The Egyptian Journal of Hospital Medicine (July 2017) Vol.68 (3), Page 1364-1367

Role of PET/CT in Monitoring Response in Treatment of Non-Hodgkin Lymphoma Patients

Annie Mohamed Nasr Eldin, Hossam Moussa Sakr, Aml Ibrahim Ahmed, Wesam Kamel El Afify
Radiodiagnosis Department, Faculty of Medicine, Ain Shams University
Corresponding author email: wesam _km@yahoo.com, Phone no: 01067893907

ABSTRACT
Aim of the work: positron emission tomography (PET) response assessment of residual nodal masses in patients with lymphoma after completion of therapy is performed visually using Douveille as the reference. The primary objective of this study was to define the role of PET in response assessment of Non Hodgkin Lymphoma patients and define various response criteria.
Patients and methods: our prospective study included 40 patients with Non Hodgkin's lymphoma diffuse large B cell type assessed for response assessment after completion of therapy, two readers independently assessed response by IHP and Deauville criteria. The addition of morphological parameters on CT was assessed in relation to therapy response.
Results: Non Hodgkin lymphoma is one of chemosensitive tumors with high ability of nodal and extranodal spread and PET /CT is more sensitive than CT in monitoring response to treatment in non Hodgkin lymphoma diffuse large B cell type patients.
Conclusions: PET/CT is the best tool for evaluation of the response to treatment in patients with Non Hodgkin lymphoma diffuse large B cell type, as well as Douveille criteria represent the accurate indicator of response categories determination.PET/CT has an obvious impact on clinical practice according to the response results and activity of residual lesion.
Keywords: Fluorodeoxyglucose 18F, Positron emission tomography, Computed tomography, Lymphoma and Therapy.

INTRODUCTION

Non-Hodgkin lymphoma (NHL) is one of the most common hematologic malignancies worldwide. The incidence of NHL has been rising for several decades; NHL incidence among males is significantly higher than in females [1].

One of the most evident advantages of FDG-PET was its ability to detect significant changes in glucose metabolism or even complete remission. This enables clinicians to detect much earlier the effectiveness of a given antineoplastic treatment, as compared to the traditional CT imaging alone [2].

Evaluating response to treatment; PET is a significant predictor of progression free survival (PFS) and overall survival (OS). Early (18) F- PET imaging also has a potential to identify patients with delayed response and no favorable prognosis despite achieving a clinical complete response [3].

PET/CT scanning after completion of therapy should be performed within two months and preferably at six to eight weeks after chemotherapy [4].

PET/CT provides information on tumor characteristics both morphologic and functional. As mentioned above, patients who have undergone therapy often have residual tissue at sites of previously active disease. The viability of this residual tissue cannot be assessed by CT alone. In such cases, PET/CT is used to determine whether treated tissue is active disease or inactive fibrosis/scar [5].

PATIENTS AND METHODS

This study was conducted on 40 patients complaining of NHL referred by their clinicians to radiology Department at Tanta Cancer Center. All patients were performed CT for initial staging, then the patient underwent full chemotherapy protocol ranging from 6 to 8 cycles with 3 to 4 weeks in between cycles. Then, after finishing chemotherapy by 4 to 8 weeks they underwent PET/CT.

Patients included in our study will be selected with the following inclusion criteria*:*

- Age group: no age predilection.
- Both sexes.
- Diagnosed cases with diffuse large B-cell type (DLBC) NHL.
- Histological confirmed.
- Presenting to Tanta Cancer Center since Jan 2011.
- Receiving treatment.

The acquisition of co registered CT and PET images were performed in one session. Images were reconstructed and viewed on work

Received: 12/ 06 /2017
Accepted: 21/ 06 /2017
DOI: 10.12816/0039675

station (Syngo Multimodality Workplace, Siemens Medical Solutions), which is provided multi-planar reformatted PET, CT and fused PET/CT images with linked cursors as well as MIP PET images in video mode.

Statistical analysis of the collected retrospective data was done to determine the role of PET/CT as a monitoring tool in assessment of response to treatment in non Hodgkin lymphoma patients.

RESULTS

This study included 40 patients with pathologically confirmed non Hodgkin lymphoma (diffuse large B cell) who underwent PET/CT study after they had finished their treatment protocol. The PET/CT exam of each patient was interpreted for the assessment of treatment response at end of the treatment.

Patients characteristics at presentation are summarized in the following table:

Characteristics	Patients (n= 40) Percent (%)	
Age (yrs)		
Range	22-67	
Mean ± SD	**44.58 ± 13.46**	
Gender		
Male	**22**	**(55%)**
Female	**18**	**(45%)**
B – symptoms		
Absent(-ve)	**27**	**(67.5%)**
Present (+ve)	**13**	**(32.5%)**
LDH measurement		
Normal	**21**	**(52.5%)**
Elevated	**19**	**(47.5%)**
Stage at presentation		
Stage I	**5**	**(12.5%)**
Stage II	**10**	**(25%)**
Stage III	**12**	**(30%)**
Stage IV	**13**	**(32.5%)**

A- Lymph node involvement

The sites of the lymph nodes groups involved were classified as being either supra-diaphragmatic, infra-diaphragmatic or both.

Sites of lymph nodes groups	Number of patients	Percent
Supra and infra	**11**	**(34.4%)**
Infra	**4**	**(12.5%)**
Supra	**17**	**(53.1%)**
Total	**32**	**100**

With cervical nodal involvement was the more frequent nodal site by more than 67% of patients with nodal involvement.

B- **Extranodal organ involvement**

Different sites of extra nodal involvement were found with spleen the most expressed extranodal site.

Sites of extranodal involvement	Number of patients	Percent %
Spleen	**10**	**(25%)**
Liver	**5**	**(12.5%)**
Pleuro-pulmonary	**6**	**(15%)**
Other GIT	**5**	**(12.5%)**
Bone & Bone Marrow	**3**	**(7.5%)**
Genitor-Urinary	**1**	**(2.5%)**
Head & Neck	**7**	**(17.5%)**
Skin & Soft tissue	**1**	**(2.5%)**
CNS	**0**	**(0%)**

After end of treatment, fifteen patients had a CR, twenty patients had PR, one patient had a SD and four patients had PD. In comparison, by the basis of PET/CT and Deauville criteria, 28 patients had a CR (Deauville 1, 2 and 3), 10 had a PR, no patient had SD and 2 patients had PD.

PET/CT had high sensitivity in assessment of complete remission after the end of treatment also PET/CT had high sensitivity in detection of active residual disease with significant specificity.

Post Treatment CT	Post treatment PET CT					
	Negative		Positive		Total	
	N	%	N	%	N	%
Negative	15	53.57	0	0.00	15	37.50
Positive	13	46.43	12	00.00	25	62.50
Total	28	100.00	12	00.00	40	100.00

DISCUSSION

Aggressive types of NHL constitute the most short survival, but chemo-sensitive lymphomas and high curability chance with combination chemotherapy; Diffuse Large B Cell lymphoma (DLBC) as one of the aggressive types of NHL are constituting the commonest of the haematological malignancies [6].

The nodal involvement expressed in more than 60% of patients with NHL and usually being the most accessible site for biopsy and histo-pathological diagnosis , while extra nodal involvements are expressed in approximately 40% of patients [7].

Interpretation of the PET CT findings in our study are matching with the results of ***Romera et***

al. [8]***;*** they were qualitative and semi-quantitative studies.

Our study showed the sites of the lymph nodes groups involved as being either supra-diaphragmatic, infra-diaphragmatic or both**.** 17 out of 40 patients had supra-diaphragmatic lymph nodes involved, 4 patients had infra-diaphragmatic lymph nodes involved and 11 patients had both supra and infra-diaphragmatic involvement.

Both CT and PET/CT have demonstrated high sensitivity for extra-nodal lesions, but PET/CT may be particularly helpful in discriminating benign from malignant lesions .These results are in concordance with those of ***Biggi et al.*** [9].

The overall comparison between CT and PET/CT in all patients in our study showed a significant sensitivity of PET/CT in nodal and extranodal affection. Even though diagnostic confidence is strongly improved with PET/CT, several lesions cannot be definitively stated and thus further confirmation by biopsy is needed for accurate diagnosis and this is in concordance with previous study done by ***Paes et al.*** [10].

In our study, visual assessment using Deauville Criteria-five-point scale were suited to assess different degrees of response after end of the treatment and has been developed to score images. Deauville Criteria classified into scores that represent lesions activity with **Score 1** showing no uptake above background, **score 2** showing uptake at an initial site that is less than or equal to mediastinum, **score 3** showing uptake at an initial site that is greater than mediastinum but less than or equal to liver, **score 4** showing uptake at an initial site that is moderately increased compared to the liver at any site and **score 5** showing uptake at an initial site that is markedly increased compared to liver [11]

Assessment of treatment response in our study using Deauville Criteria and Laugano classification stated that: scores 1, 2 or 3 are interpreted as complete metabolic response (CR), irrespective of a persistent mass on CT. Partial response (PR) in Deauville score of 4 or 5, provided uptake is decreased compared with baseline and absence of structural progression development on CT. Stable disease (SD), also called no metabolic response: a Deauville score of 4 or 5 without significant change in FDG uptake from baseline. Progressive disease (PD): a Deauville score of 4 to 5 with increasing intensity compared to baseline or any interim scan and/or any new FDG-avid focus consistent with malignant lymphoma.

Our study revealed high sensitivity and specifity of PET/CT over CT alone and this is in concordance with some trials such as ***Okada et al.*** [12]***; Wang***[13] ***a*****nd *Metser et al.*** [14]. Also we revealed that end of treatment PET is better for remission assessment than CT and this is matched with the results of ***Barrington and Mikhaeel*** [15] For those patients who do not achieve end of treatment complete response (CR) should be considered for further treatment after biopsy confirmation.

CONCLUSION

- Aggressive NHL usually presented by nodal and or extra-nodal involvement and although it is an aggressive lymphoma, many cases show complete remission denoting that it is a chemo-sensitive tumors.
- PET/CT is the technique of choice for patients with Non Hodgkin lymphoma as It has been demonstrated that 18F-FDG PET/CT is extremely useful tool for therapy response assessment especially for those patients with residual disease.
- Response assessment according to the Deauville criteria classification appears to represent a practical frame work used for proper assessment of response after treatment of NHL patients.
- PET/CT as a tool of assessment of response can discriminates between active lesion and non active necrotic or fibrotic lesion.

The present study had some limitations and challenges:

- Pathological confirmation was not available for most of the residual lesions, for which diagnosis was based on imaging criteria, Clinical /laboratory data and follow-up.
- Small sample size of post treatment patients so our results in this group need to be further evaluated on a larger sample size
- The proposed five-point scale is a visual measure of FDG PET/CT response assessment; the risk of a degree of subjectivity in the interpretation of FDG avidity has not been eliminated.

REFERENCES

1. (1)**Horesh N, Horowitz NA(2014) :** Does gender matter in non-Hodgkin lymphoma? Differences in epidemiology, clinical behavior and therapy. Rambam Maimonides Med.J., 5(4):29-38.
2. (2)**Gallamini A, Barrington SF, Biggi A, *et al*. (2014):** The predictive role of interim positron

emission tomography for Hodgkin lymphoma treatment outcome is confirmed using the interpretation criteria of the Deauville five-point scale. Haematologica.J. ,99(6):1107-1113.

3. (3)**De Oliveira Costa R, Hallack Neto A, Siqueira S,*et al* (2016):** Interim fluorine-18 fluorodeoxyglucose PET-computed tomography and cell of origin by immunohistochemistry predicts progression-free and overall survival in diffuse large B-cell lymphoma patients in the rituximab era. Nucl. Med. Commun., 37(10):1095-11001.
4. (4)**Seam P and Cheson BD(2007):** The role of FDG-PET scans in patients with lymphoma. Blood , 110(10):3507-3516.
5. (5)**Hutchings M and Barrington SF (2009):** PET/CT for therapy response assessment in lymphoma. J. Nucl. Med. , 50 21-30.
6. (6)**Smith A, Crouch S, Howell D, *et al*.(2015):** Impact of age and socioeconomic status on treatment and survival from aggressive lymphoma: a UK population-based study of diffuse large B-cell lymphoma. Cancer Epidemiol., 39(6):1103-1112.
7. (7)**Chiappella A, Castellino A and Vitolo (2016):** State of the art Therapy for Advanced-stage Diffuse Large B-cell Lymphoma. Hematol. Oncol. Clin.North., 30(6):1147-1162.
8. (8)**Romera M, Gámez Cenzano C and Caresia Aróztegui AP (2012):** Utility of the PET-CT in the evaluation of early response to treatment in the diffuse large B-cell lymphoma. Preliminary results. Rev. Esp. Med. Nucl. Imagen Mol., 31(3):135-141.
9. (9)**Biggi A, Gallamini A, Chauvie S *et al*. (2013):** international validation study for interim PET in ABVD-treated, advanced-stage Hodgkin lymphoma: Interpretation Criteria and Concordance Rate among Reviewers. Journal of Nuclear Medicine, 54: 683-690.
10. (10)**Paes FM, Kalkanis DG, Sideras PA *et al*. (2010):** FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease. Radiographics, 30(1):269-291.
11. (11)**Awan UE, Siddiqui N, SaadUllah M *et al.* (2013):** FDG-PET scan in assessing lymphomas and the application of Deauville Criteria. J Pak. Med. Assoc., 63(6):725-730.
12. (12)**Okada M, Sato NIshii K *et al.* (2010**): FDG PET/CT versus CT, MR imaging, and 67Ga scintigraphy in the post therapy evaluation of malignant lymphoma. Radiographics, 30(4):939-957.
13. (13)**Wang X (2015)**: PET/CT: appropriate application in lymphoma**.** Chin. Clin. Oncol., 4(1):4-13.
14. (14)**Metser U, Mohan R, Beckley V *et al. (*2016):** FDG PET/CT Response assessment criteria for patients with Hodgkin's and non-Hodgkin's lymphoma at end of therapy: a multiparametric approach. Nucl .Med .Mol Imaging, 50(1):46-53.
15. (15)**Barrington SF and Mikhaeel NG(2016)**: PET scans for staging and restaging in diffuse large B-Cell and follicular lymphomas. Curr. Hematol. Malig. Rep., 11(3):185-195.