



Review Article

Primary Central Nervous System Lymphoma (PCNSL): Challenging A Paradigm.

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ABSTRACT

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Primary central nervous system lymphoma (PCNSL) is a subtle and intrusive extranodal non-Hodgkin lymphoma (NHL) that is restricted to the, eyes, brain, leptomeninges or spinal cord without efficient entanglement. The overall prognostication, diagnosis, and execution of PCNSL alter from those for other forms of NHL. Instantaneous prognosis and inception of medication are crucial for developing analytical issues. PCNSL is susceptible to radiation treatment; however, whole-brain radiotherapy (WBRT) incompetently controls the ailment when it is used alone, and its deferred neurotoxicity neurocognitive deterioration, specifically in elderly subjects. High-dosage methotrexate (HD-MTX)-established induction chemotherapy with or without autologous stem cell transplantation (ASCT) or decrease-dosage WBRT leads to reliable ailment control and lesser neurotoxicity. The excellent medication has yet to be prescribed; however, HD-MTX-based induction chemotherapy is advised standard for newly prognosticated PCNSL. Currently randomized trials are addressing the aspects of rituximab and consolidative medication with ASCT or reduced-dosage of WBRT. Despite high tumor response rates with the antecedent medication, many subject's recurrence with a very poor diagnosis. The excellent medication for relapsed or refractory PCNSL is ill defined. The preferred salvage medication depends on a subject's age, previous medication and response, performance status, and comorbidities at the time of recurrence.

INTRODUCTION:

Primary central nervous system lymphoma (PCNSL) has been acknowledged by various other names, including diffuse histiocytic lymphoma, microglioma, and reticulum cell sarcoma, the procreation of names emulates primary scepticism about the corpuscle of origin.

PCNSL is now acknowledged to be a type of extranodal, high-grade non-Hodgkin B-cell neoplasm, commonly large corpuscle or immunoblastic form. It emanates in the eyes, leptomeninges, spinal cord, brain, generally remains incarcerated to the CNS; and infrequently escalates outside the nervous system. Therefore, it can be classified as phase 2 ailment. Formerly a strange cyst accounting for less than 2% of cerebral neoplasms, PCNSL is being observed with rising recurrence in immunocompetent subjects. Despite the corpuscles of origin are lymphocytes, PCNSL should be treated as a brain cyst, because its curative challenges simulate those of other brain cyst. In precise, drug transmission is damaged by the blood-brain barrier, and cerebral toxicity restrains the use of applicable medication modalities.

Most of PCNSLs (about 90%) are disseminated large B-cell lymphomas (DLBCLs); the rest 10% are ill-defined low-grade lymphomas, Burkitt lymphomas, and T-cell lymphomas. Initial manifestation may result

from local mass repercussion due to raised intracranial pressure, from ocular involvement, or from focal deposits on cranial or spinal nerve roots.

ETIOLOGY:

Established peril aspect for CNS lymphomas, both primary and secondary, include accomplished and/or ingrained immunodeficiency states. PCNSL is an AIDS-construing ailment related with low CD4 corpuscle count (<50 cells/L) and Epstein Barr virus (EBV). In efficient AIDS-associated lymphomas, EBV flu of the cyst may be anticipated of increased uncertainty for secondary CNS entanglement. Ingrained immunodeficiency states such as serious-combined or frequently-variable immunodeficiency, Wiskott-Aldrich or ataxia-telangiectasia ailment are related with a ~4% peril of evolving PCNSL. Post-emigrate lymphoproliferative disorder (PTLD) involving the CNS develops in 1–2% of renal emigrate recipients and 2–7% recipients of cardiac, alveolus and liver emigrates. CNS PTLT is strongly related with EBV in the setting of iatrogenic T-cell immunodeficiency induced by agents such as mycophenolate mofetil. Among PCNSL subjects without clue of immune suppression, EBV ailment of the lymphoma is subtle.

Recent and active randomized controlled trials for PCNSL

S.No.	Trial	Regimen	Status
1	G-PCNSL-SG1	HD-MTX-based induction +/- WBRT consolidation	Active
2	IELSG-20	HD-MTX +/- HD-Ara-C- > WBRT consolidation	Active
3	IELSG-32	Myeloablative vs. WBRT consolidation	Accrual complete
4	Alliance 51101	Intensive vs. myeloablative consolidation	Active
5	PRECIS	Myeloablative vs. WBRT consolidation	Active
6	Matrix/IELSG43	Intensive vs. myeloablative consolidation	Active

DISCUSSION:

Over the course of the prior half-century the oncology/ haematology association has made momentous progress in the medication of PCNSL, a contentious variant of large B-cell lymphoma. We can now foresee that between 40–50% of PCNSL subjects will exhibit long-term continuity and a compelling proportion may be ameliorated. It is expected that in the next five years of clinical trials will target on development of interference established upon high-dose chemotherapy.

At least 40–50% of PCNSL subjects will advance ailment refractory to the entrenched apparatus of agents, it is now crucial that additional analyses explore the possible efficacy of selective agents that aim candidate defiance mechanisms in high-risk PCNSL subjects. For example, pharmacologic agents that assess disruption of pathways entangling the B-cell receptor, toll-like receptor, JAK-STAT, mTOR, and PIM kinases should be treated high preference in initial phase investigation in PCNSL. Another key target is MUM-1/IRF-4, targeted by the IMiD category of small molecule agents such as pomalidomide or lenalidomide, presently under appraisal in PCNSL in initial phase clinical trials (122). Clarification of a molecular diagnostic index for peril-adapted medication in PCNSL is also a key goal for analysis in this field. Transformational advances are recommended in PCNSL given its propensity for an aging populace that cannot condone dosage-intensive chemotherapy or WBRT. The peril is 2-6% in AIDS subjects according to clinical data and will possibly further increase with the length of survival in these subjects. Emigrate subjects carry a peril of 1-5% to grow a PCNSL. The peril is 2-7% for cardiac, alveolus or liver and 1-2% for renal emigrate recipients. Subjects with ingrained immune deficiency have a peril of 4%. PCNSL may also show as a secondary malignancy.

CONCLUSION:

Immunological analysis has suggested a role for Epstein-Barr virus in the formation of this cyst. Although subtypes exist, non-

Hodgkin's lymphoma of the CNS most generally subsists of histiocytic corpuscle or large immunoblastic corpuscle bearing B corpuscle surface markers in closeness to the third ventricles and lateral. Sixty percent of these deposits are multiple, and subarachnoid aggression is observed in one-quarter of subjects. Vitreous entanglement of the eye appearing prior to and during the course of CNS lymphoma has been observed in up to 25% of subjects. The entanglement of multiple areas of the eye, and multiple intracranial sites often appears in the absence of conspicuous systemic lymphoma. Curative trials of brain radiation medication a related with median survivals of less than 1 year. Homogenous complete responses of intracranial deposits are reported following chemotherapy with high-dose intravenous methotrexate, Oncovin (vincristine), CHOP (cyclophosphamide, hydroxy daunomycin/doxorubicin, and prednisone), high-dose cytosine arabinoside, and intra-arterial methotrexate with barrier modification.

REFERENCES:

1. Miller DC, Hochberg FH, Harris NL, Gruber ML, Louis DN, Cohen H. Pathology with clinical correlations of primary central nervous system non-Hodgkin's lymphoma. The Massachusetts General Hospital experience 1958-1989. *Cancer*. 1994 Aug 15. 74(4):1383-97.
2. Ding Y, Xing Z, Liu B, Lin X, Cao D. Differentiation of primary central nervous system lymphoma from high-grade glioma and brain metastases using susceptibility-weighted imaging. *Brain Behav*. 2014 Oct 10.
3. Sugita Y, Tokunaga O, Nakashima A, Shigemori M. SHP-1 expression in primary central nervous system B-cell lymphomas in immunocompetent patients reflects maturation stage of normal B cell counterparts. *Pathol Int*. 2004 Sep. 54(9):659-66.
4. Montesinos-Rongen M, Schmitz R, Courts C, et al. Absence of immunoglobulin class switch in primary lymphomas of the central

- nervous system. *Am J Pathol.* 2005 Jun. 166(6):1773-9.
5. Gill KZ, Iwamoto F, Allen A, Hoehn D, Murty VV, Alobeid B, et al. MYC Protein Expression in Primary Diffuse Large B-Cell Lymphoma of the Central Nervous System. *PLoS One.* 2014. 9(12):e114398.
 6. Pulczynski EJ, Kuittinen O, Erlanson M, Hagberg H, Fosså A, Eriksson M, et al. Successful change of treatment strategy in elderly patients with primary central nervous system lymphoma by de-escalating induction and introducing temozolomide maintenance: results from a phase 2 study by The Nordic Lymphoma Group. *Haematologica.* 2014 Dec 5.
 7. Kranick SM, Goncalves PH, Stetler-Stevenson M, Aleman K, Polizzotto MN, Little RF, et al. Paradoxical central nervous system immune reconstitution syndrome in acquired immunodeficiency syndrome-related primary central nervous system lymphoma. *Haematologica.* 2014 Oct 10.
 8. Corboy JR, Garl PJ, Kleinschmidt-DeMasters BK. Human herpesvirus 8 DNA in CNS lymphomas from patients with and without AIDS. *Neurology.* 1998 Feb. 50(2):335-40.
 9. Gomez-Brouchet A, Delisle MB, Vital A, Brousset P. Immunohistochemical assessment of human herpesvirus 8 infection in primary central nervous system large B cell lymphomas. *J ClinPathol.* 2001 Aug. 54(8):617-8.
 10. Levin N, Soffer D, Grissaru S, Aizikovitch N, Gomori JM, Siegal T. Primary T-cell CNS lymphoma presenting with leptomeningeal spread and neurolymphomatosis. *J Neurooncol.* 2008 Oct. 90(1):77-83.
 11. Lenarz M, Durisin M, Becker H, Lenarz T, Nejadkazem M. Primary central nervous system lymphoma presenting as bilateral tumors of the internal auditory canal. *Skull Base.* 2007 Nov. 17(6):409-12.
 12. Khong P, Pitham T, Oowler B. Isolated neurolymphomatosis of the cauda equina and filum terminale: case report. *Spine.* 2008 Oct 1. 33(21):E807-11.
 13. Fischer L, Martus P, Weller M, Klasen HA, Rohden B, Röth A, et al. Meningeal dissemination in primary CNS lymphoma: prospective evaluation of 282 patients. *Neurology.* 2008 Sep 30. 71(14):1102-8.
 14. Voloschin AD, Betensky R, Wen PY, Hochberg F, Batchelor T. Topotecan as salvage therapy for relapsed or refractory primary central nervous system lymphoma. *J Neurooncol.* 2008 Jan. 86(2):211-5.
 15. Grimm SA, McCannel CA, Omuro AM, Ferreri AJ, Blay JY, Neuwelt EA, et al. Primary CNS lymphoma with intraocular involvement: International PCNSL Collaborative Group Report. *Neurology.* 2008 Oct 21. 71(17):1355-60.
 16. Korfel A, Elter T, Thiel E, et al. Phase II study of central nervous system (CNS)-directed chemotherapy including high-dose chemotherapy with autologous stem cell transplantation for CNS relapse of aggressive lymphomas. *Haematologica.* 2013;98:364-70. [PMC free article] [PubMed]
 17. Wieduwilt MJ, Valles F, Issa S, et al. Immunochemotherapy with intensive consolidation for primary CNS lymphoma: a pilot study and prognostic assessment by diffusion-weighted MRI. *Clin Cancer Res.* 2012;18:1146-55.
 18. Rubenstein JL, Gupta NK, Mannis GN, et al. How I treat CNS lymphomas. *Blood.* 2013;122:2318-30.
 19. Rubenstein JL, Hsi ED, Johnson JL, et al. Intensive chemotherapy and immunotherapy in patients with newly diagnosed primary CNS lymphoma: CALGB 50202 (Alliance 50202) *J ClinOncol.* 2013;31:3061-8.
 20. Cingolani A, Gastaldi R, Fassone L, et al. Epstein-Barr virus infection is predictive of CNS involvement in systemic AIDS-related non-Hodgkin's lymphomas. *J ClinOncol.* 2000;18:3325-30.

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