JCOMS eISSN:2783-3127 https://journalofcoms.com

Journal of

Current Oncology and Medical Sciences

Vol. 3, No.4

Case report Free Access

Synchronous primary malignancies of the lung and breast: a rare case report

Abeer Mundher Ali [1], Ahmed Dheyaa Al-Obaidi [2], Mazin Judy Ibrahim [2], Mustafa Najah Al-Obaidi [2], Muhammad Khuzzaim Khan [3]*, Hashim Talib Hashim [2]

[1] Al-Kadhimiya Teaching Hospital, Baghdad, Iraq

[2] University of Baghdad, College of Medicine, Baghdad, Iraq

[2] Dow University of Health Sciences, Karachi, Pakistan

Abstract

Introduction: Multiple Primary Malignant Tumors (MPMT) are two or more distinct primary cancers in a single patient, either occurring simultaneously (synchronous) or at different times (metachronous). MPMTs are very rare, with an incidence of 0.73% to 11.7% among cancer patients. Breast and lung cancers are the most common malignancies in women, but their coexistence as MPMT is uncommon.

Case presentation: We report the case of a 51-year-old non-smoking woman who had a productive cough with bloody sputum for a week, after a two-month history of dry cough. She was diagnosed with a high-grade, poorly differentiated non-keratinizing squamous-cell carcinoma in the right lung. A PET scan also revealed a poorly defined soft tissue mass in the central sector of the right breast, which was confirmed to be a primary invasive ductal carcinoma.

Discussion: The etiology and pathogenesis of MPMT are unclear, but several factors such as genetic predisposition, environmental exposure, immunodeficiency, and treatment-related effects have been proposed. The diagnosis and management of MPMT are challenging, as they require careful evaluation of each tumor and individualized treatment plans. The prognosis of MPMT depends on the stage and histology of each tumor, as well as the patient's performance status and comorbidities.

Conclusion: This case report highlights the rare occurrence of synchronous primary malignancies in the lung and breast, underreported in the medical literature. This case adds to the existing knowledge of MPMT and may stimulate further research on this topic. Clinicians should be aware of the possibility of MPMT in cancer patients and perform thorough investigations to rule out secondary or metastatic tumors.

Keywords: Small cell carcinoma, Breast cancer, Synchronous, Metachronous, Histopathology, Immunochemistry,
Recieved: 2023.10.20, Accepted: 2023.12.25

Corresponding Authors: Muhammad Khuzzaim Khan

✉ Email: khuzzaimkhan@yahoo.com

Recieved: 2023.8.13, Accepted: 2023.10.24

Introduction

Multiple primary malignant tumors (MPMT) are two or more separate primary cancers in one patient. They can be synchronous (discovered within six months) or metachronous (discovered after six months). MPMT are very rare, affecting 0.73% to 11.70% of cancer patients (1). Small-cell lung cancer (SCLC) and invasive ductal carcinoma (IDC) are the most common cancers in women, but their coexistence as MPMT is uncommon. SCLC is a fast-growing and aggressive lung cancer linked to smoking (2). IDC is the most frequent type of breast cancer, making up 75% of all cases (3). Usually, when both cancers are found, one is a metastasis from the other. Chest X-rays and CT scans are used to diagnose lung metastases from breast cancer or primary lung tumors (4). However, our case report describes a rare situation: a patient with both breast cancer and primary lung cancer detected by PET scan. The breast cancer was confirmed to be a separate primary tumor. This unusual case challenges the conventional understanding and highlights the complexity of MPMT. The purpose of this article is to report this rare case and contribute to the existing knowledge and research on MPMT.

Case presentation

A 51-year-old female, a non-smoker, presented with a distressing clinical profile. She experienced a productive cough accompanied by bloody sputum for one week. This was preceded by a two-month history of dry cough, which coincided with the onset of gradually increasing shortness of breath, notable fatigue, decreased appetite, and significant weight loss. Her weight had declined from 67 kg to 58 kg within three months. She denied any chest pain or fever. Her medical history, surgical history, and family history did not reveal any predisposition to cancer.

Initial evaluation included a chest X-ray that revealed severe right-sided pleural effusion. Subsequently, a contrast-enhanced chest CT scan depicted moderate right-sided pleural effusion (as depicted in Figures 1A and 1B). The scan also unveiled complete occlusion of the bronchus intermedius, along with total collapse of the right middle lobe (Figure 1C). Additionally, the right upper lobe exhibited interlobular septal thickening, and the right lower lobe displayed partial collapse accompanied by extensive fibrotic changes (figure 1D). While no definitive obstructive mass was evident, the presentation prompted further investigation through bronchoscopy.

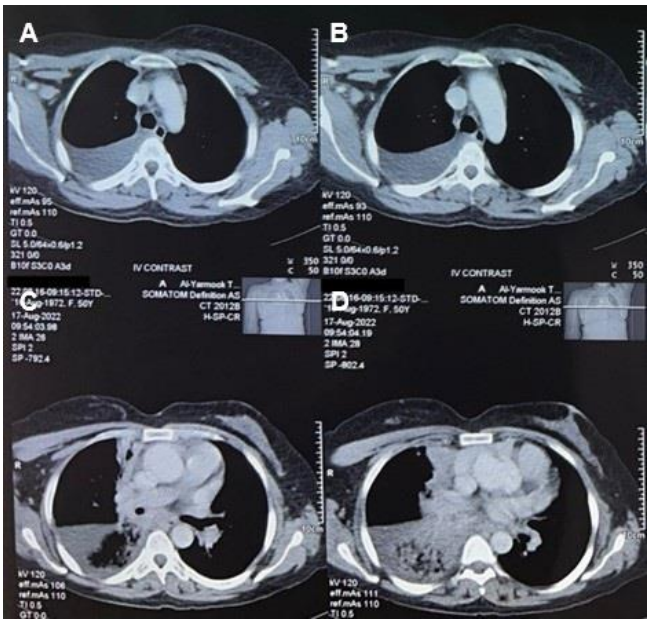

Figure 1. chest CT scan findings. Chest CT scan with IV contrast displaying distinct aspects of the patient's condition: A and B: Moderate right-sided pleural effusion. C: Total occlusion of the bronchus intermedius along with complete collapse of the right middle lobe. D: Interlobular septal thickening in the right upper lobe, accompanied by partial collapse of the right lower lobe, revealing extensive fibrotic changes.

Bronchoscopy, conducted under local anesthesia, revealed partial occlusion of the bronchus intermedius, attributed to mass effect, leading to obstruction of the middle and lower lung lobes. Subsequent lung biopsy disclosed a histopathological profile consistent with high-grade, poorly differentiated non-keratinizing squamous-cell carcinoma. Noteworthy characteristics included tumor infiltration in single and solid sheets with dense desmoplastic fibrosis, limited lymphocytic infiltration between tumor cells, and absence of stromal lymphovascular and peri-neural tumor involvement. Immunohistochemistry confirmed positive cytokeratin 5/6.

Further investigations were carried out to assess metastatic spread. A PET scan revealed Fluorodeoxyglucose (FDG) uptake in several regions. An ill-defined mass lesion in the right lung hilum (6.14.5 cm) exhibited maximum standardized uptake

value (SUVmax) of 19.2 (Figure 2A). FDG uptake was also noted in prevascular lymph nodes, bilateral paratracheal, right hilar, and subcarinal (Figure 2B, 2D). The largest node measured 3.11.7 cm with SUVmax 4.4. Additionally, a poorly defined soft tissue dense lesion (1.5*0.8 cm) in the central sector of the right breast displayed SUVmax of 5.9 (figure 2C). A smaller, benign-appearing nodule was observed in the upper inner quadrant of the right breast (Figure 2C).

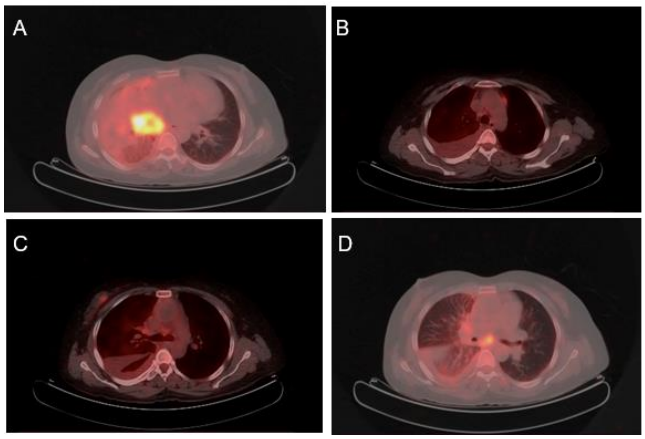

Figure 2. FDG-PET scan results. FDG-PET scan images showcasing notable observations: A: Reveals FDG uptake in an ill-defined mass lesion located in the hilar region of the right lung, involving bilateral paratracheal and right hilar lymph nodes. B: Illustrates FDG uptake in the prevascular lymph nodes. C: Demonstrates FDG uptake in an unwell-defined, dense soft tissue mass lesion in the central sector of the right breast. Additionally, it reveals the absence of significant FDG uptake in a smaller, dense soft tissue nodule located in the upper inner quadrant of the right breast. D: Displays FDG uptake in the subcarinal lymph nodes.

Ultrasonography of the right breast revealed an irregular ill-defined hypoechoic mass (16.6*10mm) within the subareolar region, along with internal echogenic foci (calcifications) classifying it as BI-RAD score four (Figure 3).

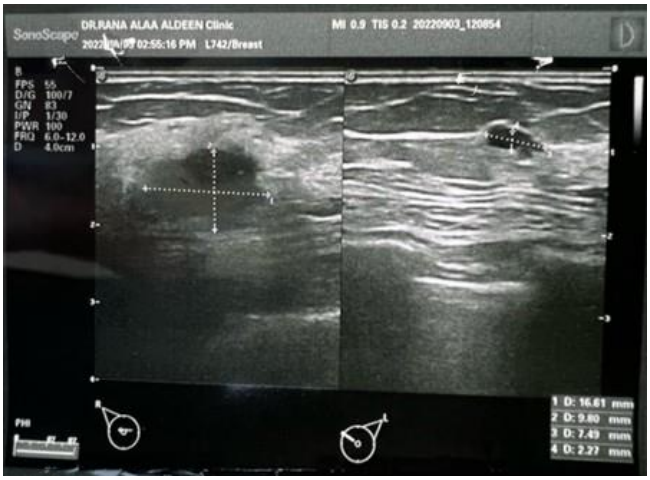

Figure 3. Breast ultrasonography findings. Breast ultrasonography image presenting specific features of interest: This image demonstrates: An irregular and ill-defined hypoechoic mass in the right breast, measuring 16.6 mm by 10 mm. The presence of internal tiny echogenic foci, indicative of calcifications. Notably, the mass is situated within the subareolar region.

Subsequent fine-needle aspiration (FNA) confirmed malignant features, displaying hyperchromatic irregular nuclei in clusters and scattered epithelial cells within a necrotic background (Figures 4A and 4B).

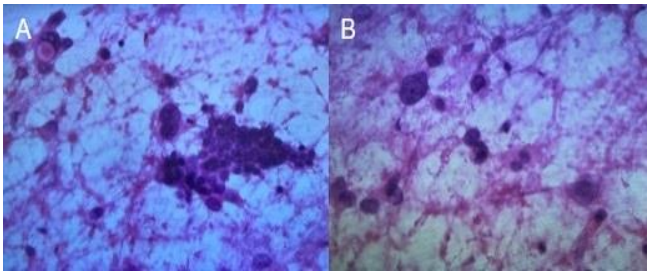

Figure 4. Cytological smears with H&E staining. Cytological smears stained with H&E, highlighting specific cellular characteristics: A and B: Depict clusters and scattered malignant epithelial cells, featuring hyperchromatic irregular nuclear borders and pleomorphic nuclei. These cells are set against a necrotic background.

Utilizing ultrasound guidance, a cell-block preparation of the right breast mass exhibited hyperchromatic and pleomorphic malignant cells with intermediate-grade nuclear atypia. Focal tubular differentiation and infiltration into fatty tissue were evident (Figures 5A and 5B). These findings corresponded to invasive ductal carcinoma (not otherwise specified), supported by immunohistochemistry results including positive CK7 and negative p63.

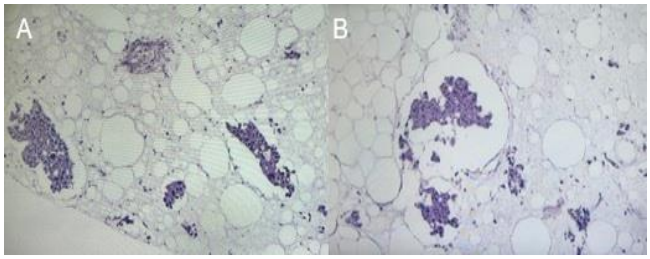

Figure 5. Cell-block preparation with H&E staining.

Cell-block preparation stained with H&E, emphasizing distinctive cellular attributes: A and B: Display hyperchromatic and pleomorphic malignant cells exhibiting intermediate-grade nuclear atypia. Notably, a focal region of tubular differentiation is also evident within the preparation.

Slide review and immunohistochemistry of the lung biopsy highlighted scattered malignant cells intermingled with inflammatory cells. Positive CK7 and absence of p63 confirmed epithelial origin, excluding lymphoma and small-cell carcinoma. The overall histopathology and immunohistochemistry aligned with poorly differentiated carcinoma exhibiting positive ER (3+5 8/8) and HER2 (score +3).

Collectively, these findings indicated the presence of two distinct cancerous lesions, each originating in different tissue types, with no evidence of metastasis between sites. The patient was eligible for palliative chemotherapy with trastuzumab and carboplatin, targeting both lung and breast cancers. Trastuzumab is a monoclonal antibody that binds to the HER2 protein, which is overexpressed in some cancers, and blocks its activity and triggers immune reactions that kill cancer cells. Carboplatin is a platinum-based drug that damages the DNA of cancer cells and prevents them from dividing. This combination is effective and well-tolerated in patients with HER2-positive breast cancer and may also have activity in HER2-positive lung cancer. The patient received an 8 mg/kg loading dose of trastuzumab followed by 6 mg/kg every three weeks, along with 5 mg/kg carboplatin every three weeks for at least six cycles. The expected outcomes of this treatment were to control the disease progression, reduce the tumor burden, and improve the quality of life. The potential side effects of this treatment included nausea, vomiting, fatigue, hair loss, low blood counts, infection, allergic reaction, kidney damage, nerve damage, and heart damage. The patient was monitored for these side effects and received supportive care as needed.

Discussion

Multiple primary malignant tumors (MPMT) are becoming more recognized due to improved diagnostic methods. However, diagnosing multiple primary lung cancers is still challenging, especially when they have the same histology. Gene mutation analysis can help to differentiate between primary and metastatic tumors (5). Synchronous breast and lung cancers are very rare, accounting for less than 0.5% of breast cancer cases. A study by Burstein et al. showed that 55% of lung lesions in women with breast cancer were primary lung cancers, 37% were metastases, and 8% were benign (6). This highlights the need for accurate histological diagnosis of lung lesions, as some of them may be treatable. This also follows the criteria by Warren and Gates for diagnosing MPMT, which require biopsy confirmation, distinct pathology, and exclusion of metastasis (6). De Luca et al. reported a case of synchronous skin and breast cancer and discussed the frequent co-occurrence of dual primary breast and lung cancers. They attributed this to three factors: the high prevalence of breast cancer in women, the good prognosis of early-detected breast cancer leading to an increased risk of secondary tumors, and the increased susceptibility of breast cancer survivors to develop primary lung tumors (7). Jin et al. described another rare case of a woman with lesions in the left breast and both lower lung lobes. They found that the lung lesions had different EGFR gene mutations, indicating genetic heterogeneity among primary malignancies (8). Hu et al. also studied the relationship between breast and lung cancers and found a strong correlation between EGFR mutation in lung cancer and hormone receptor expression in lung tissue. However, they did not find any association between EGFR mutation and HER2 expression, suggesting a possible role of sex hormones in lung cancer development in these patients (9). Besides breast and lung cancers, patients with breast cancer may also develop primary tumors in other organs, such as the ovaries, uterus/endometrium, colorectum, kidneys, pancreas, and thyroid. These occurrences may manifest synchronously or metachronously, often influenced by factors such as hormonal treatment for the primary breast tumor

(notably, a strong link exists between endometrial cancer and tamoxifen), genetic predispositions (e.g., BRCA1 and BRCA2 mutations), and obesity. Incidence rates fluctuate, with reported figures ranging from 4.1% by Kim and Song in a study tracking 108 breast cancer patients, to 16.4% by Weir et al., who followed a larger cohort of 301,963 patients (10). However, the convergence of multiple distinct cancer types, exemplified by the case presented here, remains a rare phenomenon.

This case report presents a rare occurrence of synchronous primary malignancies in both the lung and breast, which is underreported in the medical literature. This case adds to the existing knowledge of MPMT and may stimulate further research on this topic. Future directions for research may include genetic profiling, targeted therapies, or novel treatment approaches that could improve our understanding and management of these rare synchronous malignancies.

Our study has some limitations that should be considered when interpreting our results. First, our sample size was small, consisting of only one patient with synchronous primary malignancies in both the lung and breast. Therefore, our findings may not be generalizable to other patients with similar conditions. Second, our study was a case report, which is a descriptive and observational type of study that does not provide causal evidence or test hypotheses. Therefore, our study cannot establish the etiology, pathogenesis, or prognosis of these rare synchronous malignancies. Further studies with larger and more diverse samples are needed to confirm and expand our findings.

Author contribution

MKK, **MJI**, and **AMA** contributed to the conception and design of the manuscript. **MKK**, **MJI**, **HTH**, and **AMA** supervised the project. **MKK**, **MJI**, **MNA**, **HTH**, and **ADA** provided the materials and contributed to data collection and processing. **ADA**, **MJI**, **MKK**, **MNA**, **HTH** and **AMA** contributed to the interpretation and analysis of the project. **ADA**, **HTH**, and **MNA** contributed to the literature review and writing of the manuscript respectively. **ADA**, **MNA** and **AMA** critically revised the manuscript.

IRB approval

The case report was approved for publication by the University of Baghdad's Institutional Review Board under the ethics code UB/2023/022.

Ethics Statement

The manuscript complies with the ethical recommendations of the Declaration of Helsinki of the World Medical Association

Conflict of interest

The authors declare no conflict of interest.

Funding/Support

No institutional or financial support was received.

References

1. Jin B, Zhang S, Chuang X, Yu P, Chen Y, Teng Y, et al. Breast cancer and synchronous multiple primary lung adenocarcinomas with heterogeneous mutations: A case report. BMC Cancer. 2018;18(1):2–7.
2. Holly A. Swartz, Jessica C. Levenson and EFU. HHS Public Access Small-cell lung cancer. Physiol Behav. 2012;43(2):145–53.
3. Waks AG, Winer EP. Breast Cancer Treatment: A Review. JAMA. 2019;321(3):288-300. doi:10.1001/jama.2018.19323
4. Paul Spiteri Meilak B. The relationship between primary breast and primary lung cancer: A case series. Int J Case Reports Images. 2020;11(July):1.
5. Lekos A, Glantz MJ. Diagnosis in oncology. J Clin Oncol. 1997;15(8):3019–20.
6. De Luca A, Frusone F, Vergine M, Cocchiara R, Torre G La, Ballesio L, et al. Breast cancer and multiple primary malignant tumors: Case report and review of the literature. In Vivo (Brooklyn). 2019;33(4):1313–24.
7. Hu Z, Zou X, Qin S, Li Y, Wang H, Yu H, et al. Hormone receptor expression correlates with EGFR gene mutation in lung cancer in patients with simultaneous primary breast cancer. Transl Lung Cancer Res. 2020;9(2):325–36.
8. Vogt A, Schmid S, Heinimann K, Frick H, Herrmann C, Cerny T, et al. Multiple primary tumours:

Challenges and approaches, a review. ESMO Open. 2017;2(2):1–12.
9. Kim JY, Song HS. Metachronous double primary cancer after treatment of breast cancer. Cancer Res Treat. 2015;47(1):64–71.
10 . Weir HK, Johnson CJ, Thompson TD. The effect of multiple primary rules on population-based cancer survival. Cancer Causes Control. 2013;24(6):1231–42.