

3 Breast Neoplasms

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Case 3.1: Ductal Carcinoma In Situ of Breast

History

A 45-year-old female with biopsy-proven diagnosis of ductal carcinoma in situ of right breast. PET/CT was performed for initial staging.

Findings (Fig. 3.1)

Hypermetabolic right breast mass, SUVmax 13.8 (*black arrow*). Intensely hypermetabolic right axillary lymph nodes (LN), most avid LN demonstrates SUVmax 16.4 (*yellow arrow*).

Impression

Hypermetabolic right breast mass with at least two hypermetabolic right axillary LN, consistent with biopsy-proven malignancy.

Pearls and Pitfalls

Positron emission tomography (PET) with fluorine 18 fluorodeoxyglucose (FDG) is used to diagnose, stage, and monitor breast cancer. FDG-PET has the capability to depict abnormal metabolic activity before any anatomic change occurs. The most important advantage of FDG-PET/CT compared with other imaging modalities is the capability of detecting unsuspected distant metastases during a single whole-body examination. However, the results of most studies show that the capability of PET to depict lesions smaller than 1 cm in diameter is constrained by limited spatial resolution. PET also is of limited use for identifying tumors that are well differentiated histologically, such as ductal carcinoma in situ, and slow-growing cancers such as tubular carcinoma [1].

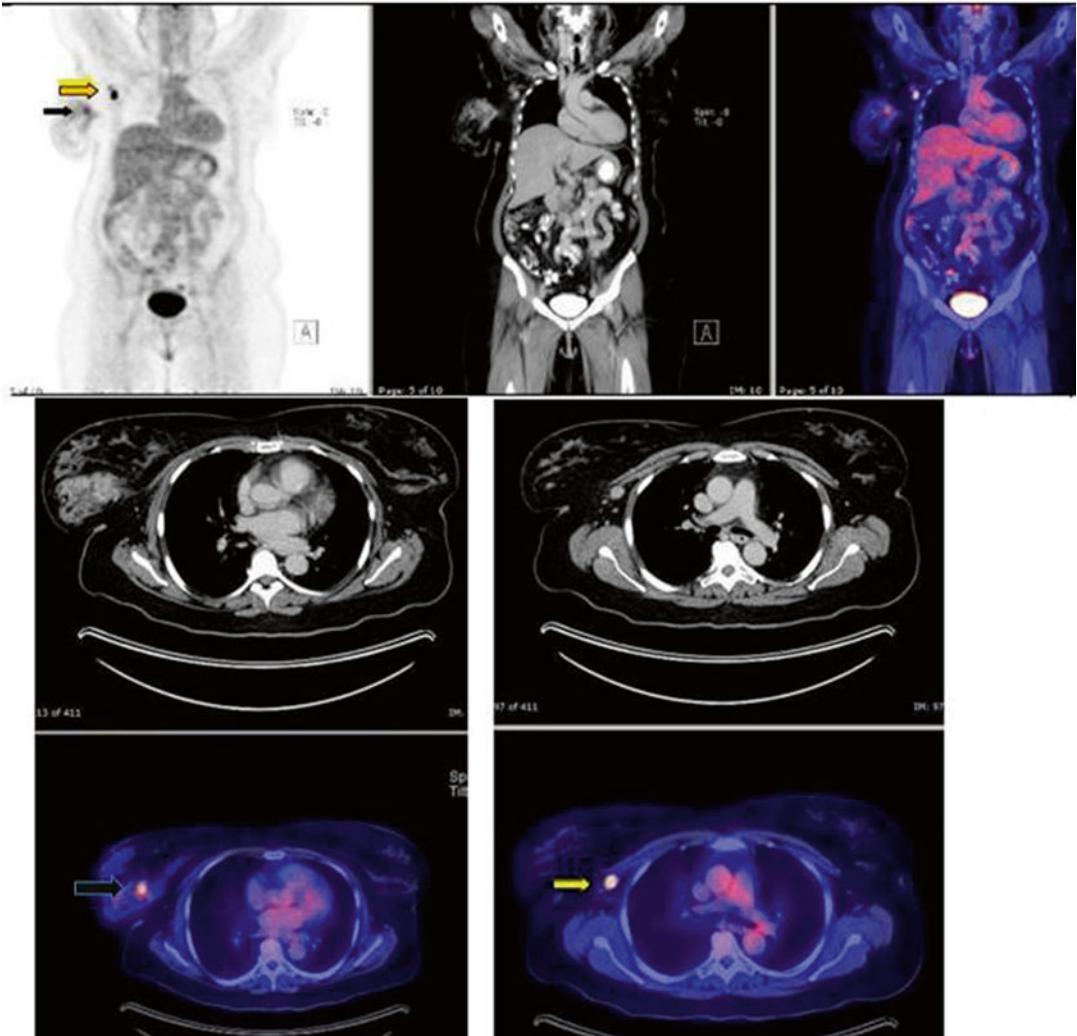


FIG. 3.1

Discussion

DCIS is defined as proliferation of epithelial cells confined to mammary ducts. The frequency of the diagnosis of DCIS has increased markedly in the United States since the widespread use of screening mammography [2]. DCIS comprises of a heterogeneous group of histopathological lesions that have been classified into several subtypes based primarily on architectural pattern: micropapillary, papillary, solid, cribriform, and comedo. Comedo-type DCIS appears to be more aggressive, with a higher probability of associated invasive ductal carcinoma [3].

Treatment options for patients with DCIS [2]:

1. Breast-conserving surgery and radiation therapy with or without tamoxifen
2. Total mastectomy with or without tamoxifen
3. Breast-conserving surgery without radiation therapy

Case 3.2: Invasive Breast Cancer

History

A 31-year-old female diagnosed with invasive right breast cancer and positive axillary metastases. She underwent modified radical mastectomy (MRM) and sentinel lymph node dissection, followed by chemotherapy.

Findings (Fig. 3.2)

(Right breast) Irregular enhancing mass measuring approximately $1.7 \times 1.3 \times 2.8$ cm, approximately 6 cm from the nipple, in the deep outer right breast (*white arrow*). No scan evidence of overlying skin, underlying muscle, or nipple involvement. (Left breast) No occult masses or abnormal areas of enhancement or adenopathy.

Findings (Fig. 3.3)

Hypermetabolic mediastinal lymph nodes seen best in coronal image on *left* (subcarinal lymph node showed SUVmax 6.6). Postsurgical changes in the right axilla. Minimally lytic, hypermetabolic lesion at L4, SUVmax 6.6 (*coronal view and bottom right axial image*).

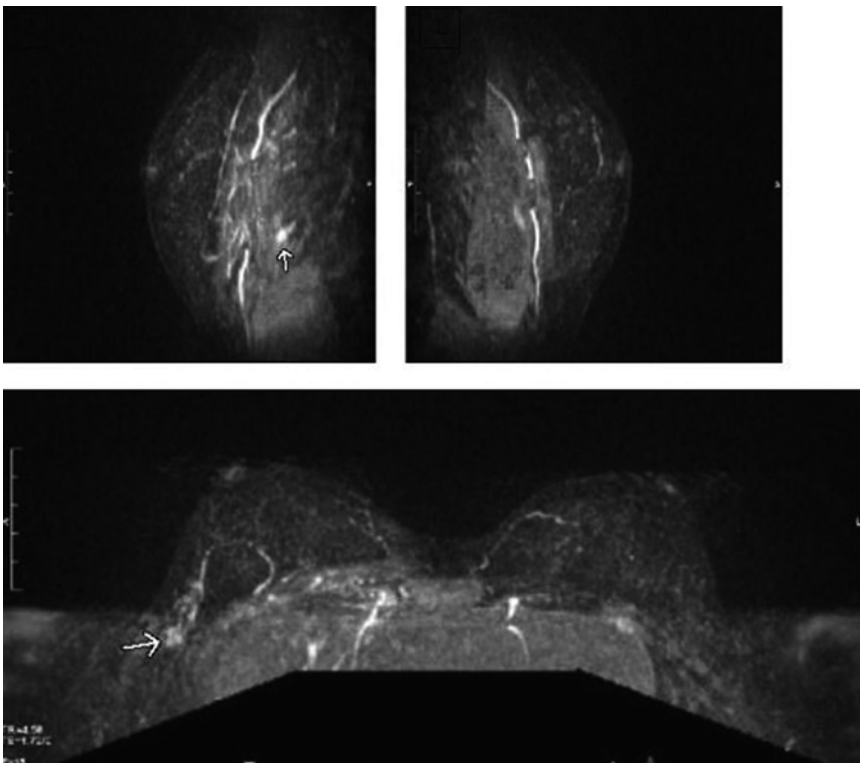


FIG. 3.2

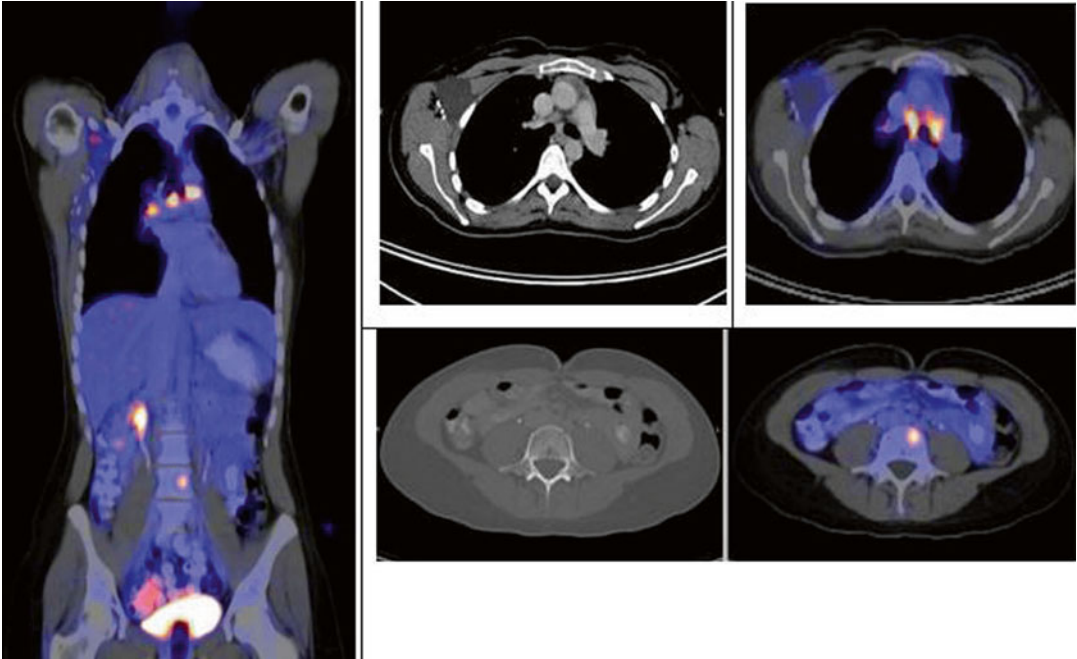


FIG. 3.3

Findings (Fig. 3.4)

Follow-up PET/CT (obtained 2 years from initial diagnosis and chemotherapy). Metabolic activity in the surgical bed of right axilla may represent chronic postsurgical changes versus residual disease. Resolution of hypermetabolic lymphadenopathy in the mediastinum. Resolution of hypermetabolic, L4 lytic lesion, now replaced by inactive, dense sclerosis, consistent with treated disease.

Impression

Interval resolution of activity within previously seen hypermetabolic mediastinal lymph nodes and L4 lytic lesion. Mild activity at the right axillary tail, likely postsurgical inflammation. No scan evidence of local recurrence.

Pearls and Pitfalls

FDG-PET is valuable for monitoring the effects of chemotherapy [4, 5]. Clinical examination and mammography are of limited use for monitoring the treatment response because of the difficulty in distinguishing fibrosis from residual tumor [1].

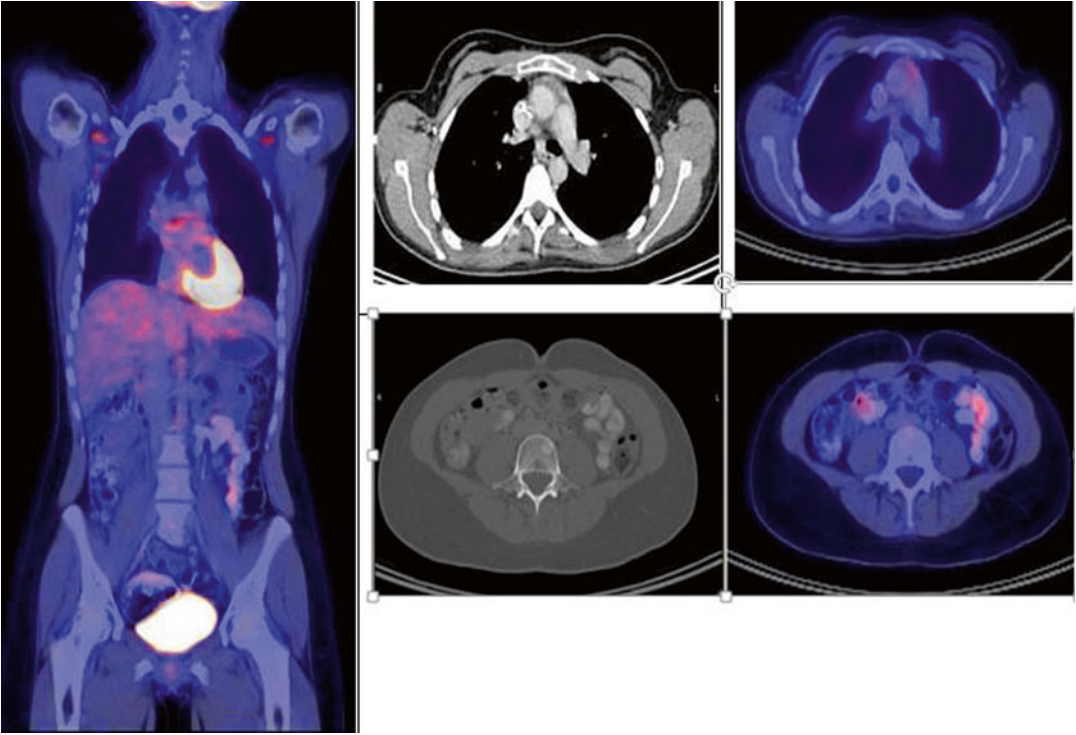


FIG. 3.4

However, false-positive FDG uptake has been observed in some benign breast diseases, e.g., in the presence of fibrocystic change, atypical ductal hyperplasia, ductal ectasia, and phyllodes tumor [1].

Discussion

PET can demonstrate changes in tumor metabolism before morphologic changes occur; thus, unresponsive tumors can be identified quickly. The uptake of FDG in a tumor after chemotherapy is predictive of the response to therapy; a treatment-induced reduction in metabolic activity correlates with a positive clinical response [1].

Practice guidelines from the SNM, National Comprehensive Cancer Network (NCCN), and other professional groups summarized for Breast Cancer (March, 2012):

1. Initial staging of patients with locally advanced or metastatic breast cancer when conventional staging studies (e.g., CT or bone scan) are equivocal or suspicious
2. Follow-up or surveillance of patients with breast cancer when conventional studies (e.g., CT or bone scan) are equivocal or suspicious

Case 3.3: Osseous Metastatic Disease Secondary to Intraductal Breast Carcinoma

History

A 54-year-old female, previously diagnosed with intraductal carcinoma (IDCA) of right breast, refused therapy, and now presents with stage IV disease.

Findings (Fig. 3.5)

Hypermetabolic, right subareolar mass also involving skin (known primary neoplasm), SUVmax 13.0, hypermetabolic satellite lesion lateral to the primary lesion (*yellow arrow*), right axillary lymph nodes, hypermetabolic contralateral left internal mammary lymph node (*axial PET image*), hypermetabolic retroperitoneal and pelvic lymphadenopathy (*coronal PET/CT images*). Multiple hypermetabolic osseous lesions (*coronal PET/CT images*) involving C5, left scapula, sternum, T7, L3 vertebrae. Pathologic compression fracture of L5. Hypermetabolic lesion involving sacral promontory, predominantly lytic left iliac bone lesion extending to the posterior left acetabulum (*red arrow*).

Impression

Stage IV, metastatic breast cancer with hypermetabolic nodal disease above and below the diaphragm and multiple osseous metastases.

Pearls and Pitfalls

¹⁸F-FDG-PET/CT may be an independent prognostic factor for disease recurrence in patients with invasive ductal carcinoma [6]. Intraductal carcinoma also refers to as ductal carcinoma in situ (DCIS).

Discussion

Skeletal metastases of breast cancer mainly occur from lymphatic spread and hematogenous dissemination. A part of the sternal metastasis could occur via lymphatic vessels to parasternal lymph node. The prognosis of patients with solitary metastatic bone lesions, especially sternal metastasis, may be different from that of multiple skeletal metastasis, because

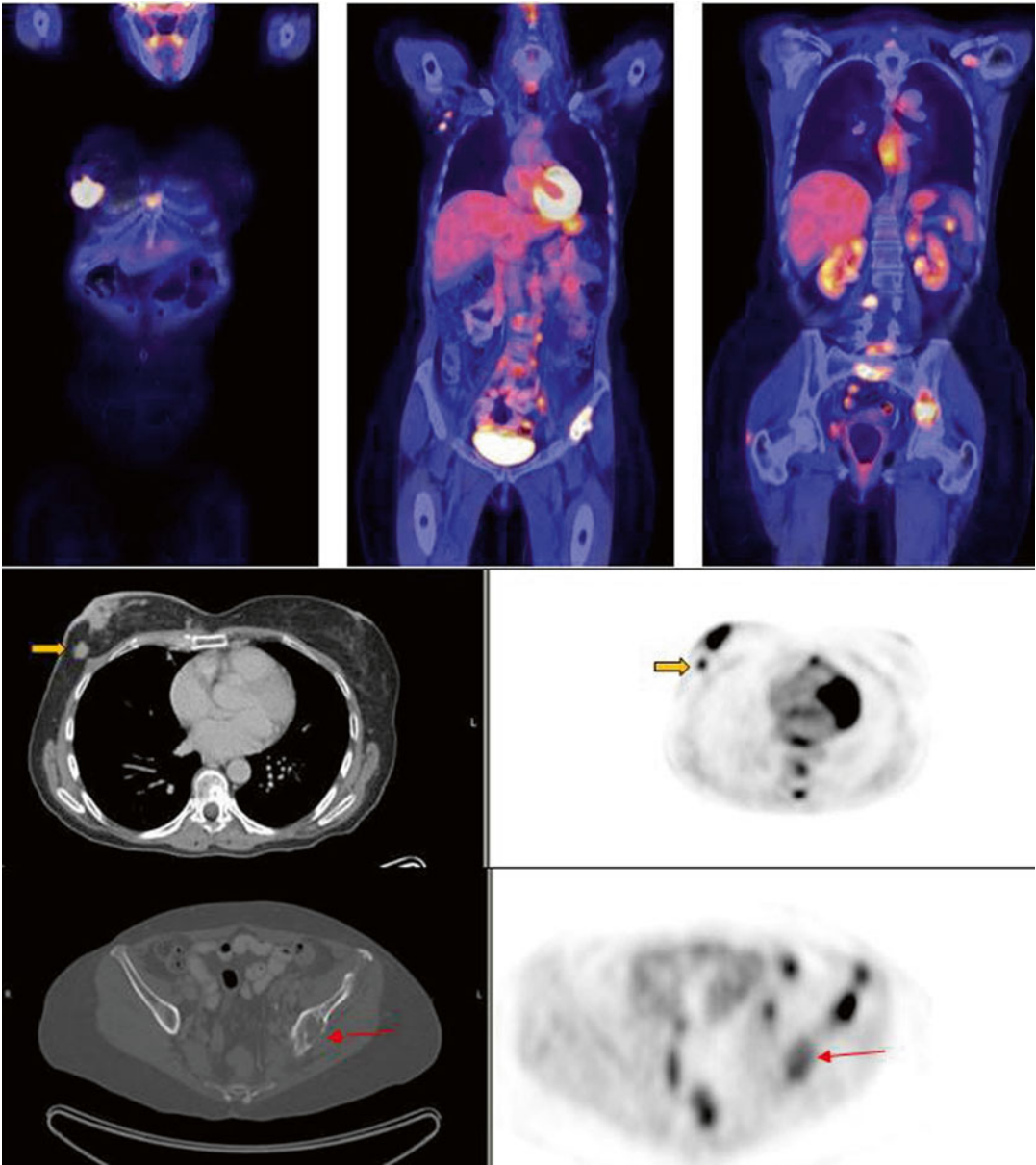


FIG. 3.5

sternal metastasis may be caused by local tumor invasion from either the primary site or adjacent lymph nodes [7]. Coleman et al. [8] reported that important prognostic factors for survival after the development of osseous metastasis in breast cancer depended on the histopathological grade of the primary tumor, ER status, presence of skeletal metastasis at initial breast cancer diagnosis, disease-free interval, and age.

Case 3.4: Metastatic Breast Cancer

History

A 5-year-old female with right breast cancer and hepatic metastases, on chemotherapy.

Findings (Fig. 3.6)

(Top row image) Hypermetabolic solitary right axillary LN, SUVmax 6.8, consistent with metastatic disease. (Middle row image) Hypermetabolic

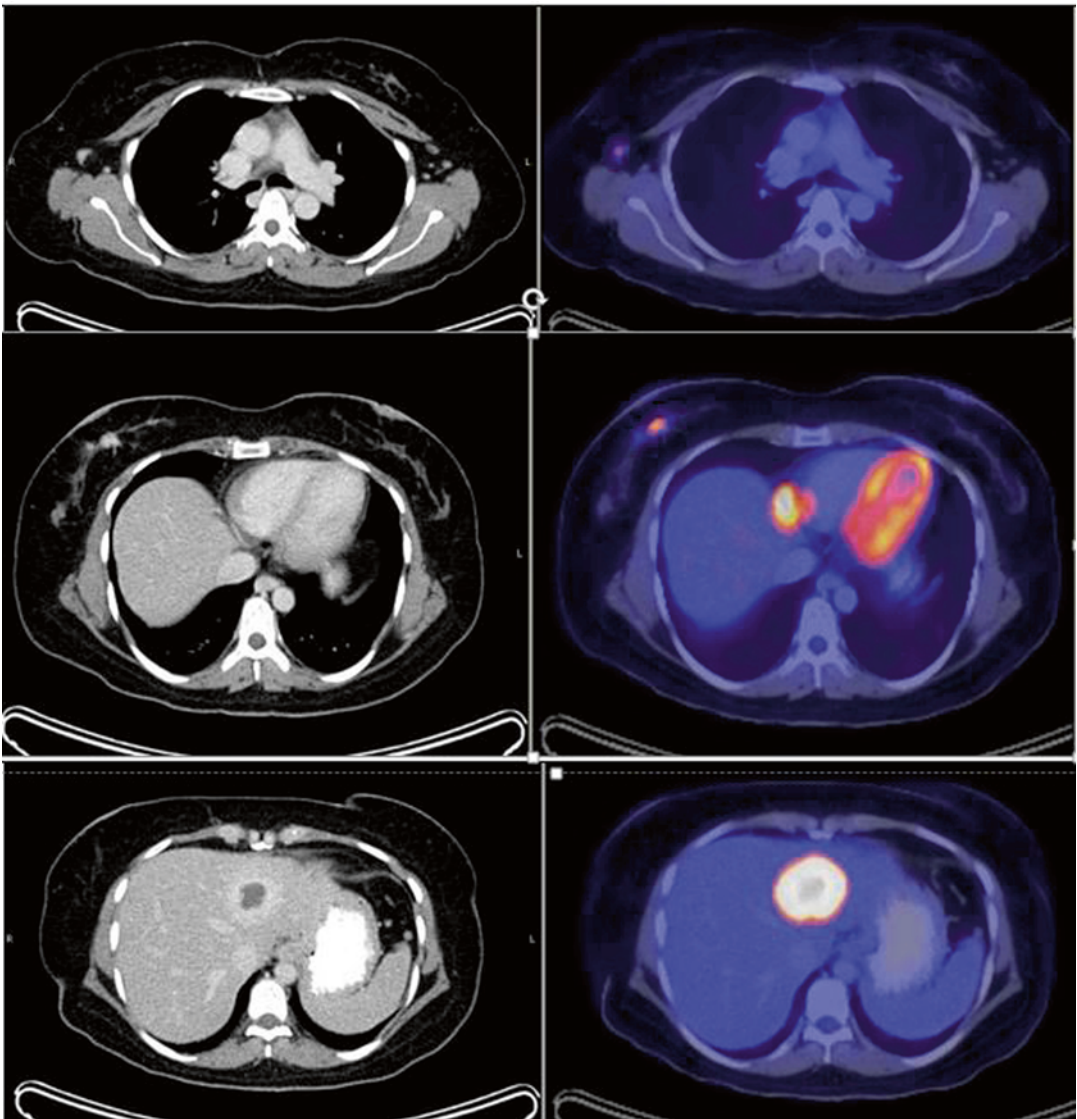


FIG. 3.6

soft tissue density in the medial quadrant of the lower right breast, SUVmax 8.3, consistent with known breast primary. (*Bottom row image*) Large hypermetabolic left hepatic lobe lesion, SUVmax 14.0, with central necrosis.

Impression

Hypermetabolic right breast primary neoplasm with ipsilateral right axillary LN metastasis and hypermetabolic hepatic metastasis.

Pearls and Pitfalls

PET/CT may be more sensitive than serum tumor markers in detecting relapse of breast cancer [9].

Discussion

⁹⁰Y radio embolization (selective internal radiation therapy [SIRT]) has emerged as a valuable therapeutic option in unresectable, chemotherapy-refractory hepatic metastases from breast cancer. The change in SUV (max) as assessed by (18)F-FDG-PET/CT before and 3 mos after SIRT was identified as the only independent predictor of survival in patients with hepatic metastases of breast cancer [10].

Case 3.5: Stage IV Breast

History

A 55-year-old female presented with pathologic fracture of the left femoral neck. Shown below are images from the initial PET/CT (*top row in figs 3.7, 3.8, 3.9, 3.10*) and follow-up PET/CT (performed 6 months following chemotherapy, *bottom row in figs 3.7, 3.8, 3.9, 3.10*).

Findings (Figs. 3.7, 3.8, 3.9, and 3.10, top rows)

Pretherapy images showed focally hypermetabolic, spiculated right breast lesion, SUVmax 5.2, with mildly hypermetabolic right axillary lymph node, SUVmax 2.4, and FDG avid right hilar lymph node. Intense activity at the left femoral neck corresponds to a lytic lesion causing pathologic fracture, seen best in Fig. 3.10 (*top*).

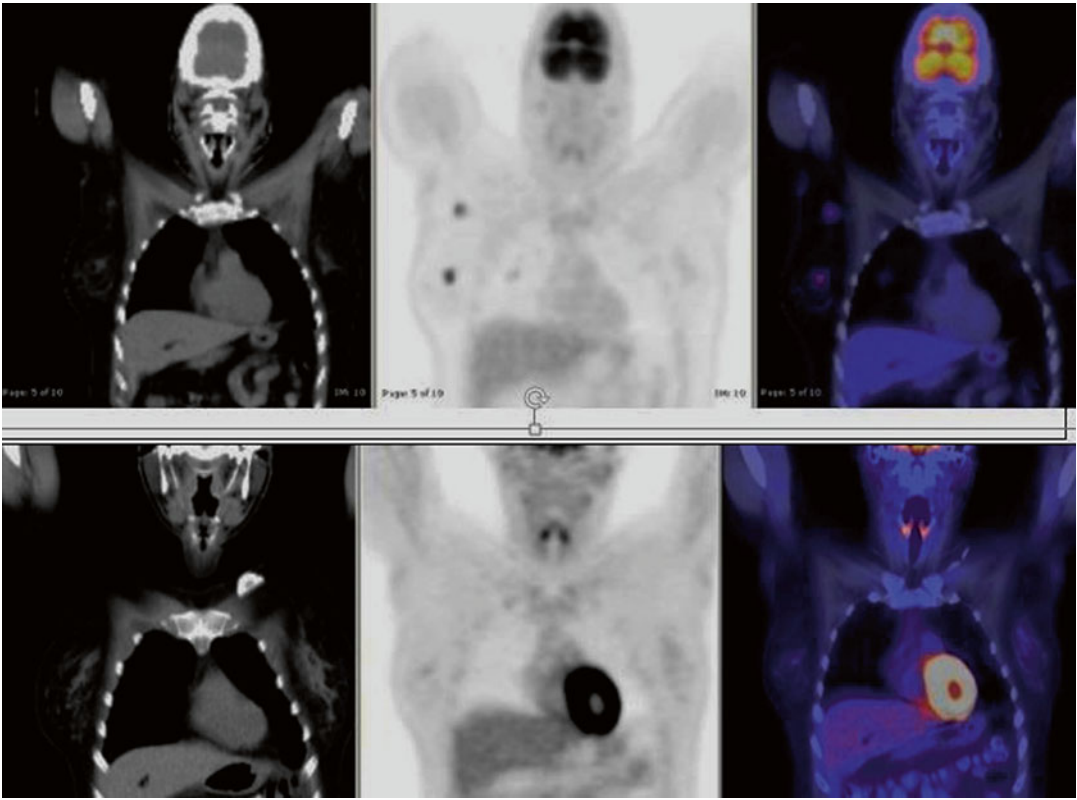


FIG. 3.7

Findings (Figs. 3.7, 3.8, 3.9, and 3.10, bottom rows)

Post-therapy images showed resolution of metabolic activity within previously noted primary breast neoplasm and hypermetabolic right axillary lymph node.

No abnormal activity in the right breast (status post lumpectomy), resolution of metabolic activity within previously noted hypermetabolic right axillary lymph node. Status post left hip arthroplasty, with resection of previously noted hypermetabolic osseous lesion. No scan evidence of metabolically avid disease elsewhere.

Impression

Stage IV breast cancer demonstrating excellent response to chemotherapy by scan pattern.

Pearls and Pitfalls

FDG-PET/CT can improve staging and alter therapeutic options in patients suspected to have breast cancer recurrence with or without distant metastatic disease, primarily by demonstrating local or distant nodal

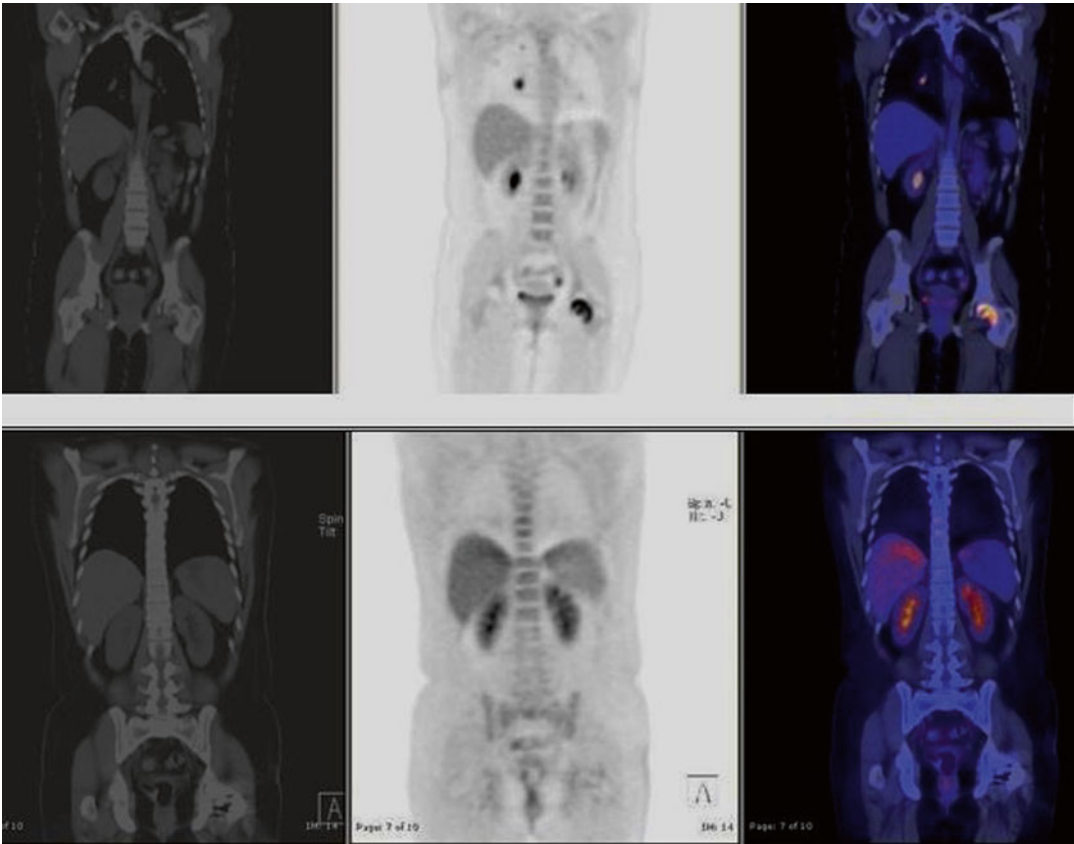


FIG. 3.8

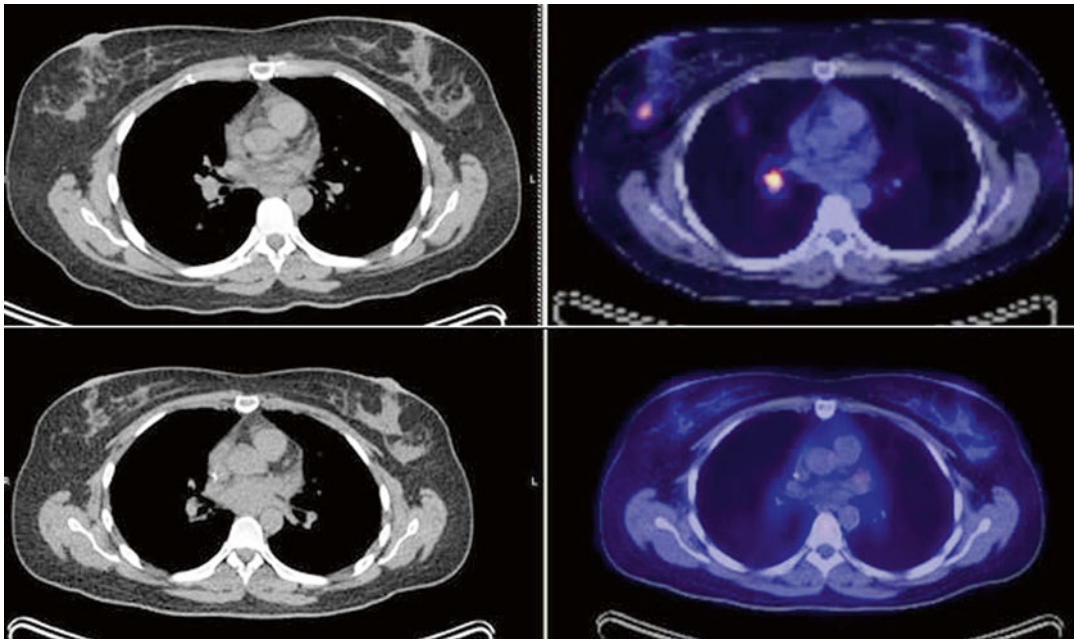


FIG. 3.9

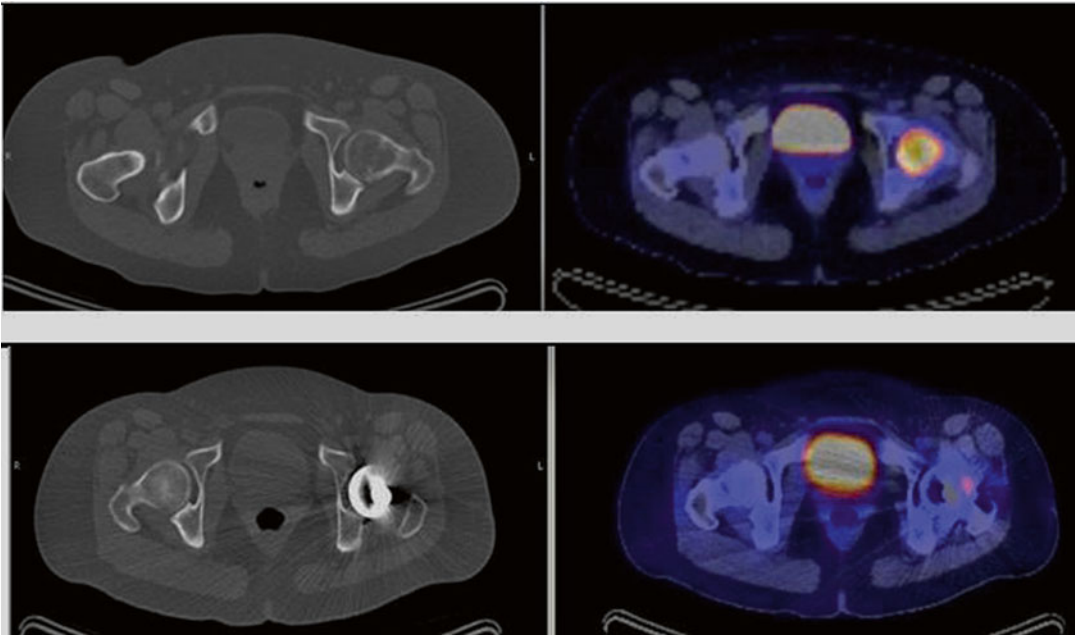


FIG. 3.10

involvement, which may present as occult at other imaging studies [11]. FDG-PET is complementary to bone scintigraphy, which remains the standard imaging procedure for surveying the skeleton for metastatic involvement. FDG-PET can be particularly useful in this setting to evaluate the response of metastatic breast cancer to systemic therapy, since conventional imaging is often challenging in this setting.

Discussion

There are two major patterns of disease spread in metastatic breast carcinoma, excluding patients with extensive diffuse metastases [12]. Patients with ER+/PR+ tumors tend to develop osseous but not brain metastases. Patients with ER-/PR- tumors tend to develop brain but not osseous metastases. Appreciation of these distributions can aid the radiologist in detecting metastatic lesions and will help the clinician to estimate the likelihood of metastases to various organ systems as well as to potentially target therapy.

Case 3.6: Invasive Ductal Carcinoma

History

A 53-year-old female, undergoing workup for invasive ductal carcinoma of right breast.

Findings (Fig. 3.11)

(Right breast; top left) Retroareolar spiculated mass corresponding to known invasive ductal carcinoma. Evidence of nipple involvement including enhancement and inversion, diffuse skin thickening and enhancement, consistent with inflammatory breast carcinoma. BI-RADS 6. An additional 1.5 cm enhancing mass at the 11:00 axis. The position of this second mass relative to the retroareolar mass above results in a total span of disease of approximately 5.6 cm. BI-RADS 5. Multiple abnormal level one right axillary lymph nodes, the largest of which measures approximately 4.4 cm AP×3.2 cm ML×2.3 cm SI, consistent with metastases. BI-RADS 5. (Left breast; top right): Normal appearing 1.1 cm intramammary lymph node. No significant MR abnormalities identified. BI-RADS: 1

Findings (Figs. 3.12 and 3.13)

Hypermetabolic primary neoplasm with satellite lesion in the right breast, presence of metastatic right axillary lymph node (seen best in coronal images, Fig. 3.12) with overlying skin thickening, demonstrating inflammatory changes (Fig. 3.13).

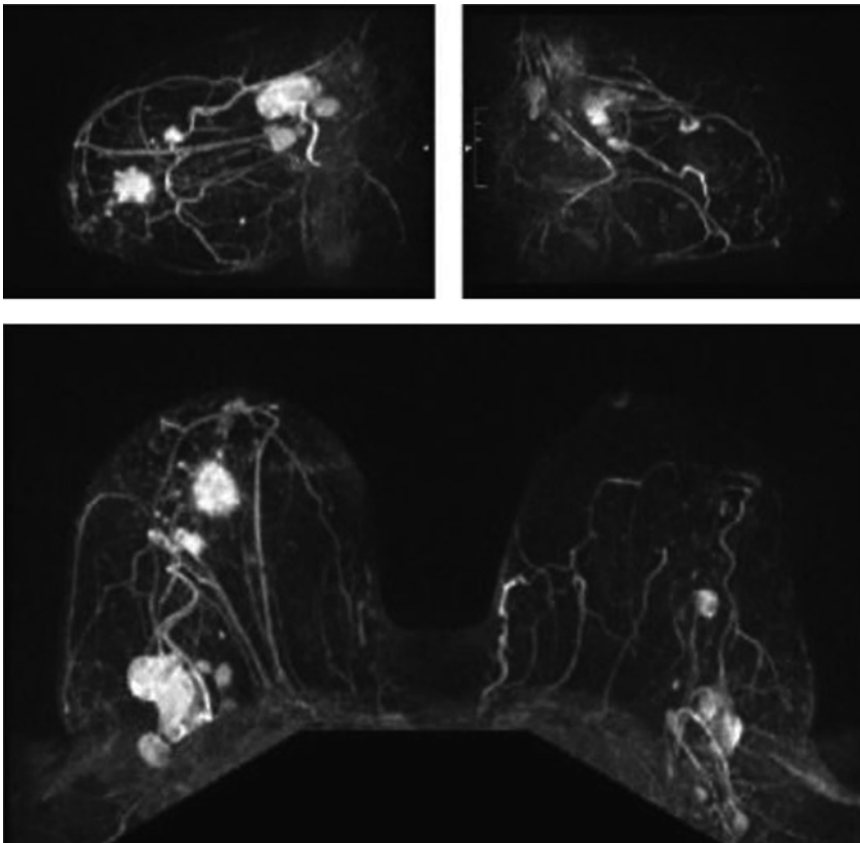


FIG. 3.11

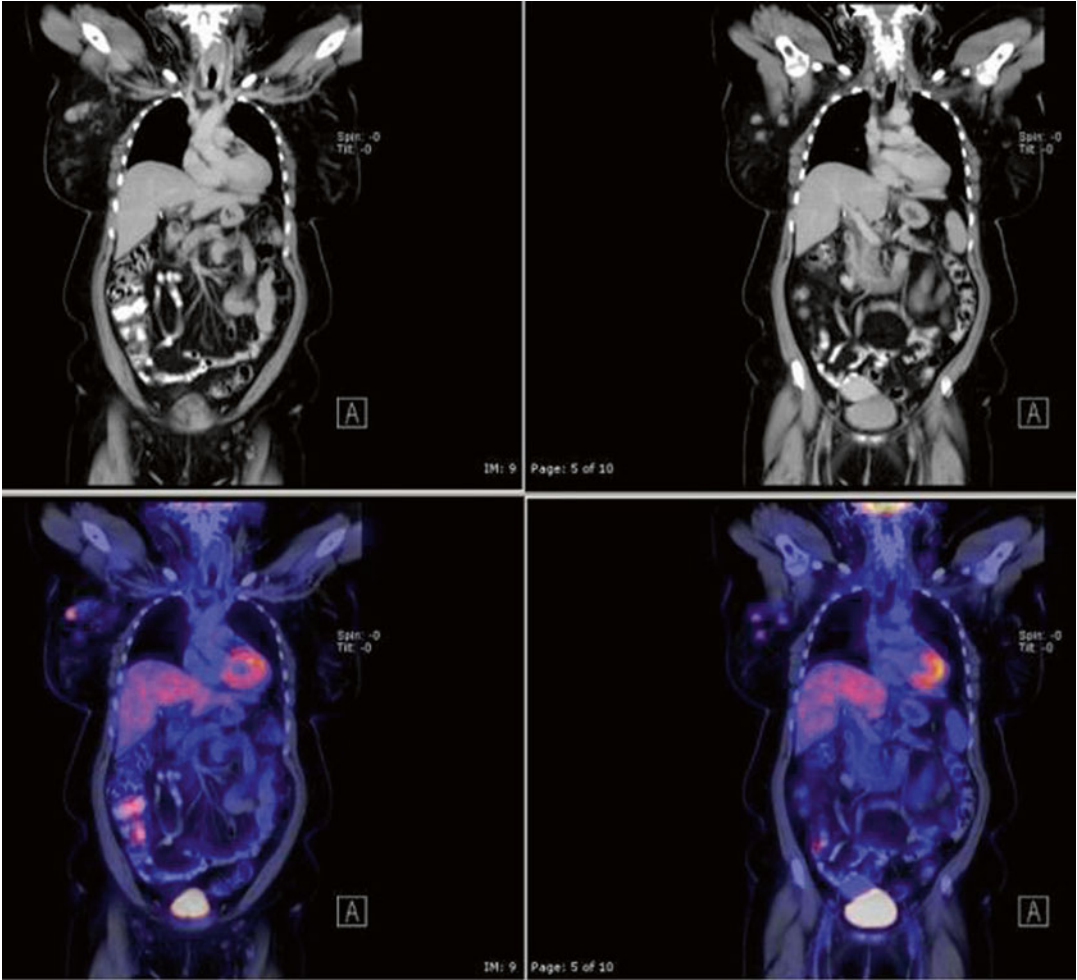


FIG. 3.12

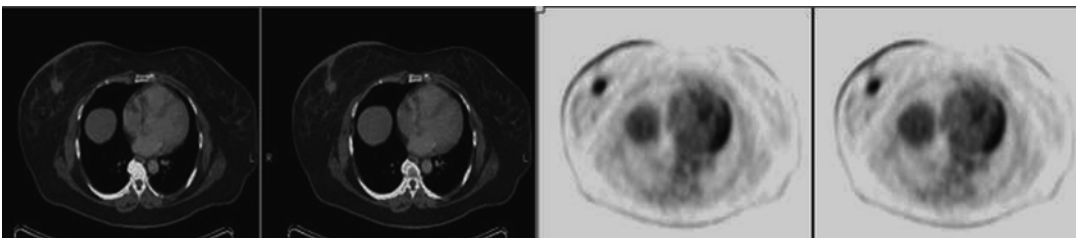


FIG. 3.13

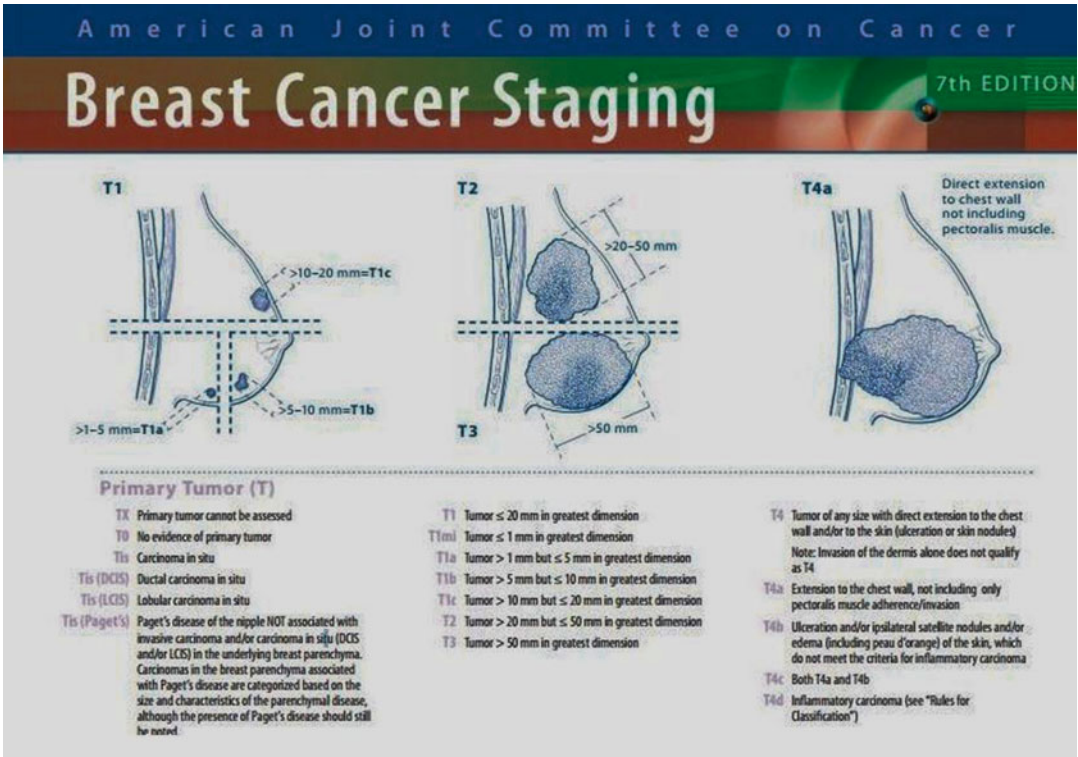


FIG. 3.14

Impression

Stage IIIB, breast cancer.

Discussion (Fig. 3.14)

The most common system used to describe the stages of breast cancer is the American Joint Committee on Cancer (AJCC) TNM system [13].

Case 3.7: Male Breast Cancer

History

A 73-year-old male with history of right breast carcinoma, status post (s/p) right mastectomy, showed disease progression over the course of 4 years.

Findings (Fig. 3.15)

Initial PET images showed hypermetabolic metastatic disease in T6 and T9 vertebrae and the left hepatic lobe. Similar study obtained 4 years later showed disseminated osseous metastasis, numerous hepatic lesions, metastatic pleural disease, and metastatic nodal disease.

Impression

Progression of hypermetabolic metastatic disease in a case of male breast ca, s/p mastectomy.

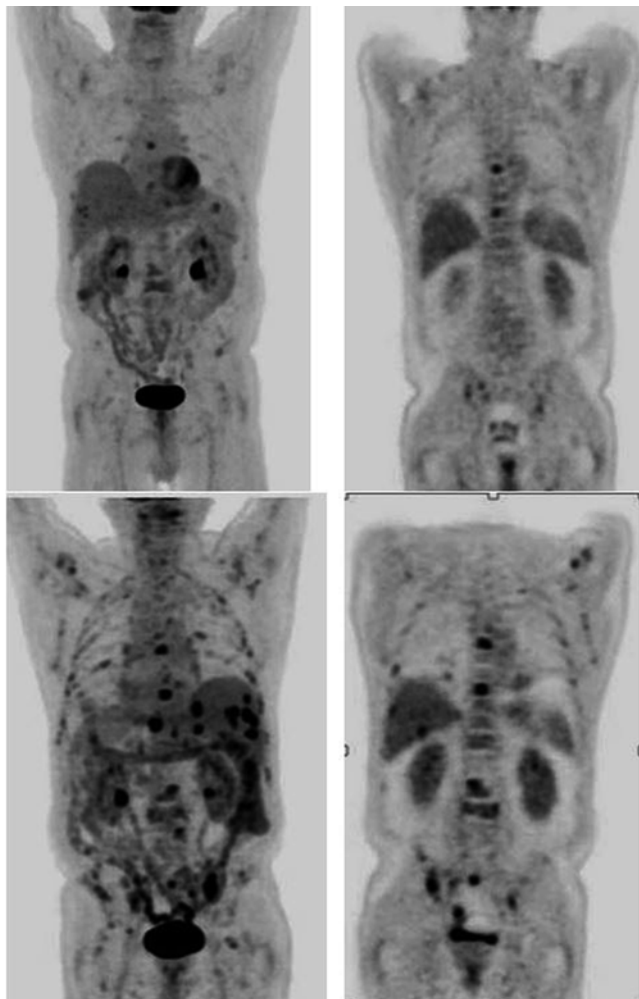


FIG. 3.15

Discussion

Men at any age may develop breast cancer, but it is usually seen in men between 60 and 70 years of age. Male breast cancer makes up less than 1 % of all cases of breast cancer. Risk factors for breast cancer in men may include the following [14]:

1. History of radiation exposure
2. Having a disease related to high levels of estrogen in the body, such as cirrhosis (liver disease) or Klinefelter syndrome (a genetic disorder)
3. Having several female relatives who have had breast cancer, especially relatives who have an alteration of the BRCA2 gene

Case 3.8: Role of Positron Emission Mammography (PEM) in Breast Cancer

History

A 50-year-old female, newly diagnosed with invasive breast cancer in the upper outer quadrant of the right breast.

Findings (Fig. 3.16)

(Right breast; top left) In the central 10 o'clock axis approximately 5 cm deep to the nipple, there is a $2.9 \times 2.6 \times 2.2$ cm spiculated enhancing mass, consistent with the site of biopsy-proven invasive malignancy. No evidence of nipple, skin, or chest wall involvement. No satellite lesions identified. Remainder of the breast and the right axilla appears unremarkable. Right breast MRI BI-RADS: 6. (Left breast; top right): No occult masses, abnormal areas of enhancement, or adenopathy. Left breast MRI BI-RADS: 1.

Findings (Fig. 3.17)

Known breast neoplasm demonstrating intense FDG uptake in the 10 o'clock axis of the right breast, $SUV_{max} = 8.2$. The remainder of the right breast was normal. Right breast PEM BI-RADS: 6. (No abnormality in the left breast; left breast PEM BI-RADS1—image not shown).

Impression

Intensely hypermetabolic right breast mass, corresponding to known primary neoplasm, proven on biopsy.

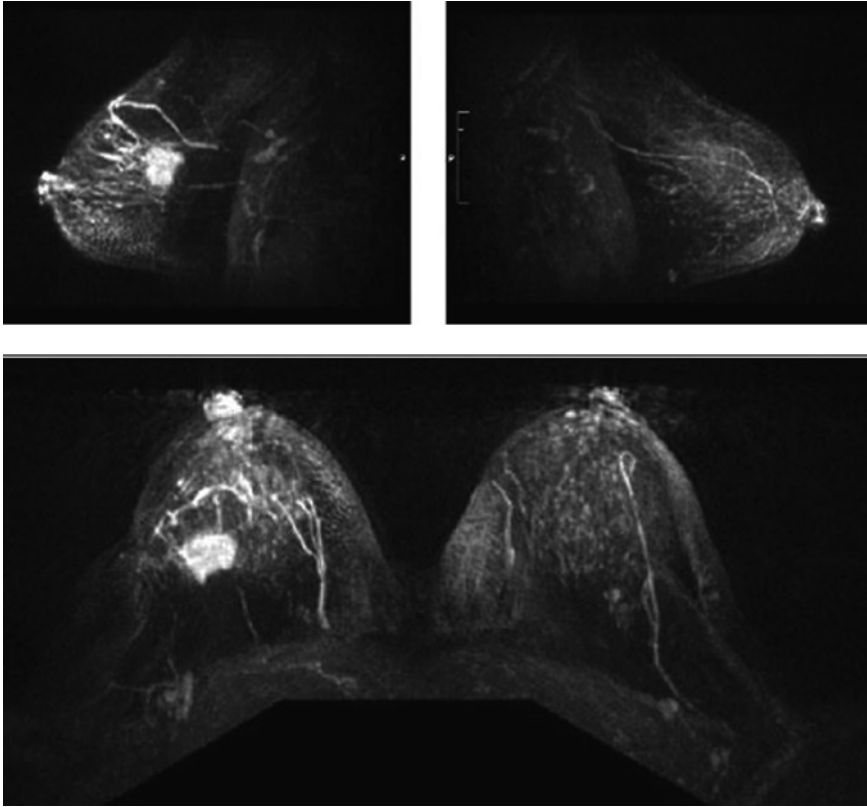


FIG. 3.16

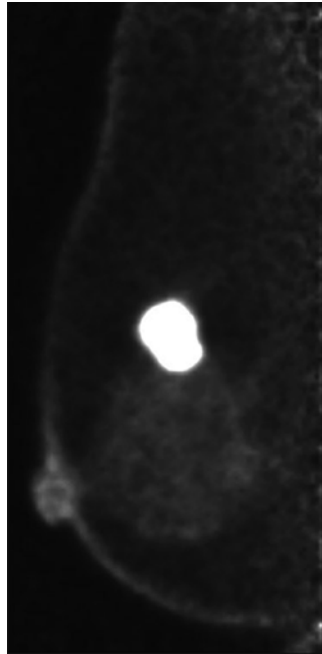


FIG. 3.17

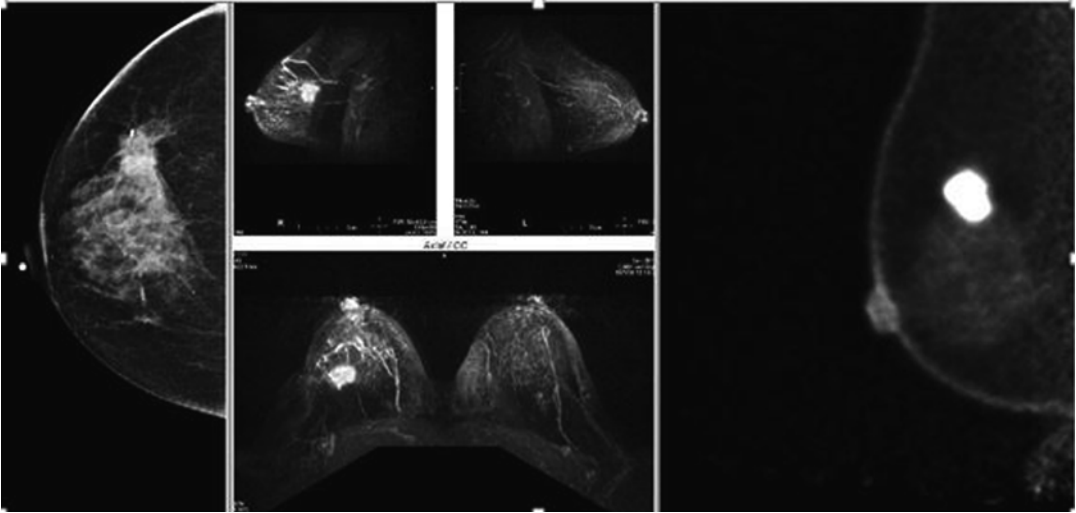


FIG. 3.18 Comparison view, mammogram, MRI breast, and PEM of the same patient

Discussion

Dedicated breast positron emission mammography (PEM) units have been developed to overcome the limitations of whole-body PET and to provide a positron emission imaging platform capable of detection and depiction of primary breast carcinoma [11]. In general, these systems consist of two planar detectors placed opposite a gently compressed breast. The advantages of such dedicated systems include improved geometric sensitivity, higher spatial resolution, shorter imaging time, and reduced attenuation compared with whole-body PET systems. They also have a small physical footprint, which makes their use in a breast imaging facility feasible and allows correlation of the results with those of conventional breast imaging as well as PEM-guided biopsy.

Case 3.9: Breast Activity in a Case of Nodal Non-Hodgkin's Lymphoma

History

A 38-year-old female, newly diagnosed with NHL following biopsy of a left neck mass.

Findings (Fig. 3.19)

Asymmetric, diffuse left breast activity (SUVmax 4.3), corresponding to dense left breast tissue on concurrent CT. Diffuse, increased FDG activity involving medial two-third of left clavicle and adjacent soft tissue, medial head of left clavicle, shows SUVmax 4.4, corresponding to biopsy-proven diagnosis of NHL.

Impression

Finding consistent with preferential lactating breast status in a setting of active NHL.

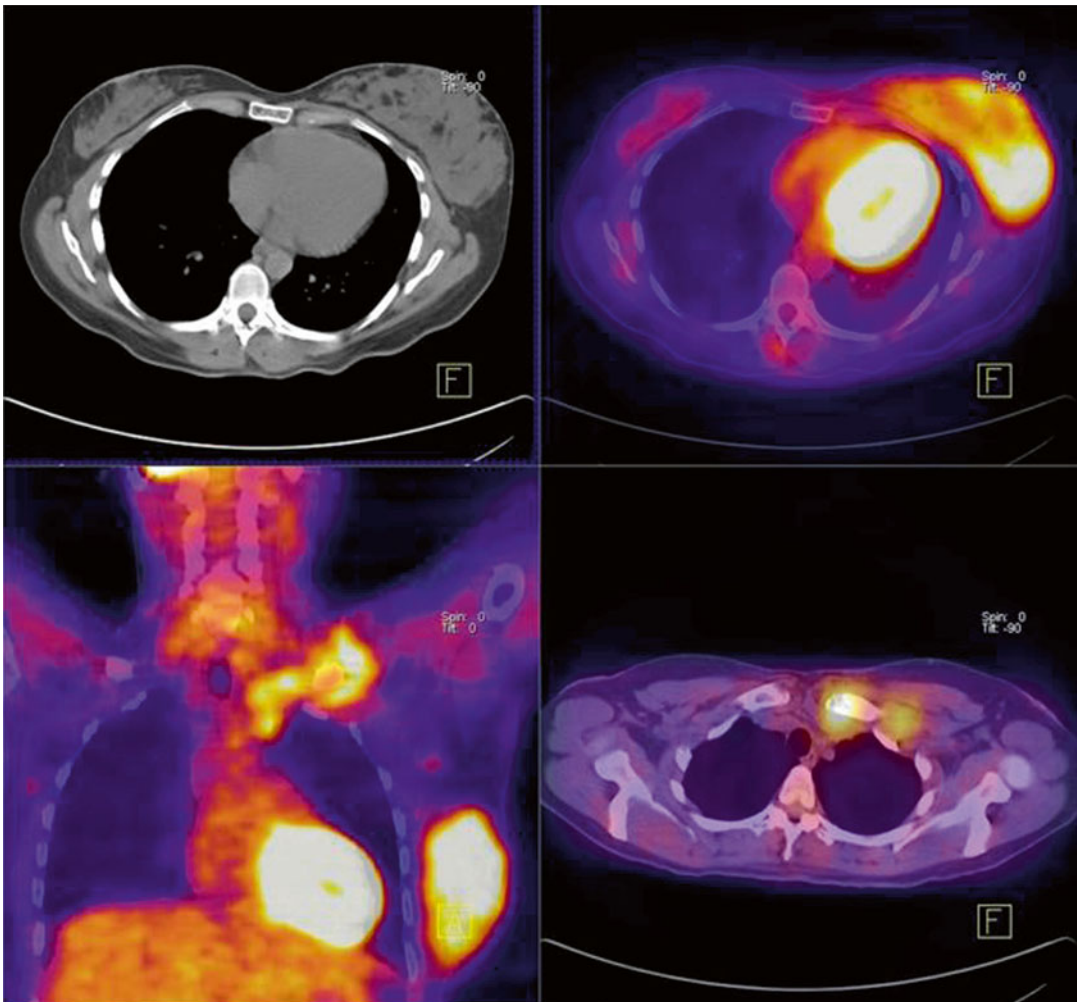


FIG. 3.19

Pearls and Pitfalls

The lactating breast has been reported to show FDG uptake related to increased glucose trapping in active glandular tissue, causing false-positive readouts. Tissue density and hormonal status also affect the uptake of FDG in the breast; dense breasts have significantly greater FDG uptake than do fatty breasts. However, the ability to discriminate between benign and malignant breast lesions is unlikely to be affected by normal physiologic uptake in the breast, because the average SUV of normal breast tissue is low [1].

Discussion

Some of the administered ^{18}F -FDG might be excreted in small amounts in breast milk. Normally, the scan should be delayed until breast-feeding has stopped. But if the scan is needed urgently, then it is advisable to collect milk before the scan, so that this can be used to provide a feed after the scan [15]. Furthermore, milk should be collected and discarded for 2 h after the scan. Normal breast-feeding can resume after that.

Case 3.10: Diffuse Large Cell Lymphoma of Breast

History

A 48-year-old female presents with diffuse large cell lymphoma (DLBCL) of the right breast.

Findings (Fig. 3.20)

Hypermetabolic soft tissue density anterior to the right breast implant, SUVmax 7.5. Left breast tissue is relatively less dense with low-grade activity, possibly related to postsurgical changes following left breast implant removal.

Impression

Diffuse soft tissue activity within the right breast consistent with biopsy-proven diagnosis of DLBCL. Likely postsurgical changes in the left breast.

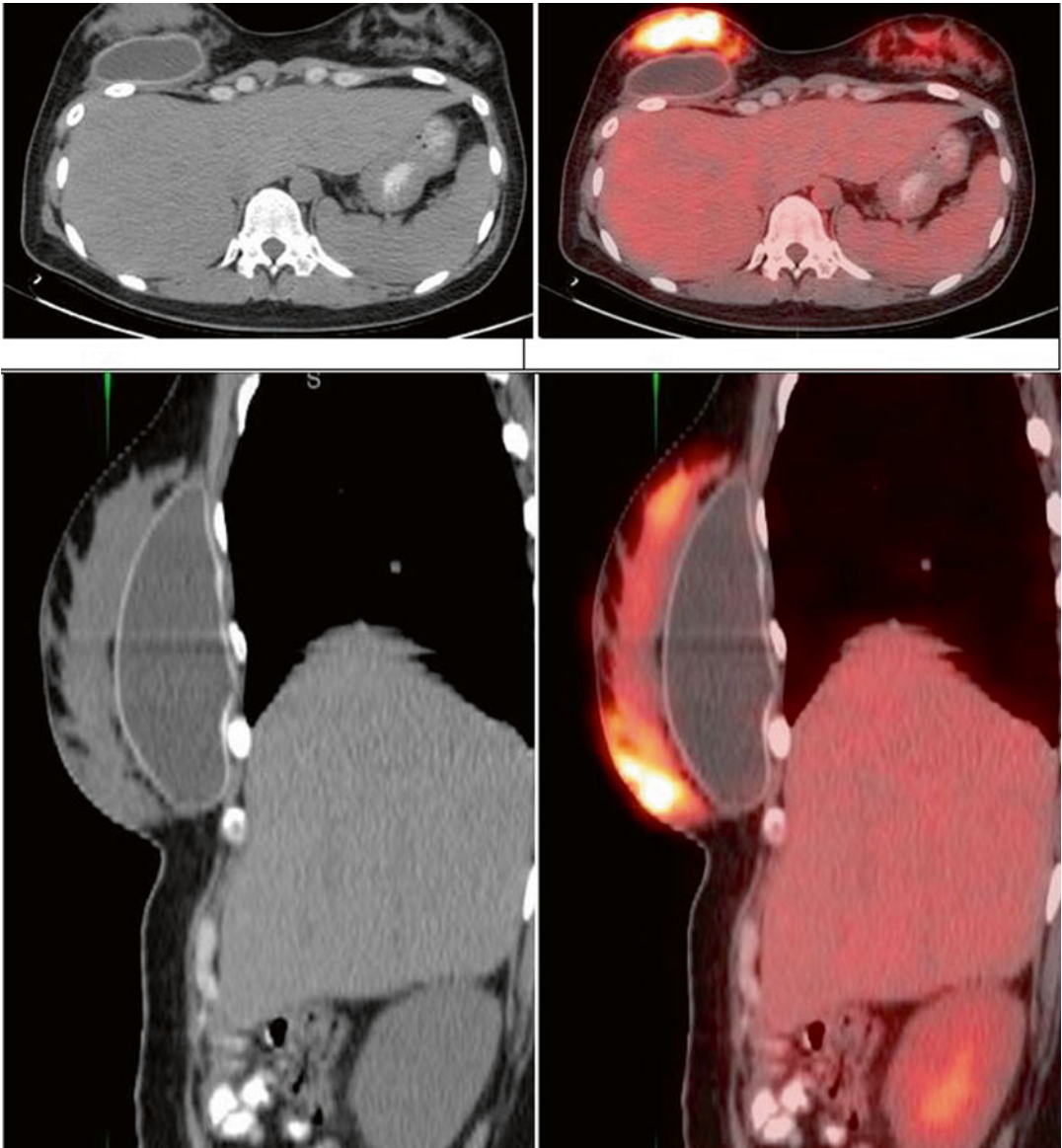


FIG. 3.20

Discussion

Primary breast lymphoma (PBL) and breast involvement in systemic lymphoma are rare [16]. Primary breast DLBCL appears to have a worse prognosis than early stage DLBCL in nodal or other extra nodal sites.

There is no consensus on the question of how to best treat PBL. Mastectomy offers no benefit in the treatment of PBL. The combined

therapy approach, with chemotherapy and radiotherapy, is the most successful treatment. PBL is poorly represented in rituximab-containing trials in DLBCL patients; there is not much experience with this agent in breast DLBCL. Because of the high incidence of central nervous system (CNS) involvement in PBL patients, many authors strongly believe that patients with aggressive forms of PBL should receive CNS infiltration prophylaxis [17].

REFERENCES

1. Lim HS, Yoon W, et al. FDG PET/CT for the detection and evaluation of breast diseases: usefulness and limitations. *Radiographics*. 2007;27:S197–213. doi:10.1148/rg.27si075507October.
2. Ductal carcinoma in situ. <http://www.cancer.gov/cancertopics/pdq/treatment/breast/healthprofessional/page4>.
3. Fisher ER, Dignam J, Tan-Chiu E, et al. Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) eight-year update of protocol B-17: intraductal carcinoma. *Cancer*. 1999;86(3):429–38 [PUBMED Abstract].
4. Jansson T, Westlin JE, Ahlstrom H, Lilja A, Langstrom B, Bergh J. Positron emission tomography studies in patients with locally advanced and/or metastatic breast cancer: a method for early therapy evaluation? *J Clin Oncol*. 1995;13:1470–7.
5. Bassa P, Kim EE, Inoue T, et al. Evaluation of preoperative chemotherapy using PET with fluorine-18-fluorodeoxyglucose in breast cancer. *J Nucl Med*. 1996;37:931–8.
6. Song BI, Lee SW, et al. ¹⁸F-FDG uptake by metastatic axillary lymph nodes on pretreatment pet/ct as a prognostic factor for recurrence in patients with invasive ductal breast cancer. *J Nucl Med*. 2012;53(9):1337–44.
7. Koizumi M, et al. Comparison between solitary and multiple skeletal metastatic lesions of breast cancer patients. *Ann Oncol*. 2003;14(8):1234–40. doi:10.1093/annonc/mdg348.
8. Coleman RE, Smith P, Rubens RD. Clinical course and prognostic factors following bone recurrence from breast cancer. *Br J Cancer*. 1998;77:336–40.
9. Diagnosis of breast cancer metastasis with PET/CT in patients with elevation of tumor markers. http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=100&abstractID=60273.
10. Haug AR, Tiega Donfack BP, et al. 18F-FDG PET/CT predicts survival after radio embolization of hepatic metastases from breast cancer. *J Nucl Med*. 2012;53(3):371–7. Epub 2012 Feb 13.
11. Rosen EL, et al. FDG PET, PET/CT, and breast cancer imaging. *Radiographics*. 2007;27:S215–29. doi:10.1148/rg.27si075517October.
12. Maki DD, et al. Patterns of disease spread in metastatic breast carcinoma: influence of estrogen and progesterone receptor status. *AJNR Am J Neuroradiol*. 2000;21:1064–6.
13. Cancer staging poster series. <http://www.cancerstaging.org/staging/index.html>.
14. Male breast cancer. <http://www.cancer.gov/cancertopics/pdq/treatment/malebreast/Patient/page5>.

15. Radiation protection of patients. https://rpop.iaea.org/RPOP/RPoP/Content/InformationFor/HealthProfessionals/6_OtherClinicalSpecialities/PETCTscan.htm#PETCT_FAQ08.
16. Pisani F, et al. Diffuse large B cell lymphoma involving the breast: a report of four cases. *J Exp Clin Cancer Res.* 2006;25(2):277–81.
17. Mouna B, et al. Primary malignant non-Hodgkin's lymphoma of the breast: a study of seven cases and literature review. *World J Surg Oncol.* 2012;10:151. doi:10.1186/1477-7819-10-151.