



Contribution of 18-fluorodeoxyglucose positron emission tomography (FDG PET) imaging in the detection of underlying carcinoma in a woman with nonspecific mastitis

Doprinos snimanja pozitronskom emisionom tomografijom pomoću 18-fluorodeoksiglukoze u otkrivanju skrivenog karcinoma kod žene sa nespecifičnim mastitisom

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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 diseases; breast neoplasms; mastitis; diagnosis, differential; positron-emission tomography.

Apstrakt

Uvod. Razlikovanje malignih i inflamatornih procesa još uvek je dijagnostički izazov. Mamografija (MG) i ultrasonografija (US) imaju nisku senzitivnost i specifičnost u gustinom tkiva dojke da bi se mogao prepoznati malignitet. S druge strane, na snimanju magnetnom rezonancom (MRI) lezije maligne mase mogu takođe biti maskirane difuznim inflamatornim procesom. Snimanje pozitronskom emisionom tomografijom pomoću 18-fluorodeoksiglukoze (PDG PET) može biti alternativna metoda koja obećava u proceni sumnjivih masi dojke, posebno kod bolesnica sa pratećim inflamatornim oboljenjima dojke. **Prikaz bolesnika.** Prikazujemo neobičan slučaj bolesnice sa sumnjivim malignitetom desne dojke na fizikalnom pregledu i radiološkim nalazima koji su išli u prilog mastitisa. Pomoću MS i US nije otkrivena lezija koja bi odgovarala mastitisu. Osim toga, MRI nalazi primarno su bili razmatrani kao infektivni ili granulomatozni mastitis. Međutim, pomoću FDG PET određene su tačne granice tumora i diseminacije karcinoma dojke, sa superiornošću u odnosu na druge, konvencionalne radiološke metode. **Zaključak.** Ovaj prikaz bolesnika naglašava doprinos FDG PET snimanja ostalim konvencionalnim radiološkim metodama u dijagnostikovanju primarnog tumora, određivanju mesta biopsije i, takođe, gradiranju bolesti, posebno kod bolesnica koje imaju prateće inflamatorno oboljenje dojke.

Ključne reči:

dojka, bolesti; dojka, neoplazme; mastitis; dijagnoza, diferencijalna; tomografija, kompjuterizovana, emisiona.

Introduction

Differentiation between a malignancy and inflammatory process is still a diagnostic challenge. There is no radiologic criterion to allow definitive diagnosis both for 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 entities¹. 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 taken³. 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 the 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 the 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 malignancy 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 (Figures 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.



Fig. 1 – Nipple retraction, orange peel appearance and enlargement is seen in the right breast.

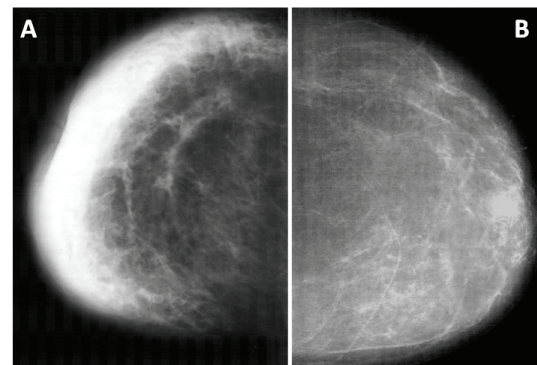


Fig. 2 – Craniocaudal views of (A) right and (B) left breast on mammography show nipple retraction, diffuse skin thickening and marked trabecular thickening in the right breast and normal parenchyma in the left breast.

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 conditions. Nearly half of the patients have clinical and radiological findings suggesting a malignant tumor. Punch biopsy and histopathologic examination are often necessary to determine a definitive diagnosis⁴.

The pathophysiology of breast cancer presenting as mastitis is unclear. It is possible that it is 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 of chronic infection. Another possible explanation may be related to recurrent infection of the necrotic areas within the tumor. Thus, these results in atypical manifestation of breast cancer as inflammatory mastitis⁵.

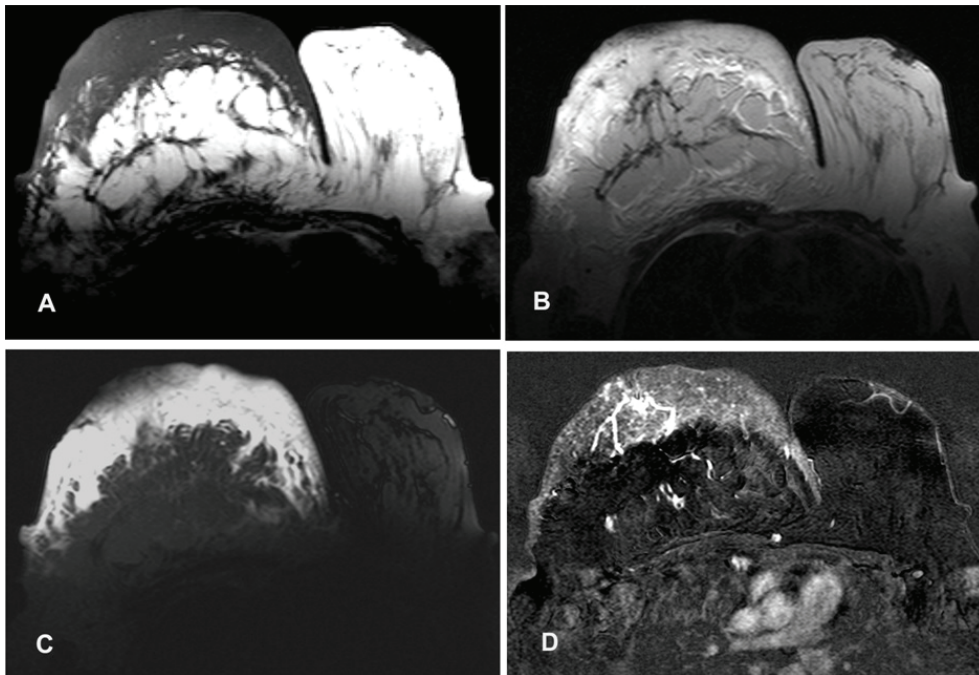


Fig. 3 – A) Axial turbo spin echo (TSE) T1-weighted (TR 550 msec; TE 11 msec; thickness 4 mm); B) TSE T2-weighted (TR 4000 msec; TE 120 msec; thickness 4 mm) and C) fat saturated TSE T2-weighted images were obtained. An axial 3-dimensional (3D) T1-weighted fast field echo (FFE) sequence (TR 6.5 msec; TE 3.2; flip angle 25; thickness 4 mm) was acquired before and after administration of intravenous paramagnetic contrast media. 3D T1-weighted postcontrast sequence was repeated five more times and post-processing of images included subtraction of postcontrast series from precontrast one (D) and calculation of time-signal intensity curves. A) Diffuse areas of low signal intensity on T1-weighted and B, C widespread hyperintense areas on T2-weighted images suggesting edema were seen. D) These edematous areas demonstrated marked contrast enhancement. However, no focal abnormal signal changes suggesting malignancy was observed.



Fig. 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 axillar 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).

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 malignant 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 diagnosis⁶. IBC was excluded by several excisional biopsies in our case.

MG and US 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 of inflammatory breast diseases and breast cancer using US and MG since both could have false negative findings⁷.

Since MRI is highly sensitive in detecting breast cancer, it is often used as a diagnostic tool to evaluate equivocal mammographic findings. Although MRI can not replace to MG or US for a complete diagnostic evaluation due to its high cost and limited specificity⁸, it may play an important role in differentiation of breast tumor from 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 cases⁶. 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 those with benign mastitis or IBC. A vessel adjacent to the lesion is another indicator suggesting malignancy on MRI⁹.

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 in breast cancer 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 tumor¹⁰. It is 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 as FDG PET has difficulty in detecting small-sized tumors, especially lesions smaller than 1 cm may show low FDG uptake¹¹.

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 reported¹³. The use of a dual-time-point imaging would add to diagnostic accuracy, especially for lesions with lower standardized uptake values (SUVs) and in differentiating inflammation from malignant lesions¹². However, it is 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 presentation¹³.

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.

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