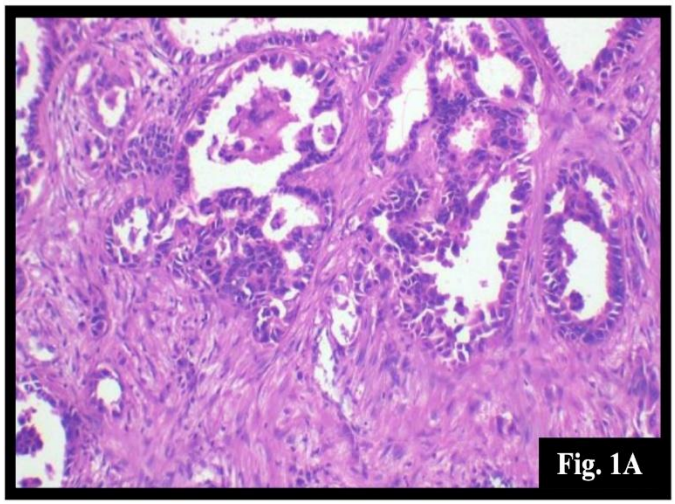

Fig. 1A: Photomicrograph showing Adenocarcinoma (H&E)

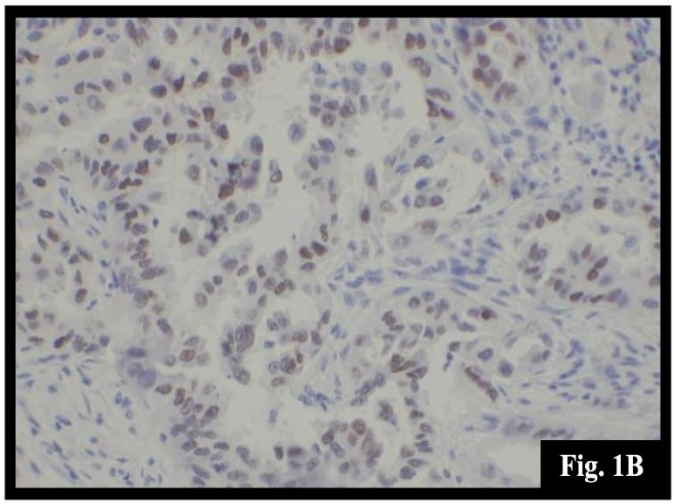

Fig. 1B: Photomicrograph showing positive staining with TTF1 (IHC)

Discussion

The diagnosis of pulmonary malignancies has become increasingly challenging with the incorporation of molecular biomarkers in addition to immunohistochemistry. The 2015 WHO classification of lung cancer was the first to introduce IHC to reflect the biologic differences of Adenocarcinoma and Squamous Cell carcinoma[1]. Additionally, assessing the true origin of the tumour also requires a detailed history to be communicated to the pathologist for clinical correlation. The delay in diagnosing primary lung adenocarcinoma, for the case in question, epitomizes this aspect. With the history of a breast lumpectomy, the initial IHC panel only incorporated ER, PgR, and Her2neu. The papillary histology did not correlate with its ER negativity. In majority of cases, invasive papillary carcinoma is ER and PgR positive[2]. This prompted us to evaluate further but were limited by logistical constraints.

As chemotherapy could not be delayed any further, due to the symptom burden, Nabpaclitaxel + Carboplatin was initiated keeping in mind its response rates in both metastatic breast cancer[3] as well as

non-small cell lung cancer (NSCLC)[4]. A substantial overall survival benefit has also been observed in elderly population in NSCLC[5]. Our patient, being elderly, tolerated the infusions well with no Grade 3 toxicities and had a partial response.

The role of biomarker testing in NSCLC cannot be understated. Driver mutation testing for EGFR, ALK, and ROS1 is a category IA recommendation as per the Pan-Asian adapted Clinical Practice Guidelines[6]. Recent data suggests that 26% of NSCLC patients who underwent mutational testing had an EGFR activating mutation[7]. NSCLC with an oncogenic driver mutation carries a better prognosis, which is forfeited if the patient does not receive the corresponding target therapy. The median survival of metastatic NSCLC patients with an oncogenic driver mutation who received target therapy was 3.49 years versus 2.38 years in those that did not receive the corresponding target therapy[8]. Thus, on detection of driver mutation, we shifted the patient to EGFR based therapy.

Needle tract metastasis to chest wall/breast have been previously reported in literature as a rare complication following percutaneous procedures[9 – 11]. To our knowledge, this is the first case report describing an intercostal drainage tract metastasis to the breast.

Conclusion

Our case highlights the role of clinicopathologic correlation in diagnosis of malignancies. The history and clinical findings influence the pathologists' choice of relevant IHC markers. The non-communication led to a delay in the diagnosis of a driver mutation positive NSCLC. However, our patient responded well the chemotherapy and current target therapy use would improve her survival outcomes while maintaining quality of life. To summarise, clinico-radio-pathologic correlation and multidisciplinary approach are of prime importance in the diagnosis and management of malignancies.

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