European Journal of Nuclear Medicine and Molecular Imaging (2020) 47:523–524
https://doi.org/10.1007/s00259-019-04518-x

EDITORIAL

^{18}F-FDG PET/CT in patients with post-transplant lymphoproliferative disorders: so far so good

Giorgio Treglia [1,2,3,4] · Luca Ceriani [1,4,5]

Received: 20 August 2019 / Accepted: 29 August 2019 / Published online: 4 September 2019

Post-transplant lymphoproliferative disorders (PTLD) are a heterogeneous group of lymphoproliferative diseases occurring after solid organ transplant (SOT) or allogeneic hematopoietic cell transplant (HCT). Epstein-Barr virus (EBV) serology mismatch among recipient and donor, type of transplanted organ, and intensity and type of immunosuppression are considered as established risk factors for developing PTLD. The risk is also higher among children compared with adults [1].

According to the recent update of the WHO classification of tumors of hematopoietic and lymphoid tissues, PTLD are classified in early lesions (non-destructive PTLD), monomorphic PTLD (B cell, T cell, and NK cell subtype), polymorphic PTLD, and classical Hodgkin lymphoma PTLD. Monomorphic PTLD (in particular diffuse large B cell lymphoma) is the most frequent PTLD subtype [2]. Notably, PTLD is characterized by a high incidence of extranodal disease [1].

As PTLD are serious post-transplant complications associated with significant morbidity and mortality, a timely and accurate diagnosis of these disorders is needed. The diagnosis of PTLD can be challenging due to the nonspecific clinical presentation and heterogeneity in histopathologic and immunophenotypic presentation; therefore, histopathology and adequate immunophenotyping are essential to confirm the diagnosis of PTLD [1].

About the imaging methods, current National Comprehensive Cancer Network (NCCN) guidelines recommend chest/abdomen/pelvis contrast-enhanced computed tomography (CECT) and/or whole-body fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) as part of initial diagnostic workup for PTLD [3]. According to the recent evidence-based guidelines from the American Society of Transplantation, ^{18}F-FDG PET/CT may provide additional useful information for staging and end of treatment response assessment in adults and children with PTLD [4].

The article of Montes de Jesus et al. recently published in EJNMMI provides further evidence on the usefulness of ^{18}F-FDG PET/CT in the management of patients with PTLD [5]. In this retrospective study, the authors evaluated the diagnostic performance of ^{18}F-FDG PET/CT in a significant population ($n = 91$) of patients with suspected PTLD examining the factors affecting the diagnostic yield of ^{18}F-FDG PET/CT. Sensitivity, specificity, positive and negative predictive value, and accuracy of ^{18}F-FDG PET/CT for the diagnosis of PTLD were 85%, 90%, 83%, 92%, and 89%, respectively, with good inter-observer agreement ($k = 0.78$). Among the main clinical features, only increased lactate dehydrogenase levels seemed to be correlated with a true positive ^{18}F-FDG PET/CT scan in PTLD patients. EBV-DNA load and timing of ^{18}F-FDG PET/CT after transplantation did not affect the diagnostic performance of ^{18}F-FDG PET/CT in PTLD [5]. The good diagnostic performance reported in this study suggests that ^{18}F-FDG PET/CT is a valuable imaging modality for detecting PTLD. These findings are in agreement with the results of previous published studies on the same topic [6–8] that, however, presented a different methodology compared to the study of Montes de Jesus et al.

This article is part of the Topical Collection on Hematology

✉ Giorgio Treglia
giorgio.treglia@eoc.ch

1 Clinic of Nuclear Medicine and PET/CT Center, Imaging Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Switzerland

2 Department of Nuclear Medicine and Molecular Imaging, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

3 Health Technology Assessment Unit, Academic Education, Research and Innovation Area, General Directorate, Ente Ospedaliero Cantonale, Via Lugano 4F, CH-6500 Bellinzona, Switzerland

4 Clinic of Nuclear Medicine and PET/CT Center, Imaging Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Lugano, Switzerland

5 Institute of Oncology Research, Bellinzona, Switzerland

A recent evidence-based article reported that ^{18}F-FDG PET/CT is currently the most frequently investigated imaging modality for the diagnosis and staging of PTLD [9]. In this setting, ^{18}F-FDG PET/CT may contribute to confirm the clinical suspicion of PTLD identifying hypermetabolic targets for possible diagnostic biopsy. Moreover, ^{18}F-FDG PET/CT may detect additional PTLD lesions compared to conventional imaging modalities in about 28% of cases, mainly in extranodal sites, resulting in possible disease upstaging [9]. Nevertheless, false-negative results (due to PTLD lesions located in anatomical regions with high physiological background activity and early PTLD lesions) and false-positive results (mainly due to inflammatory conditions or other tumors) of ^{18}F-FDG PET/CT should be taken into account [9]. However, it should be underlined that some false-positive findings for PTLD at ^{18}F-FDG PET/CT, such as infections or other tumors, represent common complications after SOT or HCT; the detection of these findings in the post-transplant period by ^{18}F-FDG PET/CT is usually clinically relevant [10].

Beyond diagnosis and staging of PTLD, ^{18}F-FDG PET/CT is emerging as a useful imaging modality to evaluate the treatment response in patients with PTLD. In this setting, ^{18}F-FDG PET/CT findings may alter or provide additional treatment guidance in 29% of cases [9]. Recent published data demonstrated that negative interim and/or negative end of treatment ^{18}F-FDG PET/CT may identify PTLD patients with low risk of disease recurrence, due to its high negative predictive value, providing clinically relevant information, in particular in patients with partial response based on conventional imaging evaluation [11, 12].

In conclusion, ^{18}F-FDG PET/CT is emerging as a useful imaging modality for diagnosis, staging and treatment response assessment in the heterogeneous spectrum of patients with PTLD. However, additional validation of its utility in these settings is required; in particular, prospective and multicenter studies including larger populations to better characterize the diagnostic performance of ^{18}F-FDG PET/CT in the different subtypes of this heterogeneous pathological entity are needed.

A comparative analysis among different imaging modalities in different patient population (pediatric or adult patients) with PTLD would also be recommended. In particular, ^{18}F-FDG PET/MRI could be a valid alternative to the ^{18}F-FDG PET/CT in children to obtain metabolic information with a significant reduction in ionizing radiation, but to date, published reports on the use of ^{18}F-FDG PET/MRI in PTLD patients are lacking.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical approval This article does not contain any study with human participants or animals performed by any of the authors.

References

1. DeStefano CB, Desai SH, Shenoy AG, Catlett JP. Management of post-transplant lymphoproliferative disorders. Br J Haematol. 2018;182(3):330–43.
2. Aguilera N, Gru AA. Reexamining post-transplant lymphoproliferative disorders: newly recognized and enigmatic types. Semin Diagn Pathol. 2018;35(4):236–46.
3. NCCN Clinical practice guidelines in oncology. B-Cell Lymphomas Version 4.2019. Available at https://www.nccn.org/professionals/physician_gls/default.aspx.
4. Allen UD, Preiksaitis JK, AST Infectious Diseases Community of Practice. Post-transplant lymphoproliferative disorders, Epstein-Barr virus infection, and disease in solid organ transplantation: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transpl. 2019;23:e13652. https://doi.org/10.1111/ctr.13652.
5. Montes de Jesus FM, Kwee TC, Kahle XU, Nijland M, van Meerten T, Huls G, et al. Diagnostic performance of FDG-PET/CT of post-transplant lymphoproliferative disorder and factors affecting diagnostic yield. Eur J Nucl Med Mol Imaging. 2019. https://doi.org/10.1007/s00259-019-04481-7.
6. Dierickx D, Tousseyn T, Requilé A, Verscuren R, Sagaert X, Morscio J, et al. The accuracy of positron emission tomography in the detection of posttransplant lymphoproliferative disorder. Haematologica. 2013;98(5):771–5.
7. Noraini AR, Gay E, Ferrara C, Ravelli E, Mancini V, Morra E, et al. PET-CT as an effective imaging modality in the staging and follow-up of post-transplant lymphoproliferative disorder following solid organ transplantation. Singap Med J. 2009;50(12):1189–95.
8. Panagiotidis E, Quigley AM, Pencharz D, Ardeshna K, Syed R, Sajjan R, et al. (18)F-fluorodeoxyglucose positron emission tomography/computed tomography in diagnosis of post-transplant lymphoproliferative disorder. Leuk Lymphoma. 2014;55(3):515–9.
9. Montes de Jesus FM, Kwee TC, Nijland M, Kahle XU, Huls G, Dierckx RAJO, et al. Performance of advanced imaging modalities at diagnosis and treatment response evaluation of patients with post-transplant lymphoproliferative disorder: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2018;132:27–38.
10. Muller N, Kessler R, Caillard S, Epailly E, Hubelé F, Heimburger C, et al. (18)F-FDG PET/CT for the diagnosis of malignant and infectious complications after solid organ transplantation. Nucl Med Mol Imaging. 2017;51(1):58–68.
11. Van Keerberghen CA, Goffin K, Vergote V, Tousseyn T, Verhoef G, Laenen A, et al. Role of interim and end of treatment positron emission tomography for response assessment and prediction of relapse in posttransplant lymphoproliferative disorder. Acta Oncol. 2019;58(7):1041–7.
12. Zimmermann H, Denecke T, Dreyling MH, Franzius C, Reinke P, Subklewe M, et al. End-of-treatment positron emission tomography after uniform first-line therapy of B-cell Posttransplant lymphoproliferative disorder identifies patients at low risk of relapse in the prospective German PTLD registry. Transplantation. 2018;102(5):868–75.