



## Successful treatment of triple primary tumor☆☆

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## ABSTRACT

**INTRODUCTION:** The occurrence of multiple primary tumors is rare. Only limited number of cases with triple malignancy have been reported. We report here a rare case of a woman presented synchronous triple tumors, in her lung, breast, skin.**PRESENTATION OF CASE:** A 56-year-old woman presented with invasive ductal carcinoma of breast, non-small cell lung cancer and malignant melanoma. The patient undergone mastectomy and malignant melanoma tumor excision on-site. After operation stereotactic radiotherapy was given to her lung tumor. Six course of chemotherapy was given to her. She is alive with no progression.**DISCUSSION:** The patient was diagnosed with melanoma and staging by FDG/PET. There is not any study about routine using PET/CT in the melanoma staging.**CONCLUSION:** This is a very rare synchronous triple tumor case.

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## 1. Introduction

Synchronous multiple primary tumors are rare.<sup>1–7</sup> Most synchronous triple tumors have been reported by Japanese authors.<sup>8</sup> Most of synchronous multiple primary tumors are seen in genitourinary system and gastrointestinal system.<sup>5–7</sup>

Herein, we report an extremely rare case of synchronous triple primary cancers of breast, lung (non-small cell lung cancer) and malignant melanoma.

## 2. Presentation of case

A 56-year-old postmenopausal female with complaints of rapidly growing hyperpigmented mass in left leg noticed 6 months ago sought medical consultant in November 2011. On examination

a colorful mole with an irregular borders in the 1/3 upper lateral side of left leg was found. Excisional biopsy of lesion showed malignant melanoma. Pathology revealed that lesion thickness 2.8 mm, Clark Level IV, epitheloid cell type, with ulceration, low mitotic rate, superficial spreading type.

An 18F-FDG PET/CT was ordered for initial staging and workup to evaluate metastatic spread of disease. The 18F-FDG PET/CT demonstrated the following: intense FDG uptake within the left breast mass on the lower inner quadrant (size 1.2 cm × 1.1 cm, SUVmax: 7.3); abnormal lymph node uptake in the left pelvis region (SUVmax: 10); abnormal uptake on the lower lobe of right lung (size 1.3 cm × 1.1 cm, SUVmax: 6.5), elevated nodular activity in the left adrenal gland (SUVmax: 6) (Fig. 1). MRI of adrenal gland ruled out any metastasis. Subsequent mammography and ultrasonography of the left breast revealed a hyperdense 1.2 cm × 1.2 cm mass within the 2 o'clock position, with ill-defined and angulated borders, assessed as a BIRADS category 5. There was a second lesion within the 11 o'clock position of the same breast, measuring 0.9 cm × 0.6 cm and 0.5 cm × 0.4 cm also considered suspicious for malignancy, assessed as a BIRADS category 4.

Trans thoracic FNAB (fine needle aspiration biopsy) of lung lesion revealed squamous cell carcinoma (Figs. 2 and 3). Given the PET-CT, chest tomography and biopsy results, this patient was diagnosed with Stage 1a non-small cell lung cancer (T1N0M0 NSCLC). The patient received a hypo-fractionated course of Stereotactic body radiotherapy (SBRT). A 3D-conformal multifield technique was used with six coplanar and one non-coplanar statics beams. A total dose of 60 Gy in three fractions over six days was prescribed to the 95% of the CTV.

☆☆ With the submission of this manuscript I would like to undertake that the above mentioned manuscript has not been published elsewhere, accepted for publication elsewhere or under editorial review for publication elsewhere; and that my Institute's (Bezmialem Vakif University Medical School) representative is fully aware of this submission.

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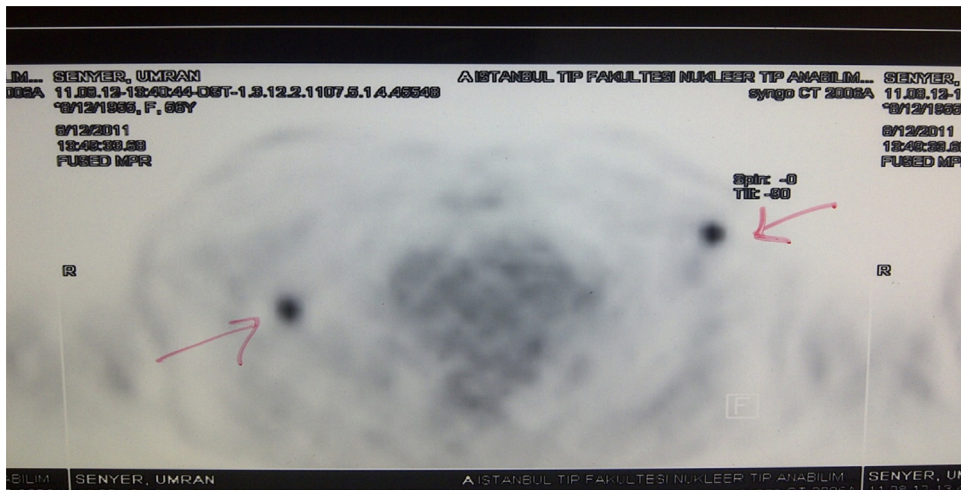


Fig. 1. PET/CT.

An ultrasound-guided core biopsy was performed of the larger breast mass, revealed an invasive ductal carcinoma of breast with negative melanoma markers. The patient underwent a subcutaneous nipple sparing mastectomy and reconstruction with the breast prosthesis and the sentinel lymph node dissection for the breast tumor and pelvic lymph node dissection for pelvic lymph nodes. Breast tumor and pelvic lymph nodes are successfully treated using a one-stage surgical approach.

Pathology of the breast surgery revealed a 1.5 cm poorly differentiated infiltrating ductal carcinoma with an extensive intraductal component. There was no any other tumor. The margins were clear. The one sentinel node identified was free of

tumor on pathological examination. Lymphovascular invasion was not identified and necrosis was not observed in the specimen. The estrogen receptors and progesterone receptors (ER and PR), c-erb B2 status were positive and the concentration of ER was 95%, PR was 90%, c-erb B2 was (+++) of the specimen (Fig. 4).

Histologically, 10 lymph nodes were removed during lower abdominal lymph node dissection and in one of them, metastasis of breast cancer was found with extracapsular extension (T1N0M1).

Six cycles of cyclophosphamide, epirubicin and 5-fluorouracil based chemotherapy and trastuzumab, anastrozole were given to the patient.

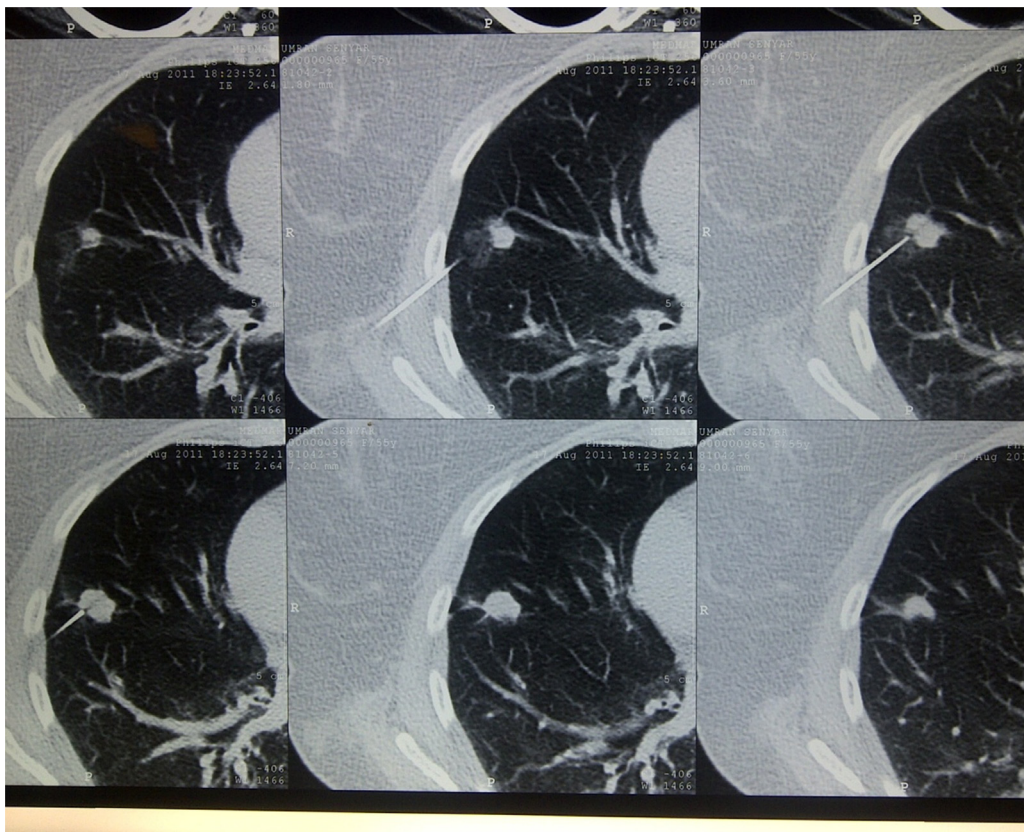
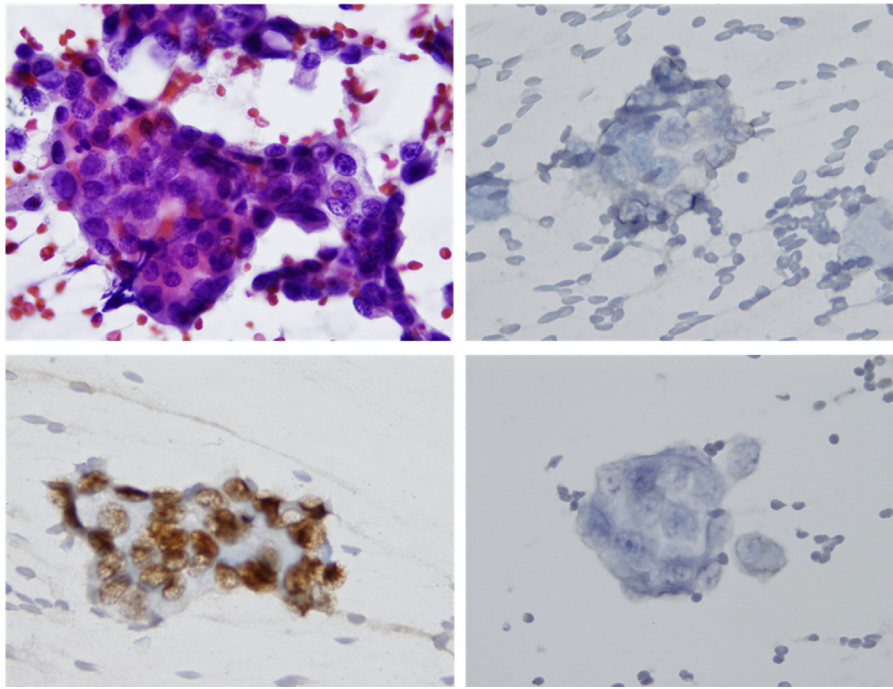
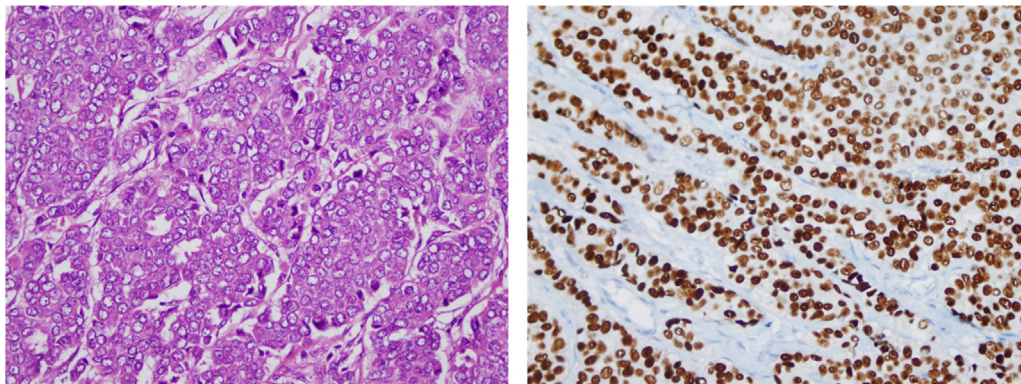


Fig. 2. Transthoracic fine needle aspiration biopsy.



**Fig. 3.** Lung FNAB. Upper left: Tumor sheets composed of atypical cells with large nuclei. They have conspicuous nucleoli and amphophilic cytoplasm. Upper right: Tumor cells have no immunohistochemical reaction with Melan-A stain. Lower left: Tumor cells have strong nuclear staining with TTF-1.



**Fig. 4.** Lymph node. Left: Metastatic lymph node with atypical cells forming solid groups. Right: ER positivity in the tumor cells with metastatic carcinoma.

Eighteen months after the diagnosis, the patient is alive and recurrence free.

### 3. Discussion

Multiple synchronous primary carcinomas are known to occur in many organ systems. The incidence of multiple primary cancers is reported about 0.73–11.7%.<sup>3</sup> Cases of synchronous primary tumors have been well documented in the lung, genitourinary, hepatobiliary/gastrointestinal, and other systems.<sup>1–4</sup>

Incidence of multiple primary malignant neoplasms increases with age. A family history of cancer and genetic predisposition may be associated with a risk of multiple malignancies.<sup>4</sup> Some studies showed the constitutional chromosomal abnormality as one of the possible high-risk factors for multiple primary cancers. A few studies provide support for the hypothesis that decreased DNA repair capacity is a contributory factor for multiple primary tumor.

The histological criteria are as follows: (1) Tumors must be clearly malignant as determined by histologic evaluation. (2) Each neoplasm must be topographically separate and distinct. (3) The

tumors should be separated by normal-appearing mucosa.<sup>1,4</sup> We confirmed all tumors histologically.

Synchronous carcinomas are those tumors diagnosed at the same time or within a 6-month period after the diagnosis of the initial cancer.<sup>4</sup>

Recently improved tumor control with relatively few complications has been achieved using high-dose, hypofractionated stereotactic radiation delivery.<sup>5</sup> We treated the lung tumor of this patient with SRS, successfully.

Adding PET/CT as a diagnostic tool improved the staging of stage III patients with increased cost.<sup>6</sup> There are a lot of studies in the literature showed that PET/CT have not any role in the initial staging of melanomas with intermediate and thin thickness.<sup>7,8</sup> There are some studies showed that PET/CT has high specificity and sensitivity identifying regional metastases in the melanomas with thick thickness.<sup>9,10</sup> However there is no study supporting the routine use of PET/CT for patients undergoing SLNB for melanoma.<sup>11</sup> Retrospective studies showed that PET/CT has changed therapeutic plan in the patients with stage 3–4 melanoma between 22% and 49%.<sup>12,13</sup> The rates in the prospective trials are between 15% and 40%.<sup>14</sup> PET/CT findings may contribute important information that led to the

modification of the original treatment plan in the melanomas with high mitotic rate, ulceration, lymphovascular invasion and thick more than 2 mm.<sup>15</sup> Our patient has 2, 8 mm thickness and ulcerative melanoma and her PET/CT findings changed therapy planning.

Recently studies suggest that mutations in the BRCA1 gene with breast-ovary cancer patients have increased risk of developing malignant melanoma by as much as 2.6 times.<sup>16</sup> There are some reports showing synchronous tumors with breast cancer and melanoma in the literature.<sup>17</sup> However we could not observe any cancer case of breast, lung and melanoma together in our clinical practice before.

#### 4. Conclusion

This case report that identifies synchronously of breast cancer, lung cancer and melonamin which is observed rarely is noteworthy.

#### Conflict of interest

We have no conflict of interest to disclose.

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None declared.

#### Ethical approval

Written informed consent was obtained from the patient for publication of this case report paper.

#### Author contributions

Dr. Sidika Kurul and Dr. Mert Basaran made data collections and study design. Dr. Esra Saglam and Dr. Sitki Tuzlali too worked on data collections and study design but made review work also. Dr. Serap Yucel participated in the study design alone, whereas Dr. Zuleyha Akgun contributed with writing works and study design.

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