Increased and normalized uptake of ^{18}F-FDG in a case of bone periprosthetic infection treated by antibiotics

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Abstract
We report the case of a 69 years old man with left hip prosthesis, who presented clinical, biochemical and imaging signs of periprosthetic infection treated with linezolid, an antibacterial agent of the oxazolidinone class. Two weeks after this treatment, a fluorine-18-fluoro-2-deoxy-d-glucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) scan showed increased uptake in the skeleton and also increased uptake in several focal areas in the spine and near the prosthesis and the surgical wound on the left gluteus medius. Bone marrow biopsy was negative; meanwhile the antibiotic therapy, after four weeks of treatment was stopped due to red blood cells and platelets toxicity. Six weeks later, the patient developed high fever again and in order to revaluate the periprosthetic inflammation, he was resubmitted to ^{18}F-FDG PET/CT which showed normal ^{18}F-FDG uptake in the whole skeleton, including the prosthesis and the subcutaneous wound. Some focal areas of increased uptake in the lumbar spine were still detected. In the next 4 weeks the patient was under a "watch and wait" follow-up in a steady state. *In conclusion*: In the case we report, since we found no other reason, we consider that the increased uptake of the ^{18}F-FDG in the skeleton was due to an increased metabolic reaction of bone marrow to infection normalized after treatment. The myelosuppressive action of linezolid could be another factor. The persistent focal areas in the lumbar spine where due to age-related bone deformities including some Schmorl's nodes. The inflammation in the bone prosthesis and the subcutaneous wound responded almost totally to the antibiotic treatment we applied.

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Introduction

Like glucose, fluorine-18-fluoro-2-deoxy-d-glucose (^{18}F-FDG) is transported into cells by a glucose transporter protein and is rapidly converted into ^{18}F-FDG-6-phosphate, which is biochemically trapped and metabolized in malignant and other tissues [1, 2].

Fluorine-18-FDG may also be accumulated in leukocytes and activated macrophages, making ^{18}F-FDG PET/CT suitable for imaging various inflammatory and infectious diseases [3]. Thus an increased uptake of ^{18}F-FDG is not always an easy to interpret finding [3-5].

The musculoskeletal ^{18}F-FDG uptake seen on whole-body PET/CT may be due to various pathologic reasons, such as primary myogenic tumors, metastases, lymphomas, infections or inflammatory conditions. Furthermore, bone marrow can be the site of higher ^{18}F-FDG uptake, determined by different pathological conditions, both malignant and benign, and by some specific therapies [1].

Case Report

We report the case of a 69 years old man, who underwent a left hip arthroplasty for coxarthrosis in June 2015. About a month later, he presented low-grade fever, swelling at the surgery site and functional, ex. impairment. Erythrocyte sedimentation rate (ESR) was 92mm for the first hour, C-reactive protein (CRP) 182mg/L- and revealed inflammation. Magnetic resonance imaging (MRI) showed periprosthetic infection. Antibiotic treatment with the glycopeptide vancomycin, 500mgx4/day and β-lactam meropenem

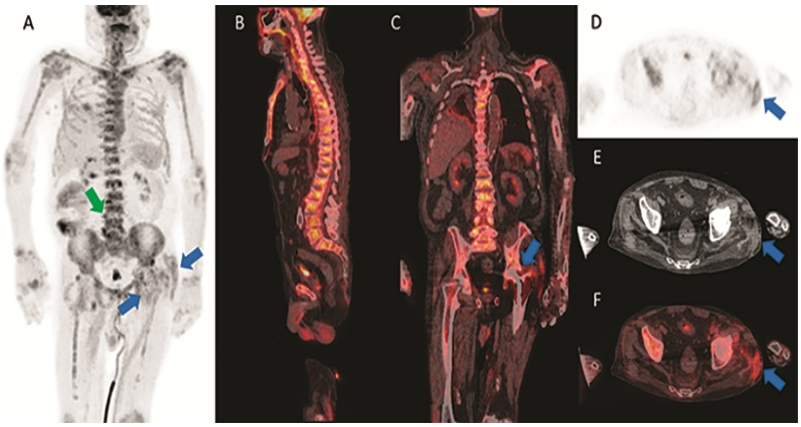

Figure 1. Fluorine-18-FDG PET/CT scan (A) MIP, (B) sagittal fusion, (C) coronal fusion (D) PET axial (E) axial CT and (F) axial fusion images. Diffusely increased ^{18}F-FDG uptake in the whole skeleton with focal "hot" areas, most evident in the lumbar spine (green arrow), sternum and pelvis (SUVmax 11.5); increased ^{18}F-FDG uptake can also be seen in periprosthetic area and in the subcutaneous area of the lateral left thigh, corresponding to the surgical wound (SUVmax 5.4) (blue arrows).

1gx3/day was administered. Because of the absence of response to this treatment, linezolid, an antibacterial agent of the oxazolidinone group in a dose of 600mgx2/day, and levofloxacin, an antibacterial agent of the fluoroquinolone group in a dose of 500mgx2/day, were administered. Pain was reduced and also the inflammatory markers (ESR, CRP). At that time, he also had a low back pain. Spine MRI was performed raising suspicion of bone infiltration. Three weeks after the beginning of antibiotic therapy, while linezolid and levofloxacin were still administered, the laboratory tests were midly decreased (ESR: 65mm for the first hour; CRP: 87mmg/L). We also found positive monoclonal component K IgG in protein electrophoresis. Fluorine-18-FDG PET/CT showed diffusely increased ^{18}F-FDG uptake with focal "hot" areas in the whole skeleton, most evident in the lumbar spine, sternum and pelvis with SUVmax of 11.5. Increased ^{18}F-FDG uptake in the periprosthetic area and in the lateral left thigh corresponding to the surgical wound with SUVmax of 5.4, were also observed (Figure 1). Bone marrow biopsy was normal.

Due to the known linezolid toxicity signs, (pancytopenia, malaise, fever, nausea and vomiting), antibiotic treatment was stopped after three weeks. The inflammatory markers were further decreased (ESR: 36mm for the first hour; CRP: 48mg/L).

Six weeks later, for persisting fever (38.0°C/100.4°F) and in order to revaluate the periprosthetic inflammation, the patient was submitted to a second ^{18}F-FDG PET/CT scan which showed normal bone uptake (SUVmax 2.0) and slightly increased ^{18}F-FDG uptake in the prosthesis and the subcutaneous wound. Some focal areas of increased activity in the lumbar spine (SUVmax 7.4) were considered as Schmorl's nodes (Figure 2). The inflammatory markers were only faintly higher than normal.

During the next 4 weeks the patient was followed by a "watch and wait" approach, being in a steady state.

Discussion

Fluorine-18-FDG bone uptake can be increased by different conditions, like carcinomas or metastases, metabolic, haematological, inflammatory and age-related degenerative deseases, administration of erythropoietin or haematopoietic growth factor or cytokine (Granulocyte Colony Stimulating Factor, Granulocyte Macrophage-Colony Stimulating Factor) [6-9]. All drugs responsible for myelosuppressive effects may therefore potentially impair the uptake of ^{18}F-FDG in the bone marrow.

Linezolid is often used for treatment of musculoskeletal or bone prosthesis infections caused by Gram-positive bacteria and also for vancomycin-resistant enterococci [10, 11]. Linezolid is generally effective and well tolerated, but if used for longer than two weeks, it may induce reversibile myelosuppression [15, 18].

Increased bone uptake of ^{18}F-FDG could be due to linezolid and other antibiotics toxicity, as also indicated by peripheral blood counts. Abnormalized uptake could be due to the reversible toxic effect of these antibiotics as shown by the normal peripheral blood counts and tests at that time. The degenerative processes of bones could have caused the ^{18}F-FDG focal uptake in the lumbar spine.

In conclusion, in the case we report, since we found no other reason, we consider that the increased uptake of the ^{18}F-FDG in the skeleton was due to an increased metabolic reaction of bone marrow to infection normalized after treatment. The myelosuppressive action of linezolid could be another factor. The persistent focal areas in the lumbar spine were due to age-related bone deformities including some Schmorl's nodes. The inflammation in the bone prosthesis and the subcutaneous wound responded almost totally to the antibiotic treatment, we applied.

The authors of this study declare no conflict of interest

Bibliography

1. Karunanithi S, Soundararajan R, Sharma P et al. Spectrum of Physiologic and Pathologic Skeletal Muscle ^{18}F-FDG Uptake on PET/CT. *AJR* 2015; 205:W141-9.

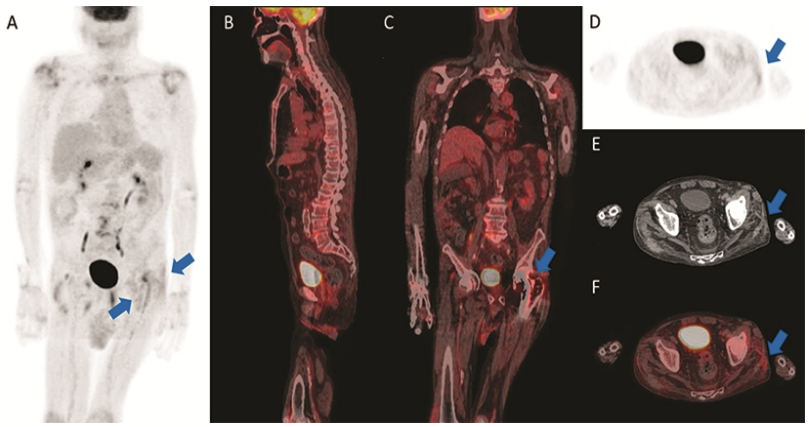

Figure 2. Fluorine-18-FDG PET/CT scan (A) MIP, (B) sagittal fusion, (C) coronal fusion (D) PET axial (E) axial CT, (F) axial fusion images. Normalization of bone marrow uptake (SUVmax 2.1); slight ^{18}F-FDG uptake in the prosthesis and the subcutaneous wound (SUVmax 3.2) (blue arrows); persistence of some focal areas in the lumbar spine (SUVmax 7.4) due to degenerative deformities and some Schmorl's nodes.

2. Aliyev A, Saboury B, Kwee TC et al. Age-related inflammatory changes in the spine as demonstrated by ^{18}F-FDG-PET: observation and insight into degenerative spinal changes. *Hell J Nucl Med* 2012; 15(3): 197-201.
3. Van der Bruggen W, Bleeker-Rovers CP, Boerman OC et al. PET and SPECT in Osteomyelitis and Prosthetic Bone and Joint Infections: A Systematic Review. *Semin Nucl Med* 2010; 40(1): 3-15.
4. Niccoli Asabella A, Notaristefano A, Pisani AR et al. Different causes of 18-Fluorine-labelled-2-deoxy-2 fluoro-D-glucose uptake in a patient with non-Hodgkin lymphoma. *Gazz Med Ital - Arch Sci Med* 2012; 171: 351-6.
5. Rubini G, Cappabianca S, Altini C et al. Current clinical use of ^{18}F-FDG-PET/CT in patients with thoracic and systemic sarcoidosis. *Radiol Med* 2014; 119(1): 64-74.
6. Hapkido H, Hidayat B, Hussein A et al. Differential Diagnosis Of Diffuse Bone Marrow Uptake On ^{18}F-FDG PET/ CT. *Int J Clin and Biomed Res* 2016; 2(1): 1-5.
7. Niccoli-Asabella A, Altini C, Notaristefano A et al. A retrospective study comparing contrast-enhanced computed tomography with ^{18}F-FDG-PET/CT in the early follow-up of patients with retroperitoneal sarcomas. *Nucl Med Commun* 2013; 34(1): 32-9.
8. Asabella AN, Cimmino A, Altini C et al. ^{18}F-FDG positron emission tomography/computed tomography and ^{99m}Tc-MDP skeletal scintigraphy in a case of Erdheim-Chester disease. *Hell J Nucl Med* 2011; 14(3): 311-2.
9. Varoglua E, Kaya B, Sari O. Chronic myeloid leukemia detected on FDG PET/CT imaging in a patient with renal cell carcinoma. *Rev Esp Med Nucl Imagen Mol* 2013; 32(1): 43-5.
10. Shaw KJ and Barbachyn MR. The oxazolidinones: past, present, and future. *Ann NY Acad Sci* 2011; 1241: 48-70.
11. Ament PW, Jamshed N and Horne JP. Linezolid: its role in the treatment of Gram-positive, drug-resistant bacterial infections. *Am Fam Physician* 2002; 65: 663-70.
12. Pfizer. 2010. Zyvox® (linezolid) package insert. Available at: http://www.pfizer.com/files/products/uspi zyvox.pdf. Accessed October 28, 2011.
13. McKee EE, Ferguson M, Bentley AT et al. Inhibition of mammalian mitochondrial protein synthesis by oxazolidinones. *Antimicrob Agents Chemother* 2006; 50: 2042-49.
14. Wang Z, Yuan L, Ma D, Yang J. ^{18}F-FDG PET/CT can differentiate vertebral metastases from Schmorl's nodes by distribution characteristics of the ^{18}F-FDG. *Hell J Nucl Med* 2016; 19(3): 241-4.
15. Timothy Chryssikos BS, Javad Parvizi, Elie Ghanem et al. FDG-PET Imaging Can Diagnose Periprosthetic Infection of the Hip. *Clin Orthop Relat Res* 2008; 466: 1338-42.
16. Zhuang H, YangH, AlaviA. Critical role of ^{18}F-labeled fluorodeoxyglucose PET in the management of patients with arthroplasty. *Radiol Clin North Am* 2007; 45: 711-18.
17. Chacko TK, Zhuang H, Stevenson K et al. The importance of the location of fluorodeoxyglucose uptake in periprosthetic infection in painful hip prostheses. *Nucl Med Commun* 2002; 23:851-5.
18. Kumar R, Basu S, Torigian D et al. Role of Modern Imaging Techniques for Diagnosis of Infection in the Era of ^{18}F-Fluorodeoxyglucose Positron Emission Tomography. *Clinical Microbiology Reviews* 2008; 209–24.