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Fluorine-18 fluorodeoxyglucose positron emission tomography findings in spondylodiscitis: preliminary results

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Abstract Nuclear medicine procedures can be helpful in diagnosing spine infections. The purpose of the study was to evaluate the findings of positron emission tomography with fluorine-18 fluorodeoxyglucose (FDG-PET) in the detection of spondylodiscitis. We performed FDG-PET in 16 patients with suspected spondylodiscitis. All the patients were operated and underwent histopathological examination. The FDG-PET findings were graded and evaluated by two independent nuclear medicine physicians. Of the 16 patients, 12 had a histopathologically confirmed spondylodiscitis. In all these 12 patients, FDG-PET was true-positive. In the four patients without spondylodiscitis, FDG-PET showed three true-negative and one false-positive result. In spondylodiscitis, the mean standard uptake

value (SUV) of FDG was 7.5 ($SD \pm 3.8$). The PET scans depicted the paravertebral soft tissue involvement in cases of spondylodiscitis. Our first results showed that FDG-PET is a very sensitive imaging procedure in the detection of spondylodiscitis. Compared to other nuclear medicine procedures, PET enables a rapid imaging with acceptable radiation dose and high spatial resolution.

Keywords FDG-PET · Spondylodiscitis · Nuclear medicine · Procedure

Introduction

The diagnosis of spine infections can be difficult, because the patient's history, subjective symptoms and physical findings are often inconclusive, particularly in the early stages. Nuclear medicine procedures, which identify pathophysiological reactions preceding morphological changes, can play a useful role in the diagnosis of spondylodiscitis. Specific tracers are used in infectious bone disease: Ga-67, Tc-99m nanocolloid, Tc-99m-HMPAO- and In-111-labeled leukocytes, Tc-99m and In-111 polyclonal human immunoglobulin, and Tc-99m-labeled monoclonal antibodies [10]. However, for diagnosing spine infections,

these procedures are still not optimal [10, 19]. On white cell imaging, up to 50% of all patients with spondylodiscitis show photopenic defects, which are not specific for infection [12].

Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) is increasingly playing an important role in the diagnosis, staging and monitoring of malignant tumours [3, 5, 15]. Not only tumours but also infections show an increased uptake of FDG. The FDG uptake depends on the increased glucose metabolism in activated inflammatory cells such as leukocytes, granulocytes and macrophages [20]. In detecting osteomyelitis with FDG-PET, first studies reported a sensitivity of up to 100% [6, 7, 9, 18]. However, there are limited experiences

in diagnosing spine infections. Therefore, we focussed in this study on evaluation of FDG-PET findings in spondylodiscitis.

Materials and methods

FDG-PET was performed in a consecutive series of 16 patients, ten female and six male, aged 15–85 years. The inclusion criteria were:

1. A suspected spondylodiscitis on the basis of anamnesis, clinical findings and imaging procedures such as radiography, com-

puter tomography (CT), magnetic resonance imaging (MRI) and bone scintigraphy, and

2. The availability of histopathological results, which made the final diagnosis.

All 16 patients were operated on and underwent histopathological examination within a matter of days after PET evaluation. The indication for surgical intervention was suspected spondylodiscitis or a destructive lesion. Individual data for the patients are listed in Table 1. Informed written consent was obtained from all study participants.

In 15 patients, MR studies were available. In 12 cases, MRI had led to the strong suspicion of spondylodiscitis. The main MR criteria for suspected spondylodiscitis were hypointensity of disc

Table 1 Individual data of the 16 patients (ESR erythrocyte sedimentation rate, CRP C-reactive protein, FDG-PET fluorine-18 fluorodeoxyglucose positron emission tomography, SUV standard uptake value, DD differential diagnosis)

Pat. no.	Age (years)	Sex	MRI findings	ESR	CRP mg/dl (norm = 0.3)	Final diagnosis, histologically confirmed (causative organism)	FDG-PET grade ^a	FDG-PET result	SUV (max. pixel value)
1	48	F	Spondylodiscitis T7–9	60	8	Tuberculous spondylodiscitis T7–T9 (<i>Mycobacterium tuberculosis</i>)	4/4	True-positive	9.2
2	78	M	Spondylodiscitis L4/L5	95	15.9	Spondylodiscitis L4/L5 (<i>Staphylococcus aureus</i>)	3/3	True-positive	6.4
3	57	F	Spondylodiscitis L4/L5	35	3.9	Postop. spondylodiscitis L4/L5 (<i>Staphylococcus aureus</i>)	3/3	True-positive	3.9
4	63	M	Spondylodiscitis L1/L2	102	13.7	Spondylodiscitis L1/L2 (<i>Staphylococcus aureus</i>)	4/4	True-positive	9.0
5	67	F	Spondylodiscitis L3/L4	50	4	Tuberculous spondylodiscitis L3/L4 (No growth)	4/4	True-positive	6.3
6	66	F	Spondylodiscitis L4/L5	92	5	Spondylodiscitis L4/L5 (<i>Streptococcus pyog.</i>)	4/4	True-positive	7.8
7	45	F	Tumour T12/L1, DD: spondylodiscitis	73	5.7	Sarcoma T12/L1 (No growth)	4/4	False-positive	17.5
8	41	F	Spondylodiscitis T3–T5	60	12	Tuberculous spondylodiscitis T3–T5 (<i>Mycobac. tuberculosis</i>)	4/4	True-positive	18.1
9	15	M	Erosive osteochondrosis C2/C3 DD: spondylodiscitis	6	0.5	Degenerative changes C2/C3 (No growth)	0/0	True-negative	0.9
10	85	F	Spondylodiscitis L1/L2	36	4	Spondylodiscitis L1/L2 (<i>Staphylococcus aureus</i>)	3/4	True-positive	4.1
11	64	F	Spondylodiscitis T12/L1	46	5.7	Spondylodiscitis T12/L1 (No growth)	3/3	True-positive	3.7
12	59	M	Spondylodiscitis L4/L5	58	11	Spondylodiscitis L4/L5 (<i>Enterobacter cloacae</i>)	4/4	True-positive	9.8
13	53	M	Spondylodiscitis L4/L5	23	9	Postop. spondylodiscitis L4/L5 (No growth)	4/4	True-positive	7.5
14	40	F	Erosive osteochondrosis L1/L2 DD: spondylodiscitis	7	1.6	Degenerative changes L1/L2 (No growth)	0/0	True-negative	0.9
15	53	M	Spondylodiscitis L4/L5	45	6.5	Spondylodiscitis L4/L5 (<i>Staphylococcus aureus</i>)	3/3	True-positive	4
16	82	F	–	29	2.3	Osteoporotic fracture L1 (No growth)	1/1	True-negative	1.2

^a Grading of reader 1/reader 2: grade 0=definitely no spondylodiscitis; 1=probably no spondylodiscitis; 2=equivocal; 3=probably spondylodiscitis; 4=definitely spondylodiscitis

and vertebral bodies on T1-weighted sequences, hyperintensity on T2-weighted sequences and contrast enhancement of the disc, adjacent vertebral bodies and involved paraspinal soft tissues [11]. In three cases there was a differential diagnosis to tumour and erosive osteochondrosis. The physicians who performed the MRI had no influence on the indication for an FDG-PET. Half of the cases had the MR studies performed at another hospital. In one patient with osteoporosis, conventional radiography and a positive bone scan led to the suspicion of spine infection. Additional CT scans (2×CT thorax) were available in five patients. Eight patients had undergone a bone scan. All bone scans were positive, with a final diagnosis of spondylodiscitis in seven and osteoporotic fracture in one.

The FDG-PET studies were evaluated visually by two independent experienced nuclear medicine physicians, who were not involved in the treatment of the patients and were blinded to the results of the other imaging procedures and to the final diagnosis. The FDG results were graded on a five-point scale of 0–4: 0=definitely no spondylodiscitis, 1=probably no spondylodiscitis, 2=equivocal, 3=probably spondylodiscitis, 4=definitely spondylodiscitis. PET scans were considered positive for spondylodiscitis if there was moderately or intensely increased FDG uptake in the spine: grade 3 or 4. PET scans were considered negative if there was no or low FDG uptake: grade 0 or 1. All cases were evaluated as true-positive, false-positive, true-negative or false-negative.

PET imaging was performed in a fasted state with a Siemens/CTI ECAT Exact 921/47 PET scanner. Between 200 and 400 MBq (5–10 mCi) FDG was administered intravenously 45 min before the start of static emission images in multiple (four or five) bed positions, starting from the base of the skull. Cross-sections were generated by filtered back projections (Hanning 0.4) and corrected by means of a measured attenuation matrix acquisition of a germanium/gallium transmission scan, prior to or after the registration of the emission scan. After reconstruction and reslicing, the slice width was 6.75 mm in all planes.

Fig. 1 Patient 8 (tuberculous spondylodiscitis): positron emission tomography (PET) scans with pathological fluorine-18 fluorodeoxyglucose (FDG) uptake in the T3–T5 vertebrae (standard uptake value, SUV, up to 18.1)

Results

Of the 16 patients, 12 had a histopathologically confirmed spondylodiscitis as final diagnosis. In nine of these cases, the spine infection was also confirmed by identification of a causative organism (Table 1). In three patients with spondylodiscitis, a causative organism was not found. Of these three patients, one had a tuberculosis and two received antibiotic therapy before surgical intervention, which may explain negative bacteriological findings.

In all 12 patients with histopathologically confirmed spondylodiscitis, the FDG-PET results were graded 3 or 4 by both readers (Table 1), giving true-positive results in all cases. Therefore, the sensitivity of PET was 100%. There was an increased FDG activity in the infected spine region, with a standard uptake value (SUV) of the maximal pixel values up to 18.1 (Fig. 1, Table 1). The mean SUV in histopathologically confirmed cases of spondylodiscitis was 7.5 (SD±3.8). FDG-PET showed true-negative results in three of the four patients found not to have spondylodiscitis on histopathological examination. In one of the four, FDG-PET was evaluated as false-positive. In this case, the histopathological analysis showed a sarcoma.

For the grading of the FDG uptake, there was a strong agreement between the two readers (Table 1). In patients with spondylodiscitis, FDG-PET also showed the paravertebral soft tissue involvement. Figure 2 illustrates the plain radiography, MRI and PET findings in patient 10 with spondylodiscitis of L1/L2.

FDG-PET allows quantification of inflammatory activity. In two patients we carried out a follow-up PET after therapy, and observed a decreased FDG uptake corresponding to clinical improvement. Table 2 shows the SUVs before therapy and at follow-up. In patient 1, the

Fig. 2a–c Patient 10. **a** Lateral radiograph shows a destructive lesion of L1/L2 due to spondylodiscitis. **b** Sagittal magnetic resonance images (sagittal T2*-weighted gradient echo sequence of the midline lumbar spine: out of phase FFE, TR/TE/flip angle=526/20/80) show spondylodiscitis of L1/L2. There is obvious hyperintensity in the L1 vertebral body and superior parts of L2, with anterior and posterior bridging. **c** Coronal and sagittal FDG-PET emission scans with increased uptake in L1/L2 due to spondylodiscitis

follow-up PET was carried out after dorsal pedicular instrumentation. The spatial resolution of PET was not affected by the metal implant.

Discussion

In the current study, FDG-PET findings were related to histopathological examination, as the gold standard for verification. The results showed a very high sensitivity in detecting spine infections using FDG-PET. In previous studies, FDG-PET has also shown a very high sensitivity in detecting infection within bone [6, 9, 18], but only a few cases of spondylodiscitis have been reported. Guhlmann et al. [6] found in 51 patients with suspected osteomyelitis, of whom 28 had infection and 23 did not, that FDG had an

Table 2 FDG-PET follow-up studies: patients 1 and 2 (see Table 1)

	Therapy	SUV (before therapy)	SUV (follow-up)
Patient 1	Surgery and tuberculostatic therapy	9.2	0.4 (6 months)
Patient 2	Surgery and antibiotic therapy	6.4	3.1 (2 months)

accuracy in the peripheral skeleton of 96% and in the central skeleton of approximately 96%; this group included only five cases of spondylodiscitis. In the infected spine regions we found a strongly increased FDG uptake, with SUVs of the maximal pixel values up to 18.1, and a mean value of 7.5. By contrast, normal bone marrow has SUVs of between 0.1 and 0.3. Underlying bony abnormalities such as recent fracture or pseudarthrosis show only slightly increased SUVs, in the range of 0.2–1.1 [7].

In diagnosing spondylodiscitis, MRI is the investigation method of choice [11]. However, nuclear medicine procedures can play a helpful role in this area. FDG-PET seems to have some potential advantages in comparison to other scintigraphic procedures. Three-phase bone scintigraphy is sensitive for the diagnosis of osteomyelitis [1], but in spondylodiscitis false-negative results are not uncommon [17]. Photopenic defects in bone scans may be due to inadequate blood supply or lytic lesion with loss of osseous tissue [14]. The blood supply can be affected by pus or vasospasm [16]. However, bone scintigraphy has its limitation as a non-specific procedure. The more specific scintigraphic procedures favoured in recent years, using radioactively labeled blood cells (WBC) and Tc-99m-labeled antigranulocyte antibodies, can not reliably detect spine infections [4, 10]. Due to the destruction of cells of the haematological system, these scintigraphic procedures frequently show areas of decreased or absent activity. The photopenic areas are not specific for spine infection, since similar bone marrow transformations are observed in bone infarct, fractures, malignant and haematological diseases and also in previously treated spondylodiscitis [2, 4, 19]. Therefore, the accuracy of WBC scintigraphy in the detection of spine infection is as low as 31–76% [13, 19]. Gallium-67 scintigraphy is another sensitive and specific procedure in diagnosing spondylodiscitis [8]. However, the use of this method may be limited, because of the relatively high radiation dose and the low spatial resolution [10].

In comparison to these scintigraphic procedures, FDG-PET has some potential advantages. PET allows rapid imaging within 1 h after the injection [18]. Using Ga-67 or WBC, clinical images are commonly obtained at 24–72 h after tracer injection. The radiation dose of FDG-PET is acceptable [18]. The effective whole-body dose is 0.74 mSv/mCi FDG. The doses received by the patients in this study were in the range of 3.7–7.4 mSv. FDG-PET shows

a high spatial resolution. We found that the surrounding soft tissue infection can be differentiated from the osseous process. This may be helpful in assessing the paravertebral abscess in spondylodiscitis.

Our series was too small to evaluate specificity. It is known, however, that FDG-PET is of limited value in discriminating between infected and malignant bony processes [7], due to the high glucose metabolism of tumour cells, which results in a high tracer uptake. This low specificity between infection and tumour is a main problem of nuclear medicine procedures [10], and was apparent in this study, where the one false-positive result was found in a patient who had a sarcoma of the spine.

It is unclear whether FDG-PET enables the differentiation of spondylodiscitis from degenerative, especially Modic type I, changes, which can be differentiated by MRI. As an increased glucose metabolism is not expected in degenerative changes, PET should enable this differentiation. However, further studies to investigate a control group of patients with degenerative disease are required.

Our experience with one patient with dorsal instrumentation and in others with joint prostheses and osteosynthesis (unpublished data) show that, in contrast to CT and MRI, the spatial resolution of PET is not affected by metal implants. As internal fixation is increasingly being used in spinal surgery, PET may become a valuable tool in assessing spine infection when metal implants are present. PET enables quantification of the inflammatory activity of an infection. In two patients, PET investigations after therapy documented a regression of the infection, which was manifest in a reduced tracer uptake. The quantification of inflammatory activity might be useful for treatment monitoring. However, these features of PET need to be studied in larger samples of patients.

PET imaging is an expensive technology. Although the cost of a single PET investigation is not much higher than the cost of a WBC scintigraphy, the usefulness of FDG-PET in diagnosing spine infections depends on its cost-effectiveness.

Our first results showed a high sensitivity of FDG-PET in detection of spondylodiscitis. Compared to other nuclear medicine procedures, PET enables a rapid imaging with acceptable radiation dose and high spatial resolution. The results warrant further studies to assess the potential use of FDG-PET in spine infections.

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