International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 04 Issue 03 March 2024

Page No: 542-545

DOI: https://doi.org/10.47191/ijmscrs/v4-i03-31, Impact Factor: 7.949

Prevalence of Central Nervous System Relapse in Diffuse Large B-Cell Lymphoma: A Comprehensive Review

Isai Gallegos Gomez[1], Melissa Anahi Chan Verdugo[2], Jennifer Aida Ortega Romero[3], Daniela Denisse Torreros Lara[4], Rodrigo Garcia Gonzalez[5], Carmen Sabrina Campaña Medina[6], Ariadna Melissa Alonso Padilla[7], Abel Gallegos Aguilar[8], Eotoniel Sanchez Romero[9]

[1,2,3,4,5,6,7,8,9] Residente Medicina Interna. Hospital General Regional #1. Instituto Mexicano del Seguro Social. Tijuana, Baja California, México

ABSTRACT

Central nervous system (CNS) relapse in diffuse large B-cell lymphoma (DLBCL) is a rare but serious complication associated with poor outcomes. The prevalence of CNS relapse in DLBCL varies widely in the literature, ranging from 1% to 30%, depending on several risk factors and diagnostic methods. This article provides a comprehensive review of the current literature on the prevalence of CNS relapse in DLBCL, focusing on risk factors, diagnostic approaches, and treatment strategies. Understanding the epidemiology and clinical characteristics of CNS relapse in DLBCL is crucial for the development of effective preventive and therapeutic strategies.

KEYWORDS: B-cell, lymphoma, nervous system.

ARTICLE DETAILS

Published On:
27 March 2024

Available on:
https://ijmscr.org/

INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma, accounting for approximately 30% to 40% of all cases. While DLBCL is considered a systemic disease, with involvement of extranodal sites being common, central nervous system (CNS) relapse is a rare but devastating complication. CNS relapse in DLBCL is associated with a significantly worse prognosis, with median overall survival ranging from a few weeks to a few months.1,2

The prevalence of CNS relapse in DLBCL is a topic of ongoing debate and investigation. Several risk factors have been identified, including high International Prognostic Index (IPI) score, involvement of certain extranodal sites (such as testes or breast), elevated serum lactate dehydrogenase (LDH) levels, and specific molecular or genetic markers (such as MYC rearrangements or double-hit lymphoma). However, the exact mechanisms underlying CNS relapse in DLBCL remain unclear.3,4

Diffuse large B-cell lymphoma (DLBCL) is the most common lymphoma among non-Hodgkin lymphomas, with a prevalence between 35% and 40%. It is an aggressive disease with high morbidity and mortality, placing a significant demand on the healthcare system for treating the underlying condition and its complications. CNS relapse in patients who have received first-line treatment for DLBCL is a rare but highly fatal event, with patient survival ranging from 2 to 5 months. The primary challenge is identifying high-risk patients to establish appropriate prophylactic measures. The Central Nervous System International Prognostic Index (CNS IPI) is currently the most robust way to identify high-risk patients. Developed by Schmitz N., this index evaluates 6 variables: renal or adrenal involvement, age over 60 years, elevated LDH, ECOG PS greater than 1, stage III/IV, and more than 1 extranodal organ affected, categorizing patients as low, intermediate, or high risk for CNS involvement. However, the patient cohort that validated the score excluded HIV-positive patients and those with spinal cord involvement.4,5,6

Diagnosis of CNS relapse in DLBCL can be challenging, as patients may present with nonspecific symptoms such as headache, altered mental status, or focal neurologic deficits. Imaging studies, such as magnetic resonance imaging (MRI) or cerebrospinal fluid (CSF) analysis, are often used to confirm the diagnosis. Treatment options for CNS relapse in DLBCL include intrathecal chemotherapy, systemic

chemotherapy, and radiation therapy, but optimal management remains a matter of debate.5,6

This article aims to review the current literature on the prevalence of CNS relapse in DLBCL, with a focus on risk factors, diagnostic approaches, and treatment strategies. By gaining a better understanding of the epidemiology and clinical characteristics of CNS relapse in DLBCL, clinicians can improve risk stratification, early detection, and management of this challenging complication.7,8

The prevalence of relapse in the central nervous system (CNS) in diffuse large B-cell lymphoma (DLBCL) is a critical concern in clinical practice. Several studies have addressed this issue, providing valuable insights into the diagnosis, prevention, and management of CNS involvement in DLBCL. The British Society for Haematology (BSH) has published a good practice paper focusing on the prevention of CNS relapse in DLBCL, emphasizing the need for consensus and uniformity in patient care. Similarly, the Spanish Lymphoma Group (GELTAMO) has issued guidelines for the diagnosis, prevention, and management of CNS involvement in DLBCL patients, based on a comprehensive review of available data. These resources offer evidence-based recommendations for clinical practice and contribute to a better understanding of CNS relapse in DLBCL.7,8,9

Furthermore, studies have investigated specific factors associated with CNS relapse in DLBCL. For instance, the absolute peripheral monocyte count at diagnosis has been identified as a predictor of CNS relapse, highlighting the potential role of immune cell populations in disease progression. Additionally, the molecular pathology of DLBCL, including the expression of MYC protein, has been linked to the prognosis of CNS involvement, shedding light on the biological features associated with CNS relapse. These findings underscore the complex interplay of clinical, biological, and molecular factors in the development of CNS relapse in DLBCL.10,11

Moreover, the management of CNS relapse in DLBCL has been a subject of investigation, with studies evaluating treatment strategies, including CNS-directed chemotherapy and stem cell transplantation. Additionally, the role of novel therapies and targeted agents, such as CAR-T cell therapy and BTK inhibitors, in the context of secondary CNS lymphoma has been explored, offering potential avenues for therapeutic intervention. These studies contribute to the ongoing efforts to optimize treatment approaches for CNS relapse in DLBCL.12

In summary, the prevalence of relapse in the CNS in DLBCL is a multifaceted issue that encompasses clinical, biological, and therapeutic dimensions. The available literature, including guidelines, predictive factors, and treatment strategies, provides a comprehensive framework for understanding and addressing CNS involvement in DLBCL.13

CLINICAL MANIFESTATIONS

The clinical manifestations of relapse in the central nervous system (CNS) in diffuse large B-cell lymphoma (DLBCL) are critical for understanding the disease progression and guiding clinical management. Despite achieving complete response with initial treatment, many patients experience relapse with a very poor prognosis. Relapse often occurs within two years, highlighting the aggressive nature of the disease. CNS relapse is associated with poor outcomes, emphasizing the need for effective preventive and therapeutic strategies. Furthermore, the risk of CNS relapse is influenced by various factors, including the molecular subtype of DLBCL and the presence of specific genetic mutations. Additionally, the aggressive clinical behavior of testicular DLBCL is associated with a tendency to relapse in the CNS, underscoring the need for vigilance in monitoring and managing potential CNS involvement.14, 15, 16, 17

Central nervous system (CNS) relapse in diffuse large B-cell lymphoma (DLBCL) can present with a variety of clinical manifestations, which can vary depending on the location and extent of CNS involvement. Recognizing these manifestations is crucial for early detection and management of CNS relapse. Common clinical features of CNS relapse in DLBCL include:

Neurological Symptoms: Patients may present with new or worsening neurological symptoms, such as headache, seizures, focal weakness, sensory deficits, or altered mental status. These symptoms are often related to the location of CNS involvement and may be focal or diffuse.
18, 19

Meningeal Signs: Meningeal involvement, known as leptomeningeal disease, can cause symptoms such as neck stiffness, photophobia, and positive Kernig's or Brudzinski's signs. Meningeal involvement is more common in patients with high-risk features, such as high International Prognostic Index (IPI) score or involvement of certain extranodal sites. 18, 19

Ocular Symptoms: Involvement of the ocular structures, known as ocular lymphoma, can cause symptoms such as blurry vision, floaters, or eye pain. Ocular involvement may occur as an isolated manifestation or as part of CNS relapse. 18, 19

Spinal Cord Compression: Rarely, DLBCL can involve the spinal cord, leading to symptoms of spinal cord compression, such as back pain, weakness, sensory deficits, and bowel or bladder dysfunction. Spinal cord compression requires urgent evaluation and management to prevent permanent neurological damage. 18, 19

Systemic Symptoms: In addition to neurological symptoms, patients with CNS relapse may experience systemic symptoms such as fever, night sweats, weight loss, and fatigue. These symptoms are nonspecific and can occur in various malignancies, including DLBCL. 18, 19

Laboratory Abnormalities: Laboratory tests may reveal abnormalities such as elevated serum lactate dehydrogenase (LDH) levels, which are associated with aggressive disease and increased risk of CNS relapse. 18, 19

Imaging Findings: Imaging studies, such as magnetic resonance imaging (MRI) of the brain and spine, may reveal evidence of CNS involvement, including leptomeningeal enhancement, parenchymal lesions, or spinal cord compression.20

Early recognition and prompt management of CNS relapse in DLBCL are essential for improving patient outcomes. Clinicians should maintain a high index of suspicion for CNS relapse in patients with DLBCL, particularly those with high-risk features, and promptly investigate any new or unexplained neurological symptoms.21

The diagnosis of CNS relapse in DLBCL involves cytologic, immunocytochemical, and molecular examination of cerebrospinal fluid, highlighting the importance of comprehensive diagnostic approaches. Moreover, the management of CNS relapse in DLBCL remains challenging, with studies evaluating the efficacy of different treatment regimens, including CAR-T cell therapy combined with targeted agents, to address relapse in the CNS. However, the effectiveness of certain prophylactic treatments, such as high-dose methotrexate, for preventing CNS relapse in DLBCL has been questioned, emphasizing the need for further research to optimize preventive strategies.22,23

CONCLUSIONS

Based on the analysis of the references, it can be concluded that the prevalence of relapse in the central nervous system (CNS) in diffuse large B-cell lymphoma (DLBCL) is a significant concern in clinical practice. The risk of CNS relapse in DLBCL patients has been the subject of extensive research, with various studies focusing on different aspects of this issue. For instance, guidelines by the Spanish Lymphoma Group (GELTAMO) provide recommendations for the diagnosis, prevention, and management of CNS involvement in DLBCL patients. Similarly, the British Society for Haematology (BSH) has produced good practice papers to address the prevention of CNS relapse in DLBCL, indicating the importance of consensus in improving patient care.

Furthermore, studies have highlighted the distinct clinical and biological features of primary testicular DLBCL and the implications for treatment failure in the rituximab era, emphasizing the need for tailored therapeutic approaches. Additionally, the use of patient-derived xenograft mouse models has been proposed to investigate tropism to the CNS and retina of primary and secondary CNS lymphoma, offering a platform to explore new therapeutic targets.

Moreover, the ineffectiveness of high-dose methotrexate for the prevention of CNS relapse in DLBCL has been reported, suggesting the need for alternative prophylactic strategies. The analysis of absolute peripheral monocyte count at diagnosis has been identified as a potential predictor of CNS relapse in DLBCL, indicating the value of biomarkers in risk stratification.

In conclusion, the prevalence of CNS relapse in DLBCL is a multifaceted issue that requires a comprehensive approach encompassing risk assessment, prophylaxis strategies, and tailored treatments. The findings from these studies underscore the complexity of CNS involvement in DLBCL and the ongoing efforts to improve patient outcomes through evidence-based guidelines and innovative research.

REFERENCES

I. (2020). The prevention of central nervous system relapse in diffuse large b-cell lymphoma: a british society for haematology good practice paper. british journal of haematology, 190(5), 708-714. https://doi.org/10.1111/bjh.16866

II. (2016). Guidelines for diagnosis, prevention and management of central nervous system involvement in diffuse large b-cell lymphoma patients by the spanish lymphoma group (geltamo). haematologica, 102(2),235-245. https://doi.org/10.3324/haematol.2016.149120

III. (2008). Understanding intraocular lymphomas. Clinical and experimental ophthalmology, 36(6), 564-578. https://doi.org/10.1111/j.1442-9071.2008.01843.x

IV. (2017). Central nervous system relapse of diffuse large b-cell lymphoma in the rituximab era: results of the uk ncri r-chop-14 versus 21 trial. Annals of oncology, 28(10), 2511-2516. https://doi.org/10.1093/annonc/mdx353

V. Warley F, Cristaldo N, Colucci G, Otero V. Recaída en sistema nervioso central en linfoma difuso de células B grandes: estudio de cohorte retrospectiva [Central nervous system relapse in diffuse large B lymphoma: a retrospective cohort study]. Rev Fac Cien Med Univ Nac Cordoba. 2021 Jun 28;78(2):142-146. Spanish. doi: 10.31053/1853.0605.v78.n2.28183. PMID: 34181848; PMCID: PMC8741305.

VI. (2015). Treatment strategies in primary vitreoretinal lymphoma. jama ophthalmology, 133(2), 191. https://doi.org/10.1001/jamaophthalmol.2014.4755

VII. (2014). Absolute peripheral monocyte count at diagnosis predicts central nervous system relapse in diffuse large b-cell lymphoma. haematologica, 100(1), 87-90. https://doi.org/10.3324/haematol.2014.114934

VIII. (2010). most primary central nervous system diffuse large b-cell lymphomas occurring in immunocompetent individuals belong to the nongerminal center subtype: a retrospective analysis

of 31 cases. Modern pathology, 23(2), 235-243. https://doi.org/10.1038/modpathol.2009.164

IX. (2001). Primary breast lymphoma: a report of 20 cases. british journal of haematology, 115(2), 253-256. https://doi.org/10.1046/j.1365-2141.2001.03047.x

X. (2017). Secondary cns relapse in diffuse large b-cell lymphoma: defining high-risk patients and optimization of prophylaxis strategies. Hematology, 2017(1), 578-586. https://doi.org/10.1182/asheducation-2017.1.578

XI. (2019). Primary testicular lymphoma: a seer analysis of 1,169 cases. Oncology letters. https://doi.org/10.3892/ol.2019.9953

XII. (2015). Primary testicular diffuse large b-cell lymphoma displays distinct clinical and biological features for treatment failure in rituximab era: a report from the international ptl consortium. Leukemia, 30(2), 361-372. https://doi.org/10.1038/leu.2015.237

XIII. (2016). Diffuse large b-cell lymphoma with testicular involvement: outcome and risk of cns relapse in the rituximab era. british journal of haematology, 176(2), 210-221. https://doi.org/10.1111/bjh.14392

XIV. (2023). Real-world experiences of cns-directed chemotherapy followed by autologous stem cell transplantation for secondary cns involvement in relapsed or refractory diffuse large b-cell lymphoma. Frontiers in oncology, 12. https://doi.org/10.3389/fonc.2022.1071281

XV. (2015). High frequency of myd88 mutations in vitreoretinal b-cell lymphoma: a valuable tool to improve diagnostic yield of vitreous aspirates. Blood, 126(1), 76-79. https://doi.org/10.1182/blood-2015-01-620518

XVI. (2022). Systemic relapse in a young adult patient with primary cns diffuse large b-cell lymphoma. Case reports in hematology, 2022, 1-9. https://doi.org/10.1155/2022/7139661

XVII. (2023). Phosphoproteome analysis of cerebrospinal fluid extracellular vesicles in primary central nervous system lymphoma. The analyst, 148(15), 3594-3602. https://doi.org/10.1039/d3an00670k

XVIII. (2021). Ineffectiveness of high-dose methotrexate for prevention of cns relapse in diffuse large b-cell lymphoma. american journal of hematology, 96(7), 764-771. https://doi.org/10.1002/ajh.26181

XIX. (2012). Isolated central nervous system relapses in primary mediastinal large b-cell lymphoma after chop-like chemotherapy with or without rituximab. Hematological oncology, 31(1), 10-17. https://doi.org/10.1002/hon.2012

XX. (2021). Prophylaxis with intrathecal or high-dose methotrexate in diffuse large b-cell lymphoma and high risk of cns relapse. Blood cancer journal, 11(6). https://doi.org/10.1038/s41408-021-00506-3

XXI. (2018). Adrenal relapse of primary central nervous system diffuse large b-cell lymphoma. Medicine, 97(38),e12482. https://doi.org/10.1097/md.0000000000012482

XXII. (2014). lmo2 and bcl6 are associated with improved survival in primary central nervous system lymphoma. british journal of haematology, 165(5), 640-648. https://doi.org/10.1111/bjh.12801

XXIII. (2022). Case report: cd19-directed car-t cell therapy combined with btk inhibitor and pd-1 antibody against secondary central nervous system lymphoma. Frontiers in immunology, 13. https://doi.org/10.3389/fimmu.2022.983934