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Diagnostic Comparison of F-18 Sodium FluorideNaF, Bone Scintigraphy, and F-18 Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in the Detection of Bone Metastasis

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Abstract

Objective: The aim of this study is to compare the diagnostic efficiency of bone scintigraphy, fluorodeoxyglucose (FDG), and sodium fluoride (NaF) positron emission tomography/computed tomography (PET/CT) in the evaluation of bone metastasis of the several malignant tumors.

Materials and Methods: A total of Thirteen13 patients (9nine Ffemales and, 4four Mmales; mean 62,.3 ± 7,.1 years) with diagnosis of different malignant tumors were included in the study. The comparison of bone scintigraphy, FDG, and NaF PET/CT results were was performed retrospectively.

Results: The NaF PET/CT demonstrated all the metastatic patients in this series; however, FDG PET/CT missed 7/13 and bone scintigrapyhy 1/13 of the patients with bone metastasis. NaF PET/CT showed significantly higher number of metastatic lesions in all the patients.

Conclusion: The lesion- based analysis showed that NaF PET/CT is significantly superior to FDG PET/CT and bone scintigraphy and patient- based analysis lower detection rate for the FDG PET/CT.

Keywords: Bone, scintigraphy, metastasis, sodium fluorideNaF, fluorodeoxyglucosefdg.

Introduction:

Bone metastasis might be difficult to estimate despite all the new technology imaging modalities in some special circumstances. Three kinds of metastatic lesions exist osteolytic, osteoblastic, and mix type. The diagnostic performance of nuclear medicine imaging modalities varies according to the components of these metastatic lesions. Bone scintigraphy is the most sensitive method in discrimination of bone changes, however, not specific at all. F-18 fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) is superior to every imaging modality in the determination of lytic bone metastasis which shows earliest in the disease course. Sodium fluoride (NaF) PET/CT is as sensitive as bone scintigraphy and considered in patients with suspicious results in bone scintigraphy and F-18 FDG PET/CT. The previous researchers showed that NaF PET/CT is able to show both osteolytic and osteoblastic bone metastasis, thus more sensitive in demonstration of bone involvement [1]. The previous studies have investigated the potential advantages of combined F-18 FDG PET/CT and NaF PET/CT in the same examination in the determination of the bone metastasis [2, 3, 4, 5]. These studies have promising results pointing out the diagnostic superiority of combination of these modalities. Sampath et al. have shown the advantages of the combined approach, especially in sclerotic bone lesions, and superiority of NaF PET/CT in discordant cases [2]. Roop et al. have demonstrated similar results for the breast cancer patients; combination of two modalities is superior in the detection of the bone metastasis compared to F-18 FDG PET/CT [3]. In addition, it has been demonstrated that this combined approach might be more cost-effective [6]. Recent NCCN guidelines recommend bone scintigraphy and NaF PET/CT in detection of bone metastasis, especially breast cancer patients in case of suspicion [7]. In case of demonstration of bone metastasis in the F-18 FDG PET/CT, there is no need for the further imaging modalities [7]. In this investigation, the study group consists of the patients with suspicious lesion in bone scintigraphy without/faint FDG uptake or conflicting results about bone metastasis. The aim of this study is to investigate and compare diagnostic efficiency of these three modalities in this special group of patients.

Materials and Methods

Patients

A total of 13 patients (nine females and four males; mean 62.3 ± 7.1 years) with

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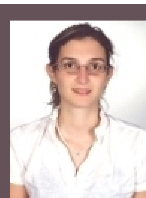
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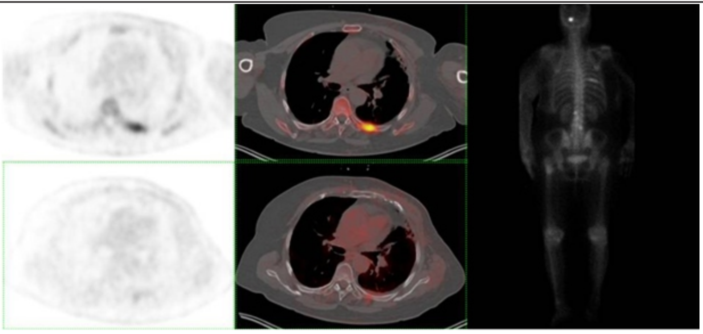

Figure 1: The patient with diagnosis of breast carcinoma, the severity of metastatic involvement is significantly different in the and sodium fluoride (NaF) positron emission tomography/computed tomography (PET/CT) NaF PET/CT compared to bone and fluorodeoxyglucose FDG PET/CT imaging and the follow-up NaF study showed significant progression.

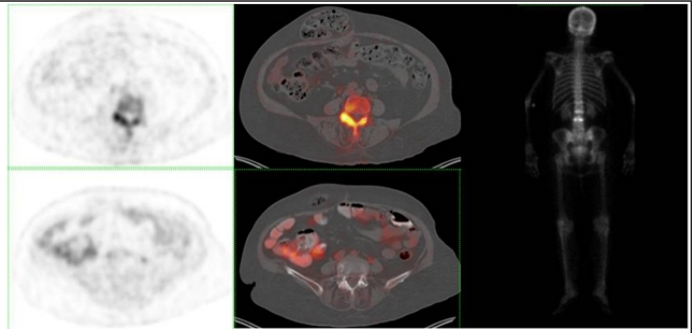

Figure 2: The patient with mild fluorodeoxyglucoseFDG accumulation in the L3 vertebra with significant metastasis in the sodium fluorideNaF positron emission tomography/computed tomography PET/CT compared to the bone scintigraphy with endometrium carcinoma.

diagnosis of malignant tumors (Ovarian, lung [n = 2], breast [n = 5], stomach carcinoma and myometrium sarcoma and endometrium carcinoma, non-Hodgkin lymphoma, and Meckel cell carcinoma) were included in the study. Suspicious metastatic lesions in the bone in either bone scintigraphy or F-18 FDG PET/CT with inconclusive results to each other, thus indicated NaF PET/CT were included retrospectively. The approval of the patients for the imaging studies and signed consent forms was obtained. The time between two imaging studies were mean 1 month interval. The inclusion criteria were having a malignant primary tumor and inconclusive bone scintigraphy-F-18 FDG PET/CT results about the metastasis. The exclusion criteria were lack of either bone scintigraphy or F-18 FDG PET/CT results, lack of suspicion of bone metastasis, and pregnancy.

Imaging

The patients were prepared for the F-18 FDG PET/CT examination with at least 6 h fasting and decreasing physical effort at least 24 h before the study. The radiopharmaceutical injection was performed (mean 370 MBq [10 mCi], according to the body weight) to each patient through venous line 60 min before the imaging. The imaging was performed by PET/CT scanner (GE, Discovery PET/CT 610, US) with additional low-dose CT scan (130 kV, 50 mAs, a pitch of 1.5, a thickness of 5 mm, in 70 cm field of view) for attenuation correction without intravenous contrast administration with oral contrast administration from the skull base to the upper thigh with the acquisition time of 1 min per bed position. The NaF PET/CT studies were performed without preparation and injection of a similar dose of 18F-NaF 60 h before the imaging. The imaging was performed by the same scanner and parameters from vertex to the toes. Bone scintigraphy imaging was performed by intravenous injection of mean 740 MBq (20 mCi) HMDP through venous line and diagnostic imaging as a whole body procedure and single-photon emission (SPECT) imaging in case of indication. The comparison of bone scintigraphy, FDG, and NaF PET/CT results was performed by an experienced Nuclear Medicine Physician retrospectively.

Results

The results of the imaging studies and the number of the metastatic lesions of the patients in bone scintigraphy, FDG PET/CT, and NaF PET/CT are summarized in Table 1. The number of metastatic lesions in the bone scintigraphy, FDG PET/CT, and NaF PET/CT was mean: 2.9 ± 1.9, 0.8 ± 1.01, and 5.2 ± 3.5, respectively. The NaF PET/CT imaging provided higher number of metastatic lesions in lesion-based analysis compared to the bone scintigraphy and FDG PET/CT. In addition, in patient-based analysis, the number of metastatic patients was higher in NaF PET/CT compared to both bone scintigraphy and FDG PET/CT. Every patient considered metastatic according to NaF PET/CT; however, one patient was non-metastatic according to bone scintigraphy and seven patients for FDG PET/CT. Most of the false-negative lesions in FDG PET/CT were sclerotic lesions. The bone scintigraphy had inconclusive results in two patients. All the patients confirmed to be metastatic according to follow-up results. The diagnostic accuracy of the bone scintigraphy, NaF, and FDG PET/CT was 92%, 46%, and 100%, respectively.

Discussion

This preliminary study showed that NaF PET/CT is superior in detection rate compared to bone scintigraphy and F-18 FDG PET/CT. Bone scintigraphy could not show metastatic lesions in one patient, but NaF PET/CT showed all metastatic patients and significantly higher number of metastatic lesions compared to bone scintigraphy and FDG PET/CT. FDG PET/CT was insufficient in most of the metastatic lesions and a significant number of metastatic patients in bone metastasis detection. The insufficiency of FDG PET/CT was prominent in especially sclerotic lesions which NaF PET/CT demonstrated metastasis. Some of the bone scintigraphy results were also inconclusive (suspicious) which was clearly verified by NaF PET/CT. In this series, local metastasis of a patient demonstrated by bone scintigraphy and NaF PET/CT, but FDG PET/CT did not show metastasis, and later on, the patient died in several days. This finding may point that FDG PET/CT has lower detection rate for local invasion. In

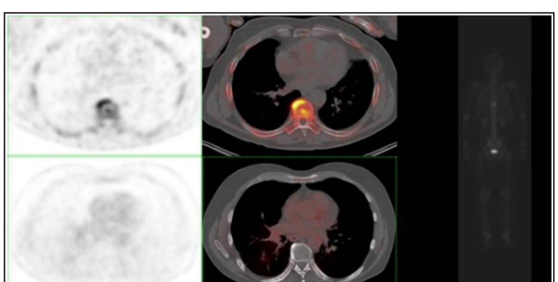

Figure 3: The patient with stable metastatic lung carcinoma in the T8-9 vertebral region with mild fluorodeoxyglucoseFDG uptake but significant activity accumulation in the sclerotic lesion in sodium fluoride positron emission tomography/computed tomography NaF PET/CT images.

Table 1: ???

Diagnosis	Bone scintigraph	NaF	FDG
Over	2	0	3
Breast 1	5	0	10
Breast 2	0	1	5
Non-Hodgkin lymphoma	7	0	4
Lung	4	3	10
Stomach	4	1	10
Uterus sarcoma	2	2	2
Breast 3	4	2	10
Merkel cell carcinoma	1	0	1
Endometrium	4	1	5
Lung	2	0	2

FDG: Fluorodeoxyglucose, NaF: Sodium fluoride

this series, SPECT and SPECT/CT were performed in addition with bone scintigraphy in some of the patients which probably increased the detection rate of bone scintigraphy. In this study, we observed that NaF PET/CT has significant superiority in the clarification of the bone metastasis, especially in problematic cases including single or suspicious metastatic lesion and sclerotic metastasis in the treatment follow-up. Although the reimbursements in our country support NaF PET/CT study in special circumstances, this study shows that NaF PET/CT is sufficient enough to show bone metastasis as a single diagnostic procedure. In the patient-based analysis, bone scintigraphy and NaF PET/CT have similar diagnostic utility, but NaF PET/CT provided more clear and confident determination of the metastatic disease in this patient group due to inconclusive results in some of the patients in this group. In this study also, metastatic involvement was shown by NaF PET/CT in FDG negative sclerotic metastatic lesions and changed patient management in more than half of the patients. Yoon et al. have similarly found that NaF PET/CT is superior to other two modalities in the osteosclerotic lesions which were the true positive results in their series with breast carcinoma [8]. In patients with sclerotic metastatic lesions might still have metastatic features in the healing phase during treatment which has osteoblastic activity in bone scintigraphy and NaF PET/CT [9]. Lapa et al. previously have shown the diagnostic superiority of NaF PET/CT in bone metastasis over both bone scintigraphy and F-18 FDG PET/CT in nearly half of their patients [10]. Furthermore, Araz et al. have demonstrated greater number of metastatic focus in 89% of their patients, especially in the lytic, blastic, and small lesions [11]. According to the previous studies, SPECT provides similar results with NaF PET/CT; however, it is not possible to perform SPECT imaging to all patients [12]. However, the SPECT imaging and SPECT/CT have clear advantage over planar scintigraphy, thus must be performed in patients with suspicion of metastasis in the whole body scan. In a previous comparative study, it has been shown that the diagnostic sensitivity of NaF PET/CT is superior to the F-18 FDG PET/CT, but it is not associated with overall survival of patients in contrast to FDG PET/CT [13]. The selection between these three modalities should depend on expectations from the examination such as soft tissue involvement or investigation of single or multiple focuses. Another comparative study including whole-body (WB) magnetic resonance imaging (MRI) as the fourth imaging modality has also demonstrated superiority of NaF PET/CT over the two studies besides feasibility of WB-MRI [14]. According to the results of a previous series including breast carcinoma patients, NaF PET/CT has changed the treatment plan in 39.3% of the patients [15]. Yoon et al. have suggested also monitoring the bone metastatic disease with sclerotic lesions by NaF PET/CT [8]. In another comparative analysis, it has been shown that NaF PET/CT might show metastatic patients that cannot be shown in both bone scintigraphy and F-18 FDG PET/CT [16]. Iagaru et al. have documented that NaF PET/CT is a superior imaging modality in disease extend evaluation than bone scintigraphy [16]. Limitations of this study are the inhomogeneous group composition (different primary tumors), small number of the patients, selection bias toward metastatic patients, and retrospective nature. In most of the patients in this study, the metastatic problematic bone lesions were sclerotic. Thus, some kind of homogeneity exists for this analysis. Lack of histopathological verification is another problematic issue; however, the patients had follow-up imaging results.

Conclusions

NaF PET/CT fulfills our expectations in the detections of bone metastasis compared to the bone scintigraphy and FDG PET/CT. However, NaF PET/CT cannot be a first-line imaging modality due to high costs but might be indicated, especially in the sclerotic hypometabolic bone lesions.

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