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Original Research

Primary Central Nervous System Lymphomas: A Single-Center Experience

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Abstract

Objectives: Primary central nervous system lymphoma (PCNSL) is a rare and aggressive form of non-Hodgkin lymphoma (NHL). This study aimed to investigate the characteristics, treatment approaches, and outcomes of patients with PCNSL in a single institution.

Methods: We retrospectively analyzed 11 patients with PCNSL treated at our institution between October 2022 and July 2024. Patient demographics, clinical characteristics, treatment modalities, and outcomes were evaluated.

Results: The median age of the patients was 65 years, with male predominance (63.64%). The median follow-up duration was 10 months. All patients were immunocompetent, and 90.91% had diffuse large B-cell lymphoma. At diagnosis, 81% of the patients were considered fit to receive HDMTX treatment. R-MPV was the most common first-line treatment (45.45%). The complete response rate to initial treatment was 80%. The treatment-related mortality was 9.09%. Autologous stem cell transplantation (ASCT) was performed in 72.73% of the patients, with rituximab-thiotepa-carmustine as the predominant conditioning regimen (62.50%). Treatment-related toxicities occurred in 50% of patients, and 87.50% of patients experienced transplant-related complications. The transplantation-related mortality rate was 25%. The relapse rate was 25% among the patients undergoing ASCT. The mortality rate was 36.36%, and cerebellar involvement was significantly associated with a higher mortality rate (p=0.045).

Conclusion: This study demonstrated the efficacy of methotrexate-based regimens and ASCT in the treatment of PCNSL and achieved high complete response rates. However, the significant incidence of treatment-related toxicities and mortality underscores the persistent challenges of managing this disease. In addition, the association between cerebellar involvement and increased mortality requires further investigation. Larger prospective studies are needed to validate these findings.

Keywords: Non-Hodgkin lymphoma, PCNSL, primary central nervous system lymphoma

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Primary central nervous system lymphoma (PCNSL) is a rare subtype of non-Hodgkin lymphoma (NHL) that primarily involves the brain, spinal cord, and eyes, without systemic involvement.[1] The most prevalent form is diffuse large B-cell lymphoma (DLBCL), which most commonly affects the frontal lobe (60%), as well as the thalamus, basal ganglia, and periventricular brain parenchyma.[2-5]

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PCNSL accounts for approximately 2% of all brain tumors and 4-6% of NHL lymphomas, with an estimated incidence rate of 0.45 per 100,000 population.[6] While no clear predisposing factor has been identified in immunocompetent individuals, the duration, type, and nature of immunosuppression may affect the risk of PCNSL in immunocompromised individuals.[7] Epstein-Barr virus (EBV) has also been implicated in certain demographic groups.[8]

Historically, untreated PCNSL patients had a median survival of only two–three months.[9] However, recent advancements in treatment modalities, including high-dose methotrexate, immunotherapy, and radiation therapy, have significantly improved patient outcomes.[10,11]

This study aimed to investigate the characteristics, treatment responses, and adverse events of treatment for patients with PCNSL at our institution, contributing to the growing body of knowledge on this rare and challenging malignancy.

Methods

This study was conducted in compliance with the Declaration of Helsinki and was approved by the local Institutional Ethics Committee on August 6, 2024 (approval number: 4486). It was designed as a single-center, retrospective analysis of medical records and conducted from October 2022 to July 2024.

The medical records of 14 patients diagnosed with non-Hodgkin lymphoma (NHL) through cranial mass biopsy were retrospectively analyzed. Positron emission tomography-computed tomography (PET-CT) and spinal magnetic resonance imaging (MRI) were performed for staging of all patients. Patients with systemic involvement, either concurrent with or prior to central nervous system (CNS) lymphoma diagnosis, were excluded from the study (n=3).

The remaining medical records of 11 patients with primary central nervous system lymphoma (PCNSL) were thoroughly reviewed, and relevant data were extracted. These data included demographic information, clinical characteristics at diagnosis, details of CNS involvement, Memorial Sloan Kettering Cancer Center (MSKCC) prognostic score, treatment modalities, adverse events, and follow-up outcomes.

The MSKCC prognostic score stratified patients based on age and Karnofsky Performance Status (KPS), with Score 1 assigned to patients under 50 years old, Score 2 to patients aged 50 or older with a KPS of 70 or higher, and Score 3 to patients aged 50 or older with a KPS below 70.[12]

Treatment response was evaluated using the International Primary CNS Lymphoma Collaborative Group (IPCG) criteria.[13] Adverse events were classified and assessed according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.[14]

Artificial Intelligence (AI) and AI-assisted Technologies

This article was prepared by the authors, with ChatGPT-4 (OpenAI, 2024) used solely to assist in correcting grammatical errors and refining language for clarity. The authors carefully reviewed and approved the final manuscript to ensure accuracy and originality, with all analyses, conclusions, and interpretations developed independently of AI assistance.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics for Windows (version 25.0; IBM Corp., Armonk, NY, USA), with the normality of continuous variables evaluated through histograms and Q-Q plots. Descriptive statistics are presented as medians (minimum–maximum) for continuous variables owing to their non-normal distribution and as frequencies (percentages) for categorical variables. Continuous variables were analyzed using the Mann-Whitney U test, while categorical variables were analyzed using Fisher's exact test or the Fisher-Freeman-Halton test. Statistical significance was set at $p<0.05$.

Results

The median age was 65 years (range, 51–75 years) in 11 patients with primary central nervous system lymphoma (PCNSL). Of these, 4 (36.36%) patients were female and 7 (63.64%) were male. The Eastern Cooperative Oncology Group (ECOG) performance status was "0" in 1 (9.09%) patient, "1" in 5 (45.45%) patients, "2" in 4 (36.36%) patients, and "3" in 1 (9.09%) patient. The median Karnofsky Performance Status (KPS) score was 90 (range: 40–100). All the patients were immunocompetent.

Disease presentation included hearing loss in 1 (9.09%), aphasia in 1 (9.09%), double vision in 1 (9.09%), gait disturbance in 3 (27.27%), facial numbness in two (18.18%) patients, headache in one (9.09%) patient, dizziness in one (9.09%) patient, altered mental status in two (18.18%) patients, plegia in one (9.09%) patient, and behavioral change in one (9.09%) patient. One patient had aphasia, gait disturbance, and facial numbness, whereas another patient had both hearing loss and double vision. None of the patients had any B symptoms. All diagnoses were confirmed using contrast-enhanced magnetic resonance imaging (MRI).

The site of involvement was frontal in 3 (27.27%) patients, parietal in 3 (27.27%), cerebellar in 2 (18.18%), multicentric in 2 (18.18%), and thalamic in 1 (9.09%). The median tumor size was 30 mm (range: 12–45 mm). Two patients (18.18%) showed multifocal involvement. Cerebrospinal fluid (CSF)

cytology was performed in only 1 (9.09%) patient, with a negative result. None of the patients had systemic or ocular involvement. Histologically, 10 (90.91%) patients had diffuse large B-cell lymphoma (DLBCL), and 1 (9.09%) had follicular lymphoma.

According to the Memorial Sloan Kettering Cancer Center (MSKCC) prognostic score, 10 (90.91%) patients were classified as class 2, and one (9.09%) patient was classified as class 3. Ten (90.91%) patients received first-line therapy. Two (18.18%) patients received the MATRIX regimen (methotrexate, cytarabine, thiotepa, rituximab), 1 (9.09%) received high-dose methotrexate (MTX), 1 (9.09%) received high-dose MTX plus high-dose cytarabine (HIDAC), 5 (45.45%) patients received R-MPV (rituximab, methotrexate, procarbazine, vincristine), and 1 (9.09%) patient received a combination of rituximab, temozolomide, and ibrutinib. Only one (9.09%) patient received MATRIX as second-line treatment, and two (18.18%) patients received radiotherapy.

Treatment-related toxicity occurred in five (50.00%) patients: three (30.00%) developed treatment-related pneumonia, three (30.00%) had liver toxicity, and one (10.00%) had lung damage and COVID-19 pneumonia (two patients had both pneumonia and liver toxicity). Response to treatment was complete remission (CR) in 8 (80.00%) patients, partial remission (PR) in 1 (10.00%), and unknown in 1 (10.00%) patient due to death before evaluation.

Autologous stem cell transplantation (ASCT) was performed in 8 patients (72.73%). The conditioning regimen consisted of rituximab, thiotepa, and carmustine (R-TC) in five (62.50%) patients and thiotepa, busulfan, and carmustine (TBC) in three (37.50%) patients. Seven (87.50%) patients experienced complications during ASCT: one (12.50%) had pneumonia-sepsis (died), one (12.50%) had adrenal insufficiency, one (12.50%) developed cytomegalovirus (CMV), one (12.50%) had BK virus cystitis, two (25.00%) developed febrile neutropenia, one (12.50%) had typhlitis (died), and one (12.50%) developed pancreatitis. One patient had both CMV and BK cystitis. None of the patients had received maintenance therapy.

Two (25.00%) patients experienced relapse: one was treated with radiotherapy (RT) and the other with MATRIX and RT for relapse treatment. Overall, four (36.36%) patients died. The causes of death were disease progression in one (9.09%), COVID-19 in one (9.09%), typhlitis in one (9.09%), and cardiac arrest in one (9.09%). The median follow-up time was 10 months (range: 3–69 months). A significantly higher percentage of cerebellar involvement was observed in the mortality cases than in the other patients (p=0.045, Table 1).

Discussion

A rare and extremely aggressive type of extranodal non-Hodgkin lymphoma (NHL), known as primary central nervous system lymphoma (PCNSL), presents significant challenges for both its diagnosis and management.[15] In our study, all patients were diagnosed through histopathological examination of biopsy specimens. We found that immunocompetent patients with PCNSL achieved an 80% complete response (CR) rate with high-dose methotrexate-containing chemotherapy regimens, with R-MPV as the most commonly used first-line regimen (45.45%). However, treatment-related toxicities and transplant-related complications were common. The mortality rate was 36.36% and cerebellar involvement was associated with a significantly higher risk of mortality.

Individuals diagnosed with PCNSL typically exhibit a variety of neurological or neuropsychiatric manifestations, which can differ based on the tumor's position and dimensions. Systemic symptoms (fever, night sweats, and weight loss) are extremely rare.[16] All patients in this study, consistent with the literature, presented with neurological findings, and none complained of systemic symptoms.

Research has shown that staging with [18F]2-fluoro-2-deoxy-D-glucose positron emission tomography ([18F]FDG-PET), preferably in conjunction with contrast-enhanced CT scans, can identify systemic disease in 4–12% of cases.[17] In our study, PET-CT detected systemic disease in 3 of 14 patients (21.4%). The disease was most frequently found in the frontal lobe and other brain hemisphere areas (38%), followed by the thalamus or basal ganglia (16%), corpus callosum (14%), periventricular regions (12%), cerebellum (9%), meninges (16%), spinal cord (1%), and the cranial and spinal nerves.[17] Furthermore, research has indicated that standard magnetic resonance imaging reveals multifocal disease in 40–50% of patients.[18,19] In our study, multifocal involvement was found in 18% of the cases, which is lower than that reported in the literature. The fact that the early onset of symptoms related to tumor localization and easy and convenient access to health service providers in our country leads to early diagnosis and variables between the populations may be the reason for the current difference. PCNSL affects the cerebrospinal fluid (CSF) in 15–20% of cases and the eyes in 5–20% of cases.[20] In our study, CSF analysis was performed in only one patient and was negative for lymphoma.

Tools for assessing prognosis play a crucial role in the management of PCNSL. To predict outcomes in clinical studies, two scoring systems have been developed: the International Extranodal Lymphoma Study Group (IELSG)[21] and the Memorial Sloan Kettering Cancer Center (MSKCC)[12]

Table 1. Clinical and radiological characteristics of patients with Primary Central Nervous System Lymphoma (PCNSL) and associations with mortality

		Mortality		
	Total (n=11)	**Yes (n=4)**	**No (n=7)**	**p**
Age (n=11)	65 (51 - 75)	61 (51 - 69)	69 (52 - 75)	0.155‡
Gender (n=11)				
Female	4 (36.36%)	0 (0.00%)	4 (57.14%)	0.194#
Male	7 (63.64%)	4 (100.00%)	3 (42.86%)	
ECOG Performance Status (n=11)				
0	1 (9.09%)	0 (0.00%)	1 (14.29%)	1.000¶
1	5 (45.45%)	2 (50.00%)	3 (42.86%)	
2	4 (36.36%)	2 (50.00%)	2 (28.57%)	
3	1 (9.09%)	0 (0.00%)	1 (14.29%)	
Karnofsky Performance Status (n=11)	90 (40-100)	80 (70-90)	90 (40-100)	0.839‡
Immunocompetent (n=11)	11 (100.00%)	4 (100.00%)	7 (100.00%)	N/A
History of lymphoma (n=11)	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Disease presentation (1) (n=11)				
Hear loss	1 (9.09%)	1 (25.00%)	0 (0.00%)	0.364#
Aphasia	1 (9.09%)	1 (25.00%)	0 (0.00%)	0.364#
Double vision	1 (9.09%)	1 (25.00%)	0 (0.00%)	0.364#
Gait disturbance	3 (27.27%)	2 (50.00%)	1 (14.29%)	0.491#
Facial numbness	2 (18.18%)	1 (25.00%)	1 (14.29%)	1.000#
Headache	1 (9.09%)	0 (0.00%)	1 (14.29%)	1.000#
Dizziness	1 (9.09%)	0 (0.00%)	1 (14.29%)	1.000#
Change of mental status	2 (18.18%)	1 (25.00%)	1 (14.29%)	1.000#
Plegia	1 (9.09%)	0 (0.00%)	1 (14.29%)	1.000#
Behavior change	1 (9.09%)	0 (0.00%)	1 (14.29%)	1.000#
B symptoms (n=11)	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Type of imaging at diagnosis (n=11)				
Contrast enhanced MRI	11 (100.00%)	4 (100.00%)	7 (100.00%)	N/A
Contrast enhanced CT	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Site of involvement (n=11)				
Frontal	3 (27.27%)	0 (0.00%)	3 (42.86%)	0.045¶
Parietal	3 (27.27%)	0 (0.00%)	3 (42.86%)	
Cerebellar	2 (18.18%)	2 (50.00%)	0 (0.00%)*	
Multifocal	2 (18.18%)	1 (25.00%)	1 (14.29%)	
Thalamus	1 (9.09%)	1 (25.00%)	0 (0.00%)	
Maximum tumor size, mm (n=5)	30 (12-45)	30 (30-30)	35 (12-45)	0.717‡
PET positive (n=11)	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
CNS fluid cytology (n=11)				
Performed	1 (9.09%)	1 (25.00%)	0 (0.00%)	0.364#
Not performed	10 (90.91%)	3 (75.00%)	7 (100.00%)	
CNS fluid cytology (n=1)				
Positive	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Negative	1 (100.00%)	1 (100.00%)	0 (0.00%)	
Systemic involvement (n=11)	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Ocular involvement (n=11)	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Diagnosis (n=11)				
Diffuse large B cell lymphoma	10 (90.91%)	4 (100.00%)	6 (85.71%)	1.000#
Follicular lymphoma	1 (9.09%)	0 (0.00%)	1 (14.29%)	

Table 1. CONT:

	Mortality			
	Total (n=11)	**Yes (n=4)**	**No (n=7)**	**p**
MSKCC prognostic score (n=11)				
Class 1	0 (0.00%)	0 (0.00%)	0 (0.00%)	1.000#
Class 2	10 (90.91%)	4 (100.00%)	6 (85.71%)	
Class 3	1 (9.09%)	0 (0.00%)	1 (14.29%)	
First line treatment (n=11)	10 (90.91%)	3 (75.00%)	7 (100.00%)	0.364#
Type of first line treatment (n=11)				
None	1 (9.09%)	1 (25.00%)	0 (0.00%)	0.697¶
MATRIX	2 (18.18%)	0 (0.00%)	2 (28.57%)	
High dose MTX	1 (9.09%)	0 (0.00%)	1 (14.29%)	
MTX + HIDAC	1 (9.09%)	0 (0.00%)	1 (14.29%)	
R-MPV	5 (45.45%)	3 (75.00%)	2 (28.57%)	
Rituximab + Temozolomide + Ibrutinib	1 (9.09%)	0 (0.00%)	1 (14.29%)	
Second line treatment (n=11)	1 (9.09%)	0 (0.00%)	1 (14.29%)	1.000#
Type second line treatment (n=11)				
None	10 (90.91%)	4 (100.00%)	6 (85.71%)	1.000#
MATRIX	1 (9.09%)	0 (0.00%)	1 (14.29%)	
Radiotherapy (n=11)	2 (18.18%)	0 (0.00%)	2 (28.57%)	0.491#
Treatment related toxicity (1) (n=10)	5 (50.00%)	1 (33.33%)	4 (57.14%)	1.000#
Pneumonia	3 (30.00%)	0 (0.00%)	3 (42.86%)	0.475#
Liver toxicity	3 (30.00%)	0 (0.00%)	3 (42.86%)	0.475#
Lung damage-COVID 19 pneumonia (died)	1 (10.00%)	1 (33.33%)	0 (0.00%)	0.300#
Treatment response (n=10)				
CR	8 (80.00%)	2 (66.67%)	6 (85.71%)	0.533¶
PR	1 (10.00%)	0 (0.00%)	1 (14.29%)	
SD	0 (0.00%)	0 (0.00%)	0 (0.00%)	
PD	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Not evaluated	1 (10.00%)	1 (33.33%)	0 (0.00%)	
ASCT (n=11)	8 (72.73%)	2 (50.00%)	6 (85.71%)	0.491#
Conditioning regimen (n=8)				
R-TC	5 (62.50%)	0 (0.00%)	5 (83.33%)	0.107#
TBC	3 (37.50%)	2 (100.00%)	1 (16.67%)	
TEAM	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Complications during stem cell transplantation (1) (n=8)	7 (87.50%)	2 (100.00%)	5 (83.33%)	1.000#
Pneumonia –sepsis (died)	1 (12.50%)	0 (0.00%)	1 (16.67%)	1.000#
Adrenal insufficiency	1 (12.50%)	0 (0.00%)	1 (16.67%)	1.000#
CMV	1 (12.50%)	1 (50.00%)	0 (0.00%)	0.250#
BK virus cystitis	1 (12.50%)	1 (50.00%)	0 (0.00%)	0.250#
Febrile neutropenia	2 (25.00%)	0 (0.00%)	2 (33.33%)	1.000#
Typhlitis (died)	1 (12.50%)	1 (50.00%)	0 (0.00%)	0.250#
Pancreatitis	1 (12.50%)	0 (0.00%)	1 (16.67%)	1.000#
Maintenance therapy (n=11)	0 (0.00%)	0 (0.00%)	0 (0.00%)	N/A
Relapse (n=8)	2 (25.00%)	1 (100.00%)	1 (14.29%)	0.250#
Treatment after relapse (n=2)				
RT	1 (50.00%)	1 (100.00%)	0 (0.00%)	1.000#
MATRIX	1 (50.00%)	0 (0.00%)	1 (100.00%)	
Follow-up time, months (n=11)	10 (3-69)	6 (3-10)	16 (6-69)	0.058‡

Descriptive statistics are presented using median (minimum - maximum) for continuous variables and frequency (percentage) for categorical variables. (1) Patients may have more than one of the followings. ‡ Mann-Whitney U test, # Fisher's exact test, ¶ Fisher-Freeman-Halton test, * Statistically significant category, N/A: Not applicable. Statistically significant p-values are shown in bold. ECOG: Eastern Cooperative Oncology Group; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; PET: Positron Emission Tomography; CNS: Central Nervous System; MSKCC: Memorial Sloan Kettering Cancer Center; MATRIX: Methotrexate, Cytarabine, Thiotepa, Rituximab; MTX: Methotrexate; MTX + HIDAC: Methotrexate and High-Dose Cytarabine; R-MPV: Rituximab, Methotrexate, Procarbazine, Vincristine; CR: Complete Remission; PR: Partial Remission; SD: Stable Disease; PD: Progressive Disease; ASCT: Autologous Stem Cell Transplantation; R-TC: Rituximab, Thiotepa, Carmustine; TBC: Rituximab, Thiotepa, Busulfan, Carmustine; TEAM: Thiotepa, Etoposide, Cytarabine, Melphalan; CMV: Cytomegalovirus; RT: Radiotherapy.

prognostic scores.[22] We used the MSKCC prognostic score in our study and found that 90.91% of the patients fell into class 2 and 9.09% fell into class 3. However, there was no difference in overall survival between the scores. This may be because of the small number of patients included in our study. Despite the presence of the two previously mentioned prognostic scoring systems, risk evaluation at the time of diagnosis remains inadequate.[15] Our findings support this notion, as we observed a significant association between cerebellar involvement and mortality (p=0.045), a factor that was not explicitly included in these scoring systems.

Age, comorbidities, and neurocognitive dysfunction are important factors in determining personalized treatment approaches. Treatment strategies should be customized not only according to age but also based on the patient's ability to tolerate intensive therapies. Patient selection for treatment must encompass a comprehensive evaluation, including assessment of performance status (PS), organ function, existing comorbidities, and overall patient frailty. Although pre-treatment PS can guide the determination of treatment intensity, this measure is dynamic and can change throughout the course of treatment, necessitating reassessment after the initial treatment cycle. If PS improves, it allows for adjustments in treatment goals to optimize patient care.[16] Treatment approaches for PCNSL have significantly advanced, with high-dose methotrexate-based chemotherapy (≥3 gr/m^2) emerging as the cornerstone of therapeutic strategies. The Radiation Therapy Oncology Group (RTOG) 9310 protocol initially established high-dose methotrexate as the standard treatment.[23] Subsequently, the International Randomized Phase II IELSG32 study critically compared multiple induction protocols, with the MATRix regimen demonstrating substantially improved progression-free and overall survival rates. Notably, patients receiving consolidation therapy following the MATRix regimen exhibited a remarkable 70% overall survival rate at 7 years, solidifying MATRix's position as a recommended induction treatment protocol.[24,25] However, this treatment has a treatment-related mortality (TRM) rate of 6%. Our study reflects this trend, with various methotrexate-based regimens being utilized as first-line treatments, and the TRM rate was 9.09%. Notably, 45.45% of our patients received R-MPV, which is consistent with current practices. Studies have shown that regimens utilizing high-dose methotrexate, such as R-MPV, followed by high-dose chemotherapy with TBC and ASCT, have demonstrated excellent disease control and overall survival rates.[26] Our findings support this approach, as 72.73% of our patients underwent ASCT, and 37.50% received TBC as the conditioning regimen. However, it is important to consider the effects of these treatments on complications and mortality.

Treatment-related toxicity occurred in five (50.00%) patients, and seven (87.50%) patients experienced complications during ASCT. The treatment-related toxicities increased with increasing treatment intensity. TRM was found to be 10-11% in patients who underwent ASCT after a TBC conditioning regimen.[26,27] In our cohort, two patients (25%) died of transplant-related complications. This high mortality rate may be attributed to the small sample size in our study. The optimal treatment approach is still being studied; however, the 2024 guidelines from the European Hematology Association (EHA) and the European Society for Medical Oncology (ESMO) recommend MTX-based therapy for all patients, regardless of whether they are eligible for ASCT. For patients eligible for ASCT, ThioTepa-based conditioning regimens are recommended as the preferred approach following appropriate initial induction therapy.[16] There is no established standard of care for patients who are not eligible for HD-MTX-based KT. Whole-brain radiation therapy (WBRT), corticosteroids, oral alkylating agents with or without rituximab (not EMA or FDA approved), immunomodulators, and Bruton's tyrosine kinase (BTK) inhibitors, are among the recommendations in the guidelines, though they are supported by a low level of evidence.[16] In our study, only one patient received MTX-free induction therapy (Rituximab + Temozolomide + Ibrutinib) because of a history of autoimmune hepatitis and achieved CR. This is an encouraging result for the use of this combination of therapies in patients who are not eligible for HD-MTX. The efficacy of ibrutinib, PD-1 blockers, and CAR-T therapies has been demonstrated in small patient groups, especially in patients with relapsed refractory PCNSL. However, current new treatment strategies still lack evidence from large-scale prospective trials.[28]

Several studies have suggested that maintenance therapies, including ibrutinib, lenalidomide, and procarbazine, administered after induction chemotherapy have yielded encouraging outcomes in small groups of elderly PCNSL patients.[29] To date, no maintenance therapy agent has received approval from the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA) for treating PCNSL.[29] In our study, none of the patients had received maintenance treatment. Treatment options for relapsed PCNSL include high-dose methotrexate rechallenge, diverse chemotherapy protocols, whole-brain radiation therapy, HSCT, as well as targeted and immunotherapy approaches.[30] In our study, we observed relapse in 2 patients (25%) who underwent stem cell transplantation. These patients received either radiotherapy or a MATRIX regimen for relapse.

The present research is constrained by methodological limitations, including a restricted sample size and retrospective study design, which consequently diminishes the broader applicability of the observed results. As this was a single-center study, the results may not be applicable to other institutions or regions. The short median follow-up period of 10 months restricts conclusions regarding the long-term outcomes. Additionally, the study did not evaluate prognostic factors such as blood biomarkers or cognitive scores, which could provide further insights. Variations in the treatment regimens may also influence the interpretation of treatment outcomes and toxicities. Comprehensive, multi-institutional research is necessary to confirm and validate these findings.

Conclusion

In conclusion, our study offers valuable insights into the management of primary central nervous system lymphoma (PCNSL). Chemotherapy protocols based on methotrexate have demonstrated effectiveness in producing high rates of complete response, while stem cell transplantation has shown promising outcomes. However, treatment-related toxicities and high mortality rates remain major challenges. The association between cerebellar involvement and increased mortality warrants further investigation for improved risk stratification. Although our findings align with the existing literature, they emphasize the need for larger multicenter studies to validate these results and identify novel prognostic factors and treatment strategies. Continued research is crucial to enhance patient outcomes and quality of life for patients diagnosed with PCNSL.

Disclosures

Ethics Committee Approval: The study was approved by the Sisli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee (date: 06.08.2024, no: 4486).

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