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F18-FDG PET-CT IN DIAGNOSING, TREATING AND MONITORING SPINAL INFECTIONS*

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ABSTRACT

Spinal infections are important problems that occur due to various factors, show different pathological processes, cause pain, spinal compression and neurological deficit, and lead to high morbidity and mortality. Scanning methods provide great facilities in the diagnosis and monitoring of these infections. MRI is quite sensitive in evaluating spinal infections. However, they may remain incapable in certain cases. Nuclear medicine imaging techniques can be used in the cases where MRI remains incapable. Three patients that have presented to our clinic with the prediagnosis of infection were evaluated by F18-FDG PET-CT and 3-phase bone scintigraphy-SPECT-CT to make definite diagnosis and for treatment monitoring. By means of these cases, we demonstrated that PET-CT, which is an adjuvant method to MRI, can be used in making diagnosis as well as in evaluating the extent of infection, residual disease, response to treatment and duration of treatment in spinal infections where MRI remains incapable.

Keywords: Spine infection, F18-FDG PET-CT, Diagnosis, medical treatment

Level of evidence: Case series, Level IV.

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INTRODUCTION

Spinal infections are important problems that occur due to various agents, show different pathological processes, cause pain, spinal compression and neurological deficit, and lead to high morbidity and mortality. Spinal infections have increased in number with the increasing number of spinal interventions, antibiotic-resistant bacteria strains, and immunocompromised patients. The diagnosis is delayed in many patients as the onset of the disease is insidious and infection-specific signs are absent in the beginning. Delayed diagnosis results in permanent neurological deficit, even death [(4)].

Technological advancements in imaging methods have provided substantial convenience in identifying the focus of infection and in making diagnosis. Furthermore, evaluation of the extent of infection, as well as prognosis, residual disease and treatment response, is among the other required qualifications of imaging methods [(19)].

MRI is quite sensitive in diagnosing spinal infections. However, it is difficult to make differential diagnosis using radiological diagnostic methods in early stage bone and soft tissue infections where morphological changes have not occurred yet or in baseline chronic infection that has been exposed to anatomical changes due to trauma or surgery. Radiological methods may not be beneficial in prosthetic infections because of metal artifact. MRI may remain incapable in assessing residual disease and response to treatment. At this stage, nuclear medicine imaging methods make contribution to the diagnosis of spinal infections. Owing to the recently developed hybrid imaging methods and PET agents, the nuclear medicine gains increasing importance in assessing infection and inflammation as well as many diseases[(3,6,7,23)].

Radiopharmaceuticals (RF), which are being used in nuclear medicine to assess infection and inflammation, localize the infection by means of pathophysiological events such as increased tissue perfusion,

increased capillary permeability, and leukocyte migration, which occur in case of inflammation, usually independent from the structural changes and etiological factors. Thus, they allow the diagnosis of infection by visualizing inflammation at early phase before the development of structural changes. Nuclear medicine imaging methods are able to perform not only regional imaging but also whole body imaging without need for additional radiation dose (excluding hybrid imaging with CT) or cost.Along with the availability of hybrid imaging methods in the recent years such as SPECT-CT, PET-CT and PET-MRI, pathophysiological data from SPECT and PET and morphological data from CT and MRI have been obtained at the same time and this has started a new period in the evaluation of inflammation and infection as well as many diseases[1,9,16,19].

CASE REPORTS

CASE REPORT-1

A 63-year-old female patient, who had undergone L4-L5 vertebra surgery 13 years ago with laminectomy of L4, presented with low back pain. MRI demonstrated postoperative changes in L4-5 vertebra and lesions consistent with spondylodiscitis in T5-6 and T6-7 vertebras. Pre-diagnosing with spondylodiscitis /metastasis, she was evaluated by 3-phase bone scintigraphy SPECT- CT and F18-FDG PET-CT before treatment and by F18-FDG PET-CT after treatment. Bone scintigraphy failed to demonstrate blood supply and blood pool phase of T5-T7 vertebras clearly because of massive cardiac activity. During bone phase of whole body and SPECT/CT images, increased activity uptake was observed in the lower end plate of T5 vertebra and upper end plate of T6 vertebra and T7 vertebra. PET-CT demonstrated lytic sclerotic changes with massive FDG uptake (SUVmax: 11.1, late SUVmax: 12.6) in T5-T7 vertebras and the discs supporting the pre-diagnosis of spondylodiscitis, as well as images of orthopedic instruments at the level of L3-L5 vertebras and mildly increased FDG uptake suggesting postoperative changes on the posterior surface around the instruments. Brucella infection was detected in the patient (Brucella agglutination test coombs: 1/320). She treated with streptomycin, rifampicin and tetracycline. She was evaluated by PET-CT on the 3rd month after treatment for Brucella; mildly increased FDG uptake (SUV max: 3.6 late SUVmax: 4.2) with remarkable metabolic response to treatment was observed in the T5-6 and T6-7 intervertebral space and in the T6 vertebra (Figure 1A,1B-2A,2B). Antibiotic treatment stopped at 3 months.

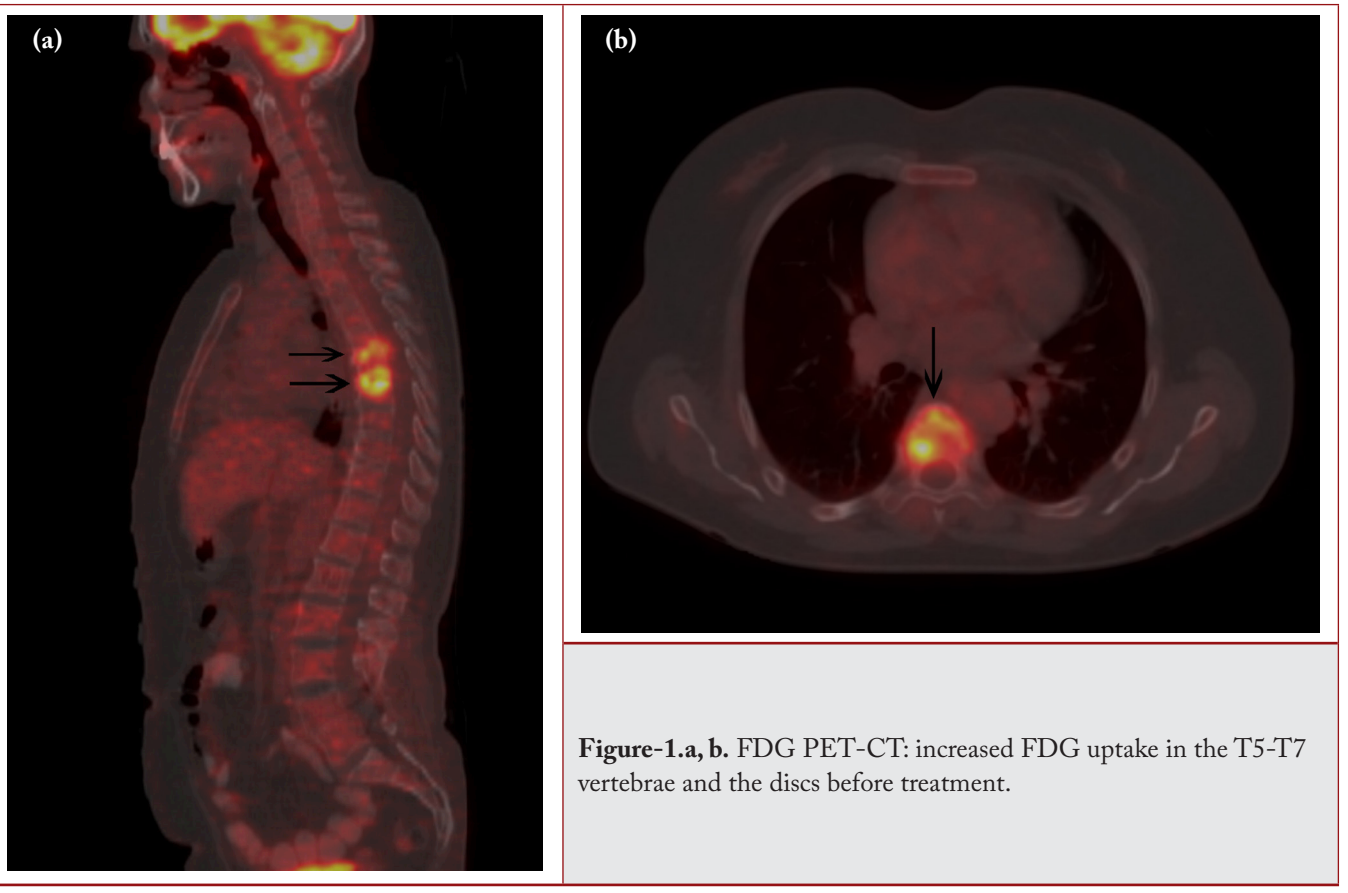
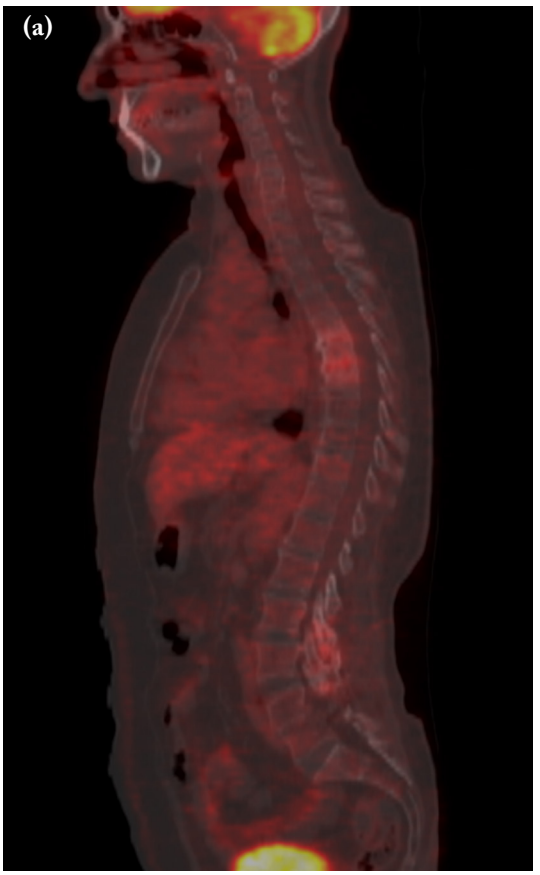


Figure-1.a, b. FDG PET-CT: increased FDG uptake in the T5-T7 vertebrae and the discs before treatment.



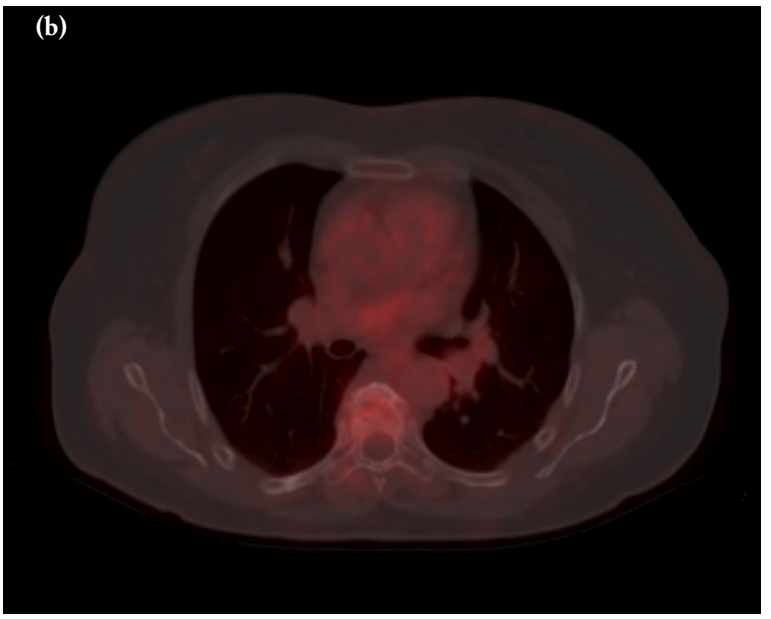


Figure-2.a,b. FDG PET-CT: remarkable decrease in FDG uptake in the vertebrae and discs on the 3rd month after treatment for Brucella.

CASE REPORT-2

A 66-year-old female patient presented with back pain and fever. She was evaluated by CT, and a lesion was detected in the T9-10 vertebras. Pre-diagnosing with malignancy, 3-phase bone scintigraphy/SPECT-CT and F18-FDG PET-CT were performed. Bone scintigraphy demonstrated hyperemia at the level of T9-T10 vertebra, whereas bone phase of SPECT-CT demonstrated diffusely increased activity uptake in the T9-T10 vertebras accompanied by soft tissue component. PET-CT revealed a lesion in theT9-10 vertebras with massive FDG uptake (SUVmax: 12.3) destructing the vertebras, which was accompanied by paravertebral soft tissue component. Spondylodiscitis could not be distinguished from malignancy. MRI primarily suggested spondylodiscitis. Histopathological evaluation was recommended; true-cut biopsy results were consistent with active chronic inflammation. Staphylococcus aureus was grown in the culture. She had medical treatment with cefazolin and ciprofloxacin.

CASE REPORT-3:

A 61-year-old female patient with diabetes mellitus and chronic renal failure, who have been receiving hemodialysis via intravenous catheter, underwent MRI for low back pain. MRI revealed spondylodiscitis in the T11-T12 and L1-L2 vertebras and also findings suggesting paravertebral abscess at the level of T11-T12 vertebra. Pre-diagnosing with spondylodiscitis, she was evaluated by three-phase bone scintigraphy/SPECT-CT and F18-FDG PET-CT. Bone scintigraphy demonstrated mild hyperemia at the level of T12 vertebra, SPECT-CT demonstrated loss of height in the T12 vertebra, destruction of vertebra corpus, increased RF uptake and concomitant soft tissue thickening at the corpus neighborhood, and increased RF uptake between T11 and L2 vertebras accompanied by soft tissue component suggesting spondylodiscitis and in L5-S1 vertebras primarily suggesting degenerative/arthritic changes. PET-CT demonstrated lytic-sclerotic hypermetabolic lesions (SUVmax: 7.4, late SUVmax: 9.5) betweenT11 and L2 vertebras accompanied by soft tissue components. Evaluating these findings together with clinical and laboratory findings, primarily spondylodiscitis was considered. Enterococcus faecalis was grown in blood culture. She had medical treatment with teicoplanin and ciprofloxacin.

DISCUSSION

Spinal infections have increased in number along with increasing number of spinal interventions, antibiotic-resistant bacteria strains and immunosuppressive patients[4]. One of the presented cases was an immunosuppressive patient with Diabetes mellitus and chronic renal failure.

Among imaging methods, MRI is still valid in assessing spinal infections as was in the present cases. Many studies have demonstrated that F18-FDG PET-CT is an adjuvant and complementary method in spinal infections[12,15].The studies have also revealed that F18-FDG PET-CT is effective in acute and chronic osteomyelitis, even in chronic osteomyelitis treated with antibiotics, spondylodiscitis, spondylodiscitis accompanied by soft tissue involvement, in discriminating modic changes from pyogenic spondylodiscitis, in discriminating degenerative from infectious end plate pathologies, in diagnosing infection in the patients with metallic implant and prosthesis, and in discriminating pyogenic from tuberculosis spondylitis. In a meta-analysis comparing different imaging methods in chronic osteomyelitis, F18-FDG PET was determined to be not only the most sensitive method but also the method with the highest specificity. The sensitivity of F18-FDG PET, bone scintigraphy and signed leukocyte scintigraphy was found to be 96%, 76% and 84%, respectively and the specificity was found to be 91%, 84% and 60%, respectively. Accordingly, it was concluded that it is the method with the highest diagnostic accuracy in detecting or excluding chronic osteomyelitis particularly in the axial bones[22]. F18-FDG PET-CT is used to evaluate response to treatment and residual disease via SUV measurement not only in the oncological diseases but also in the infectious and inflammatory diseases; thereby, it is superior to MRI and scintigraphy methods. The use of F18-FDG PET-CT in detecting biopsy point in the infection area is another advantage [8,11,22]. In our study, F18-FDG PET-CT helped us in determining biopsy point in two cases.

In addition to the visual evaluation, PET-CT also enables evaluation by standardized uptake value (SUV), which is a quantitative parameter calculated using PET imaging. SUV value is used to evaluate benign, infectious or inflammatory diseases as well as malignant disease. Although a SUV value of 2.5 is traditionally considered as the threshold value in discriminating benign from malignant lesion, it is known that SUV value lower than 2.5 can be measured in certain types of cancer or extremely high SUV value can be measured in certain infectious pathologies[2,17]. In our cases with proven infection, all had SUV value was over 7.

Double phase imaging can be performed to discriminate benign from malignant pathology and to enhance diagnostic specificity. Standard imaging is performed nearly 4-60 min after IV injection. In double-phase imaging, the 2nd imaging is performed 90-270 min after injection. In substantial proportion of the studies, increased SUV values were determined in the majority of (80-90%) malignant lesions during late imaging after RF injection, whereas increased SUV values were determined in the majority of benign lesions. This situation appears to be more valid in evaluating inactive and chronic infections. Unfortunately, increased SUV value can be detected during late imaging in some active granulomatous and infectious lesions as is in the malignant diseases, which hinders correct interpretation of double-phase imaging[2,17]. Double-phase imaging was performed in two of the present cases and increased late SUV values were determined.

Scintigraphy methods are being used for years in the spinal infections. It was determined that FDG-PET-CT is an excellent alternative to the scintigraphy methods in visualizing infection and inflammation. Some advantages of F-18-FDG PET-CT have made it preferred in detecting infection and inflammation.F-18 has convenient physical characteristics and convenient kinetics as it is rapidly collected in the lesion. Since it has short half-life, the patient receives lesser dose of radiation. Completion of the method in two hours owing to its physical characteristics is a critical advantage in terms of early outcome and patient comfort. In addition, PET devices have better resolution and contrast than scintigraphy devices. PET or PET-CT, as well as scintigraphy methods, enables whole body scanning and therefore is able to detect multifocal infections. In contrast to CT and MRI, artifacts due to metallic implants do not inhibit F18-FDG uptake in PET. CT enhances the advantage of PET as it provides anatomical detail. It is able to discriminate aseptic from septic inflammation. It can be used in elder and immunosuppressed patients. It is non-invasive with good interpreter consistency. It is easy to discriminate inflammatory cell from infiltrated bone marrow since FDG uptake is low in normal bone marrow. FDG uptake in bone can rapidly return to the normal after 3-4 months of trauma or surgery, which is another superiority to the bone scintigraphy. It has high sensitivity in chronic infections. One of the disadvantages of F18-FDG PET-CT is not being specific to infection and inflammation. Suspicious foci adjacent to the organs with physiologically high F18-FDG uptake might be reported as false negative or false positive [7,15,21]. In Case 2, the discrimination of infection from malignant pathology could not be made and therefore, biopsy was taken.

F18-FDG PET-CT is an adjuvant method to MRI with high negative predictive value and high sensitivity in evaluating spinal infections. Regardless of combining with CT, the sensitivity and specificity of F18-FDG PET in musculoskeletal infections are 95 % and 75-99 %, respectively. F18-FDG PET-CT has high negative predictive value and high sensitivity [12,15].Studies have demonstrated that F18-FDG PET-CT is superior to MRI in evaluating low-grade spondylitis or discitis and end plate anomalies, in detecting multiple infectious foci and directing for minimal invasive surgery, and in determining duration of antibiotic therapy [5,10,13,15,20].

Spondylodiscitis is a serious disease with high risk and cost and requires long-term antibiotic therapy. F18-FDG PET-CT is the second line method after MRI with similar accuracy in directing the cases where MRI is not convenient or diagnostic. Its specificity is higher than MRI in evaluation and in terminating the treatment [18].

Nanni et al. evaluated 34 spondylodiscitis patients by PET before and 2-4 weeks after treatment and concluded that 34 % decrease

in SUV value on interim PET is the strong predictor of complete treatment response and is more effective than CRP for follow-up[14]. In the present study, the case with Brucella spondylodiscitis was evaluated by PET before and on the 3rd month of treatment for Brucella, and 68 % decrease was determined in SUV value.

Although there is high number of studies demonstrating that F18-FDG PET and PET-CT have high sensitivity and diagnostic accuracy, they have been conducted in a limited number of patients. Meta-analyses with larger sample size are required to identify clinical use and cost-effectivity [22].

In conclusion, F18-FDG PET-CT is a method adjuvant to MRI in diagnosing spinal infections and in evaluating extent of the disease, treatment response and duration of treatment where MRI remains incapable.

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