The role of ^{18}F-FDG PET/CT in evaluation of Primary CNS lymphoma: The path less travelled

Sharjeel Usmani,[1] Anjali Jain,[1] Khulood Al Riyami,[1] Shah P Naumani,[2] Rashid Al-Sukaiti,[1] Muhammad Shahzad Shamim[3]

Abstract

Primary central nervous system lymphoma (PCNSL) is a rare but highly aggressive lymphoma with increasing incidence in immunocompromised patients. MRI is the modality of choice in evaluating brain lesions. However, MRI is often challenging in the detection of early recurrence, assessing residual disease and response evaluation in PCNSL. ^{18}F-FDG PET/CT has superior diagnostic performance compared with body CT in the evaluation of lymphoma. ^{18}F-FDG PET-CT is helpful in evaluating evaluation of disease extent and differentiating primary CNS lymphoma from systemic lymphoma. Besides diagnostic and prognostic value in primary CNS lymphoma, it might also be helpful in response assessment. The role of FDG-PET in PCNSL is not fully defined. In this article we have reviewed the potential role of ^{18}F-FDG PET/CT in initial diagnosis, baseline staging, restaging, evaluation of treatment response, prognostication, and survival analysis of PCNSL.

Keywords: ^{18}F-FDG PET/CT; CNS lymphoma; brain tumors.

DOI: 10.47391/JPMA.23-59

Literature Review

Primary central nervous system lymphoma (PCNSL) is a rare form of extra nodal lymphoma that arises within the brain, eyes, leptomeninges, or spinal cord in the absence of systemic disease at the time of diagnosis. The annual incidence of PCNSL is 0.5 case per 100,000, accounting for 3–5% of primary brain tumours.[1] The majority of PCNSL cases are diffuse large B-cell lymphomas likely to occur in immunodeficient patients.[2] The preferred treatment option includes chemotherapy followed by a consolidative whole-brain radiotherapy or autologous stem cell transplantation in younger patients.[3] Despite high initial complete remission rate with methotrexate-based regimens, over 50% of the patients relapse within 2 years after diagnosis.[4]

Magnetic resonance imaging (MRI) is the modality of choice in initial assessment of suspected primary CNS lymphoma due to its high soft-tissue resolution. MRI shows characteristic radiological features such as lesion location adjacent to the cerebrospinal fluid (CSF) space, strong and homogenous contrast-enhancement, moderate oedema, and absence of necrosis.[5] The radiologic findings of MRI and CT, however, are not pathognomonic for PCNSL. Similar findings can be seen in malignant gliomas, brain metastases, and inflammatory diseases.[6] MRI is often challenging in detection of early recurrence, assessing residual disease and response evaluation. 1H-MR spectroscopy can provide noninvasive biochemical information regarding in vivo tissue. Some authors have suggested that 1H-MR spectroscopy is helpful for discriminating tumours and pseudotumours, whereas others argue that it may not be so, because there is some overlap of the metabolites.[7]

^{18}F-FDG PET is commonly used in diagnostic staging, restaging, and response assessment in cancer patients to evaluate tumour glucose metabolism.[8] It is the most widely used radiotracer in lymphoma because of its high uptake by lymphoid cells and has better diagnostic accuracy compared to conventional imaging modalities in evaluating disease extent, monitoring treatment response and disease prognostication of lymphoma.[9] ^{18}F-FDG PET-CT is a more effective technique than CE-CT for the evaluation of extra-nodal involvement in Hodgkin and non-Hodgkin lymphoma patients.[10] PCNSL shows high ^{18}F-FDG uptake in almost all cases, and ^{18}F-FDG PET provides valuable information in the primary diagnosis of PCNSL (Figure 1). Multiple studies have shown that higher FDG uptake in CNS lymphoma enables differentiation from nonmalignant etiologies that may not be reliably distinguished on MRI.[11] ^{18}F-FDG PET can also differentiate PCNSL from other malignant brain tumours such as glioblastoma (GBM) and metastatic brain tumours, based on SUV max values, as PCNSL tend to be intensely avid compared to other tumours.[12] In a recent study an SUV max cut-off of 15.5 had 84% sensitivity and 80% specificity for diagnosing CNS lymphomas.[13] Lesion

[1]Department of Radiology and Nuclear Medicine, Sultan Qaboos Comprehensive Cancer Care and Research Center (SQCCCRC), Muscat Oman. [2]Department of Radiology, Stony Brook University, New York USA. [3]Aga Khan University Hospital, Karachi, Pakistan.

Correspondence: Muhammad Shahzad Shamim.

Email:shahzad.shamim@aku.edu

ORCID ID. 0000-0001-8305-8854

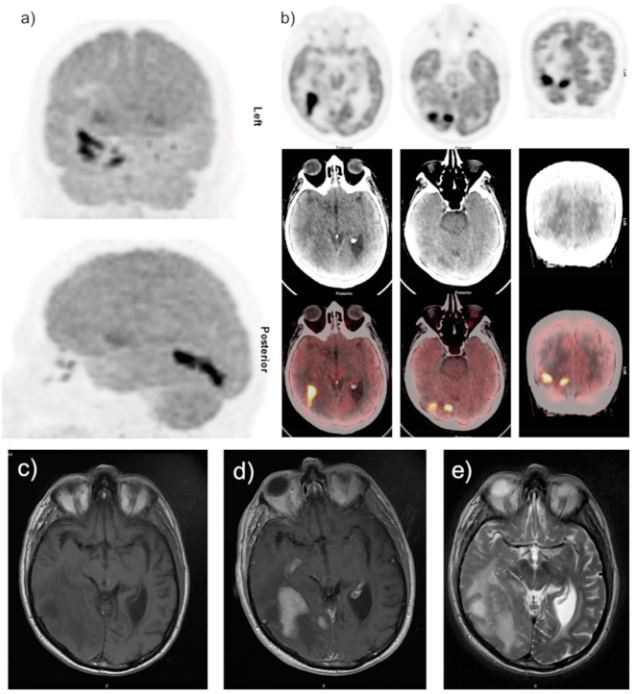

Figure-1: 78-year-old male is known case of relapse CNS NHL. a-c)^{18}F-FDG PET/CT demonstrate hypermetabolic mass lesion in right occipital/ posterior temporal lobes. Findings are consistent with disease relapse. c-e) MRI shows right occipital /posterotemporal large mass lesion (5.7 x2.6 x 3.5 cm) with irregular intensely enhancing iso-intense lesion effacing ipsilateral right occipital horn with large amount of oedema.

visualization may be limited in ^{18}F-FDG PET for leptomeningeal disease, intraocular and basal ganglia lesions. A recent meta-analysis by Zou Y et al.[14] reported a pooled sensitivity of 88% (95% CI: 80–94%) and specificity of 86% (95% CI: 73–94%). In addition, ^{18}F-FDG PET-CT also detects 4–10% of unexpected systemic involvement in suspected lymphoma confined to the brain.[15] The clinical significance of identifying systemic disease is uncertain, but detection of systemic lymphoma at the time of initial PCNSL diagnosis may play important roles regarding the origin of the disease, guiding biopsy and treatment strategies.

^{18}F-FDG PET is a useful imaging technique for monitoring response, mostly for methotrexate-based treatments, and detection of recurrence.[16] It has shown overall high accuracy in predicting treatment outcome in CNS lymphoma, both during and after completion of treatment.[17] It can be used to evaluate treatment response of PCNSL at early stage as changes in metabolic imaging occur soon after the initiation of therapy (Figure 2). Early evaluation of the initial treatment response is very important because salvage treatment may improve the outcome and quality of life. It can also predict complete remission or to diagnose tumour

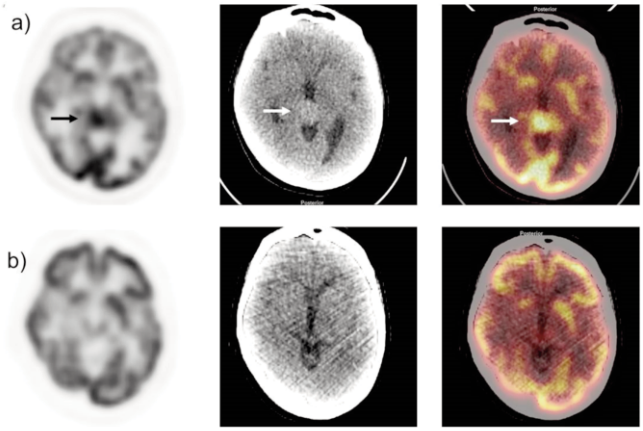

Figure-2: 37-year-old female with NHL of pineal region. a) Baseline ^{18}F-FDG PET/CT demonstrate hypermetabolic lesion at pineal gland with SUV max 20.8. b) Post chemotherapy PET/CT images show complete metabolic response to prior hypermetabolic pineal gland mass.

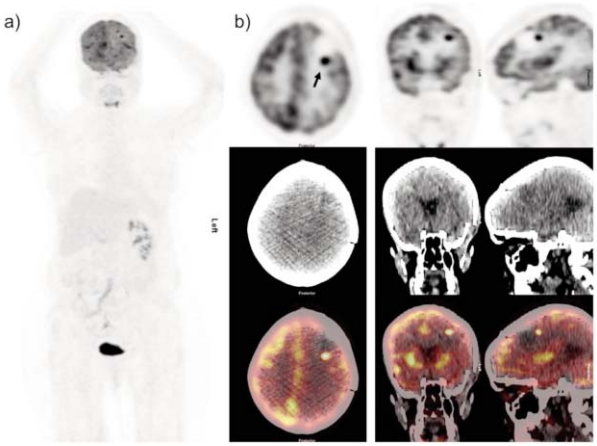

Figure-3: 48-year-old female has primary CNS lymphoma underwent surgical resection three month back. ^{18}F-FDG PET/CT demonstrate hypermetabolic lesion of SUV max 17.4 at left frontoparietal lobe (black arrow); corresponding CT localized this uptake at the periphery of post-operative brain defect. Findings are consistent with disease residual/recurrence.

recurrence of PCNSL after treatment (Figure 2). MRI is often unable to distinguish residual tumour nidus from biopsy-related scar tissue.[5] ^{18}F-FDG PET shows the real nature of residual masses after chemotherapy by distinguishing active foci from fibrotic tissue or inflammatory process (Figure 3). Although Deauville score is an established response assessment tool in HL and NHL, its application in PCNSL is still unclear and is a potential area for further research to establish its role in this group of patients.

^{18}F-FDG uptake may also have a prognostic value in PCNSL. The degree of ^{18}F-FDG uptake in terms of SUV values may represent tumour aggressiveness in PCNSL.

PCNSL with high uptake tend to exhibit poor treatment response compared to that with low to moderate uptake.[18] The overall survival time for the patients with high uptake is lower as compared to patients with low to moderate uptake. Recent study by Krebs S, et al.[19] has shown that the PET parameters such as SUV max, total lesion glycolysis (TLG), and metabolic tumour volume (MTV) correlated with progression free survival (PFS). The higher lesion metabolic parameters were inversely related to patient outcome.

Conclusions

^{18}F-FDG PET-CT has potential role in the diagnosis, initial staging, restaging, prognostication and treatment response evaluation in patients with primary CNS lymphoma.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Sierra del Rio M, Rousseau A, Soussain C, et al. Primary CNS lymphoma in immunocompetent patients. Oncologist. 2009;14:526–39.
2. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72:7-33.
3. Bhagavathi S., Wilson J.D. Primary Central Nervous System Lymphoma. Arch. Pathol. Lab. Med. 2008;132:1830–1834.
4. Thiel E, Korfel A, Martus P, et al. High-dose methotrexate with or without whole brain radiotherapy for primary CNS lymphoma (G-PCNSL-SG-1): a phase 3, randomised, non-inferiority trial. Lancet Oncol. 2010; 11: 1036–1047.
5. Maza S, Buchert R, Brenner W, et al. Brain and whole-body FDG-PET in diagnosis, treatment monitoring and long-term follow-up of primary CNS lymphoma. Radiol Oncol. 2013;47:103-110.
6. Küker W, Nägele T, Korfel A, et al. Primary central nervous system lymphomas (PCNSL): MRI features at presentation in 100 patients. J Neurooncol. 2005;72:169-177.
7. Lu SS, Kim SJ, Kim HS, et al. Utility of proton MR spectroscopy for differentiating typical and atypical primary central nervous system lymphomas from tumefactive demyelinating lesions. AJNR Am J Neuroradiol. 2014;35:270-277.
8. Fletcher JW, Djulbegovic B, Soares HP, et al. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med. 2008;49:480–508.
9. Usmani S, Ahmed DAT, Hamadah A, Al Kandari F. A rare case of Diffuse Large B-Cell Lymphoma of the Prostate on 18F-FDG PET-CT. J Pak Med Assoc. 2021;71(1(B)):388-389.
10. Ömür Ö, Baran Y, Oral A, Ceylan Y. Fluorine-18 fluorodeoxyglucose PET-CT for extranodal staging of non-Hodgkin and Hodgkin lymphoma. Diagn Interv Radiol. 2014;20:185-192.
11. Hoffman JM, Waskin HA, Schifter T, et al. FDG-PET in differentiating lymphoma from nonmalignant central nervous system lesions in patients with AIDS. J Nucl Med 1993;34:567–575.
12. Makino K, Hirai T, Nakamura H, et al. Does adding FDG-PET to MRI improve the differentiation between primary cerebral lymphoma and glioblastoma? Observer performance study. Ann Nucl Med. 2011;25:432-438.
13. Purandare NC, Puranik A, Shah S, et al. Common malignant brain tumors: Can 18F-FDG PET/CT aid in differentiation? Nucl Med Commun 2017;38:1109–16.
14. Zou Y, Tong J, Leng H, et al. Diagnostic value of using 18F-FDG PET and PET/CT in immunocompetent patients with primary central nervous system lymphoma: A systematic review and meta-analysis. Oncotarget 2017;8:41518–28.
15. Malani R, Bhatia A, Wolfe J, et al. Staging identifies non-CNS malignancies in a large cohort with newly diagnosed lymphomatous brain lesions. Leuk Lymphoma 2019;60:2278–82.
16 . de-Bonilla-Damiá Á, Fernández-López R, Capote-Huelva FJ, et al. Role of (18)F-FDG PET/CT in primary brain lymphoma. Rev Esp Med Nucl Imagen Mol 2017;36:298–303.
17. Krebs S, Barasch JG, Young RJ, Grommes C, Schöder H. Positron emission tomography and magnetic resonance imaging in primary central nervous system lymphoma-a narrative review. Ann Lymphoma. 2021;5:15.
18. Kawai N, Zhen HN, Miyake K, et al. Prognostic value of pretreatment 18F-FDG PET in patients with primary central nervous system lymphoma: SUV-based assessment. J Neurooncol. 2010;100:225-232.
19. Krebs S, Mellinghoff I, Grommes C, et al. Prognostic value of FDG-PET/CT in recurrent/refractory CNS lymphoma receiving Ibrutinib-based therapies. Eur J Nucl Med Mol Imaging 2019;46:S260–1.