Impact of Fluorodeoxyglucose-Positron Emission Tomography (FDG-PET) in the Management of Patients with Cancer and other Serious Disorders: A Clinical Case Based Approach

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Abstract

In this pictorial review, the impact of FDG-PET is illustrated with specific clinical case examples that would demonstrate the power and promise of this molecular imaging technique in managing a wide variety of disorders. The case vignettes depicted in this communication represent the ones where this modality can be utilized in the routine clinical scenario and can prove substantially beneficial to the patients of cancer and other serious disorders. Related discussions are drawn along with individual cases to enable the readers understand the further prospects of PET that are being explored at the present.

Keywords: FDG-PET, PET-CT, Oncology, Cancer, Infection, Cardiology, Neurology, Evidence Based Medicine, Personalized Medicine, Molecular Imaging.

Introduction

The specialty of Nuclear Medicine is a dynamic branch of Medicine that deals with the use of unsealed radiopharmaceuticals for the diagnosis and therapy of cancer and a wide array of disorders involving cardiology, orthopedics, neurology and psychiatry disciplines. Diagnostic imaging with conventional nuclear medicine provides a great deal of critical information in diseases involving the aforementioned systems while therapeutic nuclear medicine is of great benefit to the patients suffering from thyroid diseases (esp. thyrotoxicosis and thyroid cancer), neuroendocrine tumors, painful skeletal metastases, joint disorders and lymphomas. The recent addition of positron emission tomography (PET) to its armamentarium has added a new dimension that is being employed in the day-to-day clinical practice in the appropriate settings in cancer and other serious disorders.

A relatively new and evolving concept in the clinical domain is individualizing treatment based upon PET and PET-CT results that significantly improves patient management. The success of this new concept significantly depends upon the success of development in the field of molecular imaging, with functional imaging with current and future novel PET tracers and this is likely further enhance the scientific basis of medical practice 1,2.

A. Staging of Cancer

FDG [Fluorodeoxyglucose (18F)]-PET (Fig. 1) plays a crucial role in the staging of wide variety of malignancies (both initial staging and restaging in the subsequent course) including lymphoma, lung carcinoma, esophageal carcinoma and so on.

Case 1 A 65 year old female, known patient of Diffuse large B cell lymphoma.(Fig. 2)
Case 2. A recently diagnosed patient of primitive neuroectodermal tumor (PNET) of right proximal tumor who was referred for disease evaluation. Patient did not receive any treatment at the time of FDG-PET imaging. (Fig. 2)

Fig. 1: FDG-PET demonstrates extensive disease involving bilateral neck nodes, axillary and mediastinal nodes, paraaortic and iliac nodes in the abdomen and inguinal nodes.

Fig. 2: In this known patient of PNET, there is intense FDG uptake at the site of primary with central photopenia suggesting necrosis within the tumor. Also note the FDG uptake in the bone marrow of vertebrae, pelvis and upper limbs bilaterally and proximal left femur suggesting bone marrow metastasis.
Learning Point

I. Introduction of FDG-PET has completely replaced CT for staging patients of lymphoma and provides two discrete advantages:
1. FDG-PET provides whole body status in a single examination.
2. A baseline scan forms the basis of evaluation of further treatment response.

II. Metastasis to the skeleton starts at the red bone marrow and FDG-PET is superior to bone scan in this respect as it detects metastasis at the level of bone marrow. The result of FDG-PET rivals MRI in this respect.

B. Early Response Assessment in Patients of Cancer by FDG-PET

Case 3 and Fig. 3 FDG-PET images at diagnosis (left panel: A) and following 3 cycles of chemotherapy (right panel: B) in a 30 year old male, a known patient of Diffuse large B cell Lymphoma demonstrating avid FDG uptake in the chest and abdomen that shows near total resolution after 3 cycles of chemotherapy.

Learning Point

Early identification of non responders to primary chemotherapy by FDG-PET imaging following 2-3 cycles of chemotherapy is a major advance in the management of lymphoma since the non-responding patients can be moved into the salvage schedules utilizing aggressive strategies earlier without administering ineffective chemotherapy that is not only expensive but also toxic and result in significant morbidity without benefit.

Case 4. A 45-year-old man presented with a 12X 10-cm sized mass (with central necrosis) abutting the body and tail of pancreas and left kidney (but intervening fat plane was maintained) on baseline CT scan. The mass extended from the level of pancreatic body up to the level of aortic bifurcation. The baseline FDG-PET (Fig. 4a) showed uptake at the periphery of mass (arrow-marked). The 1-month post-treatment FDG-PET (Fig. 4b) showed disappearance of the FDG uptake from the periphery of the mass indicating a complete metabolic response (CMR). The CT scan at this time showed persistence of the mass (Fig. 4c and d) with contrast enhancement (reprinted with permission3).
Learning Point

The dramatic change in the tumor metabolic activity following successful therapy (chemotherapy, radiotherapy or molecular targeted therapy e.g. in GIST) has made FDG-PET the modality of choice for monitoring therapeutic response in several malignancies and revolutionized the management by reliably segregating responding patients from non responders where alternative therapies can be employed at the very outset.

C. Assessment of Disease Viability and Differentiating them from Post-Treatment Fibrosis

Case 5 (Fig. 5) A 65 yr old male, diagnosed patient of sacral chordoma (Tumour involving S3-5 and coccyx), post surgery and radiotherapy. CT and MRI were inconclusive on the nature of soft tissue residue at the site of primary tumor for differentiating post radiotherapy fibrosis and viable active disease. The patient had complaints of low backache just right to the midline.

Fig. 5: FDG-PET showing intense focal uptake in the region of the sacrum suggesting persistent active disease at the site of primary.
**Case 6** and Fig 6. In this known patient of second primary malignancy of brain there was query with regard to the viability of the disease. MRI was inconclusive. FDG-PET demonstrated intense focal uptake at the mentioned site suggesting persistent active disease.

**Learning Point**

Differentiating viable disease following treatment from viable active disease is a challenge to the attending physicians. This problem particularly pertains to patients in whom a remnant of what was originally a large mass is still visible on CT or MR. It is in this setting of the “residual mass”, that to date PET has been shown to have the greatest utility.

**D. Patients of thyroid Cancer with raised tumor marker and normal radiiodine scan**

**Case 7** and Fig 7. A 23 year old female, a diagnosed patient of Papillary Carcinoma Thyroid, who recently demonstrated serum thyroglobulin (Tg) level (tumor marker of thyroid carcinoma) of 414ng/ml, $^{131}$I whole body scan was normal. FDG-PET demonstrated multiple diseased nodes in lower neck that helped determining the sites of disease and the reason for raised Tg in this patient. These were confirmed after excision.

**Learning Point**

In our preliminary experience, this group of surgically amenable disease is around 25% of patients. In these patients this modality makes an impact in patient management.

**E. Patients of Colorectal carcinoma with raised tumor marker levels**

**Case 8** and Fig 8. In this patient of colorectal carcinoma, FDG PET was done for rising carcinoembryonic antigen (CEA) levels (tumor marker of colorectal malignancy). The FDG-PET 3D MIP image shows extensive metastasis in right
scapula, spine, pelvis and an inguinal node suggesting timorous involvement at those sites.

Learning Point

FDG-PET is a highly sensitive modality and is used routinely in clinical parlance in patients of colorectal and ovarian malignancy with rising tumor marker levels for doing whole body survey.

F. Perfusion-Metabolism Mismatch in Hibernating Myocardium

Case 9 and Fig. 9. A classical example of hibernating myocardium is demonstrated where there is a perfusion defect (left panel: arrow) is noted in a patient who suffered from myocardial infarction. The FDG-PET cardiac study (right panel: arrow) shows hypermetabolism in the same defect region suggesting this to be viable myocardium.

Learning Point

Myocardial hibernation is defined as a state of persistent ventricular myocardial dysfunction at rest (downregulation of contractile function) resulting from reduced myocardial blood flow with preserved viability. Identifying hibernating myocardium is of major interest in the cardiology practice as this represent myocardium that can be salvaged. “Flow-metabolism” mismatch is hallmark of this entity and presently considered as the gold standard for detecting hibernating myocardium.

G. FDG-PET in Dementia

Case 10 and Fig 10. In this patient with memory disturbances and a clinical suspicion of dementia, FDG-PET demonstrates the typical pattern of reduction in glucose metabolism in temporo-parietal cortices with relative preservation of primary visual and sensoriomotor cortices, striatum, and cerebellum which is considered typical for Alzheimer’s Disease (AD).
Learning Point

FDG-PET is a sensitive and accurate method for an early diagnosis of AD, when combined with traditional medical evaluation.

Other important uses of PET in evaluating Neurological Disorders include the following:

- Detecting Seizure focus in temporal lobe epilepsy: The efficacy of FDG-PET imaging is in localization of the epileptogenic site for surgical excision and potential cure. FDG-PET is very useful in detecting such sites with a sensitivity of 85% to 90% (2).

- Evaluation of movement disorders: Fluorine-18-6-fluoro-L-DOPA (FDOPA) or radiopharmaceuticals that bind to the dopamine transporter sites and therefore allow detecting the degree of the loss of the pre-synaptic dopaminergic neurons, has great potential to be routinely employed for the early and accurate diagnosis of Parkinson’s disease and other movement disorders. Differentiating among various types of parkinsonian syndromes especially in the early stages is difficult by either clinical or conventional imaging (MRI) assessment, where this modality can be of significant help (2).

H. FDG-PET in Infection and Inflammatory Disorders

Case 11. A 44-year-old man after heart transplant presented with fever of unknown origin and inconclusive radiologic studies, including CT.

Fig 11. Coronal PET images demonstrates a focus of increased FDG activity in the aortopulmonary window and represents the source of infection. The patient completely recovered following drainage of the infected site in the mediastinum (reprinted with permission).

Case 12. A 52-year-old man, who was treated with antitubercular drugs for 1 year without any benefit for an initial diagnosis of tuberculosis, and was referred for further evaluation. A rebiopsy of the inguinal nodes for a definitive diagnosis was confirmatory of sarcoidosis. He had a history of hypothyroidism, which is a frequent accompaniment of sarcoidosis due to the association of autoimmunity in this population.
Fig. 12. Baseline FDG-PET study at diagnosis (upper panel) demonstrates multiple abnormal foci in bilateral neck nodes, mediastinal, axillary, and multiple abdominal (para-aortic and inguinal) nodes, and the liver, spleen, and thyroid. He was treated with oral corticosteroids and was referred for reassessment of his disease status with FDG-PET following 6 weeks of therapy. The post-treatment FDG-PET images (lower panel) showed remarkable improvement with near total resolution of the FDG hypermetabolism at the initially involved sites (reprinted with permission).

Learning Point

The Case 12 underscores the value of FDG-PET imaging in whole-body monitoring of early response to therapy in patients of sarcoidosis (particularly those with extensive disease) that can be of great value in managing these patients.

Conclusion

This brief pictorial review was designed to illustrate to the readers certain specific clinical examples demonstrating the utility and impact of FDG-PET-based molecular imaging in the day-to-day medical practice. The potential prospect of this modality in assessing a variety of benign and malignant disorders for both research and clinical purposes is growing and is limitless. While initially its application was restricted to neurological disorders, oncology soon became the field where it was employed with great success. Detection of infection and inflammation is very fast becoming the second most common clinical application of FDG-PET imaging, furthering its role as an indispensable clinical modality. The 6 infective conditions in which FDG-PET has demonstrated its utility include (1) chronic osteomyelitis, (2) complicated lower-limb prostheses, (3) complicated diabetic foot, (4) fever of unknown origin, (5) acquired immunodeficiency syndrome (ie, AIDS), and (6) vascular graft infection.
and fistula. Studies have reported success in detecting inflammatory processes in disorders such as regional ileitis, sarcoidosis, rheumatologic disease, and vasculitis. The introduction of novel PET tracers has revolutionized clinical assessment of certain specific tumors e.g. gallium-68 labeled PET tracers (e.g. $^{68}$Ga-DOTA-TOC, $^{68}$Ga-DOTA-NOC) has added a new dimension to the management of patients with Neuroendocrine tumors. Imaging tumor proliferation with $3'$-deoxy-$3'$-[18F]-Fluorothymidine (FLT) and tumor hypoxia with [18F]Fluoromisonidazole (FMISO), $^{18}$F-fluoroazomycin arabinoside (FAZA) and Cu-60 diacetyl-bis (N(4)-methylthiosemicarbazone [(60)Cu-ATSM]) aids in understanding the tumor characteristics from different perspectives that can have important implications for targeted therapy based upon tumor biology. Several new PET tracers based upon certain distinct biochemical pathways are in the process of evolution and will likely enhance the role and reliability of this powerful imaging technique in near future.

References


