Mycobacterial Lymphadenitis in a Human Immunodeficiency Virus-Infected Patient: Usefulness of 18F-Fluorodeoxyglucose Positron Emission Tomography for Diagnosis and Monitoring the Response to Treatment

Abstract

Lymphadenitis, due to typical or atypical *Mycobacterium*, is a clinical condition frequently associated with human immunodeficiency virus (HIV) infection. Differential diagnosis between benign and malignant causes may be a challenge for clinicians. In this regard, the role of positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (^{18}F-FDG) has still not been fully explored. We describe a case of 30-year-old male, infected by HIV, with mycobacterial lymphadenitis, in which ^{18}FDG-PET and PET-derived parameters resulted useful for guiding diagnosis and monitoring the response to treatment.

Keywords: *^{18}F-fluorodeoxyglucose positron emission tomography, human immunodeficiency virus, lymphadenitis, Mycobacterium*

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A 30-year-old male patient with significant and unintentional weight loss over the previous 6 months was admitted to our hospital for persistent fever. One month before, he was diagnosed with bronchitis on the basis of symptoms and had performed antibiotic therapy with amoxicillin (250 mg 3 times a day) without any significant benefit. On physical examination, he presented abdominal pain radiating to the upper right quadrant. Laboratory investigation showed hemoglobin 11.8 g/dL (range 13.5–17.5), platelet count 393,000/mL (range 140,000–440,000), total white cell count 5500 cells/µL (range 4000–9600), absolute neutrophil count 3874 cells/µL (range 1800–7000), absolute lymphocytic count 784 cells/µL (range 1000–4800), and CD4+ T-lymphocyte 15 cells/µL (range 460–1600). Human immunodeficiency virus (HIV) test resulted positive with HIV RNA levels of 141,006 copies/ml. He started prophylaxis therapy with cotrimoxazole, azithromycin, and fluconazole. Due to the persistence of abdominal pain, the patient underwent ultrasonography examination that showed multiple enlarged lymph nodes in the abdomen, confirmed by a subsequently performed contrast-enhanced computed tomography (CT) scan. He underwent bone marrow biopsy that resulted negative for lymphoproliferative disease. Polymerase chain reaction (PCR)-based detection of typical and atypical *Mycobacterium* resulted negative.

Due to his ingravescent clinical condition, the patient was submitted to ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/CT scan. The patient fasted 6 h before tracer administration and underwent PET/CT scan 60 min after the intravenous administration of 3.7 KBq/kg of ^{18}F-FDG. The PET/CT device consisted of a Discovery ST (GE, Milwaukee, USA) with bismuth germanate crystal units arranged to form 24 rings combined with a 16-Slice Light Speed Plus CT scanner. The average full width at half maximum axial resolution of PET is 5.2 mm and system sensitivity is 9.3 cps/KBq for three-dimensional (3D) acquisition mode. Scanning was performed from the neck to the proximal tight in 3D modality, with an acquisition time of 3 min/bed/position. Images were reconstructed using an ordered subset expectation maximization iterative

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algorithm (OSEM-SV, VUEPoint HD, GE, 2 iterations, 15 subsets). The CT was performed immediately before PET in the identical axial field of view using a standardized protocol, consisting of automatic tube current modulation with auto mA, tube rotation time of 0.5 s/rotation, and slice thickness of 3.75 mm. The CT data were resized from 512 × 512 matrix to 256 × 256 matrix to match the PET data. The data were transmitted to a nuclear medicine database, fused, and displayed using a dedicated software Advantage 4.7, (GE Healthcare, Wisconsin, U.S.A).

18F-FDG-PET examination showed some hypermetabolic supra-diaphragmatic lymph nodes and a conglomerate mesenteric lymphadenopathy [Figure 1]. Metabolic active volume (MAV) was defined on the PET scan using a dedicated software (PET VCAR, GE Healthcare). Every lesion was segmented with a threshold of 42% of the maximum standardized uptake value (SUV_{max}) value within the bounding box of the lesion. Total lesion glycolysis (TLG) was calculated as the product of MAV × SUV_{mean}. All the lesions in the body were considered; thus, whole-body TLG (wb) was the sum of the TLG of each lesion.

Afterward, the patient underwent a PET imaging-guided biopsy of the mesenteric mass through laparoscopic approach. Histology demonstrated lymph node almost completely employed by foamy macrophages with multiple corpuscles in the cytoplasm that turned intensely bright red at Ziehl–Neelsen (ZN) staining [Figure 2]. On this basis, diagnosis of mycobacterial lymphadenitis was made. The patient started intravenous antimycobacterial therapy with good benefits. Furthermore, he also started antiretroviral therapy with emtricitabine, tenofovir, and efavirenz. Two months after the beginning of antimycobacterial therapy,
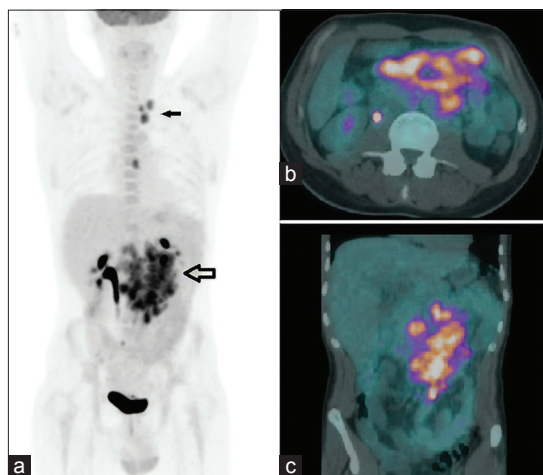
18F-FDG-PET/CT was repeated and demonstrated complete response of the supra-diaphragmatic lymph nodes and significant regression of the mesenteric lymphadenopathy [Figure 3]. When the change between wbTLG measured at baseline and that assessed after therapy was calculated, a reduction of 85.6% was found. This metabolic response was in agreement with a complete relief of the clinical symptoms.

Lymphadenopathy is a common clinical condition in HIV-infected patients, but its differential diagnosis may be a challenge for physicians.[1] Lymphadenopathy, in fact, may be due to benign processes (i.e., aspecific phlogosis), infection (i.e., mycobacteriosis), or malignancies (i.e., lymphoma).[2] In case of suspected mycobacterial infection, the detection of *Mycobacterium* DNA through peripheral blood-based PCR technique has been shown to present low sensitivity when compared to the gold standard methods, such as ZN stain and the acid-fast bacilli culture.[3] Although PET-CT with 18F-FDG and other tracers represents a well-established imaging method in oncology,[4] especially as concerns lymphoproliferative disorders, its role for the imaging and follow-up of the patients with mycobacterial tuberculosis has still to be fully explored. Tubercular granulomas contain mostly blood-derived macrophages, epithelioid cells, and multinucleated giant cells, surrounded by activated T-lymphocytes. Since activated lymphocytes highly increase their glucose consumption with an enhancement of the glycolytic pathway,[5] PET with 18F-FDG has been applied in patients affected by tuberculosis for early detection and monitoring the response to therapy. In this regard, Sathekge *et al.* evaluated the relationship between the severity/extension of tuberculosis, assessed through PET/CT with 18F-FDG, and the response to treatment in 24 consecutive patients affected by HIV-associated tuberculosis.[6] Of note, the authors applied a dual-phase protocol for PET/CT scan
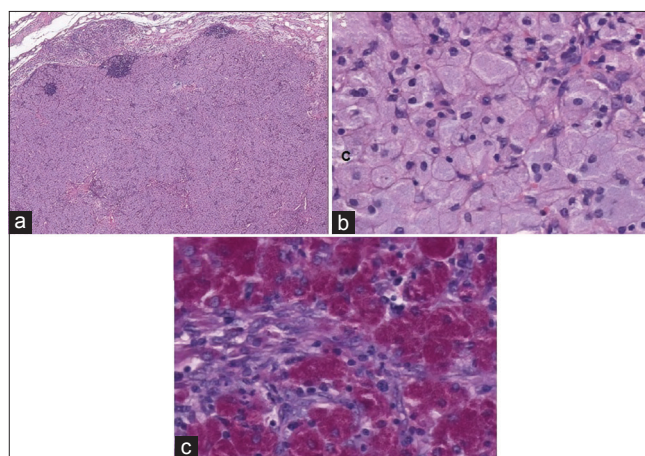

Figure 1: Whole-body 18F-fluorodeoxyglucose positron emission tomography–computed tomography (a, maximum intensity projection image) demonstrates highly increased fluorodeoxyglucose uptake corresponding to supra-diaphragmatic lymph nodes (black arrow) and to a conglomerate mass in the abdomen (black countered arrow), as well evident in the fused axial (b) and coronal (c) positron emission tomography–computed tomography corresponding slices. The calculation of the whole-body total lesion glycolysis resulted of 2128.5 g

Figure 2: (a) Biopsy of the conglomerate mass in the abdomen. Lymph node almost all completely employed by foamy macrophages (H and E stain, 4×). (b) Foamy macrophages containing many corpuscles in the cytoplasm (H and E stain, ×50). (c) Corpuscles in the cytoplasm resulting strongly positive for acid-fast organisms (ZN stain, ×50)
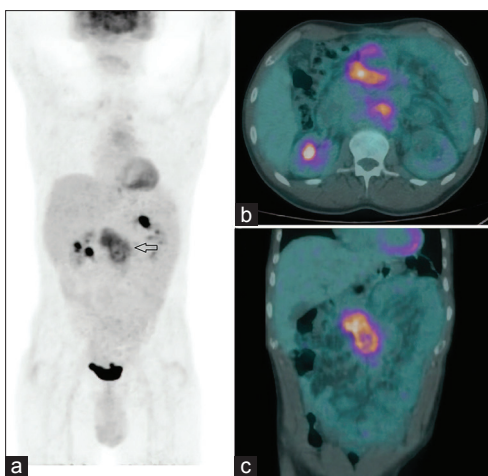
Figure 3: Whole-body 18F-fluorodeoxyglucose positron emission tomography–computed tomography (a, maximum intensity projection image) acquires 2 months after antimycobacterial therapy demonstrates complete regression of the supra-diaphragmatic lymph nodes and significant regression of the conglomerate mass in the abdomen, as well evident in the fused axial (b) and coronal (c) positron emission tomography–computed tomography corresponding slices. The calculation of the whole-body total lesion glycolysis resulted of 304.7 g

acquisition at 45 and 120 min after tracer injection; therefore, the percentage change in SUV_{max} from early to delayed images was calculated in sites of tracer uptake. The response to tuberculostatic treatment was evaluated at 4 months and the patients were divided into two groups: responders and nonresponders. It has to be pointed out that the SUV_{max} and the number of involved lymph nodes were significantly higher in nonresponder than in responder subjects, while no difference in the percentage of SUV_{max} between early and late scan was found between two groups. These preliminary results indicated PET/CT with 18F-FDG as potentially useful tool not only for the initial evaluation of HIV-associated tuberculosis but also for the assessment of resistance to tuberculostatic treatment.

A published report from Lefebvre *et al*. on 18 patients affected by lymph node tuberculosis, although it was not specifically focused on HIV-infected patients, demonstrated that PET with 18F-FDG may result helpful for aiding diagnosis and monitoring the response to treatment.[7] Of note, in the previously cited paper, the authors found a reduction in SUV_{max} of 82.8% in cured patients and of 43.7% in noncured subjects. However, it has been demonstrated that SUV_{max} may present some limitations in evaluating response to treatment, since this parameter takes into account only the uptake of the lesion without any consideration of its volumetric features. This issue may be a particularly problematic in case of conglomerate adenopathy tissue, in which therapy is aimed not only to reduce the activity but also to reduce the mass effect of the lesions. To overcome these drawbacks, several PET-derived parameters (such as MAV and TLG) have been introduced to provide a more complete overview of the lesion's characteristics, since they take into consideration both activity and volume.[8]

In the case we have described, PET-CT with 18F-FDG represented a useful imaging modality for identifying the most appropriate site for performing biopsy in an HIV patient with suspicion of mycobacterial infection. Furthermore, the use of PET-derived parameters, such as TLG, resulted of value for monitoring the response to treatments.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for her images, and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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