



Unveiling the Diagnostic Mystery: ¹⁸F-FDG PET and Bone Scan Negative in Bone Metastases of Lobular Breast Cancer: A Case Report

Tanısal Gizemin Çözülmesi: Lobüler Meme Kanseri Kemik Metastazlarında ¹⁸F-FDG PET ve Kemik Taraması Negatif Bir Olgu Sunumu

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Abstract

Identifying osseous metastases by imaging is essential and may be challenging in patients with lobular breast cancer. We present a case of a 66-year-old woman with lobular breast cancer who underwent ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) for staging purposes. ¹⁸F-FDG PET/CT reveals minimal FDG uptake in the primary tumor cells. Prominent sclerotic lesions with low FDG avidity are seen in the spinal and pelvic bones. The subsequent Tc-99m methylene diphosphonate bone scan is unremarkable. The magnetic resonance multiple imaging (MRI) reveals bone metastases. MRI may be beneficial in invasive lobular carcinoma. MRI facilitates improved metastatic evaluation, especially in bone-only and bone-predominant metastatic malignancies, when assessment with ¹⁸F-FDG PET/CT may be difficult and constrained.

Keywords: Lobular breast cancer, ¹⁸F-FDG PET/CT, osseous metastases, MRI

Öz

Lobüler meme kanserli hastalarda kemik metastazlarının görüntüleme ile tespiti önemlidir ve tanısal anlamda zorlayıcı olabilir. Evreleme amacıyla ¹⁸F-fluorodeoksiglukoz pozitron emisyon tomografisi/bilgisayarlı tomografi (FDG PET/BT) taraması yapılan 66 yaşında lobüler meme kanserli bir kadın olguyu sunuyoruz. ¹⁸F-FDG PET/BT, primer tümör hücrelerinde minimal FDG tutulumu göstermiştir. Spinal ve pelvik kemiklerde FDG içermeyen belirgin sklerotik lezyonlar görülmüştür. Ardından yapılan Tc-99m metilen difosfonat kemik taraması normal saptanmıştır. Manyetik rezonans görüntüleme (MRG), çoklu kemik metastazlarını ortaya koymaktadır. MRG, invaziv lobüler karsinomda potansiyel olarak faydalı olabilir. MRG, özellikle sadece kemik ve kemik ağırlıklı metastatik malignitelerde, ¹⁸F-FDG PET/BT ile değerlendirmenin zor ve kısıtlı olabileceği durumlarda, metastazların daha iyi değerlendirilmesine yardımcı olur.

Anahtar kelimeler: Lobüler meme kanseri, ¹⁸F-FDG PET/BT, kemik metastazları, MRG

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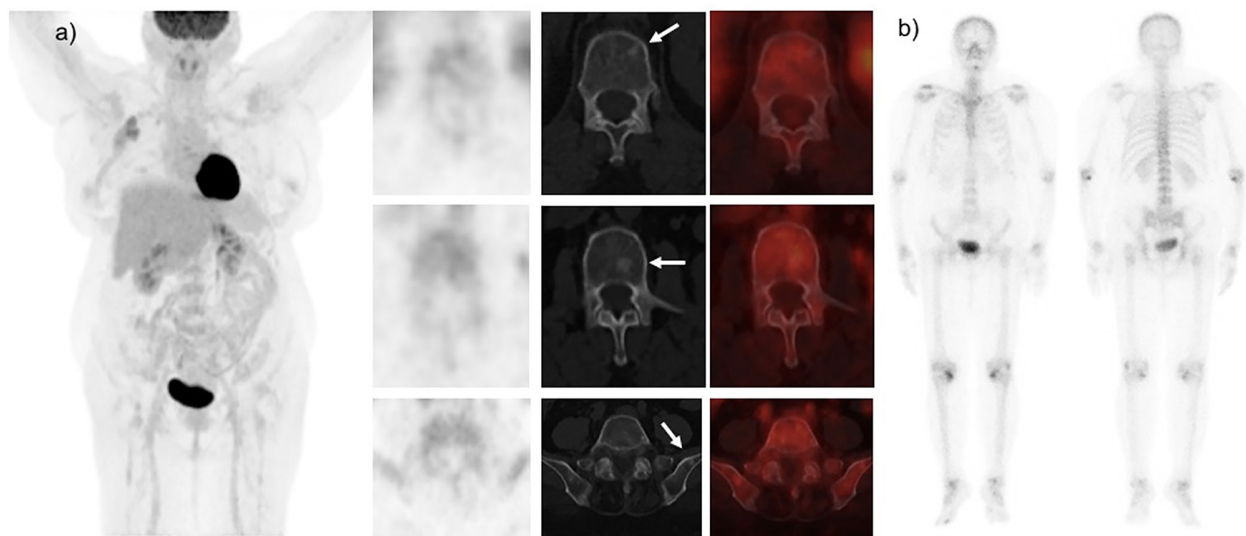


Figure 1. A 66-year-old female has a documented diagnosis of locally advanced grade 2 right lobular breast cancer, which is estrogen receptor-positive; progesterone receptor-positive; and human epidermal growth factor receptor 2-negative. ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) performed for preliminary staging. (a) Mild FDG uptake is seen in the primary tumor of the right breast. Diffuse heterogeneous ^{18}F -FDG uptake is seen in the skeleton, matching CT reveals ill-defined sclerotic lesions, most noticeable at the body of T12, L2 vertebrae, and bilateral iliac bones (white arrow) with no significant ^{18}F -FDG avidity. (b) The whole body Tc-99m methylene diphosphonate bone scan is unremarkable.

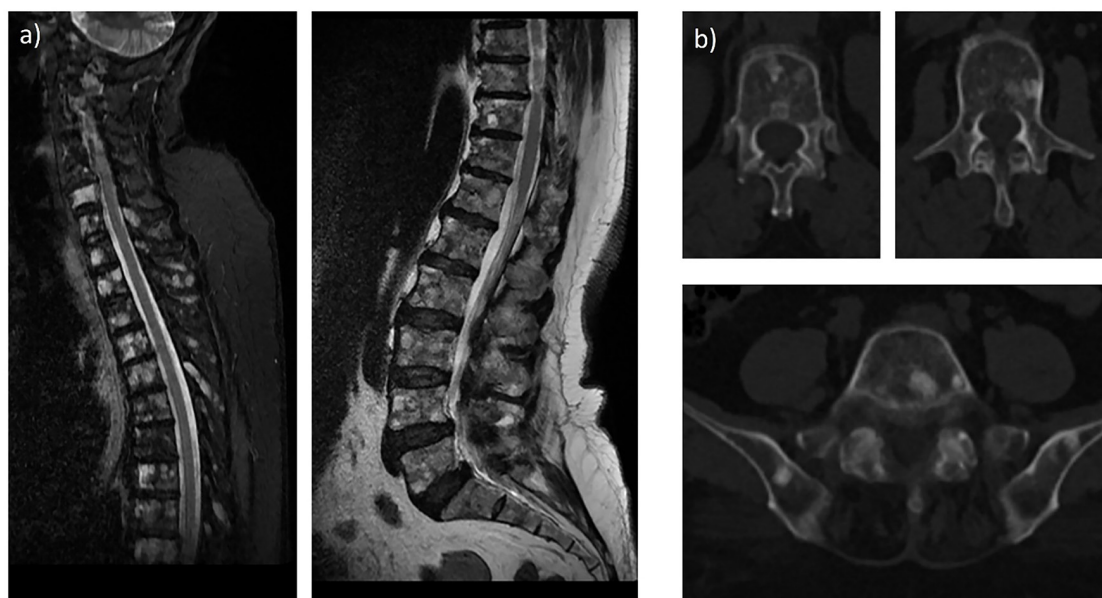


Figure 2. (a) The contrast-enhanced T2 images of magnetic resonance imaging (MRI) showed abnormal bone marrow signals across almost the entire spine, ribs, shoulder blades, hips, and pelvis, suggestive of widely spread bone metastases. (b) Follow-up computed tomography (CT) imaging demonstrates that several bony lesions have become denser (increased sclerosis), suggesting the healing response. Invasive lobular carcinoma (ILC) accounts for a notable portion of invasive breast carcinomas, developing insidiously in roughly 10-15% of cases.

^{18}F -fluorodeoxyglucose positron emission tomography/CT (FDG PET) plays a meaningful role in the staging and restaging of breast cancer. However, its sensitivity and detection rates are lower in lobular carcinoma, attributable to the lessened FDG-avidity of malignant cells (1). ILC demonstrates lower maximum standardized uptake values than invasive ductal carcinoma (IDC) on account of multiple mechanisms, such as lower tumor cell density, reduced proliferation rates, diffuse infiltration into encompassing tissues, and diminished GLUT-1 expression (2). In women with breast cancer, bone is the principal site of distant metastasis. It is also the primary site of metastasis in 50% of patients (3). Individuals

diagnosed with lobular breast cancer display a greater tendency for bone metastases compared to those with ductal malignancies and more often appear sclerotic on CT scans than those with IDC. ^{18}F -FDG PET/CT is more sensitive in detecting lytic bone metastases in breast cancer patients, while Tc-99m methylene diphosphonate bone scintigraphy demonstrates greater sensitivity for detecting sclerotic bone metastases. Recently, a study by Usmani et al. (4) showed low sensitivity and precision of ^{18}F -FDG PET/CT in identifying bone metastases in patients with lobular breast cancer. The absence of uptake on whole body bone scan despite the presence of sclerotic lesions presents an intriguing diagnostic phenomenon. This discordance may be attributed to several factors, including the subtle nature and small size of the sclerotic lesions, which could fall below the resolution threshold of bone scintigraphy. Additionally, these findings might represent very early metastatic disease that is currently undetectable. Another consideration is the possibility of low osteoblastic activity despite the sclerotic appearance on CT, suggesting a unique biological behavior of these metastatic lesions. MRI demonstrates superior accuracy in the diagnosis of bone metastasis associated with lobular breast cancer. It detects bone metastases at an earlier stage than other imaging techniques. It can identify subtle changes in bone marrow that may not be visible on bone scan, ^{18}F -FDG PET or CT scans. The rate of misdiagnosis associated with MRI in identifying bone metastasis in lobular breast cancer is comparatively low (5). In untreated patients with ILC, non-FDG-avid sclerotic osseous metastases were found to be significantly more prevalent than in those with IDC. The diagnostic confidence is lower in ^{18}F -FDG PET/CT in ILC when evaluating for osseous metastases and consideration given to performing a biopsy/MRI or obtaining follow-up imaging before excluding metastatic disease. Our case highlights the need for careful evaluation of any sclerotic lesion in lobular breast cancer patients, even if negative on ^{18}F -FDG PET/CT, and to consider alternative imaging modalities or more specific PET tracers such as ^{18}F -fluoroestradiol and ^{68}Ga -fibroblast activation protein inhibitor-04 as alternative options for comprehensive evaluation of lobular breast cancer metastases (6,7). Furthermore, PET/MRI emerges as a promising hybrid modality that could enhance diagnostic accuracy in such cases. This hybrid technology demonstrates higher sensitivity for detecting bone metastases compared to PET/CT, making it particularly valuable in cases of ILC where metabolic activity is characteristically low. The integration of PET/MRI into the diagnostic algorithm for ILC could potentially bridge the current imaging gaps, though availability and cost considerations may influence its implementation in clinical practice.

Ethics

Informed Consent: The consent was obtained for image use.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.U., K.A.R., A.J., A.A.B., N.A., Concept: S.U., K.A.R., A.J., Design: S.U., V.V.J., S.K., Data Collection or Processing: S.U., K.A.R., A.J., A.A.B., P.D., V.V.J., S.K., N.A., Analysis or Interpretation: S.U., A.J., A.A.B., Literature Search: S.U., N.A., Writing: S.U., K.A.R., N.A.

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References

- Hogan MP, Goldman DA, Dashevsky B, Riedl CC, Gönen M, Osborne JR, Jochelson M, Hudis C, Morrow M, Ulaner GA. Comparison of

^{18}F -FDG PET/CT for systemic staging of newly diagnosed invasive lobular carcinoma versus invasive ductal carcinoma. *J Nucl Med.* 2015;56:1674-1680.

- Bos R, van Der Hoeven JJ, van Der Wall E, van Der Groep P, van Diest PJ, Comans EF, Joshi U, Semenza GL, Hoekstra OS, Lammertsma AA, Molthoff CF. Biologic correlates of (18)fluorodeoxyglucose uptake in human breast cancer measured by positron emission tomography. *J Clin Oncol.* 2002;20:379-387.
- Hamaoka T, Madewell JE, Podoloff DA, Hortobagyi GN, Ueno NT. Bone imaging in metastatic breast cancer. *J Clin Oncol.* 2004;22:2942-2953.
- Usmani S, Al Riyami K, Jain A, Alajmi AA, Albaimani K, Dumasig P, Al Busaidi A, Al Sukati R. Enhancing precision in bone metastasis diagnosis for lobular breast cancer: reassessing the role of 18 F-FDG PET/CT. *Nucl Med Commun.* 2024;45:858-864.
- Rong Y, Ren H, Ding X. MRI and bone scintigraphy for breast cancer bone metastase: a meta-analysis. *Open Med (Wars).* 2019;14:317-323.
- Sahin E, Kus T, Aytekin A, Uzun E, Elboga U, Yilmaz L, Cayirli YB, Okuyan M, Cimen V, Cimen U. ^{68}Ga -FAPI PET/CT as an alternative to ^{18}F -FDG PET/CT in the imaging of invasive lobular breast carcinoma. *J Nucl Med.* 2024;65:512-519.
- Ulaner GA, Jhaveri K, Chandarlapaty S, Hatzoglou V, Riedl CC, Lewis JS, Mauguen A. Head-to-head evaluation of ^{18}F -FES and ^{18}F -FDG PET/CT in metastatic invasive lobular breast cancer. *J Nucl Med.* 2021;62:326-331.