Immunopathologia Persa
DOI:10.34172/ipp.2025.34472
http immunopathol.com

Immunohistochemical evaluation of CD10, BCL6, BCL2, MUM1 and MYC in diffuse large B-cell brain lymphoma; diagnostic and prognostic significance

Farahnaz Bidari Zerehpoosh[1], Masoomeh Farahmandfar[2*], Guive Sharifi[3], Omidvar Rezaei[4], Latif Gachkar[5]

[1]Department of Pathology, Shahid Beheshti University of Medical Sciences, Loghman Hakim Hospital, Tehran, Iran
[2]Department of Pathology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Department of Neurosurgery, School of Medicine, Skull Base Research Center Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Department of Neurosurgery, School of Medicine, Skull Base Research Center Loghman Hakim Hospital Shahid Beheshti University of Medical Sciences, Tehran, Iran
[5]Department of Infectious Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

***Correspondence to**
Masoomeh Farahmandfar,
Email: drmasomfar@gmail.com

Received 23 Aug. 2024
Revised: 10 Jan. 2025
Accepted 25 Jan. 2025
ePublished 22 Feb. 2025

Keywords: Diffuse large B-cell lymphoma, Primary nervous system lymphoma, Immunohistochemical biomarkers, Patient survival, Prognosis

Citation: Bidari Zerehpoosh F, Farahmandfar M, Sharifi G, Rezaei O, Gachkar L. Immunohistochemical evaluation of CD10, BCL6, BCL2, MUM1 and MYC in diffuse large B-cell brain lymphoma; diagnostic and prognostic significance. Immunopathol Persa. 2025;11(2):e34472. DOI:10.34172/ipp.2025.34472.

Abstract

Introduction: Although the prognosis of primary central nervous system lymphoma (PCNSL), a progressive neoplasm of the central nervous system, has improved with the use of current therapies, the overall survival rate of patients is still low.

Objectives: Since the identification of factors that affect the survival of these patients can help physicians choose the best treatment and prognosis, this study aimed to investigate the diagnostic and prognostic significance of immunohistochemical biomarkers in patients with diffuse large B-cell lymphoma (DLBCL), as the most common type of PCNSL.

Patients and Methods: In this descriptive-cross-sectional, 30 histological block samples from patients diagnosed with DLBCL were subjected to tissue preparation and immunohistochemical staining with multiple myeloma oncogene-1 (MUM1), B cell lymphoma-6 (BCL-6), B cell lymphoma-2 (BCL-2), cluster differentiation 10 (CD10), and MYC antibodies, and their expression rates were determined subsequently. Patients' characteristics, including survival status and survival time after diagnosis, were extracted from patients' records.

Results: Immunohistochemistry positivity for MUM1, BCL-6, BCL-2, CD10, and MYC biomarkers were seen in 25 (83%), 21 (70%), 25 (83%), 2 (7%), 25 (83%) and 0 (0%), respectively. According to the Hans algorithm, 24 patients (80%) were activated B cell (ABC) and 6 patients (20 %) were germinal center B cell (GCB). Totally, 23 (77%) patients have died during the study period. The mean survival time of patients was 12 months (95% CI: 14.47-33.24). There was no significant difference in death rate for different categories of variables such as demographic characteristics, DLBCL subgroup, and biomarker positive rates (P>0.05). According to the univariate cox model, the immunohistochemistry (IHC) reactivity rate for the studied biomarkers did not significantly affect the survival. In contrast, chemotherapy and radiotherapy reduce the hazard of death by 72% and 65%, respectively.

Conclusion: The results of the present study revealed that the expression rate of MUM1, BCL-6, BCL-2, CD10, and MYC could not be used as a proper prognostic biomarker for DLBCL patients.

Introduction

Primary central nervous system lymphoma (PCNSL) is a type of non-Hodgkin's lymphoma and is a rare, highly invasive, and progressive central nervous system (CNS) neoplasm. It should be noted that although the response to PCNSL treatment is better than other CNS neoplasms, it has a poor prognosis compared to other lymphomas (1). PCNSL accounts for 4% of all CNS neoplasms in immunocompetent individuals (2), Increased prevalence of acquired immunosuppressive diseases and immunosuppression following organ transplantation lead to increase in the PCNSL prevalence (3).

Morphologically, more than 90% of these tumors are diffuse large B-cell lymphoma (DLBCL), based on the latest WHO classification (4). According to the type of gene expression, DLBCLs are divided into two subgroups of tumors similar to the B-cell germination center (GCB) and tumors similar to activated B cells (ABCs) (5). Although the prognosis and survival of these patients have been improved by systemic treatment of high-dose methotrexate, the overall survival of most patients is still low (6,7). The results of some studies have indicated that this morphological classification cannot predict the survival rate of patients with PCNSL

Key point

The results of the present study revealed that the expression rate of multiple myeloma oncogene-1 (MUM1), B cell lymphoma-6 (BCL-6), B cell lymphoma-2 (BCL-2), cluster differentiation 10 (CD10), and MYC could not be conducted as a proper prognostic biomarker for patients with diffuse large B-cell lymphoma (DLBCL), as the most common type of primary central nervous system lymphoma (PCNSL).

(8,9). Due to the increasing incidence of PCNSL (even in people with good immunity), genetic heterogeneity of patients, and numerous problems in the management and treatment of these patients, introduction of new prognostic and diagnostic biomarkers in PCNSL had given significant attractions during the last years (10). Different biomarkers have been studied in a number of studies with contradictory results. For example, the expression of B cell lymphoma (BCL)-6 marker in PCNSL was associated with a poor prognosis in the studies conducted by Chen et al (9) and Kreher et al (11). On the other hand, in the study performed by Lossos et al, the expression of this biomarker was reported to be associated with a better prognosis in these patients (12).

Objectives

The present study aimed to evaluate the diagnostic and prognostic significance of immunohistochemical biomarkers of multiple myeloma oncogene-1 (MUM-1), B cell lymphoma -6 (BCL-6), B cell lymphoma -2 (BCL-2), and cluster differentiation (CD10), MYC in DLBCL patients.

Patients and Methods

Study design

In this descriptive-cross-sectional study was conducted on the histological block samples (n=30) from patients who were histopathologically diagnosed with DLBCL at the Loghman Hakim hospital, Tehran, Iran, during 2012-2019. Initially, the patients' characteristics, including age, gender, type of treatment, survival status, and duration of survival after diagnosis was extracted from the patients' records. The samples were taken for the preparation of an immunohistochemical slide after the confirmation of the diagnosis.

Immunohistochemical staining

First, tissue sections with a thickness of 4 to 5 microns were cut from the molded samples, then the slides are immersed in xylene to remove the paraffin and then hydrated with descending does of ethanol (99%, 95%, and 70%). In the next step, the slides were treated by 5% hydrogen peroxide for 10 minutes to quench the activity of endogenous peroxidase and then washed by tape water. The samples were then placed in a 0.01 M sodium citrate buffer in a microwave oven for 1 min at 98 °C for antigen retrieval. The slides were transferred to Tris buffer saline (TBS) for 5 minutes. Primary antibodies against MUM1, BCL-6, BCL-2, CD10, and MYC were added at a dilution of 1:200 and kept at 4 °C for one hour. Afterward, washing had done twice by the TBS. The slides were blocked by 10% normal goat serum for 5 min and excess serum was removed. The samples were then incubated with secondary antibody at a dilution of 1:500 for 45 min and washed again twice (each time for 5 minutes) with TBS. Subsequently, the chromogenic reaction was conducted by diaminobenzidine (DAB), and the counter-stain was performed with hematoxylin. Eventually, the samples were examined under a light microscope.

Evaluation of antibody expression rate

Microscopic examination of antibody-labeled sections was performed on the prepared immunohistochemical slides using a light microscope. At least 1000 cells per slide were counted by eye, and the percentage of stained cells was determined as well. Subsequently, the percentages of brown and blue stained cells in each tissue were compared, and the extent of staining was reported in terms of the percentage of stained cells. Staining was considered positive for MUM-1, BCL-6, and CD10, when >30% of cells were positively stained. For BCL-2 and MYC, staining was considered positive when >50% and >40% of cell were positively stained, respectively. The DLBCL type was also determined based on the Hans algorithm (13).

Statistical analysis

The data analysis was performed by statistical software STATA version 16. Variables presented by frequency (percentage) and mean (SD). Meanwhile, the chi square test was conducted to compare dead and survived patients. We have considered the duration between admission and death of patients as the survival time. Intergroup survival time comparison was done by Kaplan-Meier curves and log-rank test for all variables. Univariate cox model was carried out to have a better estimation of hazard ratio (HR) ant its confidence interval for each variable. A *P* value less than 0.05 was considered statistically significant.

Results

Out of 30 patients, 14 (46.67%) and 16 (53.33%) patients were male and female, respectively. Moreover, 63.33% of patients (19 patients) were less than 60 years and 11 (36.67%) were more than 60 years old. Chemotherapy and radiotherapy treatment were performed on 24 (80%) and 11 (37%) patients, respectively. The DLBCL subtype was ABC in 24 (80%) patients and GCB in 6 (20%) patients, based on Hans algorithm. Positive immunohistochemistry (IHC) staining for MUM1, BCL-6, BCL-2, CD10, and MYC biomarkers were seen in 25 (83%), 21 (70%), 25 (83%), 2 (7%), and 25 (83%), 0 (0%) respectively. In addition, double-hit lymphoma (Co-expression of MYC and BCL-2 or MYC and BCL-6) and triple-hit lymphoma (co-expression of MYC & BCL-2 and BCL-6) were

not found in the samples. During the study, 23 (77%) patients have died. We used chi-square test to compare the difference between survived and dead patients. There was no significant difference in death rate for different categories of variables (Table 1).

The IHC reactivity rate for the studied biomarkers did not significantly affect the survival. Intergroup survival time comparison by log-rank test for various variables showed only significant difference for chemotherapy and radiotherapy variables. In addition, according to the univariate cox model, HR for chemotherapy and radiotherapy were 0.28 and 0.35, respectively. In other words, chemotherapy and radiotherapy reduce the hazard of death by 72% ((1-0.28)×100) and 65% ((1-0.35)×100) respectively (Table 2).

The mean and median survival time of patients was 12 months (95% CI: 14.47 - 33.24) and 12 months, respectively. Table 3 shows mean and median survival time of patients according to demographic characteristics, treatment type, DLBCL subgroup, and biomarker positive

Table 1. Demographic characteristics and clinical features of patients

	Survived	Dead	Total	χ2	*P* value
Gender					
Female	3 (18.75%)	13 (81.25%)	16 (53.33%)	0.402	0.526
Male	4 (28.57%)	10 (71.43%)	14 (46.67%)		
Age					
Less than 60 years	6 (31.58%)	13 (68.42%)	19 (63.33%)	1.97	0.161
More than 60 years	1 (9.09%)	10 (90.91%)	11 (36.67%)		
Chemotherapy					
No	0 (0.0%)	6 (100.0%)	6 (20.0%)	2.28	0.131
Yes	7 (29.17%)	17 (70.83%)	24 (80.%0)		
Radiotherapy					
No	3 (15.79%)	16 (84.21%)	19(63.33%)	1.65	0.199
Yes	4 (36.36%)	7 (63.64%)	11 (36.67%)		
MUM1					
Negative	2 (40.0%)	3 (60.0%)	5 (16.67%)	0.931	0.334
Positive	5 (20.0%)	20 (80.0%)	25 (83.33%)		
BCL-6					
Negative	2 (22.22%)	7 (77.78%)	9 (30.0%)	0.009	0.925
Positive	5 (23.81%)	16 (76.19%)	21 (70.0%)		
BCL-2					
Negative	2 (22.22%)	7 (77.78%)	9 (30.0%)	0.009	0.925
Positive	5 (23.81%)	16 (76.19%)	21 (70.0%)		
CD10					
Negative	7 (25.0%)	21 (75.0%)	28 (93.33%)	0.652	0.419
Positive	0 (0.0%)	2 (100.0%)	2 (6.67%)		
MYC					
Negative	7 (23.33%)	23 (76.67%)	30 (100.0%)		
Subtype					
GBC	2 (33.33%)	4 (66.67%)	6 (20.0%)	0.419	0.517
ABC	5 (20.83%)	19 (79.17%)	24 (80.0%)		

ABC: Activated B cell, BCL-2: B cell lymphoma -2, BCL-6: B cell lymphoma -6, CD 10: cluster differentiation 10, GBC: Germinal center B cell, MUM1: Multiple myeloma oncogene-1.

Table 2. Intergroup survival time comparison (Log-rank test) and univariate cox model according to the patients' characteristics, and studied biomarkers

Characteristics	Log-rank χ^2 (*P* value)	Univariate cox model		
		HR	*P* value	95% CI
Age (≥60 versus <60 years)	1.58 (0.208)	1.68	0.237	0.71–3.95
Gender (male versus female)	0.78 (0.376)	0.69	0.401	0.30–1.63
Chemotherapy (yes versus no)	8.49 (0.003)	0.28	0.010	0.10–0.73
Radiotherapy (yes versus no)	5.53 (0.018)	0.35	0.031	0.13–0.91
MUM1 (positive versus negative)	1.35 (0.249)	1.97	0.276	0.58–6.71
BCL-6 (positive versus negative)	0.03 (0.863)	0.93	0.870	0.37–2.28
BCL-2 (positive versus negative)	0.27 (0.601)	1.27	0.618	0.49–3.26
CD10 (positive versus negative)	2.79 (0.095)	3.16	0.146	0.67–14.91
Subtype (ABC versus GBC)	0.19 (659)	1.26	0.675	0.43–3.73

ABC: Activated B cell, BCL-2: B cell lymphoma -2, BCL-6: B cell lymphoma -6, CD 10: cluster differentiation 10, GBC: Germinal center B cell, HR: Hazard ratio, MUM1: Multiple myeloma oncogene-1.

Table 3. Mean survival time and its confidence interval of demographic variables and clinical features of patients

	Mean survival time (95% CI)	Median survival time
Gender		
Female	17.56 (7.61-27.51)	11.00
Male	29.25 (14.20-44.30)	12.00
Age		
Less than 60 years	25.42 (14.20-44.30)	13.00
More than 60 years	17.64 (3.17-32.10)	4.00
Chemotherapy		
No	5.33 (0.00-12.71)	1.00
Yes	28.48 (17.59-39.38)	13.00
Radiotherapy		
No	13.53 (5.22-21.83)	2.00
Yes	38.84 (23.28-54.39)	45.00
MUM1		
Negative	31.00 (14.83-47.17)	24.00
Positive	21.46 (11.27-31.64)	8.00
BCL-6		
Negative	18.89 (6.87-30.91)	13.00
Positive	24.54 (12.93-36.16)	12.00
BCL-2		
Negative	26.11 (6.94-45.28)	13.00
Positive	21.19 (11.71-30.67)	11.00
CD10		
Negative	25.41 (15.60- 35.23)	12.00
Positive	2.00 (2.00-2.00)	2.00
MYC1		
Negative	12.00 (14.47-33.24)	12.00
Subtype		
GBC	22.50 (4.90-40.10)	12.00
ABC	23.18 (12.84-33.53)	11.00
Total	12.00 (14.47-33.24)	12.00

ABC: Activated B cell, BCL-2: B cell lymphoma -2, BCL-6: B cell lymphoma -6, CD 10: cluster differentiation 10, GBC: Germinal center B cell, HR: Hazard Ratio, MUM1: Multiple myeloma oncogene-1.

rates. In addition, for all variables, the Kaplan-Meier survival curves is drawn to compare the estimated survival time of the groups (Figure 1). The Kaplan-Meier survival curves for subgroup in Figure 2 shows as the same survivals estimation for germinal center B cell (GCB) and ABC.

Discussion

The present study was conducted on 30 samples from DLBCL patients, and the results showed that most of them were ABC type. Moreover, about 75% of the patients had died during study follow-up, and the mean survival time of patients was 12 months. Demographic characteristics, DLBCL subgroup, and biomarker positivity did not significantly affect the patient's survival. Intergroup survival time comparison showed only significant difference for chemotherapy and radiotherapy variables According to the univariate cox model, chemotherapy and radiotherapy reduce the hazard of death by 72% and 65%, respectively.

The importance of diagnostic and prognostic biomarkers in the identification of the disease origin, estimation of the prognosis or response to treatment, and monitoring of treatment regimens is clear. In our study, as a previous study unlike systemic DLBCLS, the majority of cases were ABC with a low expression of GC markers (CD10 and BCL-6) and high expression of the activated B cell marker (MUM-1). Generally, PCNSL is a rare low-incidence condition that is difficult to study, and there is a need for personalized treatments due to the differences between patients from a cellular and molecular perspective. Therefore, it is clinically important to determine the best treatment for each patient individually and identify cellular biomarkers and measure their relationship with demographic characteristics and patients' survival (14). Various studies have investigated the prognostic significance of biomarkers, such as MUM1, BCL-6, BCL-2, MYC, and CD10 in these patients. However, the results of these studies are often contradictory. Some studies have reported that BCL-6 is a factor for better prognosis (15-17), while such a result has not been reported in some other studies (18-22). Yin et al examined the relationship between the expression rate of CD10, BCL-6, MUM1, BCL-2, and MYC biomarkers and the prognosis on 47 patients and reported that the expression rates of BCL-2 (over 70%) and MYC (over 40%) were not associated with patients' survival (23). The results of a study performed by Liu et al on 89 patients in China indicated that the expression rates of CD10, BCL-6, MUM1, and BCL-2 biomarkers were 16.9%, 51.7%, 92.1%, and 73.3%, respectively, and that none of these could predict patients' prognosis (24). In the same line, Kreher et al, found no relationship between MUM1 expression rate and patients' prognosis (11). Niparuck et al reported the expression rate of 19%, 86%, 91%, 91%, and 23% for CD10, BCL-6, MUM1, BCL-2, and MYC biomarkers in 43 patients, respectively, and reported that CD10 and BCL-2 were associated with good and poor prognosis, respectively (25). In a study conducted on 86 patients in India, MUM1, BCL-6, CD10, and C-MYC were expressed in 80.2%, 32.6%, 2.3%, and 4.6% of patients, respectively. Only BCL-6 was associated with a slightly better prognosis (15). Based on the study performed by Gomes Candido Reis et al, MYC overexpression was associated with a poor prognosis (26). Son et al also reported that MYC was a prognostic factor associated with PCNSL (27). Our findings, did not find any significant correlations between IHC positivity of the studied biomarkers and patient's survival. Also, no significant difference was observed between ABC and GCB on survival time, which is according with earlier studies.

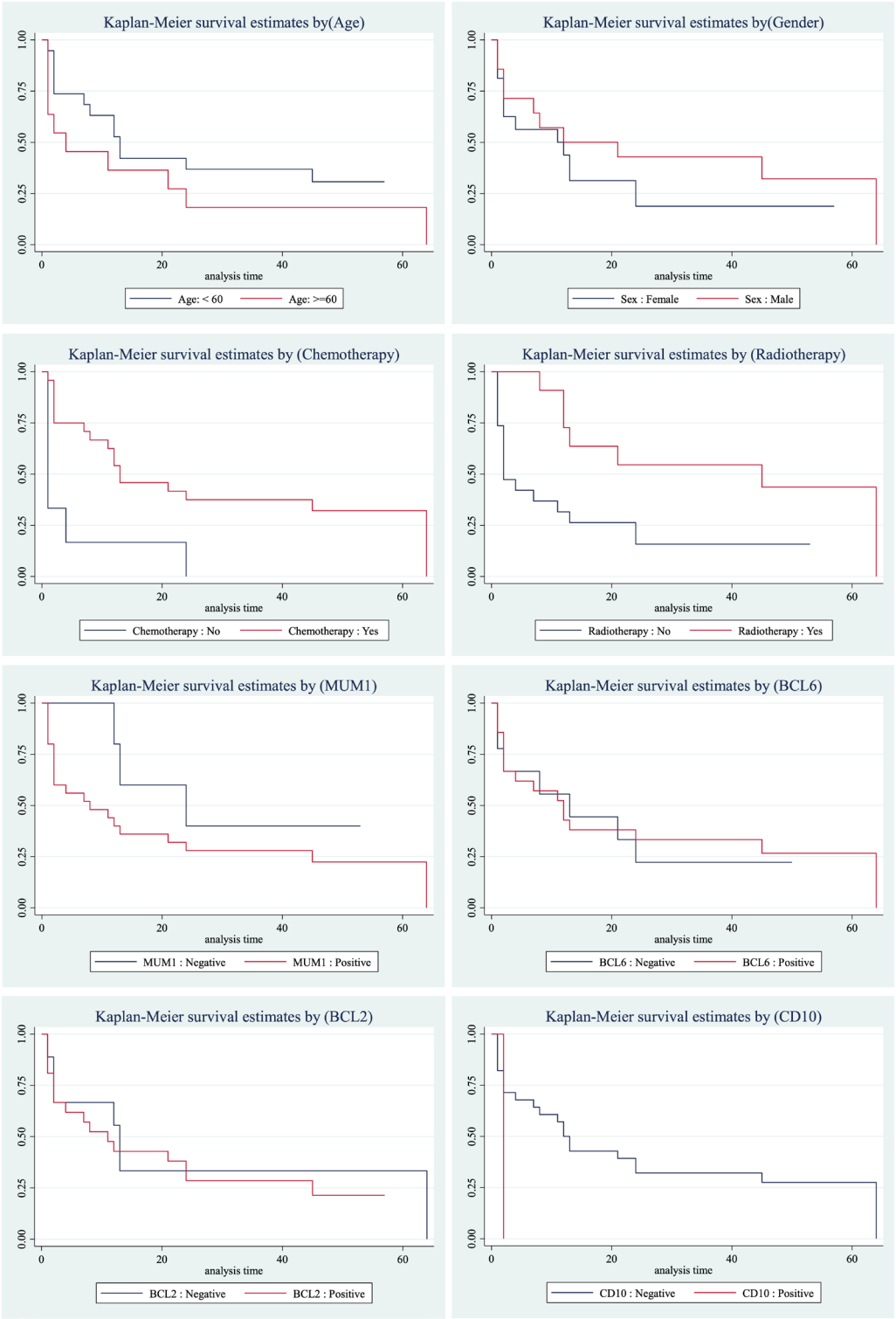

Figure 1. The Kaplan-Meier survival curves for gender; age and clinical features.

Regarding the conflicting results obtained in the above-mentioned studies, it is impossible to reach a single conclusion in terms of the effectiveness of biomarkers in the prognosis of patients due to the rarity of the disease and the small sample size of the studies. However, due to the increasing incidence of this disease for various reasons, such as organ transplantation and the widespread use of immunosuppressive drugs, studies with larger sample sizes are required to investigate the factors affecting the patients' prognosis and treatment.

Conclusion

The results of the present study revealed that the expression rate of MUM1, BCL-6, BCL-2, CD10, and MYC biomarkers

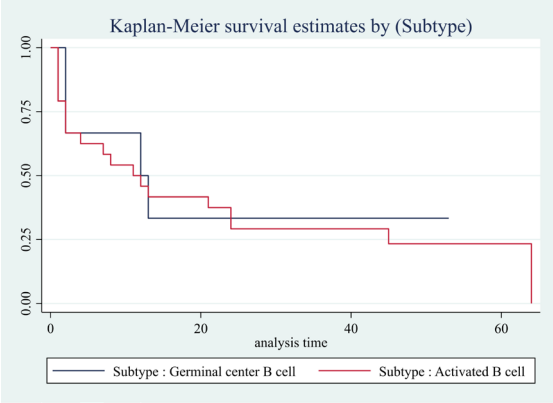

Figure 2. The Kaplan-Meier survival curves to compare germinal center B cell and activated B cell.

did not significantly affect the patients' survival and hence could not be suggested as an appropriate prognostic biomarker in DLBCL patients.

Limitations of the study

One of the most important limitations of this study is the low sample size. However, due to the rareness of the disease, most similar studies also have a sample size.

Author's contribution

Conceptualization: Masoomeh Farahmandfar, Farahnaz Bidari Zerehpoosh.
Data curation: Masoomeh Farahmandfar.
Formal analysis: Masoomeh Farahmandfar.
Investigation: Masoomeh Farahmandfar.
Methodology: Masoomeh Farahmandfar, Farahnaz Bidari Zerehpoosh.
Project Administration: Farahnaz Bidari Zerehpoosh, Masoomeh Farahmandfar.
Resources: Masoomeh Farahmandfar.
Supervision: Farahnaz Bidari Zerehpoosh.
Validation: Masoomeh Farahmandfar, Farahnaz Bidari Zerehpoosh, Guive Sharifi, Omidvar Rezaei, Latif Gachkar.
Writing-original draft: Masoomeh Farahmandfar.
Writing-review and editing: Masoomeh Farahmandfar, Farahnaz Bidari Zerehpoosh, Guive Sharifi, Omidvar Rezaei, Latif Gachkar.

Conflicts of interest

The authors declare no conflict of interest.

Ethical issues

The research adhered to the principles outlined in the Declaration of Helsinki. The Ethics Committee of Shahid Beheshti University of Medical Sciences approved the study (IR.SBMU.RETECH.REC.1399.759). Written informed consent was obtained from all participants prior to any intervention. This study was extracted from M.D thesis of Dr. Masoomeh Farahmandfar at the Department of Pathology at this university (Thesis #24841). Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

References

1. Grommes C, DeAngelis LM. Primary CNS Lymphoma. J Clin Oncol. 2017;35:2410-8. doi: 10.1200/JCO.2017.72.7602.
2. Villano JL, Koshy M, Shaikh H, Dolecek TA, McCarthy BJ. Age, gender, and racial differences in incidence and survival in primary CNS lymphoma. Br J Cancer. 2011;105:1414-8. doi: 10.1038/bjc.2011.357.
3. Corn BW, Marcus SM, Topham A, Hauck W, Curran WJ, Jr. Will primary central nervous system lymphoma be the most frequent brain tumor diagnosed in the year 2000? Cancer. 1997;79:2409-13. doi: 10.1002/(SICI)1097-0142(19970615)79:12<2409::AID-CNCR17>3.0.CO;2-V.
4. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood. 2011;117:5019-32. doi: 10.1182/blood-2011-01-293050.
5. Provencher S, Ferlay C, Alaoui-Slimani K, Devidas A, Lepretre S, de Prijck B, et al. Clinical characteristics and outcome of isolated extracerebral relapses of primary central nervous system lymphoma: a case series. Hematol Oncol. 2011;29:10-6. doi: 10.1002/hon.944.
6. Omuro A, Correa DD, DeAngelis LM, Moskowitz CH, Matasar MJ, Kaley TJ, et al. R-MPV followed by high-dose chemotherapy with TBC and autologous stem-cell transplant for newly diagnosed primary CNS lymphoma. Blood. 2015;125:1403-10. doi: 10.1182/blood-2014-10-604561.
7. Rubenstein JL, Hsi ED, Johnson JL, Jung SH, Nakashima MO, Grant B, et al. Intensive chemotherapy and immunotherapy in patients with newly diagnosed primary CNS lymphoma: CALGB 50202 (Alliance 50202). J Clin Oncol. 2013;31:3061-8. doi: 10.1200/jco.2012.46.9957.
8. Raoux D, Duband S, Forest F, Trombert B, Chambonnière ML, Dumollard JM, et al. Primary central nervous system lymphoma: immunohistochemical profile and prognostic significance. Neuropathology. 2010;30:232-40. doi: 10.1111/j.1440-1789.2009.01074.x.
9. Chen XL, Li XY, Wang W. Effect of B Cell Differentiation Markers on the Prognosis of Primary Central Nervous System Lymphoma. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2017;25:1410-4. doi: 10.7534/j.issn.1009-2137.2017.05.022.
10. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127:2375-90. doi: 10.1182/blood-2016-01-643569.
11. Kreher S, Jöhrens K, Strehlow F, Martus P, Borowiec K, Radke J, et al. Prognostic impact of B-cell lymphoma 6 in primary CNS lymphoma. Neuro-Oncology. 2015;17:1016-21. doi: 10.1093/neuonc/nov046.
12. Lossos C, Bayraktar S, Weinzierl E, Younes SF, Hosein PJ, Tibshirani RJ, et al. LMO2 and BCL6 are associated with improved survival in primary central nervous system lymphoma. Br J Haematol. 2014;165:640-8. doi: 10.1111/bjh.12801.
13. Wn Najmiyah WAW, Azlan H, Faezahtul AH. Classifying DLBCL according cell of origin using Hans algorithm and its association with clinicopathological parameters: A single centre experience. Med J Malaysia. 2020;75:98-102.
14. Krzyszczyk P, Acevedo A, Davidoff EJ, Timmins LM, Marrero-Berrios I, Patel M, et al. The growing role of precision and personalized medicine for cancer treatment. Technology. 2018;6:79-100. doi: 10.1142/s2339547818300020.
15. Radotra BD, Parkhi M, Chatterjee D, Yadav BS, Ballari NR, Prakash G, et al. Clinicopathological features of primary central nervous system diffuse large B cell lymphoma: Experience from a Tertiary Center in North India. Surg Neurol Int. 2020;11:424. doi: 10.25259/sni_314_2020.
16. Braaten KM, Betensky RA, de Leval L, Okada Y, Hochberg FH, Louis DN, et al. BCL-6 expression predicts improved survival in patients with primary central nervous system lymphoma.

Clin Cancer Res. 2003;9:1063-9.
17. Lin CH, Kuo KT, Chuang SS, Kuo SH, Chang JH, Chang KC, et al. Comparison of the expression and prognostic significance of differentiation markers between diffuse large B-cell lymphoma of central nervous system origin and peripheral nodal origin. Clin Cancer Res. 2006;12:1152-6. doi: 10.1158/1078-0432.Ccr-05-1699.
18. Aki H, Uzunaslan D, Saygin C, Batur S, Tuzuner N, Kafadar A, et al. Primary central nervous system lymphoma in immunocompetent individuals: a single center experience. Int J Clin Exp Pathol. 2013;6:1068-75.
19. Camilleri-Broët S, Crinière E, Broët P, Delwail V, Mokhtari K, Moreau A, et al. A uniform activated B-cell-like immunophenotype might explain the poor prognosis of primary central nervous system lymphomas: analysis of 83 cases. Blood. 2006;107:190-6. doi: 10.1182/blood-2005-03-1024.
20. Chang CC, Kampalath B, Schultz C, Bunyi-Teopengco E, Logan B, Eshoa C, et al. Expression of p53, c-Myc, or Bcl-6 suggests a poor prognosis in primary central nervous system diffuse large B-cell lymphoma among immunocompetent individuals. Arch Pathol Lab Med. 2003;127:208-12. doi: 10.5858/2003-127-208-eopmob.
21. Villa D, Tan KL, Steidl C, Ben-Neriah S, Al Moosawi M, Shenkier TN, et al. Molecular features of a large cohort of primary central nervous system lymphoma using tissue microarray. Blood Adv. 2019;3:3953-61.doi:10.1182/bloodadvances.2019000989.
22. Yuan XG, Huang YR, Yu T, Xu Y, Liang Y, Zhang XH, et al. Primary central nervous system lymphoma in China: a single-center retrospective analysis of 167 cases. Ann Hematol. 2020;99:93-104. doi: 10.1007/s00277-019-03821-9.
23. Yin W, Xia X, Wu M, Yang H, Zhu X, Sun W, et al. The impact of BCL-2/MYC protein expression and gene abnormality on primary central nervous system diffuse large B-cell lymphoma. J Neurooncol. 2019;12:2215-23. doi: 10.1007/s11060-018-2990-6.
24. Liu J, Wang Y, Liu Y, Liu Z, Cui Q, Ji N, et al. Immunohistochemical profile and prognostic significance in primary central nervous system lymphoma: Analysis of 89 cases. Oncol Lett. 2017;14:5505-12. doi: 10.3892/ol.2017.6893.
25. Niparuck P, Boonsakan P, Sutthippingkiat T, Pukiat S, Chantrathammachart P, Phusanti S, et al. Treatment outcome and prognostic factors in PCNSL. Diagnostic Pathol. 2019;14:56. doi: 10.1186/s13000-019-0833-1.
26. Gomes Candido Reis D, Levy D, Lage L, Culler HF, Rocha V, Bydlowski SP, et al. New genetic prognostic biomarkers in primary central nervous system lymphoma (PCNSL). Brain Behav. 2021;11:e02061. doi: 10.1002/brb3.2061.
27. Son S-M, Ha S-Y, Yoo H-Y, Oh D, Kim S-J, Kim W-S, et al. Prognostic impact of MYC protein expression in central nervous system diffuse large B-cell lymphoma: comparison with MYC rearrangement and MYC mRNA expression. Mod Pathol. 2017;30:4-14. doi: 10.1038/modpathol.2016.56.