

## FDG-PET/CT Limitations in the Diagnosis of Spinal Implant Infection

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### Abstract

Here, we present a case of a false-negative 18F-FDG-PET/CT in a patient with an implant-associated infection with *Cutibacterium acnes* which negatively affected treatment. By discussing possible error sources concerning the method and the pathogen, we want to highlight the occurrence of false-negative 18F-FDG-PET/CT-examinations.

### Keywords

FDG-PET/CT, *Cutibacterium acnes*, Low virulence-bacteria, Spinal infection, Spinal implant, Biofilm infection

### Abbreviations

*C. acnes*: *Cutibacterium acnes*; CRP: C-Reactive Protein; CT: Computed Tomography; ESR: Erythrocyte Sedimentation Rate; FDG: 18F-Fluorodeoxyglucose; FDG-PET/CT: 18F-Fluorodeoxyglucose Positron Emission Tomography and Computed Tomography; MRI: Magnetic Resonance Imaging; NPV: Negative Predictive Value; Th5: 5<sup>th</sup> Thoracic Vertebra; Bone Scintigraphy: Technetium-99m-Diphosphonate Bone Scintigraphy; WBC: Labelled Leukocyte Imaging; 67Ga: Gallium-67 Imaging

### Introduction

The diagnosis and treatment of chronic implant infection in the postoperative spine can be challenging. The symptoms and physical findings are often non-specific and inflammatory markers have a relatively low sensitivity in low-grade and chronic infections [1]. Proper treatment is extensive, including surgical removal of the implant and long-term antibiotic treatment. Consequently, it is important that the preoperative investigation is as correct and detailed as possible, especially if the foreign material has to be replaced.

Magnetic Resonance Imaging (MRI) is the gold standard imaging method when osteomyelitis is suspected. The diagnostic certainty decreases considerably in the postoperative spine. In the presence of metal implants, it decreases even more, due to artefacts.

Several studies have proved the value of 18F-Fluorodeoxyglucose (FDG) Positron Emission Tomography and Computed Tomography (FDG-PET/CT) as a highly sensitive method in diagnosing spinal infections [2-4]. The technique

is mostly used when MRI is contraindicated or inconclusive [3]. The major considerations have concerned specificity and false-positive results, especially in the presence of spinal instrumentation. The negative predictive value (NPV) is considered to be close to 100%, so that a negative FDG-PET/CT can be considered to exclude spinal infection with a high degree of certainty [2, 3].

Here, we present a case with a false-negative result of FDG-PET/CT in a patient with an implant-associated infection of the spine with *Cutibacterium acnes* (*C. acnes*). *C. acnes* is a part of the natural skin flora in the deeper layers of the skin. Historically it has been considered as a contamination or a colonizing agent, but the clinical importance of *C. acnes* growth in bacterial cultures has been reevaluated. The bacterium is now acknowledged as a frequently occurring infectious agent, especially in orthopedic implant-associated infections. *C. acnes* is slow growing in vitro and has an expected low virulence which make these infections difficult to diagnose. It also has a high risk of reoccurrence [1, 5]. We consider all these factors to contribute to the case relevancy.

## Case Report

A 19-year-old patient was referred for an FDG-PET/CT investigation on suspicion of infection due to recurring back pain. About 2 years earlier she'd had similar symptoms which had led to diagnostic surgery of the 5th thoracic vertebra (Th5), including the insertion of a posterior spinal instrumentation. The perioperative bacterial cultures had verified a deep infection with *C. acnes* and with prolonged antibiotic treatment the patient's infection was regarded as cured.

This time the patient presented with discrete palpation tenderness at the surgery site and at level L3-4, without other focal signs of inflammation. C-reactive protein (CRP) was 8 mg/L (reference value < 3) and the erythrocyte sedimentation rate (ESR) 25 mm (reference value < 20), both slightly elevated but close to the reference values. Computed Tomography (CT) and MRI were inconclusive. A diagnosis of recurrent infection or non-fusion was suspected. The patient was referred for an FDG-PET/CT examination for further assessment, planning for revision surgery in case of signs of infection on the PET scan. The patient had been antibiotic free for 1.5 years at the time of the examination. FDG-PET/CT was performed with 4 MBq/kg (0.108 mCi/kg) on a Siemens Biograph mCT PET/CT. Scanning from the neck to proximal femur was performed 60 minutes after injection. An FDG-uptake greater than background activity in adjacent normal tissue was considered as pathological-positive. For interpretation, the PET-images without attenuation correction was assessed, as is standard [6], to avoid attenuation correction artefacts from the metallic spinal instrumentation. The examination showed no pathological FDG uptake, neither at the surgical site nor elsewhere, and no pathological findings on the CT scan.

Since, there were no signs of infection or inflammation on the FDG-PET/CT investigation, the decision was watchful waiting. In the following months, the patient's pain became

more intense and ESR rose to 37 mm. Revision surgery was performed 3 months after the FDG-PET/CT examination. Perioperatively, a small fluid filled cavity was found, without further signs of infection. 10 out of 10 perioperative bacterial cultures showed growth of *C. acnes*, proving a persistent chronic implant infection.

## Discussion

FDG is an unspecific tracer that reflects high glucose metabolism [2]. It has a fast distribution in the body, even in tissues with a low perfusion. For spinal imaging, FDG has the advantage of a naturally low uptake in bone, bone marrow and resting muscle [3, 6]. After spinal surgery the FDG-uptake typically normalizes in 4 months [3]. The high FDG uptake in infection primarily depends on the high metabolism of accumulated, activated inflammatory cells and the increased vascular permeability at the site of bacterial infection [3-5].

In our case, there was no increased FDG uptake despite a symptomatic infection with *C. acnes* and the presence of a spinal implant. The FDG-PET/CT was performed as per standard protocol and no technical factor has been identified that can explain the examination result. The patient had been without antibiotic treatment for 1.5 years at the time of the scan, which excludes that as a possible error source.

There are few reported cases of false-negative FDG-PET/CT in orthopedic spinal infections. Examination early after onset of symptoms has been shown to be false-negative [7]. In our case the symptoms had been present for about a year at the time of the examination, which should exclude this kind of time factor as a source of error. The examination was not repeated, so we can't fully exclude that a repeated FDG-PET/CT at the time of surgery would have produced another result but consider it to be unlikely.

To complement the examination with another nuclear imaging method was not considered. FDG-PET/CT has shown better performance than other methods, such as Technetium-99m-Diphosphonate Bone Scintigraphy (Bone scintigraphy), labelled Leukocyte Imaging (WBC) and Gallium-67 Imaging (67Ga). Bone scintigraphy has a low specificity and can remain abnormal even after an infection has been resolved. WBC-imaging is not recommended in spinal infection since about half of the examinations show uncertain findings. 67Ga is not specific for infection, and a positive result could be a result of the performed surgery without any complications being present. Moreover, 67Ga is no longer in use in Sweden or Western Europe [8].

In resemblance with several other bacteria *C. acnes* can adhere to implants and establish a biofilm on the avascular surface [1, 5]. The biofilm functions as a protective barrier against the immune system and against antibiotics. Even though bacteria in a biofilm in implant-associated infection are somewhat secured from the actions of the immune system, there generally is an immune response. This response causes an inflammatory reaction which FDG could be expected to detect, unless there is something that minimizes this immune

response and/or causes a reduced metabolic activity. Our patient has no identified immune deficiency. The lack of immune response is therefore suspected to be connected to the pathogen *C. acnes*, possibly its low virulence. In a study of foreign body-associated infection in a rabbit model, a significantly lower FDG-uptake was observed in infection with the low virulence bacteria *Staphylococcus epidermidis* compared to the highly virulent *Staphylococcus aureus* [9]. This supports our hypothesis and gives us reason to suspect that there are bacteria which in some circumstances do not induce an elevated FDG-uptake. FDG is known for having a low uptake in some malignant processes [6]. It is important to recognize the occurrence of this phenomenon in infectious diseases as well, especially in foreign body infections.

## Conclusion

The implementation of FDG-PET/CT in infectious disease diagnostics is expanding, especially in challenging cases. Even though false-positive examinations remain the largest issue, false-negative scans occur. They need to be emphasized since false-negative examinations can lead to delayed and inappropriate treatment and increased patient suffering. We propose that the main reasons for the false negative result are the traits of the bacteria itself with low virulence causing a low inflammatory response. Among challenging cases in infection diagnostics, patients with low virulent bacteria are expected to be a considerable fraction. Therefore, the occurrence of false-negative examinations in clinical practice must be taken in active consideration. The finding of a false-negative FDG-PET/CT in a patient with an implant-associated spinal infection with *C. acnes* is therefore highly relevant, considering the high frequency of the bacterium in implant-associated infections, the common diagnostic difficulties and the high rate of reoccurrence.

## Informed Consent

The case report is authored and published with informed consent from the patient.

## Conflict of Interest

The authors have no potential conflict of interest.

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