

Disseminated Infection Characterization on FDG-PET/CT: Clinico-Laboratory-Radiological Correlation Unraveling the Complexity

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1. Abstract

18F FDG PET/CT is a hybrid imaging technique traditionally used for various oncological indications. Recent advances have broadened its use to various non-oncological indications, such as infections and inflammatory diseases. While FDG uptake indicates increased metabolic activity, however the uptake of FDG is not specific, and it is not possible to distinguish separate infections on the basis of FDG uptake alone. We present a case, wherein through critical analysis of PET/CT images, and correlation with patient's clinical and laboratory data, we were able to identify three distinct infections on FDG PET/CT.

2. Introduction

Infections pose a serious threat globally due to the increasing problem of antibiotic resistance [1]. Early diagnosis or exclusion of infection is of utmost importance, and it is a major factor that determines the patient's prognosis [2]. In most cases, the diagnosis of infections is straightforward, using clinical and laboratory data, supplemented with structural imaging techniques such as ultrasonography, computed tomography and magnetic resonance imaging. However, they may not be able to localize the infectious foci in all cases [3]. Thus, functional and metabolic imaging techniques are often needed to complement the role of anatomical imaging methods in many clinical situations [3].

18F flourodeoxyglucose positron emission tomography/ computed tomography (18F FDG PET/CT) is an advanced hybrid imaging technique that combines the anatomic information derived from CT with the functional information derived from PET. Initially

limited to oncological indications, FDG PET/CT has expanded its scope to include non-oncological applications, such as imaging infections and inflammation as well. It allows for whole-body examination in a single session, to identify infection foci in patients [4-7]. White blood cells have a high glucose metabolism compared to other cells. Additionally, inflammatory mediators cause an upregulation of glucose transporters, leading to increased FDG uptake. Therefore, sites of infection often light up on FDG PET/CT [8]. However FDG is considered relatively nonspecific due to its limitations in differentiating infection from inflammation, as well as distinguishing different types of infections. We present an interesting case of a patient with a complex medical history, wherein FDG PET/CT helped to identify the sites of infection which further correlated with three distinct types of organisms.

3. Materials and Methods

A 53 year old gentleman presented to the emergency with multiple painful skin eruptions over the body. On examination, the patient was vitally stable and febrile to touch. There were multiple tender non-itchy pustular skin lesions over the scalp, face, neck and chest with a ~2 cm palpable left inguinal lymph node. Co-morbidities included type 2 diabetes mellitus and hypertension. His past history was significant for genitourinary tuberculosis, for which the patient received a course of anti-tubercular therapy, followed by augmentation ileo-cystoplasty for thimble bladder two months back. There was no history of immunosuppressant intake. Routine laboratory workup demonstrated raised inflammatory markers, with elevated total leukocyte count and neutrophils. Blood cultures were

sent and empirical antibiotics were started. 2-D echocardiography and 18F FDG PET/CT were done to identify the primary source of infection. Echocardiography was negative for vegetations on heart valves. Further to rule out any possibility of myocardial involvement and to look for focus of active infection, patient was referred to 18F FDG PET/CT. The patient was prepared according to infective endocarditis protocol and was instructed to follow a high fat and low carbohydrate diet for 2 days before the PET/CT scan [9]. 18F FDG PET/CT images were acquired from vertex to mid-thigh after 55 minutes of injection of 6.5 milicuries of 18F FDG (Figure 1, A). Dedicated cardiac spot images were also acquired. 18F FDG PET/CT revealed multiple metabolically active variable sized skin and subcutaneous nodular cystic lesions involving face, scalp, head & neck, anterior chest & abdominal wall, back, pelvic region and scrotum (SUVmax - 6.6 in the lesion on anterior abdominal wall, Figure 1, B). In addition, there was a thick walled cavitary lesion involving the right lung upper lobe, with peripheral FDG uptake (SUVmax - 5.0). This lesion demonstrated internal necrosis and air fluid levels within (Figure 1, C). Further, there were multiple parenchymal foci of increased FDG uptake involving bilateral renal parenchyma, persistent till delayed images (left kidney, SUVmax - 9.5, delayed SUVmax - 12.9, Figure 1, D). Moreover, irregular focal bladder wall thickening was noted involving the neo-bladder with few hypermetabolic areas (SUVmax - 18.0, delayed SUVmax - 25.3, Figure 1, E). No abnormal FDG uptake was noted in the myocardium.

We tried to correlate the 18F FDG PET/CT findings with the clinical details, laboratory parameters and follow-up imaging of the

patient. The biopsy from left inguinal lymph node was suggestive of budding yeasts with pseudohyphae, and culture of pustular skin lesions came out to be positive for *Candida albicans*. This confirmed the fungal origin of cutaneous lesions seen on 18F FDG-PET/CT. Thus, a diagnosis of disseminated Candidemia was made. Cutaneous tuberculosis was ruled out, since skin lesions were negative for acid fast bacilli. Secondly, the thick walled cavitary lesion in right lung upper lobe was initially suspected to be an aspergilloma based on the CT features [10], however a negative galactomannan assay in bronchoalveolar lavage fluid ruled out this possibility. Further, the presence of a solitary well-defined cavitary lesion with normal remaining bilateral lung parenchyma made pulmonary tuberculous involvement less likely [11]. The patient was started on intravenous caspofungin as per the culture and sensitivity reports, followed by maintenance therapy with oral posaconazole. The skin lesions gradually improved. Further, a follow-up thorax CT scan performed after three months of anti-fungal therapy showed a 50% reduction in the size of the lung lesion. This finding corroborated the possible fungal nature of this lung lesion. Thirdly, *Escherichia coli* (*E. coli*) was identified on urine culture, and ultrasonography of the kidneys demonstrated bilateral pyelonephritis. This helped in correlating metabolically active renal parenchymal lesions to pyelonephritis secondary to *E. coli* infection. Lastly, the focal hypermetabolic bladder wall thickening was correlated with the reactivation of genitourinary tuberculosis, in view of recent urine Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) positivity.

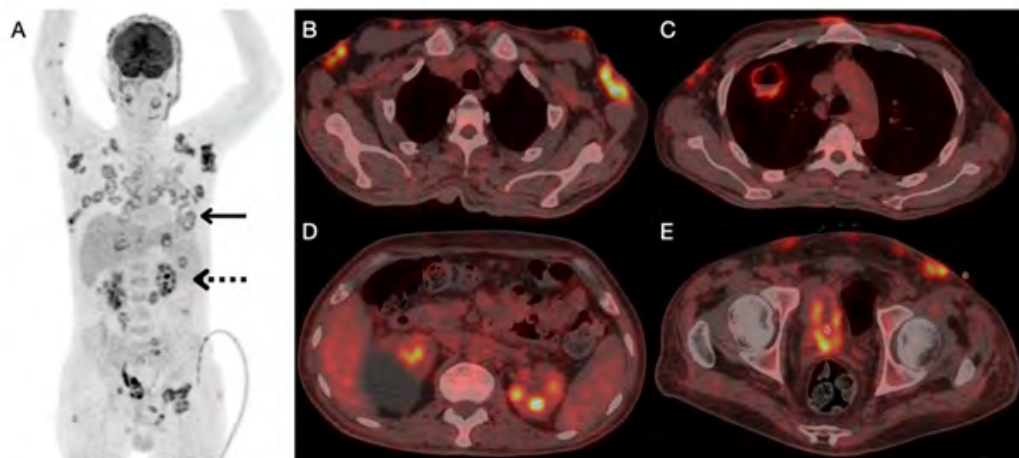


Figure 1: 18F FDG PET/CT images of the patient. A: Maximum intensity projection image, depicting multiple FDG avid oval lesions, predominantly involving the thorax (solid arrow), as well as multiple foci of increased radiotracer uptake involving bilateral kidneys (dotted arrow). B-D: Fused 18F FDG PET/CT images of the patient. B: FDG avid skin and subcutaneous lesions involving thorax and bilateral axilla. B: Peripherally FDG avid cavitary lesion involving the right lung upper lobe. C: Multiple foci of FDG uptake involving both kidneys. Ancillary evidence of right simple renal cyst. D: Focal hypermetabolism involving the thickened urinary bladder wall.

4. Results

In this case, there were distinct infective foci demonstrated on 18F FDG PET/CT involving the skin, lung, kidneys and urinary bladder by three different causative organisms. These included *Candida albicans* in skin lesions, bilateral renal parenchymal lesions attributed to *E. coli*, and reactivation of genitourinary tuberculosis in the form of bladder involvement by *Mycobacterium tuberculosis*. Moreover, the patient presented with superficial *Candida* skin lesions, and FDG PET/CT helped in detecting systemic involvement, specifically in the form of the cavitary lung lesion. This is clinically relevant, as systemic candidiasis requires more aggressive and prolonged anti-fungal therapy compared to localized skin infections [12].

5. Discussion and Conclusion

Infectious and inflammatory diseases are usually characterized by a more diffuse and less pathognomonic pattern of FDG uptake than FDG uptake for oncological indications. In addition, patients who are referred for FDG PET/CT with suspected infection or inflammation are rarely treatment naive and may have already received varying dose of antibiotics [13]. Consequently, FDG PET/CT is generally considered as nonspecific modality to distinguish infections [3, 14, 15]. However, critical analysis of the images along with clinical, laboratory and radiological correlation can widen the scope of FDG PET/CT beyond its established applications and help in correlating with different infectious processes occurring simultaneously. There is paucity of data on the role of FDG PET/CT in fungal infections. Our findings align with previous research [16, 17], which has demonstrated a potential role of FDG PET/CT in diagnosing invasive fungal infections. Moreover, although FDG PET/CT is often considered as limited utility for localizing tuberculosis involvement of the urinary tract due to the physiological radiotracer accumulation of FDG [18], a careful examination of images, acquisition of delayed images preferably post Lasix administration along with correlation with patient's history, can help overcome this limitation.

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7. Conflict of Interest: The authors declare that they have no conflict of interest.

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9. Consent from Patient: The patient has agreed to use his images for publication and provided written informed consent for the same.

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