

A Case of Triple Primary Malignancies Including the Breast, Pancreas, and Lung: The Role of ¹⁸F-FDG PET/CT

Meme, Pankreas ve Akciğeri İçeren Üçlü Primer Malignite Olgusu: ¹⁸F-FDG PET/CT'nin Rolü

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ABSTRACT Breast cancer is the most common malignancy in women and survival rates increase thanks to early diagnosis and treatment options. Secondary malignancies may develop in these cases with increased survival. On the other hand, the cases in which two distinct synchronous organ malignancies develop besides breast cancer are quite rarely found in the literature. In this case presentation, as far as we know, we have reported the first case previously diagnosed with breast cancer in whom development of synchronous lung and pancreas malignancies was detected by ¹⁸F-FDG PET/CT performed during follow-up period. Our case is interesting because of carrying synchronous and metachronous 3 distinct malignancies altogether and it presents the importance of interpretation of the ¹⁸F-FDG PET/CT imagings performed during follow-up of a primary tumor and histopathological confirmation with respect to surgical treatment possibility.

Key Words: Neoplasms, multiple primary; positron-emission tomography/ computed tomography

ÖZET Meme kanseri kadınlarda en sık görülen malignite olup erken tanı ve tedavi seçenekleri sayesinde sağkalım oranları artmaktadır. Artan sağkalım ile birlikte bu olgularda sekonder maligniteler gelişebilmektedir. Buna karşın literatürde meme malignitesi yanında senkron iki farklı organ malignitesi ortaya çıkan olgulara oldukça az rastlanılmaktadır. Biz bu olgu sunumunda meme malignitesi tanısı almış, izlem sırasında yapılan ¹⁸F-FDG PET/CT görüntüleme ile fark edilen senkron akciğer ve pankreas malignitesi gelişen ilk olguyu rapor etmekteyiz. Olgumuz senkron ve metakron üç farklı maligniteyi bünyesinde taşıması nedeniyle ilginç olup, primer bir tümör varlığında takip sırasında yapılan ¹⁸F-FDG PET/CT görüntülerinin yorumlanması ve histopatolojik konfirmasyonun cerrahi tedavi şansı açısından önemini ortaya koymaktadır.

Anahtar Kelimeler: Neoplaziler, çoklu primer; pozitron-emisyon tomografi/ bilgisayarlı tomografi

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When multiple neoplasms develop in the same person the tumors are defined as synchronous (within 6 months after the first tumor) and metachronous (after 6 months from the first tumor) according to the time between the occurrence. The tumors that developed distinctly and synchronously or metachronously in an identical patient are named as multiple primary tumors and reported to have an incidence of 0.7-11.7% in the literature.¹ The incidence of multiple primary malignancies, is rising because of improved survival rates due to early diagnosis and newly developed treatment options.²

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In the cases with malignancies; possibility of surgical treatment for secondary malignancies that may develop during follow-up period has a great importance with respect to survival. Consequently, it should be kept in mind that newly developed hypermetabolic lesions encountered by ^{18}F -FDG PET/CT during follow-up periods of the patients found with primary malignancy should be evaluated for secondary malignancies as well as possible metastatic sites. In our manuscript, we have presented a case who was operated for breast malignancy and found to have hypermetabolic lesions in the pancreatic body and upper lobe of left lung with ^{18}F -FDG PET/CT performed two years later and histopathologically diagnosed with rarely observed synchronous lung and pancreatic malignancies.

CASE REPORT

A 44-year-old female patient was operated for malignant cytology in her right breast accompanied by frozen section biopsy. She was diagnosed with malignant phyllodes tumor of breast and reactive lymph nodes according to the pathological evaluation (Figure 1). Whole body PET/CT imaging performed for primary staging and according to PET/CT, our patient was assessed as T1N0M0 stage and followed-up without treatment. Whole body PET/CT imaging performed during the follow-up period encountered a moderate-degree hypermetabolic (maximum standard uptake value (SUV_{max})= 2.6) nodular parenchymal lesion located at

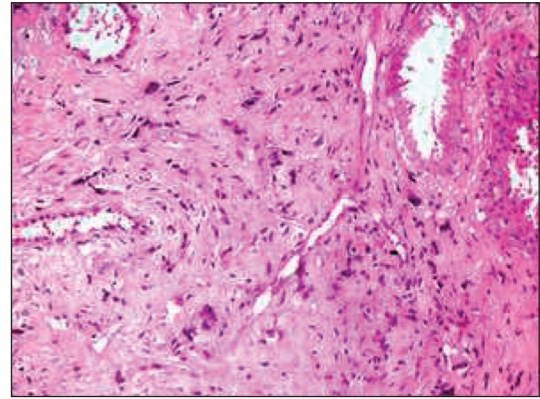


FIGURE 1: Malignant phyllodes tumor field including pleomorphic and sporadically spindle cells in the stroma between normal breast duct (H&E x100).

left upper lobe apicoposterior segment with an irregular contour and approximate size of 1.4x1.0 cm (Figure 2a) and a moderate-degree hypermetabolic (SUV_{max}=2.5) pancreatic lesion in diameter of 2.5 cm located at the body of pancreas (Figure 2b). The moderate-degree hypermetabolic lesion encountered in the body of the pancreas was evaluated as highly likely to be malignant whereas the nodular lesion with an irregular contour located at left upper lobe apicoposterior segment was interpreted as either metastasis of one of the previously existing malignancies (malignancy of breast or pancreas) or second primary cancer of lung and thus histopathological correlation was recommended for differential diagnosis. Morphological and immunohistochemical features (positive TTF1 and cytokeratin 7 and negative cytokeratin 20 of tru-cut biopsy

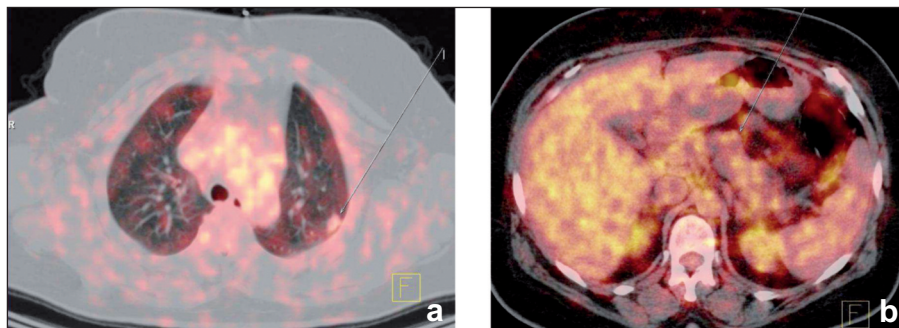


FIGURE 2: a) Transaxial PET-CT images showed moderate-degree hypermetabolic (maximum standard uptake value (SUV_{max})= 2.6) nodular parenchymal lesion located at left lung upper lobe apicoposterior segment with an approximate size of 1.4x1.0 cm (arrow). **b)** Transaxial PET-CT images showed a moderate-degree hypermetabolic (SUV_{max}=2.5) pancreatic lesion in diameter of 2.5 cm located at the body of pancreas (arrow).

SUV is an index of tracer uptake that is defined as follows:

SUV= activity concentration in the tissue (MBq/ml)/administered activity (MBq/patient weight (kg))

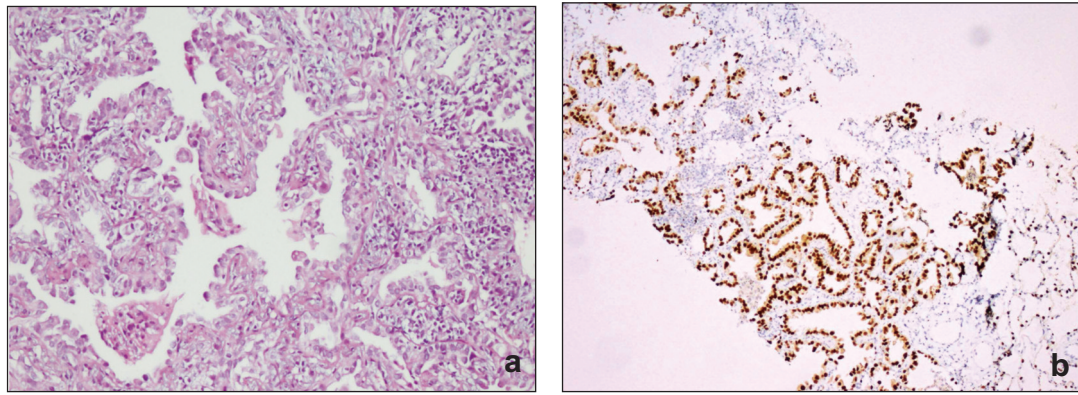


FIGURE 3: a) Adenocarcinoma fields including small papillary formations and glandular structures in the lung tru-cut biopsy specimen (H&Ex100). b) TTF1 positivity in the lung tru-cut biopsy specimen (TTF1x100).

specimen obtained from the lesion located at left upper lobe apicoposterior segment supported malignancy of primary lung (non-small cell lung carcinoma) (Figure 3a, b). Similarly with tru-cut biopsy, wedge material specimen revealed a 1.5 cm-diameter tumor. On the histopathological examination of lymph nodes with tissue samples of 5th, 6th and 9th stations reactive hyperplasia were diagnosed. No additional treatment was given according to these findings. A short time later, the lesion located at the body region of pancreas was evaluated by a cytological examination for differential diagnosis. The smears that revealed cytologically malignant features were interpreted in favor of adenocarcinoma. Whipple procedure was performed according to these results.

Its pathological examination resulted its diagnosis in favor of ductal adenocarcinoma (Figure 4 a). Metastasis was encountered in two of the 19 lymph nodules dissected from surrounding pancreas (Figure 4 b). The patient, who was performed six cures of chemotherapy following surgical operation and received the last cure at November 2012, has undergone a whole body PET/CT in December 2012 and no pathological uptake of ¹⁸F-FDG was found in pancreas and left lung after surgery (Figure 5). No relapse, metastasis and another malignancy was encountered in the patient during three year of follow-up after the administered treatment procedures and also via thoracic and whole body CT imaging performed in 2014.

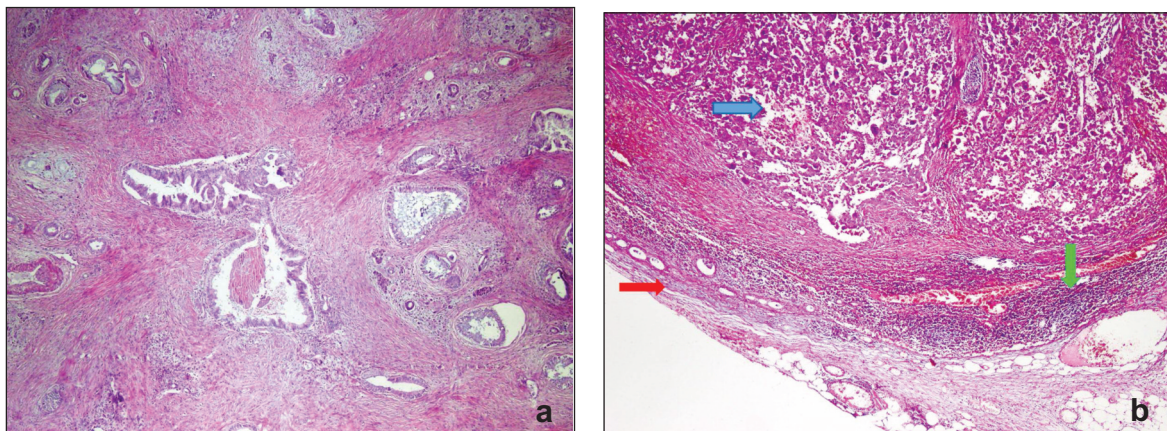


FIGURE 4: a) Tumor cells with findings of malignancy that formed glandular structures in various diameter measurements in the pancreas operation material (H&Ex50). b) Focus of normal residual lymph nodules in the lymph nodules dissected from peripancreatic region (green arrow), typical metastatic adenocarcinoma fields located as subcapsular sinuses (red arrow) and fields composed of giant cells (blue arrow) (H&Ex50).

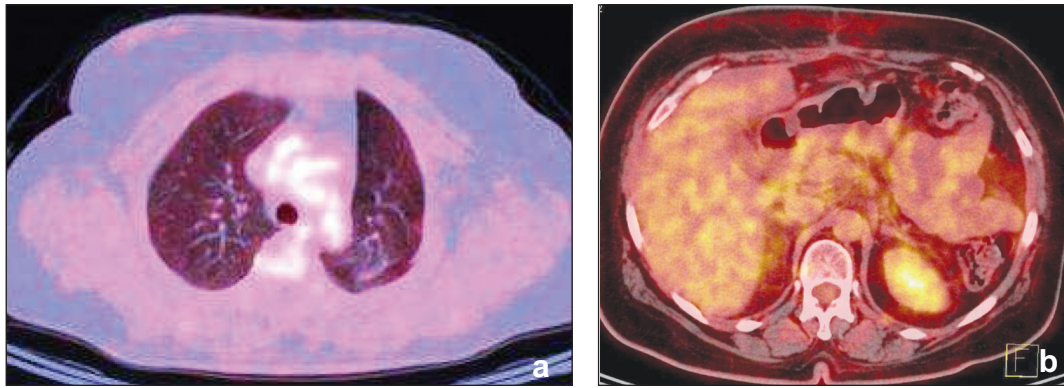


FIGURE 5: a) Transaxial fused PET/CT images showed the changes secondary to operation at the level of left upper lobe apicoposterior segment. b) Body and tail regions of the pancreas couldn't be encountered secondary to the operation on sagittal fused PET/CT.

DISCUSSION

Thanks to technological improvements in the present time, rate of early diagnosis in the malignancies progressively increases and survival durations of the cases have prolonged due to additional modern treatment options. As a consequence of all these improvements, potential of secondary malignancies in these cases increases.² Carcinogenic effects due to treatment and genetic predisposition of the patient may be responsible as a reason of this issue.³ Our cases was not given an additional treatment regimen. Therefore, tumors may be considered to be associated with genetic predisposition. The patient reported in her medical history that one of her siblings was exitus due to tongue malignancy while her other sibling was operated for breast malignancy. However, no detailed information on subtype of the tumor couldn't be obtained and this present characteristic supports our hypothesis.

A study on 40 cases has reported that a secondary malignancy develops within 1 to 22 months after the primary malignancy and lung cancer is found in 5% of the secondary malignancies that developed in the cases with malignancy of breast in a study.^{4,5} In our case presentation, lung carcinoma developed two years after as stated in the literature in addition with a synchronous pancreatic ductal adenocarcinoma. In a case series of 149 patients, possibility of a newly-developed lung nodule to be a secondary malignancy of lung was found higher

in the cases with malignancy of head-neck, breast, cervix, gallbladder, esophagus, ovary, prostate and stomach whereas metastatic potential was found higher in the cases with melanoma, sarcoma and testicular carcinoma.⁶

¹⁸F-FDG has the capability to detect multiple coexisting cancers.^{7,8} There are many studies that have investigated advantage of ¹⁸F-FDG PET or PET/CT in detecting multiple primary tumors with respect to revealing metabolic changes in contrast to conventional anatomical imagings.⁹ As far as we have investigated in the literature, this is the first reported case in whom secondarily developed primary malignancies of pancreas and lung detected via ¹⁸F-FDG PET/CT imaging performed during follow-up periods of the cases with primary malignancy of breast. Even though, it is known that multiple primary malignancies have worse progression, our case has been followed-up without detecting any relapse or metastasis thanks to early diagnosis obtained by PET/CT and histopathological confirmation.

In our report FDG PET/CT has played an important role in detection of secondary primary malignancies of lung and pancreas that developed synchronously and in the management of the patient providing an opportunity for a surgical resection accompanied by histopathological diagnosis. For this reason in patients with known malignancy, the masses which are recognised by imaging modalities such as FDG PET/CT during follow-up

periods of the cases should make us consider a metachronous tumor as well as metastatic involvement. Imaging modalities and achievement of

pathological evaluation creates the chance of early resection and carries the critic importance on survival and prognosis.

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