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Research Paper

The role of 18F–NaF PET/CT in metastatic bone disease

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ABSTRACT

Aim: To investigate the role of 18F–NaF PET/CT and compare it with 99m Tc-MDP whole body bone scintigraphy and 18F-FDG PET/CT in detecting the extent of metastatic bone disease and to present our first experience with 18F–NaF PET/CT in our country.
Materials and methods: A total of 37 histopathologically proven cancer patients (22 male, 15 female) with bone metastasis detected on Tc-99m MDP whole body bone scan were prospectively enrolled Cebeci, following ethics committee approval. 18F–NaF PET/CT was performed to the participants in Ankara University Medical Faculty Nuclear Medicine Department for evaluation of symptomatic skeletal sites which were negative on Tc-99m MDP whole body bone scan. A lesion based comparison was made between 18F–NaF PET/CT and Tc-99m MDP whole body bone scan for each patient and between 18F–NaF PET/CT and 18F-FDG PET/CT in 12/37 patients.
Results: The number of lesions demonstrated by 99m Tc-MDP bone scan and 18F–NaF PET/CT was equal in 4/37 (%11) of the cases. 18F–NaF PET/CT showed a greater number of pathological foci in 89% of participants. 18F–NaF PET/CT was able to show both lytic and blastic lesions and small lesions were better visualized due to the advantage of sectional imaging with much better resolution and higher target/background ratio. 18F–NaF PET/CT demonstrated a greater number of metastases in 10/12 (83%) of the patients when compared to 18F-FDG PET/CT. In the other two patients, bone metastasis could be demonstrated only by 18F–NaF PET/CT. The uptake of 18F-FDG was variable in blastic lesions and cranial bone involvement was missed by 18F-FDG PET/CT in some cases due to physiological brain metabolism.
Conclusion: Although further prospective clinical studies in specific cancer populations are indicated to set the place of 18F–NaF PET/CT in diagnostic scheme, the results of this pilot study from our country support the superiority of 18F–NaF PET/CT in investigation of bone metastasis over 99mTc-MDP bone scan and 18F-FDG PET/CT in various malignancies. 18F–NaF PET/CT is coming forward as a single step bone seeking study, considering all the advantages, but especially potential of detecting occult metastases and reliably directing patient management.

1. Introduction

Metastatic bone disease is the most frequent malignancy of the skeletal system [1]. Early diagnosis of bone metastases is an important step in the management of cancer as they may cause serious endocrinologic, hematologic, neurologic and orthopedic complications and intolerable pain [2,3].

The most common method for bone scanning is Technetium-99m methylenediphosphonate (99mTc- MDP) bone scintigraphy, because 99mTc- MDP is a cheap and easily available radiopharmaceutical with no toxic effects and whole body bone scintigraphy has an acceptable sensitivity, specificity, positive and negative predictive value.

Fluorine 18-Fluorodeoxyglucose positron emission tomography/computerized tomography (18F-FDG PET/CT) is now used as a useful imaging tool for staging, restaging and evaluation of therapy response for most cancers. The uptake mechanism of the radiopharmaceutical in bone metastases depends on the pathological increase in glycolytic activity of the malignant cells, therefore 18F-FDG shows specifically the malignancy of the bone. 18F-FDG PET/CT also contributes to the true evaluation of bone marrow involvement and soft tissue component of the metastasis [4].

Fluorine 18–Sodium Fluoride (18F–NaF) has been introduced as a bone-seeking agent first in 1962 by Blau et al. [5] and approved by FDA in 1972 for detection of osteogenic activity. However it lost its popularity by the easy availability of Molibdenum-99 (Mo-99) generators and better imaging characteristics of 99mTc- for gamma cameras, with respect to the high energy photons of Fluorine-18. As PET technology spread all around the world in 1990's, 18F–

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NaF PET/CT regained interest for bone scanning [6]. The kinetics of the radiopharmaceutical is quite useful for imaging. After intravenous injection, it is cleared out from the blood pool fast and it forms fluoroapetite crystals by chemoadsorbtion to the hydroxyapatite crystals [7].

The aim of this study was to investigate the role of 18F–NaF PET/CT and compare it with 99m Tc-MDP whole body bone scintigraphy and 18F-FDG PET/CT in detecting the extent of metastatic bone disease and to present the results of our first experience with 18F–NaF PET/CT practice in our country.

2. Materials-methods

2.1. Patient group

Ankara University Ethics Committee approval was taken for the study. A total of 37 histopathologically proven cancer patients (22 male, 15 female) with bone metastasis detected on Tc-99m MDP whole body bone scan were prospectively enrolled. 18F–NaF PET/CT was performed to the participants in Ankara University Medical Faculty Nuclear Medicine Department for evaluation of symptomatic skeletal sites which were negative on Tc-99m MDP whole body bone scan. Informed consent for 18F–NaF PET/CT procedure was signed by all participants. All patients were over 18 years old with a mean age of 58.91. Also, the results of other imaging modalities concurrently performed with bone scans and 18F–NaF PET/CT for staging, restaging or evaluation of therapy response were also taken under consideration. Twelve patients (32%) also had 18F-FDG PET/CT and 2 patients (0.5%) had In-111 Octreotide whole body scintigraphy and 1 patient had Ga-68 DOTATATE PET/CT. There were 9 breast, 8 lung, 6 prostate, 2 gastric cancer, 1 nasopharynx, 1 cervix, 1 bladder, 1 colon cancer, 1 renal cell carcinoma (RCC), 1 RCC and neuroendocrine tumor (NET), 1 colon and prostate, 1 lung and prostate cancer, 1 pancreas NET, 1 Hodgkin's Lymphoma (HL), 1 non-Hodgkin Lymphoma (NHL) and 1 uterine leiomyosarcoma patients. Fifteen patients have not received any chemo-radiotherapy yet while 10 received only radiotherapy, 6 received only chemotherapy, and 5 received both. One prostate cancer patient received only hormonotherapy (Table 1).

2.2. 18F–NaF PET/CT protocol

No special patient preparation was needed except for oral hydration, so that fast clearance from the background and a lower whole body radiation exposure could be obtained. The history of the disease, the chemotherapy, radiotherapy and antihormonal therapy performed were noted for evaluation. The injected doses

Table 1
Patient characteristics.

Patient	Age	Gender	Primary pathology	Therapy history	18F–NaF PET/CT	Tc-99m MDP Whole body bone scintgraphy	18F-FDG PET/CT
1	64	F	Hodgkin's Lymphoma	Chemotherapy	+	+	+
2	81	F	Breast cancer	Chemotherapy	+	+	absent
3	49	F	Gastric cancer	Chemotherapy	+	+	absent
4	80	M	Prostate cancer	No history of therapy	+	+	absent
5	46	F	Breast cancer	Chemotherapy, radiotherapy	+	+	+
6	60	M	Lung cancer	Radiotherapy	+	+	absent
7	52	M	Lung cancer	Radiotherapy	+	+	absent
8	50	M	Prostate cancer	Chemotherapy, radiotherapy	+	+	absent
9	32	M	Nasopahrynx cancer	Chemotherapy	+	+	+
10	36	M	Renal cell carcinoma	No history of therapy	+	+	absent
11	48	F	Breast cancer	No history of therapy	+	+	absent
12	77	F	Lung cancer	No history of therapy	+	+	+
13	72	F	Cervix cancer	No history of therapy	+	+	+
14	53	M	Renal cell carcinoma+neuroendocrine tumor	Radiotherapy	+	+	+
15	68	F	Uterine leiomyosarcoma	Radiotherapy	+	+	absent
16	66	M	Lung cancer	No history of therapy	+	+	absent
17	80	M	Urinary bladder cancer	No history of therapy	+	+	absent
18	39	F	Breast cancer	Chemotherapy, radiotherapy	+	+	absent
19	55	M	Lung cancer	No history of therapy	+	+	+
20	87	F	Breast cancer	No history of therapy	+	+	absent
21	34	F	Breast cancer	No history of therapy	+	+	absent
22	68	F	Colon	No history of therapy	+	+	absent
23	68	F	NonHodgkin lymphoma	No history of therapy	+	+	+
24	46	M	Colon+prostate cancer	No history of therapy	+	+	+
25	57	M	Gastric cancer	Radiotherapy	+	+	absent
26	60	F	Breast cancer	Radiotherapy	+	+	absent
27	45	F	Breast cancer	Radiotherapy	+	+	absent
28	31	F	Breast cancer	Radiotherapy	+	+	+
29	64	M	Prostate cancer	No history of therapy	+	+	absent
30	37	M	Lung cancer	No history of therapy	+	+	+
31	66	M	Pancreas neuroendocrine tumor	Radiotherapy	+	+	absent
32	59	M	Lung cancer	Chemotherapy, radiotherapy	+	+	absent
33	78	M	Prostate cancer	Chemotherapy, radiotherapy	+	+	absent
34	79	M	Prostate cancer	Hormonotherapy	+	+	absent
35	66	M	Prostate+lung cancer	Chemotherapy	+	+	absent
36	72	M	Prostate cancer	Radiotherapy	+	+	absent
37	55	M	Lung cancer	Chemotherapy	+	+	+