ACCEPTED MANUSCRIPT

Accepted manuscripts are the articles in press that have been peer reviewed and accepted for publication by the Editorial Board of the Vojnosanitetski Pregled. They have not yet been copy edited and/or formatted in the publication house style, and the text could still be changed before final publication.

Although accepted manuscripts do not yet have all bibliographic details available, they can already be cited using the year of online publication and the DOI, as follows: article title, the author(s), publication (year), the DOI.

Please cite this article: CONTRIBUTION OF FDG PET IMAGING IN THE DETECTION OF UNDERLYING CARCINOMA IN A WOMAN WITH NONSPECIFIC MASTITIS


UDC:

DOI: 10.2298/VSP161026010H

When the final article is assigned to volumes/issues of the Journal, the Article in Press version will be removed and the final version appear in the associated published volumes/issues of the Journal. The date the article was made available online first will be carried over.
Gulhane Military Medical Academy and School of Medicine, Departments of Nuclear Medicine and General Surgery*, Etlik-Ankara, Turkey.

Correspondence:
Semra Ince, MD
Gulhane Military Medical Academy and School of Medicine, Departments of Nuclear Medicine and General Surgery*
06018  Etlik-Ankara  Turkey
Phone: (+90) 312 304 48 28
Fax  : (+90) 312 304 48 00
E-mail: since@gata.edu.tr
Abstract

Introduction. Differentiation between a malignancy and inflammatory process is still a diagnostic challenge. Mammography (MG) and ultrasonography (US) have low sensitivity and specificity in dense breasts in order to detect malignancy. On the other hand, malignant mass lesions can also be masked on magnetic resonance imaging (MRI) by diffuse inflammatory process. 18-fluorodeoxyglucose positron emission tomography (FDG PET) imaging can be a promising alternative imaging method in the evaluation of suspicious breast masses, especially in patients with accompanying inflammatory breast diseases.

Case report. We report an atypical case of a patient suspected for malignancy in right breast on physical examination and radiologic findings in favor of mastitis. Neither MG nor US revealed any mass lesion consistent with malignancy. Moreover, MRI findings were primarily considered as infectious or granulomatous mastitis. However, FDG PET determined the accurate borders of tumor and dissemination of breast cancer with superiority to other conventional radiological methods. Conclusion. This case report emphasizes the contribution of FDG PET imaging to other conventional radiological methods with regard to primary tumor diagnosis, determination of the biopsy site, and also staging the disease especially in patients with accompanying inflammatory breast disease.

Key words: breast cancer; FDG PET; mastitis; MRI.

Introduction

Differentiation between a malignancy and inflammatory process is still a diagnostic challenge. There is no radiologic criterion to allow definitive diagnosis for both inflammatory carcinoma and benign inflammatory disorders including infectious and noninfectious diseases (e.g. granulomatous mastitis, mastitis/abscess formation and fat necrosis) [1, 2]. Breast edema, enlargement, skin thickening, nipple discharge/retraction,
abscess and axillary lymphadenopathy are common and nonspecific findings of all above mentioned benign and malignant inflammatory entities [1]. Because benign and malignant inflammatory conditions may have similar signal characteristics and contrast enhancement patterns, as in our case, malignant mass lesions can be masked by diffuse inflammatory process on magnetic resonance imaging (MRI) [1]. On the other hand, 18-fluorodeoxyglucose positron emission tomography (FDG PET) can depict areas of abnormal uptake with a higher sensitivity and shows the site where biopsy should be taken [3]. FDG PET imaging can be a promising alternative imaging method in the evaluation of inflammatory breast diseases and may obviate extensive use of MRI. Here, we present a woman with a mass suspected for malignancy in right breast and radiologic findings in favor of mastitis. FDG PET determined the correct location and dissemination of breast cancer with superiority to other conventional radiological methods.

**Case report**

A 35-year old woman presented with the complaints of right breast enlargement and nipple retraction. In addition to them, orange peel appearance (peau d'orange) was seen on physical examination but no focal mass was detected (Figure 1). Conventional imaging methods were planned with suspicion of inflammatory breast cancer (IBC) or invasive breast cancer. Ultrasonography (US) revealed diffuse skin thickening and edema without discrete lesion on the right side consistent with benign mastitis. Several lymphadenopathy were also noted on the right axillar region. Mammography (MG) was performed shortly after US and confirmed nipple retraction, diffuse skin thickening and marked trabecular thickening (Figure 2). The breast parenchyma was hyperdense and microcalcification or spicules contoured mass lesion consistent with malignity were not present on MG. One week later MRI was performed in order to depict any malignant focus, by using a dedicated
breast coil (Figure 3). MRI showed diffuse areas of low signal intensity on T1-weighted (Figure 3A) and widespread hyperintense areas on T2-weighted images suggesting edema (Figure 3B, 3C). These edematous areas demonstrated marked contrast enhancement (Figure 3D). However, no focal abnormal signal changes suggesting malignancy was observed, and time-signal intensity curves did not suggest malignancy. Therefore, MRI findings were primarily considered as infectious or granulomatous mastitis. Excisional biopsies made twice from the most suspicious areas were reported as chronic nonspecific mastitis. Due to continued doubts about breast cancer, patient's clinical whole-body FDG PET scan was planned one month after MRI. FDG PET images revealed heterogeneously increased FDG uptake extents in upper outer quadrant of the right breast (SUV max= 5.5), focal increased FDG uptake in 6 right axillar (SUV max= 9.2) and 1 right supraclavicular (SUV max= 3.2) lymph nodes. Moreover, FDG PET showed focal increased FDG uptake in upper part of sacrum (SUV max= 7.4) consistent with bone metastasis (Figure 4). Excisional biopsy was repeated from upper outer quadrant of the right breast according to FDG PET results, and revealed as infiltrative ductal carcinoma. Tumor size was 2.5 cm and the estrogen and progesterone receptors status were both negative. Her2 neu score was positive. Bone metastasis in sacrum was also confirmed by MRI.

**Discussion**

Mastitis is a benign inflammatory disease of the breast which may mimic breast cancer clinically and radiologically. It includes a group of acute and chronic inflammatory situations. Nearly half of the patients had clinical and radiological findings suggesting a malignant tumor. Punch biopsy and histopathologic examination are often necessary to determine a definitive diagnosis [4].

The pathophysiology of breast cancer presenting as mastitis is unclear. It’s possible to have been caused by tumor cells damaging epithelial cells and basement membrane
surrounding the ductal lumen. This causes death of ductal tissue and behaves as a source for chronic infection. Another possible explanation may be related to recurrent infection of the necrotic areas within the tumor. Thus, these result atypical manifestation of breast cancer as inflammatory mastitis [5].

It still remains a challenge to differentiate IBC from benign mastitis as well as from breast cancer since they are often misdiagnosed as in our case. Breast erythema, edema, tenderness, pain, warm breast, peau d’orange and swelling are the most common signs suggesting both benign and malign inflammatory conditions. IBC is a rare entity and constitutes 2.5% of all cases with breast cancer. It is the most aggressive variant of breast cancer and has a very poor prognosis. Skin thickening without a mass is the most common radiographic finding on MG and US for IBC as in our case. MRI plays a crucial role in the differential diagnosis of IBC. Tumor emboli blocking the dermal lymphatics are the pathognomonic features on histology which leads to diagnosis [6]. IBC was excluded by several excisional biopsies in our case.

MG and USG provide benefits in many cases for the detection of breast masses and the diagnosis of malignancy. Malign breast lesions tend to appear on MG as microcalcification (76%), soft tissue densities (11%) or both (13%) [4]. However, both of them have low sensitivity and specificity in dense breasts as in our case, and also in patients having a prosthesis or prior surgery. Additionally, it is not uncommon to experience difficulty in differentiation inflammatory breast diseases and breast cancer using US and MG since both could have false negative findings [7].

Since MRI is highly sensitive in detecting breast cancer, it is often used as a diagnostic tool to evaluate equivocal mammographic findings. Although, MRI cannot replace to MG or US for a complete diagnostic evaluation due to its high cost and limited specificity [8], it may play an important role in differentiation breast tumor form IBC. Skin
enhancement without a mass-like formation, diffuse cutaneous/subcutaneous/ prepectoral edema and skin thickening are the most important findings for IBC in MRI in most cases [6]. While tumors differ from inflammatory conditions with more localized findings, non-mass-like lesions can cause difficulty in diagnosis with MRI. Patients with breast cancers more frequently present with a lobulated or irregular margin than as in the case with benign mastitis or IBC. A vessel adjacent to the lesion is another indicator suggesting malignancy on MRI [9].

FDG PET is widely used in oncology for diagnosis, staging, re-staging and treatment evaluation. The diagnostic accuracy of FDG PET imaging in breast tumors has been shown superior to MRI, MG especially in dense breasts and after augmentation mammoplasty which have complicated conventional radiological findings to interpret [3,10]. The major advantages of FDG PET include showing multicentricity and lymph node, lung, bone metastases using only one imaging procedure. FDG uptake in tumors is well correlated with the amount of viable cancer cells in the tumor [10]. It’s reported that FDG accumulation was correlated with the pathologic grade of the tumor. Well-differentiated subtypes such as tubular or lobular carcinoma and carcinoma in situ show low FDG uptake. Tumor size is also important that FDG PET has difficulty in detecting small-sized tumors, especially lesions smaller than 1 cm may show low FDG uptake [11].

Unfortunately, since FDG is not a tumor specific agent, infectious or inflammatory mastitis may also cause false positive FDG uptake for malignancy [5, 12]. Mastitis is a well-known pitfall for FDG PET, and several cases of increased FDG uptake in acute and chronic infectious mastitis were previously reported [13]. The use of dual-time-point imaging would add to diagnostic accuracy, especially for lesions with lower SUVs and in differentiating inflammation from malignant lesions [12]. However, it’s quite
possible to differentiate inflammation from breast cancer by visual interpretation, careful clinical history and radiologic correlation.

FDG PET can be used as complementary to conventional radiological imaging techniques especially in equivocal cases or in the presence of negative radiologic findings in patients with a high clinical probability of malignancy. Additionally, FDG PET is a valuable imaging technique to show the extent of the disease regarding nodal status or distant metastases for initial staging in patients with IBC since the probability of metastases is high at presentation [13].

Conclusion

FDG PET imaging may show encouraging contribution to conventional radiological methods with regard to primary tumor diagnosis, determination of the biopsy site, and also disease staging especially in patients with accompanying inflammatory breast disease.

Consent

Informed consent was obtained from the patient for the publication of this case report and any accompanying images.

REFERENCES:


**Figure Legends**

**Figure 1:** Nipple retraction, orange peel appearance and enlargement is seen in right breast.

**Figure 2:** Craniocaudal views of (A) right and (B) left breast on mammography show nipple retraction, diffuse skin thickening and marked trabecular thickening in right breast and normal parenchyma in left breast.

**Figure 3:** Axial turbo spin echo (TSE) T1-weighted (TR 550 msec; TE 11 msec; thickness 4 mm) (A), TSE T2-weighted (TR 4000 msec; TE 120 msec; thickness 4 mm) (B) and fat saturated TSE T2-weighted (C) images were obtained. An axial 3-dimensional (3D) T1-weighted fast field echo (FFE) sequence (TR 6.5 msec; TE 3.2; flip angle 25; thickness 4 mm) was acquired before and after administration of intraveous paramagnetic contrast media. 3D T1-weighted postcontrast sequence was repeated five more times and postprocessing of images included subtraction of postcontrast series from precontrast one (D) and calculation of time-signal intensity curves. Diffuse areas of low signal intensity on T1-weighted (A) and widespread hyperintense areas on T2-weighted images suggesting edema (B, C) were seen. These edematous areas demonstrated marked contrast enhancement (D). However, no focal abnormal signal changes suggesting malignancy was observed.
**Figure 4:** Maximum intensity projection (MIP) FDG PET image shows heterogeneously increased FDG uptake in upper outer quadrant of the right breast (SUV max= 5.5) (short thin arrow), focal increased FDG uptake in 6 right axillary lymph nodes (SUV max= 9.2) (long thin arrow) and 1 right supraclavicular lymph node (SUV max= 3.2) (short thick arrow), increased FDG uptake in upper part of sacrum consistent with bone metastasis (SUV max= 7.4) (long thick arrow).