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Original Article

Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography as a diagnostic tool in therapeutic evaluation of lymphoma after completion of therapy

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ABSTRACT

Purpose: This study aimed at assessment of the role of (PET/CT) in lymphoma after completion of therapy to differentiate post-treatment fibrosis from residual viable tumor and being familiar with the limitations and interpretative pitfalls of PET/CT.

Method and materials: The present study was performed on 50 patients (27 males and 23 females). 18F-FDG was injected IV one hour before performing the study. Contrast enhanced CT was performed followed by PET.

Results: After the end of therapy; PET/CT revealed (38%) of cases showed a partial regression, (28%) of cases showed a progressive disease, (22%) of cases with complete metabolic disease remission, (8%) of cases showed a stationary disease and the remaining (4%) of cases showed mixed response to therapy. CT only agreed with PET/CT in 76% of the cases. Some physiologic uptake often occurs after treatment in (4%) of patients. PET/CT has 100% sensitivity, 68.75 % specificity, 87.17% PPV, 100% NPV and 90% accuracy in treatment response of lymphoma; compared to 94.1% sensitivity and 50% specificity, 80% PPV, 80% NPV and 80% accuracy for CECT.

Conclusion: PET/CT is a multimodality technique that can accurately monitor the treatment response of lymphoma. It can differentiate residual mass containing viable tumor from post treatment fibrosis.

1. Introduction

Lymphoma is considered a neoplastic proliferation of lymphoid cells with various stages of differentiation. It affects lymph nodes as well as the other primary lymphatic organs including bone marrow, spleen and thymus [1].

Lymphoma represent 6% of all neoplastic lesions and they are responsible for about 3% of the mortalities related to the neoplastic processes. Lymphoma can nearly affect all tissues of the body producing a variety of imaging manifestations [2,3].

Two main groups of lymphoma are known according to their pathology: Hodgkin disease and non-Hodgkin lymphoma (NHL). NHL is more common than Hodgkin disease up to eight times [3].

Nowadays, Lymphoma have high cure rate due to recent therapeutic modalities, even with advanced and recurrent cases. The prognosis of the disease and survival of the patients with lymphoma depend on the histological grade, clinical stage and lastly on the response to treatment [4].

Therapeutic response of the patient is an important substitute for other measures of clinical benefit, such as progression free survival (PFS) and overall survival (OS). It also plays an important role in decision making regarding continuation or changing of the therapy. By conventional methods, it is difficult to differentiate residual viable tumoral tissue from fibrotic scar tissue. On the other hand, Performing a biopsy for all lesions is not only impractical but also inaccurate as mixture of fibrosis and viable lymphoma may be present within the residual masses [5].

Positron emission tomography (PET) is based on the use of positron-emitting radiopharmaceuticals and the detection photons emitted following positron annihilation with an electron. 18F-fluoro-2-deoxyglucose (FDG) is commonly used as a radiotracer in oncological PET studies & this is likely related to increased glycolytic rate of malignant cells [6]. 18-fluoro-2-deoxyglucose (FDG) is now widely used for initial staging, follow-up and evaluation of response to therapy in various malignant diseases, including lymphoma [7–8].

Two main drawbacks of PET are present during tumor imaging, the

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first is its lacking of detailed anatomic landmarks while the other is lacking of specificity as sites of active inflammation are also FDG avid [4].

Recently, combined PET/CT scanner was introduced that allows PET and CT images co-registered by means of computer hardware in the same setting. This technique has dual advantages that it improves identification and definition of biological activities by PET and the display of the surrounding anatomy by CT [9–10].

In most cases of lymphoma, PET/CT examination is done after completion of the therapy. The aim of the examination at this time is to assess the therapeutic response of the neoplasm & to exclude residual neoplastic activity [11–12].

2. Aim of study

This study aimed at assessment of the role of PET/CT in lymphoma after completion of therapy and to differentiate post therapeutic fibrosis from residual tumoral activity. The diagnostic pitfalls and limitations of PET/CT were also assessed

3. Patients and methods

3.1. Patients

This prospective study was conducted between October 2013 to October 2015. It included 50 patients (27 males and 23 females. The mean age of the patients was 41.5 years and their ages ranged between 12 and 70 years). Patients included in the study were proved to have lymphoma (28 Non-Hodgkin's lymphoma and 22 Hodgkin's disease) on histopathological basis. All patients had undergone PET/CT scans for assessment of treatment response of lymphoma after completion of therapy & to differentiate post therapeutic fibrosis from residual tumoral activity.

3.2. Preparation

History was taken from patients regarding when was the tumor started, types of treatment, if patients received chemotherapy or radiotherapy and they were asked when it was ended, any other comorbidities (specially diabetes mellitus so as to control the blood glucose level), the patients were also asked to bring last biopsy histopathological report, creatinine level. Patients were asked about any newly developed complaint.

The patients were informed to stop eating for 6–8 h before the examination. All metallic items were removed from the patient, including pants with zipper, bra, belts, bracelets, etc. and the patients were given gown to wear. An intravenous (IV) cannula was inserted in the antecubital vein of the patient according to the condition of the vein for administration of both ^{18}F -FDG and IV non-ionic contrast media. We used wide pore IV cannula (20 G) for 32 patients and (18G) for 18 patients. The patients were informed to avoid heavy physical activities before the examination and after the injection of the radioisotope to minimize physiologic muscular uptake of the radiotracer as possible and they were also asked to void prior to scanning.

Weight and height of patients were measured. Serum glucose was routinely measured prior to ^{18}F -FDG injection. Patients with fasting blood glucose level of 70–150 mg/dl were permitted to undergo PET/CT. Diabetic patients (8 patients) were instructed to control blood glucose level prior to FDG administration however blood glucose level was elevated in 4 cases, one unit of rapidly acting insulin was injected /200 cc saline, and then the blood glucose level was monitored, when it was within the accepted range and this happened in 2 cases; ^{18}F -FDG was injected one hour later, but the study was postponed for the remaining 2 patients as the serum blood glucose could not be controlled.

In order to decrease brown fat metabolism: The patients were placed in a warm waiting room before ^{18}F -FDG injection and they were also

Table 1

The age and gender of the studied 50 patients with lymphoma after therapy.

Age group	Number of patients	Percentage (%)	Gender of patients	
			Male	Female
< 20	3	6%	1	2
20: < 30	12	24%	7	5
30: < 40	7	14%	4	3
40: < 50	9	18%	5	4
50: < 60	11	22%	6	5
60: 70	8	16%	4	4
Total number of patients	50	100%	27	23

asked to eat foods rich in fat and less carbohydrate 24 h prior to examination.

PET/CT was performed at least 6–8 weeks post therapy to decrease the misleading effect of FDG uptake as result of post-treatment inflammation.

3.3. Image acquisition and processing

Combined PET/CT scans were performed on (Biograph, Siemens) system, consisting of a dedicated PET scanner and a 64-slice CT scanner. This dedicated system permits the acquisition of combined CT and PET images in one session.

One and half liters of water was administered to act as neutral oral contrast agent approximately 1 h before the examination. An intravenous 10–20 mCi (1 ml/10 kg) ^{18}F -FDG was manually injected 45–60 min before examination. This time of uptake phase is necessary for the ^{18}F -FDG to be adequately bio-distributed in the body and picked up by the cells. Patients were informed to rest in a quiet isolated room, with complete physical and mental rest.

The patients were examined in a supine position and comfortable head fixation with arms up. Contrast enhanced CT scan was performed first from base of the skull to mid thigh, then a Torso PET examination. The whole study took approximately 20–30 min.

The contrast enhanced CT examination was performed following injection of 1–2 ml/kg of a low-osmolality iodinated contrast medium (ultravist) at a rate of 4 ml/s by using a automatic injector, by the following parameters: 120 kV, 100 mA, 1/s tube rotation, 4-mm slice collimation, and bed speed of 8 mm/s. One case developed minor reaction to contrast and was controlled by I.V corticosteroid.

For a Torso whole body PET/CT study (neck, chest, abdomen, and pelvis), scanning began at the level of the skull base and extended caudally to the level of the mid-thighs. Dedicated brain PET and real whole body PET/CT that extend from vault of skull to foot were not indicated to any case at this study depending on clinical base and patients' previous imaging.

PET was performed following the CT study without moving the patient. Approximately 5 to 7 bed positions are planned in the 3-dimensional acquisition mode for scanning the same area with 2–3 min acquisition at each bed position there is overlap between beds positions PET/CT scan in caudo-cranial direction.

Helical PET and CT images were first reconstructed followed by reformatting of both sagittal and coronal images that allowed better viewing. For each of these sets of PET and CT images, matching "fusion" images were generated by combining the 2 types of data.

The acquisition time for an integrated PET/CT scan was approximately 15–25 min. The co-registered images were displayed using special software and reviewed on the dedicated workstation.

3.4. Image interpretation

All CT examinations were viewed and interpreted by Two experienced radiologists and all PET/CT examinations were interpreted

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