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Clinical Experience of ^{18}F-FDG PET/CT in Soft Tissue and Osseous Sarcomas

Elgin OZKAN, Cigdem SOYDAL, Mine ARAZ, N. Ozlem KUCUK

Ankara University Faculty of Medicine, Department of Nuclear Medicine, Ankara, TURKEY

ABSTRACT

The aim of this retrospective analysis was to describe our clinical experience for fluorine-18 (^{18}F) fluorodeoxglucose (FDG) positron emission tomography/computed tomography (PET/CT) in patients with soft tissue and osseous sarcoma. Total of 26 ^{18}F-FDG PET/CT scans were evaluated in 17 patients (7 osteosarcoma, 5 Ewing's sarcoma, 3 uterine sarcoma and 2 rhabdomyosarcoma) in different stages of disease. ^{18}F-FDG PET/CT was applied on postoperative period except for one patient. The results of ^{18}F-FDG PET/CT, conventional imaging modalities (CT and/or MRI) and clinical follow-up data were reviewed retrospectively. The range of the period between conventional imaging modalities and ^{18}F-FDG PET/CT was 1-6 months. The mean follow-up period was 3.8±0.2 years. The findings of CT and/or MRI and ^{18}F-FDG PET/CT were compared on the patient basis. Concordance was seen in 7 of 17 patients and discordance in 10 of 17 patients. In the concordant group, results were normal in 4 of 7 patients. Local recurrence or distant metastases did not seen in these patients during the follow-up period. In one patient who had undergone 18F-FDG PET/CT for preoperative staging, both of ^{18}F-FDG PET/CT and CT examinations showed the primary lesion on the clavicula. Distant metastases (liver, lung, lymph nodes) were defined with the 18F-FDG PET/CT and conventional imaging modalities in two patients. In the discordant group, ^{18}F-FDG PET/CT scans were normal in 4 patients who had multiple nodules on the both lungs in CT. These patients were followed up in remission. Local recurrence and distant metastases (bone, peritonium, lymph nodes) which could not be detected by conventional imaging modalities were seen in three patients, respectively.

In this retrospective analysis we concluded that ^{18}F-FDG PET/CT is a functional imaging modality which can be used successfully in addition to conventional imaging modalities in soft tissue and osseous sarcomas.

Keywords: Soft tissue sarcomas, Osseous sarcomas, F-18 FDG, PET/CT

ÖZET

Yumuşak Doku ve Kemik Sarkomlarında ^{18}F-FDG PET/BT Klinik Deneyimi

Bu retrospektif analizin amacı yumuşak doku ve kemik sarkomlu hastalarda flor-18 (^{18}F) florodeoksiglukoz (FDG) pozitron emisyon tomografi/bilgisayarlı tomografi (PET/BT) kullanımı ile ilgili deneyimlerimizi ortaya koymaktır. Onyedi olgunun (7 osteosarkom, 5 Ewing sarkomu, 3 uterin sarkom, 2 rabdomyosarkom) hastalığının değişik evrelerinde çekilen toplam 26 ^{18}F-FDG PET/BT sonucu değerlendirildi. ^{18}F-FDG PET/BT, 1 hasta dışında tüm hastalara postoperatif dönemde uygulandı. ^{18}F-FDG PET/BT, konvansiyonel görüntüleme yöntemleri (BT ve/veya MR) ve klinik takip sonuçları retrospektif olarak gözden geçirildi. Konvansiyonel görüntüleme yöntemleri ile ^{18}F-FDG PET/BT arasındaki süre aralığı 1-6 aydı. Ortalama takip süresi 3.8±0.2 yıldı.

BT ve/veya MR ve ^{18}F-FDG PET/BT bulguları hasta bazında değerlendirildi. 17 hastanın 7'sinde uyumluluk, 10'unda ise uyumsuzluk görüldü. Uyumlu grupta 4 hastanın sonuçları normaldi. Bu hastaların takip sürelerinde lokal rekürrens ya da uzak metastaz görülmedi. ^{18}F-FDG PET/BT'nin preoperatif dönemde uygulandığı bir hastada ^{18}F-FDG PET/BT ve BT klavikuladaki primer lezyonu gösterdi. İki hastada 18F-FDG PET/BT ve konvansiyonel görüntüleme yöntemleri ile uzak metastaz (karaciğer, akciğer, lenf nodu) tanımlandı. Uyumsuz grupta BT'de her iki akciğerde birden fazla nodülleri olan 4 hastada ^{18}F-FDG PET/BT normaldi. Bu hastalar remisyonda takip edildi. ^{18}F-FDG PET/BT ile konvansiyonel görüntüleme yöntemleri ile saptanamayan lokal rekürrens ve uzak metastazlar (kemik, periton, lenf nodu) sırasıyla üçer hastada saptandı.
Bu retrospektif analizde ^{18}F-FDG PET/BT'nin yumuşak doku ve kemik sarkomlu hastalarda konvansiyonel görüntüleme yöntemlerine ek olarak başarı ile uygulanabilecek fonksiyonel bir görüntüleme yöntemi olduğu sonucuna vardık.

Anahtar Kelimeler: Yumuşak doku sarkomları, Kemik sarkomları, F-18 FDG, PET/BT

INTRODUCTION

Soft tissue and osseous sarcomas are heterogeneous tumor groups which have different clinical behavior and differentiation degree. Sarcomas are very unusual and they are responsible for 0,7% of adult malignancies and 0,2% of all primary osseous tumors.[1] Also they are more common in childhood than in adults. Six hundred newly diagnosed child or adult osteosarcoma cases are reported every year in the U.S.A.[2] Rhabdomyosarcoma is the most common soft tissue sarcoma in childhood.[3]

Sufficient data regarding to clinical usefulness of fluorine-18 (^{18}F) fluorodeoxglucose (FDG) positron emission tomography/computed tomography (PET/CT) in this patient group hasn't been reported yet because sarcomas are very rare and heterogeneous. The goal of this analysis is to describe our clinical experience for 18F-FDG PET/CT in patients with soft tissue and osseous sarcoma.

MATERIAL and METHOD

Patients

Twenty-two patients who had ^{18}F-FDG PET/CT in our department due to soft tissue and osseous sarcoma between the years 2007 and 2009 were evaluated. The results of ^{18}F-FDG PET/CT, conventional imaging modalities (CT and/or MRI) and clinical follow-up data were reviewed retrospectively. Five patients whose follow up data were not available or the patients who were developed secondary malignancies in follow-up period were excluded from the study. Total of 26 ^{18}F-FDG PET/CT scans were obtained in 17 patients (11 male, 6 female; age range: 8-51 years) in different stages of disease.

One out of 17 patients who had undergone 18F-FDG PET/CT for preoperative staging was Ewing's sarcoma. In 16/17 patients (7 osteosarcoma, 4 Ewing's sarcoma, 2 rhabdomyosarcoma and 3 uterine sarcoma), ^{18}F-FDG PET/CT was performed for postoperative staging. Six patients were in childhood or adolescent age group however the vast majority were in adult age group (mean age: 26±1.6 years). The range of the period between conventional imaging modalities and 18F-FDG PET/CT was 1-6 months. The mean follow-up period was calculated as 3.8±0.2 years.

^{18}F-FDG PET/CT

^{18}F-FDG PET/CT images were acquired with Discovery ST PET/CT scanner (General Electric, Milwaukee, Wisconsin, USA). Patients were required to be on fasting for at least 6 hour before scanning and blood glucose levels were checked before the FDG injection. An oral contrast agent was given to all patients. Intravenous contrast agents were not used. Patients were rested in a quiet room without administrating muscle relaxant during waiting period. Whole body PET/CT imaging was performed while patients were in supine position from the skull base to the mid thighs. Images were obtained approximately 1 hour after an intravenous injection of 555 MBq of FDG. CT image was obtained from the integrated PET/CT scanner with the use of a standardized protocol involving 140 kV, 70 mA, a tube rotation time of 0.5 s per rotation, a pitch of 6 and a section thickness of 5mm. Immediately after the CT part, PET images were acquired for 4 minutes per bed position. PET images were reconstructed using non-contrast CT data for attenuation correction.

Image Analysis

Whole body PET/CT images were interpreted by two experienced nuclear medicine physicians by visual inspection in least three planes (transaxial, coronal, sagittal). Comparison was made between focus increasing uptake and background and blood pool activity. After then their anatomic confirmation was made with CT images. The criterion for malignancy was accepted FDG hypermetabolism at the site of pathological changes on CT or marked focal hypermetabolism at the physiological uptake sites. Maximum standardized uptake value (SUVmax) was calculated for all pathologic lesions.

RESULTS

The findings of conventional imaging modalities (CT and/or MRI) and ^{18}F-FDG PET/CT were compared on the patient basis. Concordance was seen in 7 of 17 patients and discordance in 10 of 17 patients. Details of comparison of imaging modalities, follow-up results and characteristics of patients were summarized on Table 1.

In the concordant group, results of ^{18}F-FDG PET/CT and conventional imaging modalities were normal in 4 of 7 patients (2 Ewing's sarcoma, 1 rhabdomyosarcoma and 1 osteosarcoma). Local recurrence or distant metastases did not seen in four of them during the follow-up period. In one patient with Ewing's sarcoma who had undergone ^{18}F-FDG PET/CT for preoperative staging, both of ^{18}F-FDG PET/CT and CT examinations showed the primary lesion on the clavicula. After surgical removal, second ^{18}F-FDG PET/CT scan of this patient was totally normal. In two patients of this group, distant metastases were defined. One of them had been diagnosed to osteosarcoma and had undergone wedge resection of right lung because of lung metastases. After surgical procedure, control CT detected mass lesion on the right hilar region and multiple nodules on the left lung. ^{18}F-FDG PET/CT identified pathological FDG uptake on the lesions of hilar region and left lung. So this patient received chemotherapy for distant metastases. The last patient of this group had surgically removed uterine sarcoma and high Ca-125 levels. Abdominal CT had detected multiple liver nodules and multiple intraabdominal lymph nodes. In ^{18}F-FDG PET/CT these lesions showed patholocigal FDG uptake (liver SUV max: 9.1 and lymph nodes SUV max: 10.5). For this reason, this patient was taken to chemotherapy programme. After treatment, sizes of these lesions haven't changed so the patient is still being followed up with stable disease.

In the evaluation of discordant group, ^{18}F-FDG PET/CT scans were normal in 4 patients (2 Ewing's sarcoma, 1 rhabdomyosarcoma, 1 osteosarcoma). Four of them had multiple nodules on the both lungs in thorax CT but no pathological FDG uptake seen on these nodules. For this reason distant metastases were excluded in these patients and were followed up in remission until today. ^{18}F-FDG PET/CT showed local recurrence which could not be detected by conventional imaging modalities in three patients with osteosarcoma. Distant metastases which could not be detected by conventional imaging modalities also were identified in three patients. In the first patient with uterin sarcoma pathological FDG uptakes had been shown on the multiple foci on the left lung (SUV max: 6.3) and at sacroiliac joint (SUV max: 14.1). At the same time, sacroiliac MRI detected signal changes of this patient's iliac bone and sacrum. And these changes were accepted to be associated with edema of bone marrow. After ^{18}F-FDG PET/CT, this patient took chemotherapy for lung metastases. 1 year later, metastatic mass was showed on the sacrum and iliac bone by control MRI and patient received chemotherapy again. ^{18}F-FDG PET/CT detected pathological FDG uptake in the abdominal wall, between bowel loops (SUV max: 9.3) and right inguinal lypmh node (SUV max: 3.8) in the second patient with uterin sarcoma of this group. Fine needle aspiration biopsy was performed for inguinal lymph node and confirmed to be metastasis of malignant mesenchymal tumor. This node was excisionally removed and chemotherapy was started. The last patient of this group had surgically removed osteosarcoma and his MRI images had showed a mass lesion on the left tibia. ^{18}F-FDG PET/CT detected uptake on the proximal site of left tibia, bilaterally axillary, iliac, inguinal and left popliteal lymph nodes in this patient. After ^{18}F-FDG PET/CT patient was taken chemotherapy schedule. The sizes of axillary, inguinal, iliac and popliteal lymph nodes were decreased, so the findings of ^{18}F-FDG PET/CT assumed to be metastatic.

Table 1. Patient characteristics and results of imaging modalities and follow-up.

Patient no	No of PET/CT	Age	Gender	Histopathological subtypes	Localisation	Findings of CT MRI	Findings PET/CT	Findings of PET/CT	SUV	Treatment	Comparison of results	Recurrent disease
1	1	45	F	Uterin sarcoma	Uterus	Multiple lesions on liver and multiple lymph nodes in the abdomen.		Multiple foci on liver multiple uptake on abdominal lymph nodes	Liver (9.1), Lymph nodes (10.5)	SR, Cht	Concordant	+
2	2	8	F	Rhabdomyo-sarcoma	Right arm	Nodule on the right lung upper lobe.	Postoperative changings on the right arm.	Normal		SR,Cht,RT	Discordant	–
3	3	12	F	Rhabdomyo-sarcoma	Parapharan geal site		Postoperative changes.	Normal		Cht,RT	Concordant	–
4	4	44	M	Osteosarcoma	Right tibia	Mass on the right hilar region and nodule on the left lung upper lobe.	hilar region and left lung upper lobe	Uptake on the right (12.3), Left lung(3)	Right hilar region	SR, Cht	Concordant	+
5	5	46	F	Uterin sarcoma	Uterus	Multiple nodules on the right lung lower lobe.		Uptake on the abdom wall, between bowel loops and on the right inguinal region	Abdominal wall (9.3), Bowel loops(9.3)	SR,Cht	Discordant	+
6	6	15	M	Ewing's sarcoma	Right fibula	Milimertic nodules on the both lungs.	Pathological signal changes near the surgical defect site	Normal		Cht	Discordant	–
	7					Milimertic nodules on the both lungs in same size	Normal	Normal				
	8					Milimertic nodules on the both lungs in same size	Normal	Normal				
7	9	9	M	Ewing's sarcoma	Mandibula	Multiple lymph nodes on the neck		Minimal uptake on the lymph nodes	Lymph nodes(3.3)	Cht,RT	Concordant	–
	10					Multiple lymph nodes on the neck		Minimal uptake on the lymph nodes	Lymph nodes(4.0)			
	11							Minimal uptake on the lymph nodes	Lymph nodes(3.6)			
8	12	25	M	Osteosarcoma	Right fibula	Lung nodules on the both of lungs.		Normal		SR,Cht	Discordant	–
9	13	23	M	Ewing's sarcoma	Right humerus	Normal		Normal	SR,CT,RT	Concordant	-	

10	14	21	M	Ewing's sarcoma	Right iliac bone	Nodules on the right lung.		Normal		SR,Cht	Discordant	–
	15							Normal				
	16							Normal				
	17							Normal				
11	18	51	F	Uterin sarcoma	Uterus	Metastatic nodules on the left lung, metastatic lesion on the left liver lobe.	Signal changes on the iliac bone and sacrum (associated with edema of bone marrow).	Multiple foci on the left lung, on the right sacroiliac joint.	Lung(6.3), Sacroiliac joint(14.1)	SR,Cht,RT	Discordant	+
12	19	11	M	Ewing's sarcoma	Right clavicleula	Lymph nodes on the both sites of neck, malignant mass on the right clavicleula.		Uptake on the right clavicleula	Clavicleula(3.6)		Concordant	–
	20							Normal		SR,Cht		
13	21	50	F	Osteosarcoma	Right knee	Normal		Uptake on the distal part of right femur, on the proximal part of tibia, around the implant of the right knee.	Femur(27.6), Tibia (13.4), Implant (17.3)	SR,Cht	Discordant	+
14	22	24	M	Osteosarcoma	Right iliac bone	Normal	Right iliac bone	Iliac bone (6.61)	SR,CT,RT	Discordant	+	
15	23	20	M	Osteosarcoma	Left femur	Suspected nodule on the right lung.		Uptake on the lateral site of femur implant.	Implant (4.4)	SR,Cht,RT	Discordant	+
16	24	18	M	Osteosarcoma	Left tibia	Suspected nodule on the right lung.	Mass on the proximal site of left tibia.	Uptake on the proximal site of left tibia, bilaterally axillary, iliac, inguinal and left popliteal lymph nodes.	Left tibia(6.61), Lymph nodes(8.7)	SR,Cht	Discordant	–
17	25	28	M	Osteosarcoma	Left humerus	Normal		Normal		SR,Cht	Concordant	–
	26					Normal		Normal				

F, female; M, male; CT, computed tomography; MRI, magnetic resonance imaging; SUV, standardized uptake value; SR, surgical resection; Cht, chemotherapy; RT, radiation therapy.

DISCUSSION

CT and MRI are widely used in the evaluation of soft tissue and osseous sarcomas. However these imaging modalities just can detect anatomical changings without giving functional information. Also metallic replacement related with surgical procedure may inhibit evaluation by MR. For this reason, ^{18}F-FDG PET/CT is preferred in this patient group because it can give both anatomical and functional information. There have been reported few studies in the usefulness ^{18}F-FDG PET/CT in osseous and soft tissue sarcomas.[1-6] The relationship between SUV and differentiation degree of tumor has been described.[4] In our study, the correlation between clinical behavior of the tumor and the SUV couldn't be evaluated because ^{18}F-FDG PET/CT wasn't performed preoperatively to any of the patients except one. In the study of Charest et al.[1], sensitivity of ^{18}F-FDG PET/CT in preoperative staging had been reported as higher than the sensitivity in detection of recurrence in sarcoma patients. But this difference has not been found statistically significant. In our series, all local recurrences could be detected by ^{18}F-FDG PET/CT. Also, in the first patient with pathological signal changes in MRI and in the second patient with suspicious lymph nodes in CT, local recurrence was excluded by ^{18}F-FDG PET/CT and local recurrence hasn't observed in clinical follow up period in these two patients. At least in our series, 18F-FDG PET/CT seems to be successful in detection of local recurrence.

In sarcoma cases, sensitivity of ^{18}F-FDG PET/CT in the detection of distant metastases has been reported as lower than the local recurrences.[6] In our series, ^{18}F-FDG PET/CT detected distant metastases in 5 patients (lung, liver, lymph nodes, peritoneum and bone). Also ^{18}F-FDG PET/CT excluded distant metastases in 4 patients who had suspected lung nodules on CT. In a study where 13 sarcoma cases were evaluated, FDG-PET/CT could detect only 2 patients' distant metastases.[5] In another study, Kleis et al. reported that FDG-PET/CT had a very high sensitivity in detection of local recurrences but had mild sensitivity in detection of distant metastases.[5] However, in the literature ^{18}F-FDG PET/CT is recommended for the evaluation of treatment response in Ewing's sarcoma, osteosarcoma and rhabdomyosarcoma cases.[6-11] In our series, suspicious lung nodules were detected by CT in 6 patients (2 osteosarcoma, 2 Ewing's sarcoma, 1 rhabdomyosarcoma and 1 uterine sarcoma). Pathological FDG uptake was seen in 2 patients' lung nodules in the ^{18}F-FDG PET/CT and they were taken under chemotherapy schedule. But ^{18}F-FDG PET/CT was totally normal in 4 of them and these patients' lung nodules stayed stabile during the follow up period. Although in our series, ^{18}F-FDG PET/CT was very successful, especially it is very hard to evaluate nodules in diameter less than 5 mm. Growing in the size shows a malignant potential of the lung nodules, but it should be taken into account that the malignancy possibility of the lung nodules smaller than 5 mm is higher in childhood sarcomas than in adults. Fifty five percent of lung nodules smaller than 5 mm in childhood sarcomas were showed to be malignant in study of Kleis et al.[5]

Also in our series, ^{18}F-FDG PET/CT detected inguinal lymph node and peritoneal metastases in 1 uterine sarcoma patient. In another uterine sarcoma patient ^{18}F-FDG PET/CT detected iliac bone metastases before 1 year earlier than MRI could. In the study of Park et al. which evaluated ^{18}F-FDG PET/CT results in 8 uterine sarcoma patients, ^{18}F-FDG PET/CT detected intaabdominal recurrence in 5 uterine sarcoma patients and 1 of them was solitary intraabdominal tumor which couldn't be seen by ultrasound and CT.[12] Treatment plans of 7 patients were changed by ^{18}F-FDG PET/CT, in another study in which 19 uterine sarcoma patients were included.[9] Uterine sarcomas have very poor prognosis and rates of 5 years survival had been reported as 20-49.6%.[10,11] Generally, the predicted stage of disease is lower than the true stage at time of diagnosis in most patients. Aggressive treatment strategies can not improve survival. But, the successful staging at the beginning period can improve the quality of life via palliative treatment choices and can avoid unnecessary surgeries. ^{18}F-FDG PET/CT can be used for staging in this period.[9]

There were 2 rhabdomyosarcoma patients in our group and ^{18}F-FDG PET/CT was totally normal for both of them (1 embryonal sarcoma and 1 alveolar sarcoma). Although their follow up period was very short, in this period, no metastasis was seen in both of them. It has already been described, that ^{18}F-

FDG PET/CT could show distant metastases which could not be detected by conventional imaging procedures in rhabdomyosarcoma patients.[3,13,14]

This analysis describes our clinical experience in soft tissue and bone sarcomas. But also has some limitations. Follow up period was very short, patient group was very heterogeneuos and number of patients was very small. So we could not report long time follow up results. Also, except one patient, all patients were referred to our clinic in postoperative period. So we could not analyze the relationship between preoperative SUV and histopathological variant.

CONCLUSION

In this retrospective analysis we concluded that ^{18}F-FDG PET/CT is a functional imaging modality which can be used successfully in addition to conventional imaging modalities in soft tissue and osseous sarcomas.

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Correspondence

Dr. Çiğdem SOYDAL

Ankara Üniversitesi Tıp Fakültesi

Nükleer Tıp Anabilim Dalı

Cebeci, Ankara / TURKEY

Tel: (+90.312) 595 64 45

Fax: (+90.312) 362 08 97

e-mail:csoydal@yahoo.com