

# The relationship between primary breast and primary lung cancer: A case series

Bernard Paul Spiteri Meilak

## ABSTRACT

**Introduction:** Prior to the initiation of curative treatment, patients with a confirmed breast malignancy undergo staging to assess for the presence of any metastasis. There are instances where instead of metastatic lesions, the patient is diagnosed with a primary lung malignancy. This is identified when the patient is given chemotherapy directed at the breast primary, but the lung lesion does not improve on imaging. Lung biopsy then confirms this diagnosis.

**Case Series:** This case series highlights three such patients who were treated at Mater Dei Hospital, Malta. All three were first diagnosed with the breast malignancy and were later found to have a second primary in the lung. Management of these patients was always through a multidisciplinary team approach, involving the breast surgeons, cardiothoracic surgeons, the oncologist, respiratory physicians, breast and lung specialized radiologists, and the breast care nurses. Relevant literature is also discussed with a focus on synchronous breast and lung malignancies.

**Conclusion:** The main conclusion from this case series is that it would be beneficial if all patients with breast cancer are regularly screened for a lung malignancy/metastasis by at least a chest X-ray. It is important to keep in mind the link between the two organs and the potential presence of a separate lung primary.

**Keywords:** Incidental findings, Primary breast, Primary lung

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## INTRODUCTION

Primary breast cancer is known to metastasize mainly to the lung, and so the patients are always staged with a chest X-ray to check for lung metastasis before treatment is initiated. If a lesion is detected, further investigation with a computed tomography (CT) thorax will be carried out to characterize the lesion further. This will initially be suspected to be metastasis from the breast primary, however there are cases where this could be an incidental finding of a lung primary. If the patient is given chemotherapy and the breast tumor resolves but the lung lesion does not, it is important to consider other diagnoses. These incidental findings are then biopsied and treated appropriately. This case series illustrates three patients who had primary breast cancer with an incidental finding of primary lung cancer. This was discovered on the preoperative chest X-ray that is performed for all breast patients. In all three situations the lesion was initially thought to be metastasis from the breast, but it failed to resolve when the patient was given targeted treatment for the breast cancer. Further investigations then confirmed the true nature of the lung lesion as a new primary.

## CASE SERIES

### Case 1

Patient A, a female aged 70, felt a lump in her left breast on self-examination. She presented to her general

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practitioner (GP) who referred her to the Breast Clinic. The lump was described as hard and non-tender to palpation with no overlying skin or breast changes. A mammogram and ultrasound of the breast were performed, and these confirmed the presence of a 2.5 cm lesion in the left upper outer quadrant. The case was discussed at the weekly breast multidisciplinary meeting where it was decided to take a biopsy. Ultrasound-guided biopsy showed that it was a grade 2 invasive ductal carcinoma which was estrogen receptor (ER) positive and human epidermal growth factor receptor 2 (HER2) positive. The case was re-discussed, and it was decided to do a wide local excision and sentinel lymph node biopsy.

The patient attended the preoperative assessment clinic where the chest X-ray revealed a 1 cm nodule in the left middle lung zone (Figure 1). A CT thorax, abdomen, and pelvis was also performed which showed the breast lesion together with left pulmonary nodules, initially seen as suggestive of metastasis (Figure 2). Surgery was therefore postponed, and she was referred to oncology where she was administered chemotherapy using vinorelbine, herceptin, and letrozole. The breast lump regressed but the lung lesion persisted as shown by further imaging. The patient was referred to the cardiothoracic surgeons who performed a wedge resection of the left upper lobe. Histology showed a well-differentiated neuroendocrine carcinoma, demonstrating that this patient had two primaries.

The breast lump was no longer palpable, but ultrasound showed an irregular hypoechoic lesion still present. Further biopsies confirmed the presence of grade 1 invasive ductal carcinoma ER positive and HER2 positive. Ultrasound wire guided wide local excision and sentinel lymph node biopsy was then performed with



Figure 1: Preoperative chest X-ray showing a 1 cm nodule in the left middle lung zone.

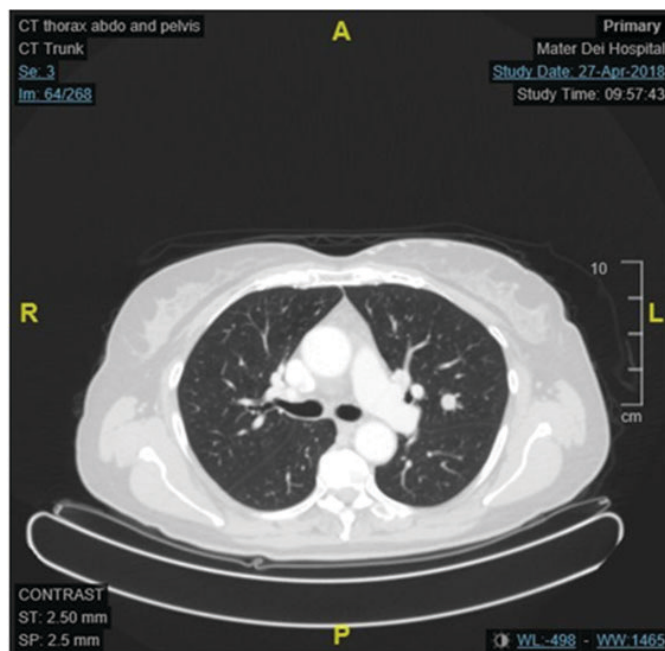


Figure 2: CT thorax, abdomen, and pelvis showing left pulmonary nodules.

complete excision of the lesion and negative lymph nodes, followed by radiotherapy.

## Case 2

Patient B, an 81-year-old female, presented with upper chest discomfort which developed over a few months. A chest X-ray was performed, and it showed air space shadowing in the right upper lobe, with a recommendation for a CT thorax. This showed a lesion in the right upper lobe with surrounding consolidation and mildly enlarged lymph nodes in the left axilla, with the findings suggestive of peripheral lung cancer with left axillary lymphadenopathy (Figure 3).

The patient was reviewed by the respiratory physicians who detected a lump in the left breast on clinical examination. They therefore referred her to a breast surgeon who ordered a mammogram. This confirmed the presence of an irregular opacity with internal microcalcifications in the left upper inner quadrant and smaller clusters in the left upper inner and left deep retroareolar region. Core biopsies were therefore performed which demonstrated grade 2 invasive ductal carcinoma with metastasis to the lymph nodes.

The impression therefore was that this patient has primary breast cancer with lung metastasis. However, CT-guided lung biopsy showed well differentiated adenocarcinoma of the lung. A right upper lobe wedge resection was then performed.

The patient was offered surgery for her primary breast cancer. However, she initially refused and was therefore given tamoxifen which caused initial regression of the tumor. She then accepted to undergo wide local excision and axillary clearance. This confirmed metastasis with

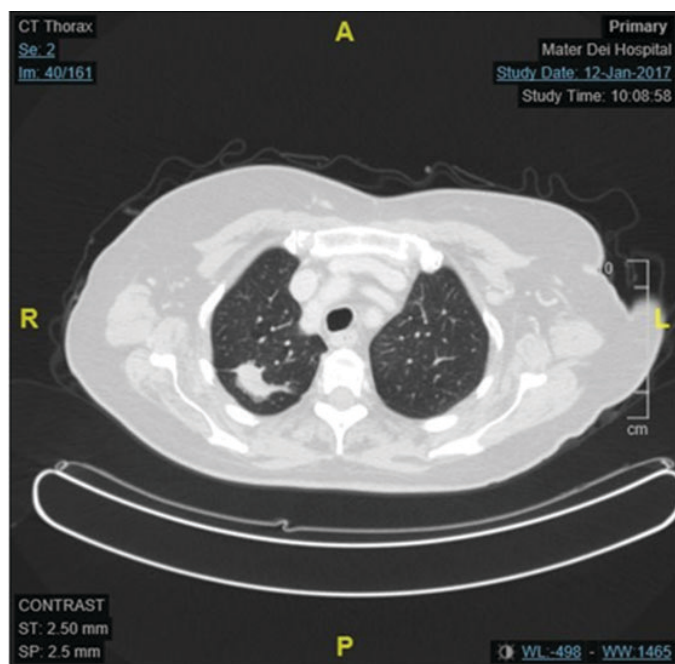


Figure 3: CT thorax showing a lesion in the right upper lobe with surrounding consolidation and left axillary lymphadenopathy.

extra capsular invasion in two out of the four lymph nodes removed. She was therefore given radiotherapy and continued on tamoxifen for a further two years. This was then changed to letrozole.

### Case 3

Patient C is an 81-year-old female who presented to the breast clinic with a painless lump in her right breast just above the areola, which was mobile with a rubbery hard consistency. No pathological lymph nodes were felt on examination. She was referred for one stop assessment where the mammogram demonstrated a spiculated opacity in the right supra-areolar region, with a smaller lesion in the right upper inner quadrant. Another spiculated lesion was detected in the left lateral breast. Core biopsies of these lesions showed three foci of grade 2 invasive ductal carcinoma, ER negative, and HER2 positive.

The patient was prepared for surgery, but during the routine chest X-ray a 1.6 cm lesion was detected in the right upper lung zone (Figure 4). Notwithstanding this, she still proceeded to bilateral wide local excision and sentinel lymph node biopsy. This confirmed grade 1 invasive ductal carcinoma on a background of low/intermediate grade of ductal carcinoma in situ (DCIS) with perineural invasion on the left, and grade 3 invasive ductal carcinoma on a background of high-grade DCIS with no angiolymphatic or perineural invasion on the right. The sentinel lymph nodes were negative bilaterally.

In view of the lung lesion, the patient underwent a CT thorax. This confirmed the presence of a 2.1 cm cavitating lesion in the right upper lobe (Figure 5). The differential diagnosis included a primary lung tumor or

a metastatic lesion from the breast. The latter option was deemed to be unlikely and so she was referred to a respiratory physician. The case was discussed at the chest team meeting which decided that the lesion appeared as a squamous cell carcinoma, later confirmed on CT-guided biopsy. Positron emission tomography (PET)/CT excluded any metastasis except for some right hilar and mediastinal lymph nodes. The patient was referred to the cardiothoracic surgeons for wedge resection.

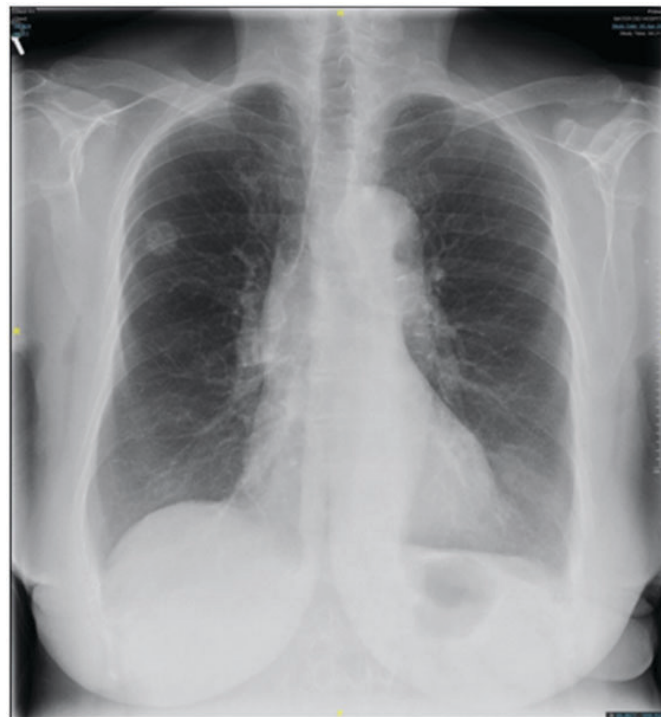


Figure 4: Preoperative chest X-ray showing a 1.6 cm lesion in the right upper lung zone.

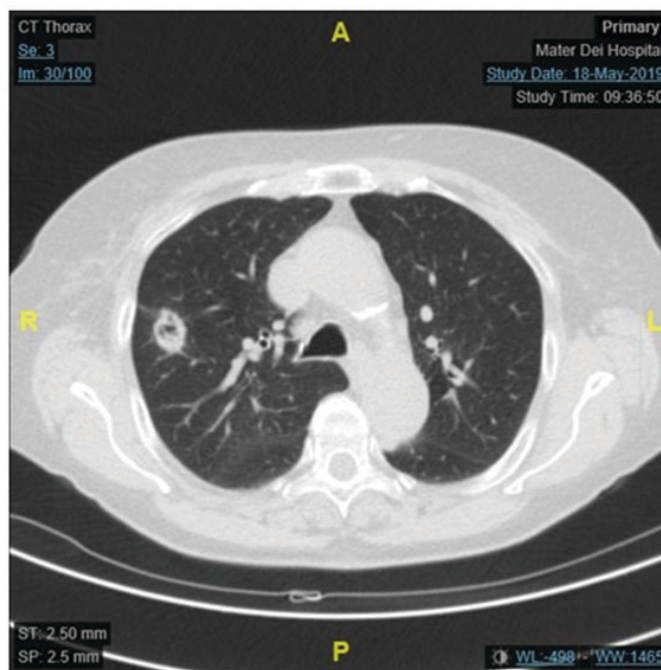


Figure 5: CT thorax showing a 2.1 cm cavitating lesion in the right upper lobe.

## DISCUSSION

The differential diagnosis of a lung lesion detected in a patient with known breast cancer is either metastatic disease or a lung primary. Synchronous breast and lung malignancy are a rare occurrence, found in less than 0.5% of breast cancer patients [1]. Burstein et al. report that lung lesions detected in women with confirmed breast cancer represent primary lung cancer in 55%, metastasis in 37%, and benign etiology in 8% [1]. This is highly significant and investigating the lung lesion further with a histological diagnosis is indicated since more than half are malignant with potential treatment options. A similar case report was published in the *World Journal of Respiriology* in 2017 by de Macedo [2]. It states that synchronous tumors have an incidence of 0.73–11.7%, and their diagnosis is increasing thanks to better diagnostic techniques and longer life expectancy [3, 4]. The author used the criteria developed by Warren and Gates [5] for the diagnosis of multiple primary malignancies where all lesions must be malignant as confirmed by biopsy, each biopsy must show different pathology and any metastasis from the initial lesion must be excluded. All these are suitable for the cases discussed above.

In a literature review carried out in a case report about a patient who suffered from a synchronous breast and skin malignancy, De Luca et al. report that double primary breast and lung cancer commonly coexist in the same patient. They found that this association could be explained by considering three important factors: malignancy of the breast is the commonest affecting women worldwide; early diagnosis of a breast malignancy results in a good prognosis with a longer life expectancy and a resultant increased risk of developing a secondary tumor; and patients with a history of a breast malignancy are at an increased risk of developing a primary lung tumor [6].

A similar case was also reported by Jin et al. in a case report which was published in 2018 in the *BMC Cancer Journal*. They describe a 57-year-old woman who presented with three lesions: one in the left breast, one in the left lung lower lobe, and another in the right lung lower lobe. Genetic studies on each of the lesions showed that they were three separate primaries, with the lung lesions being distinguished by a difference in the EGFR gene mutation [7]. This gene mutation was also observed in a study carried out by Hu et al., where they tried to identify a correlating factor between double primary breast and lung cancers. They found that in these patients, the lung cancer exhibits higher EGFR mutation rates which is directly correlated to the rates of hormone receptor expression (both estrogen and progesterone receptors) on the lung primary. HER2 was not found to have a similar relationship with the EGFR mutation, with it being undetectable in the lung tissues. Therefore, they postulated that there is a role of sex hormones in the development of lung cancer in these patients, however they advised that further studies are required to confirm this link [8].

Patients with breast cancer may have other different primaries apart from in the lung, including ovarian, uterine/endometrial, colorectal, renal, pancreatic and thyroid [9]. These may be both synchronous or metachronous and can be precipitated by hormonal treatment for the primary breast (strong association between tamoxifen and endometrial cancer), genetic factors (e.g., BRCA1 and 2), and obesity [10]. The incidence was reported to range from 4.1% by Kim and Song, who followed up 108 patients with breast cancer, to 16.4% by Weir et al., who followed up 301,963 patients [10, 11].

## CONCLUSION

The first two patients were diagnosed with the lung lesion on a preoperative chest X-ray which was performed a number of weeks after the mammogram showed a suspicious lesion and the malignancy was confirmed on biopsy. Since these patients would benefit from early diagnosis and management, waiting so long for a chest X-ray or other investigations is less than ideal. Therefore, it would be more beneficial for the patient that if a mammogram demonstrates a lesion which is highly indicative of a malignant process, they can undergo a chest X-ray to exclude the occurrence described above. It should be standard practice that all patients undergoing surgery for a breast malignancy perform a chest X-ray preoperatively, but since this occurs later than the diagnosis, one should consider earlier assessment which would allow earlier management.

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**Author Contributions**

Bernard Paul Spiteri Meilak – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that

questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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**Conflict of Interest**

Author declares no conflict of interest.

**Data Availability**

All relevant data are within the paper and its Supporting Information files.

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