

Editorial

^{18}F -FDG-PET/CT Imaging in Leukemia

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Positron Emission Tomography/Computed Tomography (PET/CT) is a noninvasive radionuclide-based whole body imaging technique which combines both a Positron Emission Tomography (PET) scanner and an x-ray Computed Tomography (CT) scanner in a single gantry system. In PET, functional images are obtained which denotes spatial distribution of metabolic or biochemical activity in the body. These images are aligned with anatomical images obtained by CT scanner in the same session resulting in a single superposed (co-registered) image [1]. Functional changes in bone/ bone marrow may precede structural changes which can be efficiently picked by PET/CT scan. Normal red marrow usually demonstrates low intensity ^{18}F -FDG uptake, thereby helping in detection of increased uptake in early marrow involvement. FDG-PET/CT is not regularly used in the assessment of acute or chronic leukemia's [2]. But, few case reports were described in the literature which demonstrated the potential role of FDGPET/CT in diagnosis and follow-up of leukemic bone marrow infiltration [3,4]. In addition to this whole-body FDG-PET is valuable for the detection of extra-medullary leukemia/myeloid sarcoma with systemic overview of tumor burden at diagnosis and relapses and can also be used for monitoring of treatment response [5,6]. FDG-PET/CT is also useful in diagnosis and prognostic stratification as well as detection of Richter's transformation in CLL cases [7-10]. FDG PET has also role in diagnosis and monitoring of Chronic Myeloid Leukemia (CML) after treatment [11,12].

Leukemia's are characterized by diffuse replacement of bone marrow with proliferating leukemic cells with circulating immature white blood cells in the blood and widespread infiltrates in the liver, spleen, lymph nodes and other sites throughout the body. Leukemia's are classified as acute or chronic and lymphoid or myeloid.

PET/CT in Acute Leukemia

Role of PET/CT is not been evaluated thoroughly in diagnosis of acute leukemia. However, it is helpful in suspecting bone marrow disease in cases in which peripheral blood smear is normal [13] or in

cases of focal bone localization of leukemia in which PET/CT scan can detected the disease, while bone marrow aspiration detected no abnormalities [14]. ^{18}F -FDGPET/CT may be useful for guiding the site of BM aspiration in cases with localized bone marrow involvement [15]. PET imaging using proliferation marker 3'-deoxy-3'-[18F] Fluoro-L-Thymidine (FLT) can be used for early assessment of treatment response in AML patients undergoing induction chemotherapy. Both during and after chemotherapy, bone marrow with low FLT uptake in AML patients who entered complete remission in contrast to higher uptake in those patients with resistant disease [16]. It is reliable in early detection of disease relapse and diagnosis of extra-medullary involvement. FDG PET/CT is useful in early detection of occult lesions in myeloid sarcoma which are non-detectable by conventional imaging techniques as CT or MRI. It identifies extra-medullary sites of involvement which facilitates biopsy and diagnosis. ^{18}F -FDG-PET/CT should be done in newly diagnosed and relapsed cases of AML to determine the extent of extra-medullary disease in AML [6]. Isolated extra-medullary relapse in AML or ALL patients with normal peripheral blood and bone marrow findings can be detected by PET/CT. It helps in determining the location and metabolic activity of relapse site compared with CT scan and can be helpful in management [17]. Cunningham et al., suggested that PET/CT can help in eradicating all foci of leukemia, and identify tumors responsible for refractory, residual, and relapsed disease [18].

PET/CT in Chronic Leukemia

FDG PET can be used for the assessment of CML patients. Nakajo et al., have reported 2 cases of CML in the chronic phase that showed increased FDG uptake in the bone marrow in pretreatment period which got reduced in follow-up FDG PET scan in a patient after termination of treatment and in the other under treatment [11]. Varoglu et al., described a case of CML in a patient of renal cell carcinoma which showed increased FDG uptake in bone marrow prominent in the vertebral bodies, pelvic bones and proximal parts of the upper and lower extremities on FDG PET/CT imaging. It was suggested that FDG PET is useful in diagnosis and monitoring of chronic myeloid leukemia after treatment [12]. Extra-medullary blast proliferation may also be detected by FDG PET/CT in CML in patients revealing normal or CML in chronic phase morphology in peripheral blood smear/ bone marrow examination. So that local radiotherapy or change in systemic chemotherapy can be offered to the patients for appropriate management [19]. Falchi et al., suggested that FDG/PET is a useful diagnostic tool in patients with CLL and suspected Richter's transformation. It can guide the site of biopsy for histologic confirmation of transformation. Patients with higher SUVmax are associated with worse clinical characteristics and worse prognosis. A SUV max > 10 associated with inferior progression-free survival and overall survival in CLL patients [10]. In patients with different CLL phases, SUVmax reflects tumor aggressiveness. It was suggested that a SUV cutoff value equal or greater than 10 to diagnose the transformation of CLL into Richter syndrome [7-10]. Histologically aggressive CLL and Richter syndrome have higher SUV max and is associated with poorer performance status, lower hemoglobin and

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platelets, and higher lactate dehydrogenase and b-2-microglobulin [7].

There are few limitations of ¹⁸F- FDG PET-CT. FDG is not a very tumor-specific substance, in as much as the leukocytes and macrophages of inflammatory processes also accumulate the tracer which is a major source of false-positive diagnoses in the application of FDG-PET in oncology. Diffuse bone marrow uptake in FDG PET/CT may be due to an inflammatory reaction, recent chemotherapy or administration of hematopoietic growth factors/ colony stimulating factor. To reduce the potentially negative impact of occasional false-positive FDG-PET results on patient management, it is absolutely mandatory to carefully select the candidates for an FDG-PET scan to wait 8-10 weeks after surgery, 10-12 weeks after local RT and 4-6 weeks after chemotherapy before an FDG PET scan is done.

To conclude, FDG PET/CT is useful in diagnosis and follow-up of patients with bone marrow malignancy. 18F-FDG PET/CT may be useful for guiding the site of BM aspiration in cases with localized bone marrow involvement. It has an important role in diagnosing extra-medullary disease in de novo or relapsed AML patients. It can guide a diagnostic biopsy and may also provide prognostic information in patients with CLL. It is also useful in detection of Richter's transformation in CLL cases. Possibility of leukemia in known case of solid malignancies also kept in mind in follow up cases in which diffuse marrow uptake may be misinterpreted as chemotherapy effect or bone marrow metastasis by solid tumors. Bone marrow aspiration/biopsy must be performed for correct diagnosis and early management.

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