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Case Report

Diagnostic Benefits of 18F-FDG PET/CT in Cases of Prosthetic Infective Endocarditis

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Abstract

Infective endocarditis (IE) is a difficult-to-diagnose provocative disease that causes significant morbidity and mortality. The first-line imaging test for the diagnosis of IE is echocardiography. However, in cases of prosthetic IE or IE associated with intracardiac devices, its sensitivity is limited. A new diagnostic tool, 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET/CT), improves diagnosis in these difficult cases. The most recent European guidelines for IE (2015) include this imaging modality as a primary diagnostic criterion. We present a case of culture-negative prosthetic IE diagnosed with 18F-FDG PET/CT.

Keywords

18F-FDG PET/CT, diagnosis, prosthetic infective endocarditis

INTRODUCTION

Infective endocarditis (IE) is an infection of the heart and great vessels' endocardium, affecting heart valves (native[B1] or prosthetic), subvalvular structures, and, in recent decades, indwelling intracardiac devices or catheters. It is a life-threatening disease with high morbidity and mortality rates that can reach 30%.[1] Globally, the incidence of IE has increased from 9.91 to 13.8 per 100000 people in the last 30 years.[2]

Despite advances in modern imaging and microbiological methods, the diagnosis of IE often faces serious difficulties and delays. An early diagnosis of IE is a key to the therapeutic approach and patients' outcome. The diagnosis of this disease is based on the Duke criteria introduced in 1994[3] and modified in 2000[4], but their specificity and sensitivity are limited in cases of prosthetic valve endocarditis (PVE) and cardiac device-related infective endocarditis (CDRIE).

18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) is a new imaging tool that has been shown to improve the diagnosis of PVE and CDRIE.[3,4] This method is widely used in oncology, for diagnosis, and treatment monitoring. As an imaging study, it can show increased metabolic activity around the prosthetic valve or the intracardiac device, as well as extracardiac foci of infection. The 2015 ESC recommendations included 18F-FDG PET/CT as a major criterion in the diagnostic algorithm of PVE.[5]

We present a case of using 18F-FDG PET SCAN in the diagnosis of prosthetic IE.

CASE REPORT

Our patient was a 67-year-old man with a past medical history of rheumatic heart disease and mitral valve replacement with a mechanical prosthesis in 2007 due to severe mitral insufficiency. He was in very good condition until April 2020, when he underwent vertebroplasty due to a L1 fracture. One month later, he was admitted to the Department of Cardiology with a three-week history of progressive complaints, including fever up to 38.9°C, headaches, weakness, a dry cough, and decreased appetite. Physical examination on admission showed blood pressure of 130/75 mmHg, tachycardia of 105 bpm, respiratory rate of 20/min, and fever of 38.6°C. Auscultation found no wheezing in the lungs and no heart murmurs, clear prosthetics sounds. Upon admission, laboratory results were as follows: white blood cells count, 7.54×10^{12}/l (3.5–10.5), hemoglobin, 115 g/l (140–180), ERS, 71 mm/h (0–20), and C-reactive protein (CRP), 88 mg/L (0–10). The dynamics of the laboratory parameters is shown in ***Figs 1, 2****.*

The PCR tests for acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were negative. The kidney and liver function were normal. Chest X-ray showed moderate pulmonary congestion and cardiomegaly. ECG showed normal sinus rhythm. Upon admission, we performed transthoracic echocardiography (TTE) and, the next day, transesophageal echocardiography (TEE). Both studies indicated normally functioning valve prosthesis, no vegetations and/or perivalvular abscess, no visual findings conclusive for infective endocarditis. The TTE and TEE were repeated twice, after 7 and 14 days, and the acquired information was the same. Three blood cultures drawn within 30 minutes were all negative. Meanwhile, we started empirical antimicrobial therapy with intravenous vancomycin 1.0 g and gentamicin 80 mg twice daily. After 14 days, we changed gentamycin with meropenem 1.0 g twice daily. Laboratory monitoring of infection, kidney, and liver function was done every 5 days.

The patient had only two minor diagnostic criteria (predisposing heart condition of prior prosthetic valve implantation and high fever) from the modified Duke criteria (MDC)

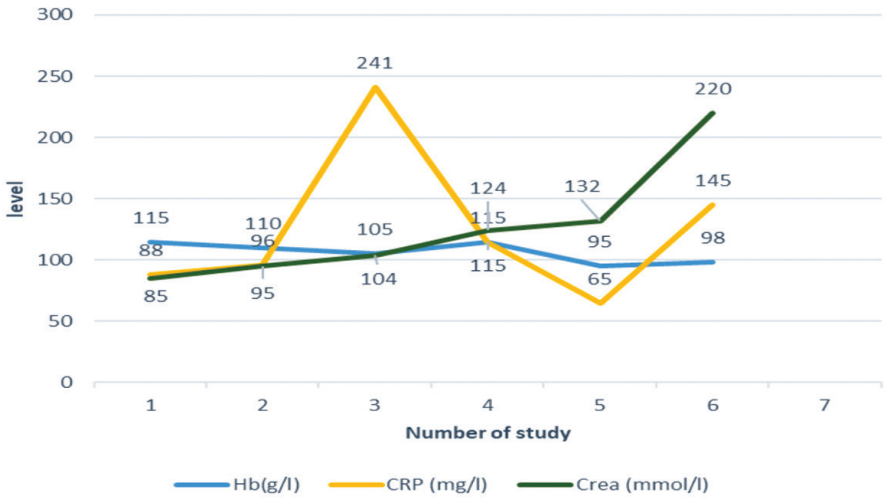

Figure 1. Dynamics of laboratory parameters: hemoglobin, C-reactive protein, and creatinine.

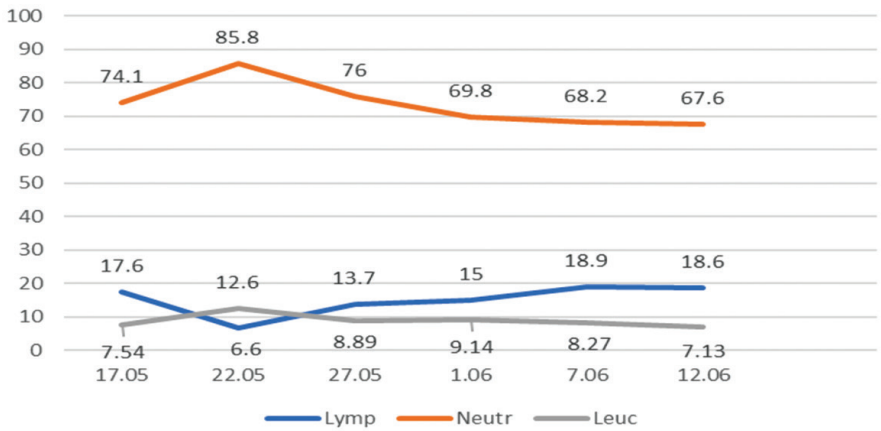

Figure 2. Dynamics of laboratory parameters: lymphocytes, neutrofils, and leucocytes.

for infective endocarditis and thus the diagnosis of IE was not confirmed.

Because of the high likelihood of infective endocarditis, we performed the 18F-FDG PET/CT at our hospital's Department of Nuclear Medicine on day 12 for diagnostic clarification. The examination was carried out after careful preparation of the patient: fasting for at least 6 hours before the study, no alkaloid drinks and sweet liquids on the day of the examination, and no smoking for the same period, blood sugar examination on site, and provision of venous access. The radiopharmaceutical for the study was 18F-fluorodesoxyglucosae (FDG). The patient underwent PET/CT whole-body examination 58 minutes after intravenous administration of 209 MBq of 18F-FDG, combined with low-dose CT on a SIEMENS PET/CT hybrid apparatus model Biograph mCT64. On the hybrid PET/CT images, increased metabolic activity around the mitral valve prosthesis was visualized, without focal character, SUV max up to 4.14. In the remaining scanned volume, PET/CT data for metabolically active lymph nodes: thoracic, right, and para-aortic – most likely in connection with the septic condition were detected ***(Figs 3, 4)****.*

After the 18F-FDG positron emission tomography scan, the patient met one major and two minor Duke criteria for infective endocarditis, thus confirming a diagnosis of possible infective endocarditis of the mitral valve prosthesis.

On the day of the nuclear examination, the patient's case was discussed by an interdisciplinary team (the heart team), including a hematologist, an oncologist, an infectious disease specialist, a cardiac surgeon, and a rheumatologist. No other disease was identified. With a diagnosis of possible IE, we continued with the double antibiotic therapy.

By day 20, there was a trend toward decrease in the inflammatory markers, and the patient was afebrile for 7 days. Then the temperature resumed and the CRP began to rise again. At the same time, the kidney function showed worsening with reduction of creatinine clearance to 37 ml/min. Due

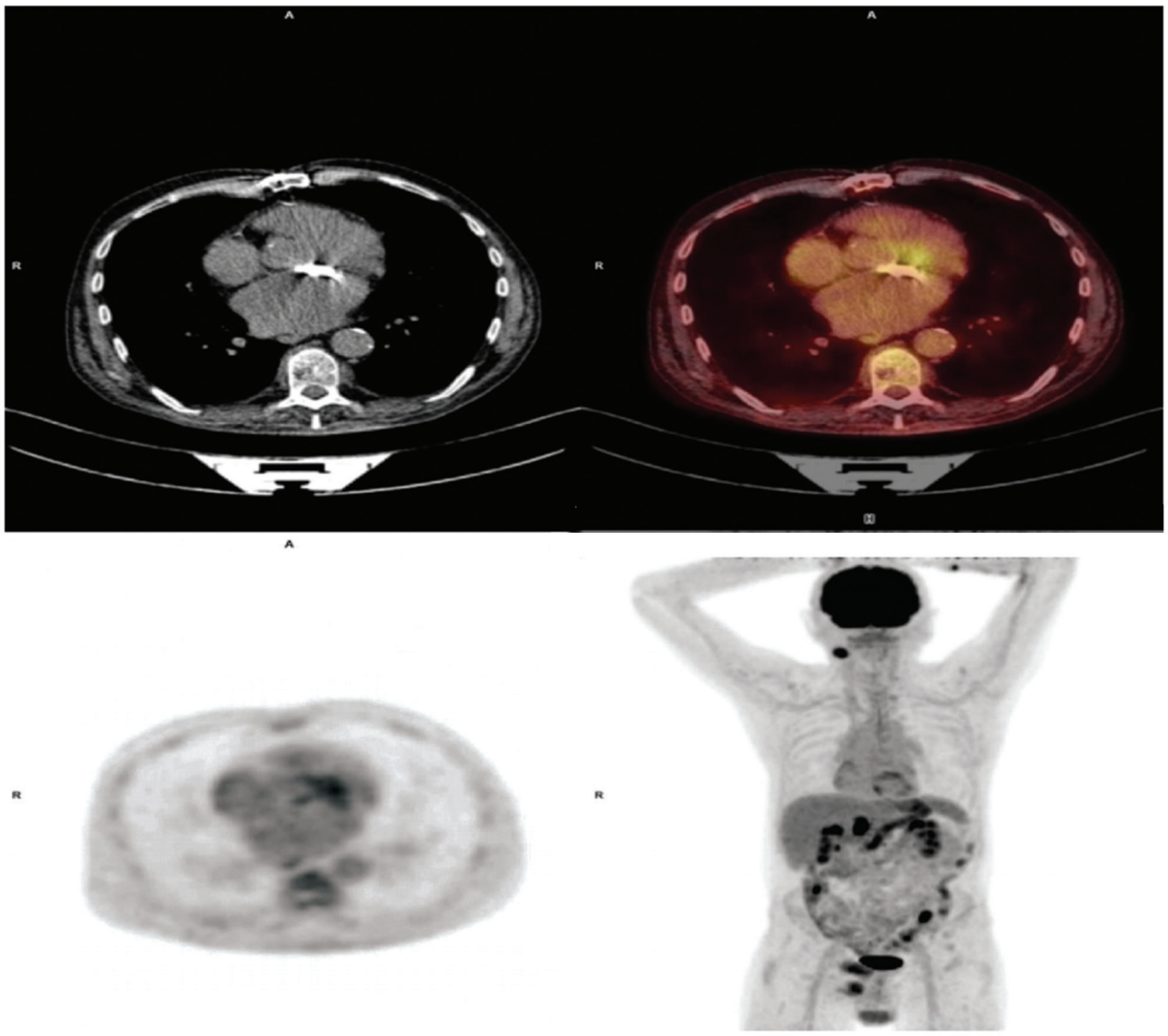

Figure 3. PET/CT data for increased metabolic activity around the mitral valve prosthesis and metabolically active lymph nodes – thoracic, right and para-aortic.

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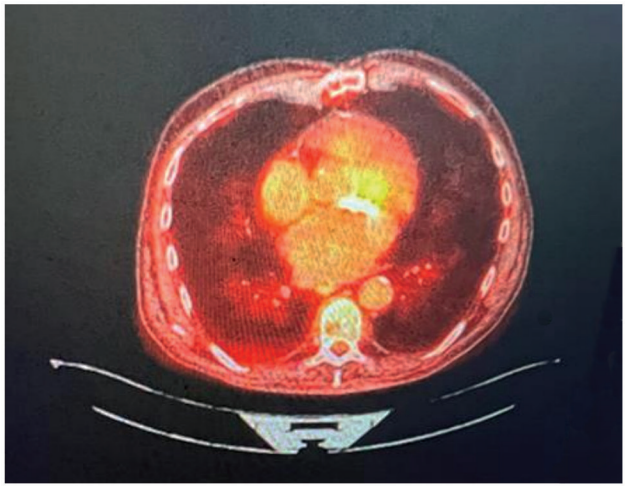

Figure 4. Increased metabolic activity around the mitral valve prosthesis.

to persistent fever, lack of response to medical treatment, initial kidney failure, the heart team decided on surgical treatment – reoperation with valve replacement. On day 25, the patient was transferred to the department of cardiac surgery, where replacement of the mitral prosthesis with biological mitral valve was performed.

Intraoperative microbiology from the valve was negative, but histology evaluation confirmed inflammatory changes of the mitral valve prosthesis. The colonies of embedded organisms with morphological characteristic of bacterial colonies are shown in ***Fig. 5****. Zones of necrosis and WBC inflammatory infiltration* ***(Fig. 6)*** *were found, thus confirming the morphologic findings correlated with the clinical diagnosis.*

After the surgical intervention, the patient's treatment continued with 6 weeks of a double parenteral antibiotic combination of vancomycin and meropenem in a dose adjusted according to the creatinine clearance. The patient stayed in the Department of Surgery for two weeks and then for four weeks in the Department of Cardiology. He was discharged fully recovered.

DISCUSSION

Infective endocarditis continues to be a diagnostic challenge because of its highly variable clinical presentation and changing patient profile. Echocardiographic evidence is one of the major Duke criteria for the diagnosis of IE, but with variable sensitivity and specificity, especially in the cases of PVE and CDRIE.[5,6] The echocardiography can be normal or nondiagnostic in about 30% of cases of PVE and CDRIE.[7] The diagnostic challenge is even greater when the blood culture is negative.

18F-FDG PET/CT is a new imaging modality that can improve the diagnostic accuracy of PVE and CDRIE. For PVE, this study has both high sensitivity and specificity for intracardiac infection. Laurens at al. reported that FDG PET/CT had a sensitivity/specificity/positive predictive value/negative predictive value for PVE of 91%/95%/95%/91%, respectively.[8] The most recent meta-analysis of this indication found similar data for PVE, but with low sensitivity (36%) and high specificity (99%) in native valve endocarditis (NVE).[9,10] 18F-FDG PET/CT can also detect extracardiac foci of infection or evidence of another disease, most commonly a malignant tumor, which may correct the initial diagnosis.[11] Low inflammatory activity (CRP<40 mg/l) and prior antibiotic treatment at the time of FDG PET/CT imaging were identified, as significant predictors of false-negative misinterpretations.[12] In our case, despite the antibiotic treatment, SUV max – 4.14 was highly diagnostic for valve inflammation. To avoid false positive results, ESC recommends performing the FDG PET/CT study three months after surgical intervention.

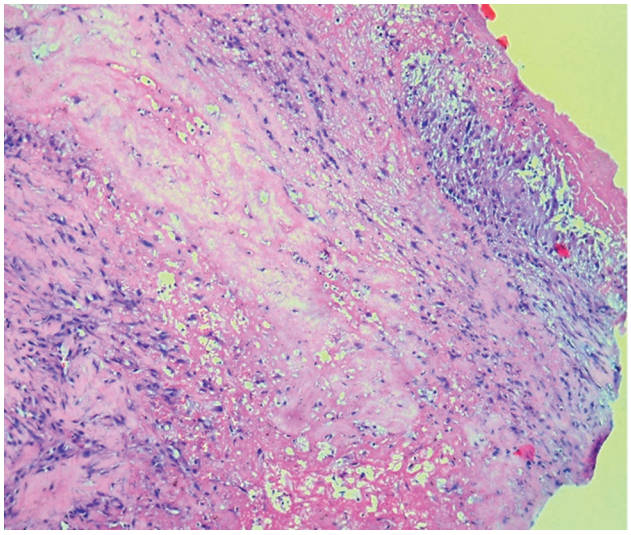

Figure 5. Colonies of embedded organisms are presented (hematoxylin-eosin ×400).

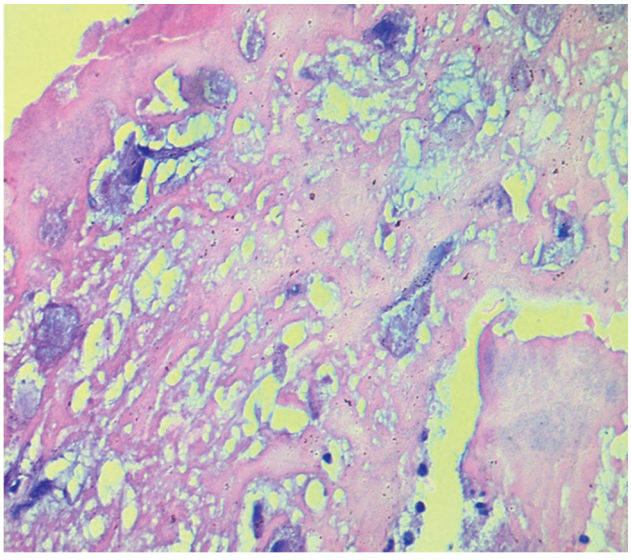

Figure 6. Necrosis and WBC inflammatory infiltration (hematoxylin-eosin ×200).

The 18F-FDG PET/CT has some limitations – false positive results, especially ≤3 months after cardiac surgery or vasculitis, tumors, foreign bodies, and post-surgical inflammation. The method has limited diagnostic accuracy in native valve IE and limited ability to assess infection in the brain and gums. It is necessary to follow restriction of carbohydrates in the diet 12-24 hours before the examination.

In our case, the patient has a high probability of IE – high risk due to the valve prosthesis; the prior operative intervention with L1 vertebroplasty could be a probable port of entry for the infection; clinical and laboratory constellation for inflammation. However, the patient does not meet Duke criteria for definite or probable IE and the diagnosis of IE would be rejected. The dilemma is that the untreated IE is life-threatening. An unnecessary 6-week hospital treatment carries other risks. A real diagnosis can be missed and delayed.

Because of the negative blood cultures and the negative TTE and TEE, we discussed a wide range of differential diagnostic possibilities. First of all, other inflammatory diseases of the heart: myocarditis, infiltrative diseases – cardiac sarcoidosis and amyloidosis, and hemopathy or neoplasm with unspecified location.[13] Each of these diseases has a specific 18F-FDG PET/CT finding. Myocarditis, sarcoidosis, and amyloidosis involve the myocardium diffusely or focally, and none of them involve solely a prosthetic valve. In addition, the absence of typical conduction and rhythm disorders rejects a major diagnostic criterion for them. Regarding the presence of insulated para-aortic lymph nodes, with a low SUV max, the possibility of hematological or neoplastic disease was ruled out after interdisciplinary discussion.

Using 18F-FDG PET/CT, we made the diagnosis of possible infective endocarditis of the mitral valve prosthesis, confirmed later by the histological examination. The treatment decision and patient's outcome strongly depend of the correct diagnosis. Nearly 50% of the patients with IE undergo surgical treatment during hospitalization.[14,15] Most bacteria are resistant to medications, and surgery is the only way to completely eliminate the infection. Indications for surgical treatment of PVE are heart failure, valvular dysfunction, periannular abscess, persistent infection, prevention of embolism, acute renal failure.[15] Uncontrolled infection is one of the most unfavorable complications of IE and is the second most frequent cause for surgery.[16]

According to the guidelines, operative treatment should not be delayed after the final diagnosis of NVE, PVE and CDRIE when indications are available and assessment of individual patient risk.[5,17,18]

CONCLUSION

Early diagnosis and detection of PVE remain difficult in clinical practice. Despite negative TEE and blood cultures in cases of high clinical probability of prosthetic IE and CDRIE, 18F-FDG PET/CT can play a critical role in the diagnosis. The use of 18F-FDG PET/CT can add value in the detection of septic emboli and/or the identification of a diagnosis other than IE. When indications are available and an assessment of individual patient risk is made, operative treatment should not be delayed after the final diagnosis of NVE, PVE, or CDRIE, according to the guidelines.

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Competing Interests

The authors have declared that no competing interests exist.

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Диагностические преимущества 18F-FDG PET/CT при протезном инфекционном эндокардите

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Резюме

Инфекционный эндокардит (ИЭ) – трудно диагностируемое провоцирующее заболевание, вызывающее значительную заболеваемость и смертность. Визуализирующим тестом первой линии для диагностики ИЭ является эхокардиография. Однако в случаях протезного ИЭ или ИЭ, связанного с внутрисердечными устройствами, его чувствительность ограничена. Новый диагностический инструмент – позитронно-эмиссионная томография с 18F-фтордезоксиглюкозой (18F-FDG PET/CT) улучшает диагностику в этих сложных случаях. Самые последние европейские рекомендации по ИЭ (2015 г.) включают этот метод визуализации в качестве основного диагностического критерия. Мы представляем случай протезного ИЭ с отрицательной культурой, диагностированный с помощью 18F-FDG PET/CT.

Ключевые слова

18F-FDG PET/CT, диагностика, протезный инфекционный эндокардит