CLINICAL IMPACT OF 18F FDG PET-CT ON MANAGEMENT OF GERM CELL TUMORS

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Abstract:

Purpose: To review the impact of 18F FDG-PET-CT scans on the management of patients with germ cell tumours [GCT] at our Centre.

Methods: 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 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, 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 (±1.5SD). The overall 5-year Disease Free Survival (DFS) was found to be: PET-CT positive patients =62%, PET-negative, CT-positive patients = 80%, 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.

Keywords: 18F FDG PET-CT, Germ cell tumour, disease free survival, SUV

Introduction:

Germinal cell tumours are categorized into pure seminomas and the heterogeneous group of non-seminomatous tumours comprising teratoma, choriocarcinoma, 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. PET-CT, with 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 hypothesized 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].

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 first-line chemotherapy residual masses are found in approximately 40% of patients,
even after normalization 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-semonias 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 & 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 germ cell tumours.

Methods:

This is a descriptive, cross-sectional, retrospective review of electronic records of patients diagnosed and treated for GCT. Study period was from December 2009 to May 2013. The details were retrieved from the hospital information system [HIS]. 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 minutes after 300 MBq (0.21 mCi/kg body weight) of F18-FDG was injected intravenously. Each patient fasted for at least 4-6 hours. 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 SUV estimation of metabolic activity.

The data was stratified on the basis of FDG PET-CT findings as; hypermetabolic residual disease [PET-CT positive], metabolically inactive residual morphologic disease [PET-negative, CT-positive] and disease free scan [PET-CT negative].

Statistics of quantitative data were 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 value <0.05 acceptable for the significance. Kaplan Meier Disease Free Survival (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. Sixteen males and four females with average age of 34.4 years (+18SD) were identified with 17 [85%] seminomatous GCT [Testicular seminoma 12, ovarian dysgerminoma 3, 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%] cases [PET-CT positive], 6 [30%] had metabolically inactive residual morphologic disease [PET-negative, CT-positive] and 6 [30%] were negative for any residual disease [PET-CT negative].

FDG PET-CT lead to change in the management plan of 12 [60%] of cases as compared to the CT-alone findings; Out of 8 with FDG avid residual disease, 5 were given further chemo-radiotherapy and 1 underwent surgical resection. 2 with additional disease sites when compared to CT-alone were put on palliative treatment rather than curative management. Similarly, 4 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 (>3cm) 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:**

Disease free survival (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, 5 got cured, 3 had progressive disease (alive with disease n=1, dead n=2). In PET-negative, CT-positive patients group, 5 were cured, 1 alive with active disease. All 6 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, 80% in PET-negative, 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.

**Table 1:** Patients’ and Disease Characteristics

| Patients | 20 |
|----------|----|
| PET-CT scans | 29 |
| Age | Mean age = 34.4 years ± 18SD |
| Gender | Male: 16 (80%) Female: 04 (20%) |

| Histopathology | Testicular seminoma | 12 |
|----------------|--------------------|----|
| Seminomatous GCT (n = 17) | Ovarian dysgerminoma | 3 |
| | Mediastinal seminoma | 2 |
| | Yolk sac tumour | 1 |
| | Sacrococcygeal teratoma | 1 |
| | Embryonal cell cancer | 1 |

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

**Figure 2:** Disease outcome during follow-up period

**Figure 1:** Kaplan Meier 5-year DFS curve showing 62% DFS in PET-CT positive patients, 80% in PET-negative, CT-positive patients and 100% in PET-CT negative patients.
Case 1: Baseline CT, PET, fusion PET-CT axial images (A) of a 29 year-male diagnosed with testicular GCT show hypermetabolic para-aortic nodal mass [SUV 6.6]. Post-chemotherapy follow-up CT, PET, 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 afterwards.

Case 2: Post-treatment scan of a 31 year-male, diagnosed with testicular GCT. Axial CT and fusion PET-CT images show progression with extensive hypermetabolic peritoneal disease.

Discussion:

Post chemotherapy residual masses are known to be present in 40% of the germ cell tumours [6]. Conventional diagnostic procedures such as CT or MRI are not able to predict the 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 up on the residual tumour size and viable cancer cells. Surgical resection of the post chemotherapy residual is reserved for lesion size of >3cm [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 over treated. FDG-PET is a better tool for assessing the viability of residual masses on the basis of its ability to visualize and quantify glucose metabolism in tumour tissue [10].

De Santis M. 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]. Giorgio et al. in their meta-analysis of 9 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 cases I comparison to CT-alone. Sharma P et al, have demonstrated diagnostic accuracy of 80.8% with 18F-FDG PET/CT for restaging patients with malignant GCTs [13]. It is a 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 germ cell tumours, 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 >3cm and normal levels of markers [4, 12].

Tumour hypermetabolism documented with FDG PET-CT has been studied in few cohorts for its impact on long term GCT survival. Buchler T 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 disease free survival 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 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.

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