

CLINICAL IMPACT OF 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY-COMPUTED TOMOGRAPHY ON THE MANAGEMENT OF GERM CELL TUMOURS

Saima Riaz¹, Humayun Bashir¹, Narjis Muzaffar², Ahmed Murtaza³, Amin Hayee⁴

¹Departments of Nuclear Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, ²Department of Medicine, Sultan Qaboos University Hospital, Muscat, Oman, ³Department of Radiology, King Saud University Hospital, Riyadh, Saudi Arabia, ⁴Department of Pathology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan

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Abstract

Purpose: The purpose of this study was to review the impact of 18F-fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET-CT) scans on the management of patients with germ cell tumours (GCT) at our centre.

Methods: A descriptive, cross-sectional, retrospective review of a total of 29 FDG PET-CT scans acquired in 20 patients with GCT between December 2009 and May 2013.

Results: Sixteen males and four females with the average age of 34.4 years (+18SD) were identified who underwent FDG PET-CT scans for treatment response/outcome evaluation on an average period of 3 months after completion of therapy. Hypermetabolic residual disease (PET-CT positive) was identified in 8 (40%). 6 (30%) had non-FDG-avid residual morphologic disease (PET negative and CT positive) and 6 (30%) were disease free (PET-CT negative). FDG PET-CT led to change in the management plan of 12 (60%) of cases as compared to the CT alone findings. Follow-up was available for a median of 2.9 years (± 1.5 SD). The overall 5-year disease-free survival was found to be PET-CT-positive patients = 62%, PET-negative and CT-positive patients = 80% and PET-CT-negative patients = 100%.

Conclusion: FDG PET-CT scanning has a potential role in the evaluation of response to treatment and can predict the survival outcome.

Key words: 18F-fluorodeoxyglucose positron emission tomography-computed tomography, disease-free survival, germ cell tumour, standardised uptake value

Introduction

Germinal cell tumours are categorised into pure seminomas and the heterogeneous group of non-seminomatous tumours comprising teratoma, chorionic carcinoma, embryonal and mixed tumours.^[1] Both the treatment and outcome of germ cell tumours (GCT) have changed with the implementation of cisplatin-based chemotherapy. Conventional imaging procedures are still prone to the significant over and under staging of GCTs.

Positron emission tomography-computed tomography (PET-CT), with fluorodeoxyglucose (FDG), is a non-invasive imaging tool for defining regional metabolic processes which allows better delineation of the viable residual tumour as the metabolic changes are hypothesised to precede the computable morphologic changes.^[2]

Germ cell tumours are FDG avid with preferential accumulation by pure seminomas as compared to non-seminomatous lesions.^[3] PET scanning does not contribute in early stages of seminoma but is a possible option for defining treatment strategy in case of residual tumours.^[4] In most of the studies, PET has not been found sensitive for small (<1 cm) retroperitoneal lymph nodes and mature teratomas.^[5]

Correspondence: Dr. Saima Riaz, Department of Nuclear Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan.
Email: saimarz.dr@gmail.com

Hybrid 18F-FDG PET-CT can be regarded as a useful tool for clinical decision-making in post-chemotherapy cases with residual masses. After completion of the first-line chemotherapy, residual masses are found in approximately 40% of patients, even after normalisation of serum tumour markers.^[6]

18F-FDG PET-CT is a better tool than CT alone for discrimination of residual tumour size. NSGCT patients with residual masses do not benefit from FDG PET as the non-seminomas are FDG non-avid. In relapsing patients with a mismatch between tumour marker levels and imaging data, FDG PET may be helpful in early diagnosis of residual viable tumour/source of relapse in seminomas, particularly if salvage surgery is being considered.^[7]

In this retrospective review of patients who received treatment for GCT cancer at Shaukat Khanum Memorial Cancer Hospital and Research Centre from January 2009 to May 2013, clinical presentation, management and survival outcome have been evaluated in a targeted Pakistani population.^[8]

The objective of our current study was to determine the impact of FDG PET-CT in diagnosis and treatment planning in patients with GCT.

Methods

This is a descriptive, cross-sectional, retrospective review of electronic records of patients diagnosed and treated for GCT. The study period was from December 2009 to May 2013. The details were retrieved from the hospital information system. All scans done for staging and follow-up purposes were included in the study. Formal institutional review board approval was taken for this study.

All patients underwent FDG PET-CT scan 50–60 min after 300 MBq (0.21 mCi/kg body weight) of F18-FDG was injected intravenously. Each patient fasted for at least 4–6 h. PET-CT scan was acquired on a dedicated PET scanner (Phillips Gemini TOF) with 3 min acquisition for each 8–9 bed positions followed by CT (with IV contrast) scan over 1 min (voltage of 70–140 kVp; tube current 80 mA). Both the corrected and uncorrected PET images were evaluated for the visual assessment and standardised uptake value (SUV) estimation of metabolic activity.

The data were stratified on the basis of FDG PET-CT findings as; hypermetabolic residual disease (PET-CT positive), metabolically inactive residual morphologic disease (PET negative and CT positive) and disease-free scan (DFS) (PET-CT negative).

Statistics of quantitative data was expressed as mean + standard deviation. The categorical data were given as frequency and percentage. Significance of the results was evaluated with Chi-square test, taking $P < 0.05$ acceptable for the statistical significance. Kaplan–Meier DFS curve was generated for survival analysis.

Results

Patients' characteristics

A total of 29 F-18 FDG-PET CT scans of 20 patients were analysed. 16 males and four females with the average age of 34.4 years (+18SD) were identified with 17 (85%) seminomatous GCT (testicular seminoma 12, ovarian dysgerminoma 3 and mediastinal seminoma 2). Four (15%) patients had non-seminomatous GCT (yolk sac tumour 1, sacrococcygeal teratoma 1 and embryonal cancer 1). The demographics of patients including age and gender are detailed in Table 1.

PET-CT scan results

On review of post-treatment FDG PET-CT scans, hypermetabolic residual disease was identified in 8 (40%)

Table 1: Patients' and disease characteristics

| | | |
|----------------------------|-----------------------------------|----|
| Patients | 20 | |
| PET-CT scans | 29 | |
| Age | Mean age=34.4 years±18 SD | |
| Gender | Male: 16 (80%) Female: 4 (20%) | |
| Histopathology | | |
| Seminomatous GCT (n=17) | Testicular seminoma | 12 |
| | Ovarian dysgerminoma | 3 |
| | Mediastinal seminoma | 2 |
| Non-seminomatous GCT (n=3) | Yolk sac tumour | 1 |
| | Sacrococcygeal teratoma | 1 |
| | Embryonal cell cancer | 1 |

PET-CT: Positron emission tomography-computed tomography

cases (PET-CT positive). 6 (30%) had metabolically inactive residual morphologic disease (PET negative and CT positive) and 6 (30%) were negative for any residual disease (PET-CT negative).

FDG PET-CT leads to change in the management plan of 12 (60%) cases as compared to the CT-alone findings. Of eight with FDG-avid residual disease, five were given further chemoradiotherapy and one underwent surgical resection. Two with additional disease sites when compared to CT alone were put on palliative treatment rather than curative management. Similarly, four with morphological but metabolically inactive residual mass were put on surveillance.

In 2 (10%) cases, residual masses on CT scan though metabolically inactive were offered radiotherapy ($n = 1$) and surgical resection ($n = 1$), in view of large (>3 cm) residual masses on CT scan.

Six (30%) were disease free on PET as well as on CT and were put on surveillance. The management offered to each group has been displayed in Figure 1.

Survival analysis

DFS of patients with post-treatment PET-CT scans was estimated over an average duration of 2.9 years (± 1.5 SD). On follow-up of PET-CT-positive patients, five got cured and three had progressive disease (alive with disease $n = 1$, dead $n = 2$). In PET-negative and CT-positive patients group, five were cured and one alive with active disease. All six PET-CT-negative patients are alive and cured [Figure 2].

The overall 5-year DFS was found to be 62% in PET-CT-positive patients and 80% in PET-negative and CT-positive patients, while 100% in PET-CT-negative patients. The difference in survival between the three groups was statistically insignificant (log-rank test; $P = 0.324$), as the sample size was small. The Kaplan–Meier survival curve is shown in Figure 3.

Discussion

Post-chemotherapy residual masses are known to be present in 40% of the GCT.^[6] Conventional diagnostic procedures such as CT or MRI are not able to predict the

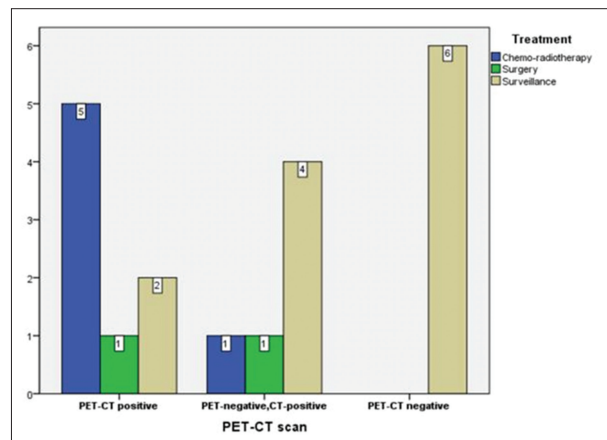


Figure 1: Display of management details based on PET-CT scan results

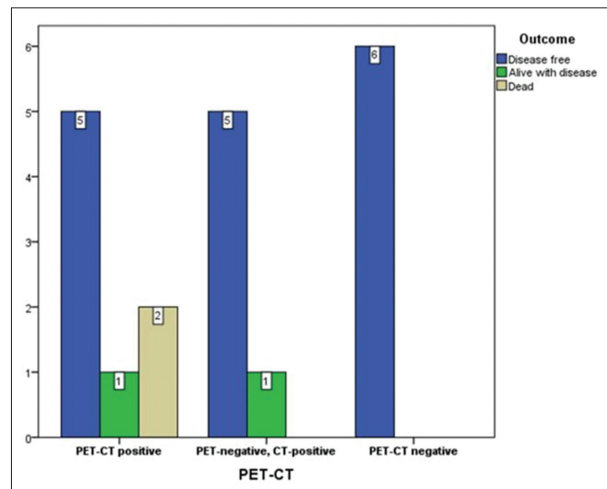


Figure 2: Disease outcome during follow-up period

viability of residual masses and remain a major diagnostic challenge in patients with GCT. The management of post-chemotherapy residual masses is either surgical resection or surveillance depending on the residual tumour size and viable cancer cells. Surgical resection of the post-chemotherapy residual is reserved for lesion size of >3 cm.^[9]

CT scan evaluates the residual disease in terms of number and size, however, cannot predict the viable cells in the residual tumour masses. Based on size, criteria alone tumour masses can be overtreated. FDG-PET is a better tool for assessing the viability of residual masses on the basis of its ability to visualise and quantify glucose metabolism in tumour tissue [Figures 4 and 5].^[10]

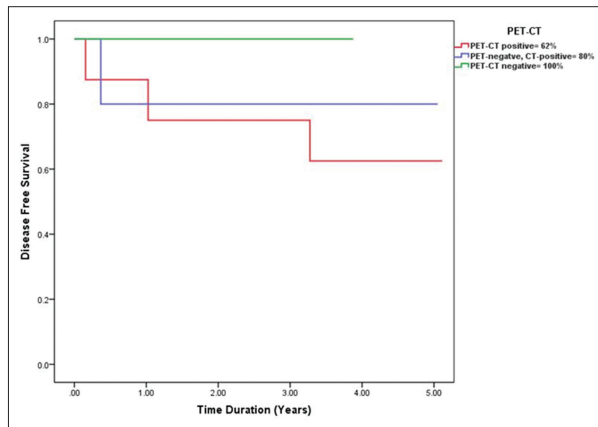


Figure 3: Kaplan–Meier 5-year disease-free scan (DFS) curve showing 62% DFS in positron emission tomography-computed tomography (PET-CT)-positive patients, 80% in PET-negative and CT-positive patients and 100% in PET-CT-negative patients

De Santis *et al.* have reported high sensitivity (80%) and specificity (100%) of PET-CT for the detection of viable tumour in post-chemotherapy seminoma in SEMPET trial.^[11] Treglia *et al.* in their meta-analysis of nine studies with 375 scans done for seminoma report a sensitivity of 78%, specificity of 86%, PPV of 58% and NPV 94%.^[2]

In our data set, we found added advantage of PET-CT in clinical decision-making of 60% of Case 1 comparison to CT alone. Sharma *et al.* have demonstrated diagnostic accuracy of 80.8% with 18F-FDG PET/CT for restaging patients with malignant GCTs.^[12] It is an extremely useful one-stop test to stage GCTs with elevated tumour markers.

In view of the established sensitivity and specificity of FDG PET-CT for GCT, it has been incorporated in international oncological guidelines for some years now. NCCN recommendation is to perform 18F-FDG PET/CT in patients with seminoma with a residual mass >3 cm and normal levels of markers.^[4,13]

Tumour hypermetabolism documented with FDG PET-CT has been studied in few cohorts for its impact on long-term GCT survival. Buchler *et al.* studied 36 patients with extragonadal GCT and showed 100% and 89% survival at 5 and 3 years, respectively, if patients had a negative end-of-treatment FDG PET-CT scans.^[14] The DFS in our limited cohort shows similar trends; however, the difference in our groups is not statistically significant. The potential prognostic role of FDG PET-CT in GCT needs to

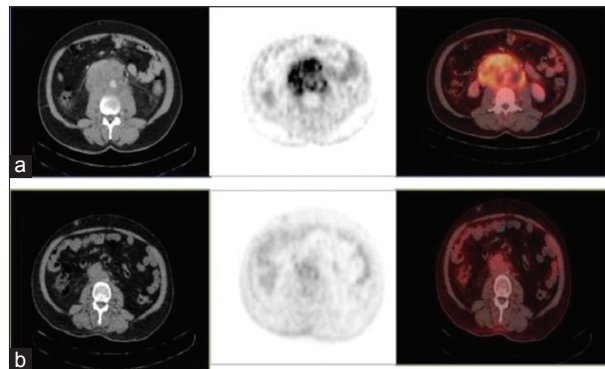


Figure 4: Baseline computed tomography (CT), positron emission tomography (PET) and fusion PET-CT axial images (a) of a 29-year-old male diagnosed with testicular germ cell tumours show hypermetabolic para-aortic nodal mass (SUV 6.6). Post-chemotherapy follow-up CT, PET and fusion PET-CT images (b) show partial morphologic and metabolic response in the para-aortic nodal mass (SUV 2.1). Patient underwent external beam radiotherapy afterward

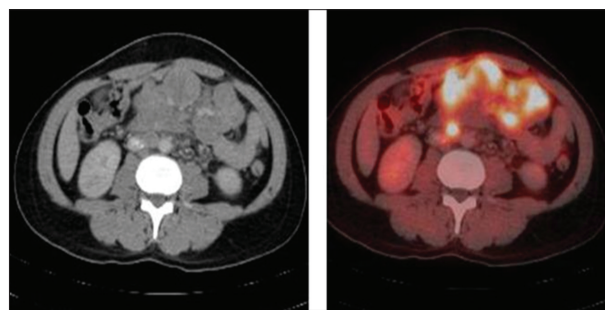


Figure 5: Post-treatment scan of a 31-year-old male diagnosed with testicular germ cell tumours. Axial computed tomography (CT) and fusion positron emission tomography-CT images show progression with extensive hypermetabolic peritoneal disease

be subjected to further validation taking into the account the primary site, histopathology and morphological residual disease after combined modality treatment.^[14,15]

Conclusion

Metabolic imaging with 18F-FDG PET/CT is useful in the assessment of residual tumours and disease recurrence in GCT. Prospective studies are required to further establish its prognostic role.

Conflict of Interest

The authors declare that they have no conflict of interest.

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