Orbital Lymphoma: Prognostic Evaluation of a Rare Variant of Non-Hodgkin's Lymphoma with ^{18}F-FDG PET-CT

[1]Afroja Sultana, [2]Md Abu Bakker Siddique, [3]Pupree Mutsuddy, [4]Tapati Mandal, [4]Papia Akhter, [5]M M Ruhul Amin, [6]A K M Fazlul Bari

[1]Medical officer & MD resident, National Institute of Nuclear Medicine & Allied Sciences (NINMAS), [2] Professor & CMO, [3]Associate Professor & PMO, 4Assistant Professor & SMO -NINMAS, [5]Assistant Surgeon & Endocrinologist, DGHS, [6] Professor & Director, NINMAS

Correspondence Address: Dr. Afroja Sultana, Medical Officer, MD-phase B resident, NINMAS, Block-D, BMU Campus, Shahbag, Dhaka -1000. Email: afrojasultanashukhi@gmail.com

ABSTRACT

Lymphomas located in the orbit and surrounding structures are uncommon cancers, accounting for just 1% of all non-Hodgkin lymphoma cases. Most non-Hodgkin lymphomas of the orbit are classified as extranodal marginal zone B-cell lymphomas of mucosa-associated lymphoid tissue type. Due to the non-specific nature of the clinical signs and symptoms, there may be some delays in reaching a diagnosis. The purpose of our study is to evaluate the prognostic value of PET-CT after therapy, as well as the clinical course of lymphomas that involve the orbit.

Keywords: ^{18}F-FDG PET/CT, orbital lymphoma, non-Hodgkin lymphoma chemiluminescence immune assay, seasonal variation, gender difference

Bangladesh J. Nucl. Med. Vol. 29 No. 1 January 2026

DOI: https://doi.org/10.3329/bjnm.v29i1.89302

INTRODUCTION

Orbital lymphomas are rare, accounting for only 1% of all non-Hodgkin lymphoma cases (1). However, they are the most common primary orbital tumors in adults aged 60 and older (2). Margo and Mulla reported in their study of more than 300 orbital malignancies a 55% incidence of orbital lymphomas (3). Most non-Hodgkin lymphomas of the orbit and orbital adnexa are extranodal marginal-zone B-cell lymphomas of mucosa-associated lymphoid tissue (MALT) type (4). Marginal zone B cell lymphoma (MZL) is an indolent non-Hodgkin lymphoma (NHL) that originates from post-germinal center marginal zone B cells and includes three distinct diseases classified together in the WHO system: extranodal marginal zone B cell lymphoma of MALT, nodal marginal zone B cell lymphoma (NMZL), and splenic marginal zone B cell lymphoma (SMZL) (5). Collectively, these three types account for about 5-10% of NHLs. Over the past decade, ^{18}F-FLUORODEOXYGLUCOSE (FDG) positron emission tomography (PET) has become increasingly important in cancer evaluation. It plays a key role in staging, detecting recurrence and metastasis, assessing therapy response, and follow-up, especially in patients with lymphoma. It can identify areas of abnormally high metabolic activity associated with malignancy. The purpose of our study is to evaluate the prognostic significance of post-therapy PET-CT and the clinical course of orbital lymphomas.

CASE REPORT

After one month of symptomatic swelling of the right upper eyelid, a 60-year-old male presented with proptosis in the oncology department. Physical examination exhibited right hypertropia, restricted right gaze, and visual field defects. There was notable swelling of the right upper eyelid with a palpable mass and hypoglobus. The patient was advised to undergo an MRI of the brain and orbit, which revealed a well-defined, ovoid lesion in the superior aspect of the right orbit, displacing the globe inferiorly. The lesion abuts the right superior rectus muscle, the lateral rectus muscle, and the right optic nerve without clear infiltration. It also appeared isointense to slightly hypointense on T1-weighted imaging compared to the surrounding orbital fat.

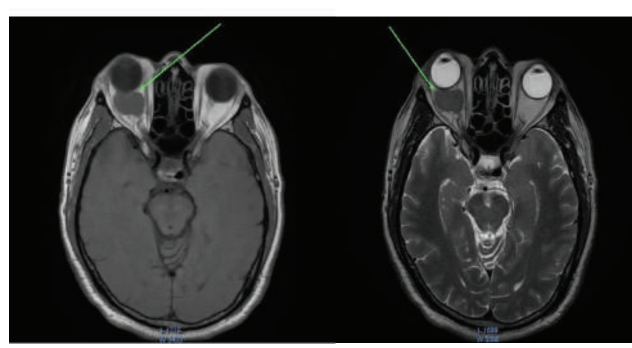

Figure 1: Axial MRI scans of the orbits show a well-circumscribed, ovoid intraconal lesion in the right orbit that is hypointense on T1-weighted image(left) and hyperintense on T2-weighted image(right).

Then, the patient was referred for an incisional biopsy due to worsening orbital swelling. He denied any prior trauma and had an unremarkable medical history. The biopsy findings showed extranodal marginal zone small atypical B-cell lymphoma. The patient was advised to undergo immunohistochemistry for further confirmation. Immunohistochemistry results showed positivity for CD20, CD3, and CD23. Ki67 was 12-18%, consistent with biopsy, imaging, and clinical findings. After the diagnosis was confirmed, the patient was recommended to undergo external beam radiotherapy (EBRT). He received 34 Gy in 17 fractions, completed within two months. Six months after EBRT, the patient was advised to undergo whole-body PET-CT to assess treatment response. The PET-CT showed a fairly well-defined, enhancing soft tissue lesion in the intraconal space of the right orbit with metabolic activity and mild adjacent fat stranding, suggesting residual disease.

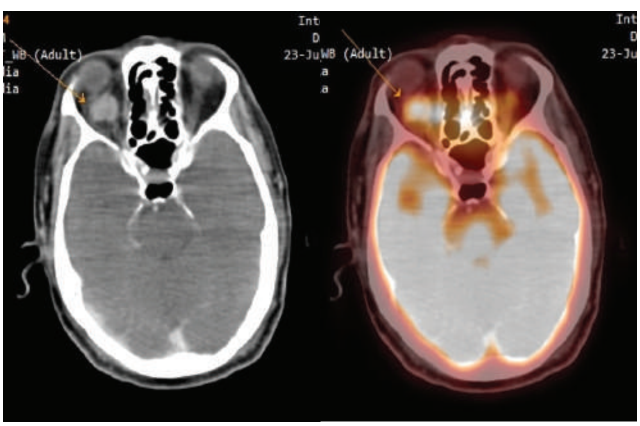

Figure 2: Axial CT and fusion PET-CT images demonstrate a well-defined, hypermetabolic (FDG-avid) soft tissue lesion within the right orbit.

After reviewing the PET-CT report, the patient was referred for chemotherapy (CHOP) with rituximab and bendamustine. The patient completed six cycles of chemotherapy within four months. Following chemotherapy, the patient was advised to undergo a whole-body PET-CT to evaluate the therapy response, which was essential for further management. The patient was then referred to NINMAS by the clinician for a whole-body PET-CT. The PET-CT showed nearly complete remission of the lesion, with only mild adjacent fat stranding area. No suspicious mass or abnormal FDG uptake was observed elsewhere in the body.

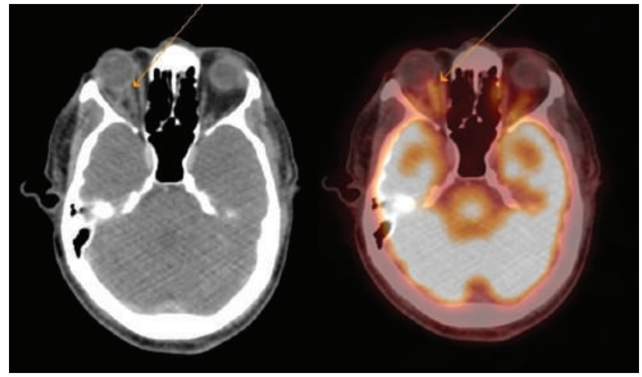

Figure 3: After chemotherapy, the PET-CT showed almost complete remission of the lesion, with adjacent fat stranding area.

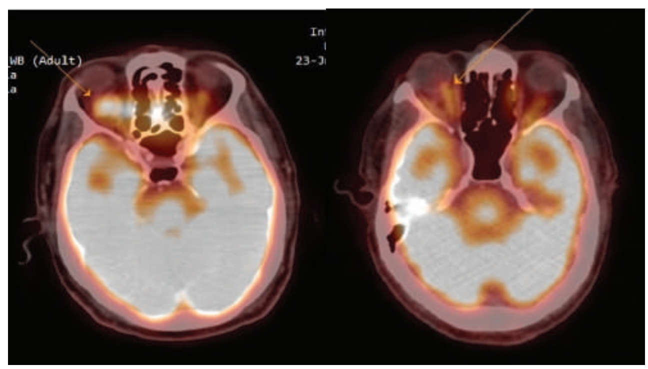

Figure 4: PET images before(left) and after(right) chemotherapy.

DISCUSSION

^{18}F-2-deoxy-D-glucose (18F-FDG) is currently the most widely used radiotracer in positron emission tomography (PET) studies to assess differences in glycolytic rate between normal and malignant cells. Combined ^{18}F-FDG-PET/CT, where PET scanner detectors integrate with a multi-detector helical CT, provides accurate localization of abnormal lesions and produces more sensitive and specific images than either modality alone (6). PET/CT plays a key role in managing aggressive and rare lymphomas by improving accuracy and optimizing treatment strategies. In 2007, the IHP (7) recommended using PET as an appropriate method for staging and measuring response after first-line treatment in Hodgkin lymphoma (HL) and aggressive NHL. The sensitivity and specificity of PET have been evaluated across both lymphoma subtypes in a meta-analysis by Zijlstra et al., with notable results (84% sensitivity and 90% specificity for HL; 72% sensitivity and 100% specificity for aggressive NHL) (8). Regarding its use in indolent lymphomas, PET is recommended only for response assessment in clinical trials (9). This consensus states that, if PET is to be used for response assessment in such patients, a pre-treatment PET is mandatory to document all positive ^{18}F-FDG lesions. We found higher accuracy with PET-CT, with an overall sensitivity of 96% for all lymphomas and 95.5% for extranodal lesions (Carrillo-Cruz et al.). Currently, no specific guidelines exist for managing ENMZL (MALT). Multiple reports confirm the efficacy of conventional treatments such as surgery, radiotherapy, or chemotherapy, alone or in combination, with no significant differences in survival (10,11,12). Surgery as the sole treatment modality should not be used because of the high risk of local relapse, as previous reports indicate (13). Radiation therapy as an initial treatment has been shown to be highly effective for MALT lymphoma of the orbit (14). Radiotherapy doses of 25-35 Gy are considered standard, as they provide local control and cure for localized orbital lymphoma (15,16,17). Interestingly, several studies have reported relatively high local or distant failure rates after successful initial radiotherapy. Jenkins and colleagues reported that 47% of their 192 patients with orbital MALT lymphoma developed extraorbital recurrence after five years (18). Hasegawa and colleagues observed a recurrence rate of 25% among 20 patients treated solely with radiotherapy for orbital MALT lymphoma, with relapses occurring after an average follow-up of 71 months (19). Given conflicting reports on EBRT, evidence suggests that combination chemotherapy may be effective for orbital lymphoma (20). Chemotherapy has never been systematically evaluated in orbital MALT lymphoma because of excellent local control rates, and it has also shown excellent responses after primary radiotherapy. Most often, chemotherapy with rituximab and bendamustine has been administered following surgery or radiotherapy.

A recent pilot study evaluated the tolerability and effectiveness of intralesional rituximab injections in five patients with orbital B-cell lymphoma, with two achieving complete remission and two achieving stable disease (21). Future clinical trials will reveal potential synergistic effects between rituximab and chemotherapy and will help better assess the role of chemotherapy in extranodal MALT lymphoma.

CONCLUSION

ENMZL (MALT) lymphomas make up the majority of orbital and periorbital non-Hodgkin lymphomas. The prognostic value of PET/CT has been crucial for all types of lymphoma. In this context, early surgical biopsy, along with proper imaging, is vital for the prompt diagnosis of orbital lymphoma. As shown in our patient, after 34 GY of radiotherapy, combined chemotherapy with rituximab and bendamustine proved effective, resulting in nearly complete remission of the lesion and symptom-free survival.

REFERENCES

1. Ahmed S, Shahid RK, Sison CP, Fuchs A, Mehrotra B: Orbital lymphomas: a clinicopathologic study of a rare disease. Am J Med Sci 2006, 331:79–83.DOI: 10.1097/00000441-200602000-00013
2. Demirci H, Shields CL, Shields JA, Honavar SG, Mercado GJ, Tovilla JC: Orbital tumors in the older adult population. Ophthalmology 2002,109:243–248.DOI: 10.1016/s0161-6420(01)00932-0
3. Margo CE, Mulla ZD: Malignant tumors of the orbit, analysis of the Florida cancer registry. Ophthalmology 1998, 105:185–190.DOI: 10.1016/s0161-6420(98)92107-8
4. Isaacson PG, Wright DH: Malignant lymphoma of mucosal associated lymphoid tissue: a distinctive type of B cell lymphoma. Cancer 1983, 52:1410–1416. https://doi.org/10.1111/j.1365-2559.1987.tb02654.xDigital Object Identifier (DOI)
5. Swerdlow SH, Campo E, Harris NL, et al. World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC Press: Lyon, 2008.
6. Seam P, Juweid ME, Cheson BD. The role of FDG-PET scans in patients with lymphoma. Blood 2007; 110(10): 3507–3516 DOI: 10.1182/blood-2007-06-097238
7. Juweid ME, Stroobants S, Hoekstra OS, et al. Imaging subcommittee of International Harmonization Project in Lymphoma. Use of positron emission tomography for response assessment of lymphoma: consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma. J Clin Oncol 2007; 25(5): 571–578.DOI: 10.1200/JCO.2006.08.2305
8. Zijlstra JM, Lindauer-van der Werf G, Hoekstra OS, Hooft L,Riphagen II, Huijgens PC. 18 F-fluoro-deoxiglucose positron emission tomography for post-treatment evaluation of malignant lymphoma: a systematic review. Haematologica 2006; 91(4):522–529.doi: 10.3324/haematol.91.4.522.
9. Cheson BD. The International Harmonization Project for response criteria in lymphoma clinical trials. Hematol Oncol Clin North Am 2007; 21(5): 841–854.DOI: 10.1016/j.hoc.2007.06.011
10. Zinzani PL, Magagnoli M, Galieni P, Martelli M, Poletti V, Zaja F, Molica S,Zaccaria A, Cantonetti AM, Gentilini P, Guardigni L, Gherlinzoni F, Ribersani M, Bendandi M, Albertini P, Tura S: Nongastrointestinal low-grade mucosaassociated lymphoid tissue lymphoma: analysis of 75 patients. J Clin Oncol 1999, 17:1254–1258.DOI: 10.1200/JCO.1999.17.4.1254

11. Zucca E, Conconi A, Pedrinis E, Cortelazzo S, Motta T, Gospodarowicz MK, Patterson BJ, Ferreri AJ, Ponzoni M, Devizzi L, Giardini R, Pinotti G, Capella C, Zinzani PL, Pileri S, López-Guillermo A, Campo E, Ambrosetti A, Baldini L, Cavalli F, International Extranodal Lymphoma Study Group: Nongastric marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue. Blood 2003, 101:2489–2495.DOI: 10.1182/blood-2002-04-1279

12. Thieblemont C, Berger F, Dumontet C, Moullet I, Bouafia F, Felman P, Salles G, Coiffier B: Mucosa-associated lymphoid tissue lymphoma is a disseminated disease in one third of 159 patients analyzed. Blood 2000, 95:802–806.https://doi.org/10.1182/blood.V95.3.802.003k19_802_806

13. Esik O, Ikeda H, Mukai K, Kaneko A: A retrospective analysis of different modalities for treatment of primary orbital non-Hodgkin's lymphomas. Radiother Oncol 1996, 38:13 DOI: 10.1016/0167-8140(95)01658-9

14. Goda JS, Gospodarowicz M, Pintilie M, Wells W, Hodgson DC, Sun A, Crump M, Tsang RW: Long-term outcome in localized extranodal mucosaassociated lymphoid tissue lymphomas treated with radiotherapy. Cancer 2010, 116:3815.doi: 10.1002/cncr.25226.

15. Smitt MC, Donaldson SS: Radiotherapy is successful treatment for orbital lymphoma. Int J Radiat Oncol Biol Phys 1993, 26:59–66. DOI: 10.1016/0360-3016(93)90173-s

16. Lee JL, Kim MK, Lee KH, Hyun MS, Chung HS, Kim DS, Shin SO, Cho HS, Bae SH, Ryoo HM: Extranodal marginal zone B-cell lymphomas of mucosa associated lymphoid tissue-type of the orbit and ocular adnexa. Ann Hematol 2005, 84:13–18DOI: 10.1007/s00277-004-0914-3

17. Stafford SL, Kozelsky TF, Garrity JA, Kurtin PJ, Leavitt JA, Martenson JA, Habermann TM: Orbital lymphoma: radiotherapy outcome and complications. Radiother Oncol 2001, 59:139–144.DOI:10.1016/S0167-8140(00)00328-5

18. Jenkins C, Rose GE, Bunce C, Wright JE, Cree IA, Plowmann N, Lightman S, Moseley I, Norton A: Histological features of ocular adnexal lymphoma(REAL classification) and their association with patient morbidity and survival. Br J Ophthalmol 2000, 84:907–913.DOI: 10.1136/bjo.84.8.907

19. Hasegawa M, Kojima M, Shioya M, Tamaki Y, Saitoh J, Sakurai H, Kitamoto Y,Suzuki Y, Niibe H, Nakano T: Treatment results of radiotherapy for malignant lymphoma of the orbit and histopathologic review according to the WHO classification. Int J Radiat Oncol Biol Phys 2003, 57:172–176.DOI: 10.1016/s0360-3016(03)00506-6

20. Galieni P, Polito E, Leccisotti A, Marotta G, Lasi S, Bigazzi C, Bucalossi A, Frezza G, Lauria F: Localized orbital lymphoma. Haematologica 1997,82:436–439.PMID: 9299857

21. Savino G, Battendieri R, Balia L, Colucci D, Larocca LM, Laurenti L, De Padua L, Blasi MA, Balestrazzi E: Evaluation of intraorbital injection of rituximab for treatment of primary ocular adnexal lymphoma:a pilot study. Cancer Sci 2011, 102:1565–1567. DOI: 10.1111/j.1349-7006.2011. 01976.x