Case Report

pISSN 1738-6217 • eISSN 2765-6608

J Korean Stereotact Neurosurg 2021;17(2):114-121

<https://doi.org/10.52662/jksfn.2021.00039>

Received: June 4, 2021

Revised: August 22, 2021

Accepted: August 23, 2021

Address for correspondence:

Yong-sook Park, MD

Department of Neurosurgery, Chung-Ang
University Hospital, Chung-Ang University
College of Medicine, 102 Heukseok-ro,
Dongjak-gu, Seoul 06973, Korea

Tel: +82-2-6299-1610

Fax: +82-2-6299-2064

E-mail: cuttage@cau.ac.kr

ORCID: <https://orcid.org/0000-0003-1152-6844>

Primary central nervous system lymphoma in the brainstem and cervical spinal cord: a case report and literature review

Ju-Sung Jang, MD, Yong-sook Park, MD

Department of Neurosurgery, Chung-Ang University Hospital, Seoul, Korea

Primary central nervous system lymphoma is an uncommon type of extranodal non-Hodgkin's lymphoma, and lymphoma in the brain stem and spinal cord is rare. We report a case of primary lymphoma that developed from the medulla oblongata to the cervical spinal cord, which was considered inflammation or glioma before the pathologic report enabled the correct diagnosis. A 56-year-old male presented with decreased light touch sensation on the left hemibody and disequilibrium that had lasted for a month. On imaging, a T2-hyperintense lesion mimicking a glioma was found extending from the medulla oblongata to the spinal cord at C2. Open biopsy at the posterior column of the C1 area was performed and histopathology indicated a diffuse large B-cell lymphoma. After a complete staging evaluation, chemotherapy was administered. Equivocal lesions on imaging should be diagnosed pathologically to provide sufficient information for proper management.

KEY WORDS: Brain neoplasms, Non-Hodgkin lymphoma, Spinal cord neoplasms, Medulla oblongata lymphoma

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is an uncommon type of extranodal non-Hodgkin's lymphoma, which involves the brain, leptomeninges, eyes, or spinal cord without evidence of systemic disease [1]. It accounts for 1.5% of non-Hodgkin's lymphomas, and lymphoma of the brain stem and spinal cord is extremely rare, accounting for 1–3% of PCNSLs [2-4]. The very low incidence of this tumor and its diverse imaging presentation makes its diagnosis difficult.

Here, we report a case of primary lymphoma occurring from the medulla oblongata to the cervical spinal cord, which was considered inflammation before the pathologic report was revealed.

CASE REPORT

A 56-year-old male, with no medical history, presented with disequilibrium and sensory changes in the arm and leg, which was more severe in the left hemibody, 1 month previously. He had felt left-sided weakness 10 days prior to his visit to our hospital. On physical examination, sensations of touch on the left side were diminished and motor weakness was grade 4+. The deep tendon reflex of the left leg was hyperactive and the other limbs were normoactive. He tested positive for the Romberg test. Magnetic resonance imaging (MRI) of the cervical spine at the time

showed a diffuse T2/fluid attenuated inversion recovery hyperintense infiltrative lesion in the medulla oblongata to C2 spinal cord with multifocal patchy enhancement in the periphery of the lesion, and mild diffusion restriction in the anterior aspect of the medulla (Fig. 1). The initial suspicion was a tumorous condition including high-grade glioma and diffuse midline glioma or demyelinating disease. Laboratory tests including infection markers and peripheral blood cell counts were within the normal range. A serologic test for human immunodeficiency virus was negative. A cerebrospinal fluid (CSF) exam showed white blood cell count 5/ μ L, red blood cell count 5/ μ L, protein 76 mg/dL, glucose 75 mg/dL, and lactate dehydrogenase 17 IU/L, which had a non-specific pattern. CSF culture revealed no growth of tuberculosis, bacteria, or virus, and there were no malignant cells in the cytology of CSF. The patient underwent open biopsy of the lesion under general anesthesia. The spinal cord was swollen from the central region to the left, so the posterior median sulcus was not clear. There were black, diffuse, and minute pigmentations on the pial membrane similar to finely-spread pepper. Small pieces of the spinal cord were obtained on the left side of the C1 area, which was enhanced in the MRI and thought to correspond to the posterior column.

In the biopsy report, hematoxylin and eosin staining showed the diffuse proliferation of round cells with a hyperchromatic nucleus

that was larger than that of a normal histiocyte nucleus. Immunohistochemistry was positive for cluster differentiation (CD) 20, CD79a, B-cell lymphoma 2, and CD10, and 40% of tumor cells were Ki-67 positive. The confirmatory result of the biopsy was diffuse large B-cell lymphoma (Fig. 2). The patient had an enhanced computerized tomography scan of the chest, abdomen and pelvis, and a positron emission tomography scan to assess the presence of a lymphoid tumor. There was no malignancy in other organs, which confirmed primary intramedullary lymphoma in the brainstem to high cervical spinal cord. He was started on chemotherapy. Five 14-day cycles of induction chemotherapy with rituximab, methotrexate, procarbazine, and vincristine were given as follows: day 1, rituximab 500 mg/ m^2 ; day 2, methotrexate 3.5 mg/ m^2 (over 2 hours), vincristine 1.4 mg/ m^2 ; day 1–7, procarbazine 100 mg/ m^2 /d (odd cycles only). After the 2nd cycle, there was a partial response on c-spine MRI (Fig. 3). He received a 3rd cycle of chemotherapy, and is going to receive reduced-dose whole brain radiotherapy. After radiotherapy, he is going to receive two consolidation high-dose cytarabine cycles (one cycle = 28 days). Currently, he is alive 20 months after his neurologic symptoms presented.

Ethical statements

Informed consent was waived by the Board.

Fig. 1. Initial brainstem and cervical spinal cord magnetic resonance imaging. (A) A diffuse infiltrative lesion from the medulla oblongata to the C2 spinal cord with high signal intensity on a T2-weighted image. (B) Multifocal patchy enhancement in the periphery of the lesion on a T1-weighted enhanced image.

Fig. 2. Pathology. (A) Immunohistochemistry shows positive CD20 staining suggesting B-cell lymphoma (×200). (B) Hematoxylin and eosin (H&E) staining shows the diffuse proliferation of round cells with hyperchromatic nuclei that are larger than the nuclei of normal histiocytes (×400).

Fig. 3. Follow-up magnetic resonance imaging after the second cycle of chemotherapy. (A) The hyperintense lesion had changed to an isointense lesion on a T2-weighted image. (B) Decreased extent of the known lymphoma on a T1-weighted enhanced image.

DISCUSSION

We reviewed recent case reports of PCNSL in the brain stem (Table 1) [5-9] and spinal cord (Table 2) [10-28]. For brain stem lesions, patients developed diplopia and dysarthria suggesting cra-

nial nerve dysfunction as well as hemibody weakness. Symptom progression tended to be fast from 2 weeks to 2 months.

For spinal cord PCNSL (Table 2), various ages, sex, and locations were noted. Locations of PCNSL were evenly distributed throughout all levels of the spinal cord from the cervical spine to

Table 1. Summary of brainstem lymphomas

Report	Age (yr)/sex	Location	Imaging characteristic	Presentation	Diagnosis	Outcome	Remark
Kim and Kim (2016) [5]	9/F	Cerebellar peduncle	Well enhanced	Diplopia, dysarthria, gait disturbance, hemibody weakness	DLBCL	Died in 10 months	Remission in 3 months after chemotherapy, died due to acute hydrocephalus crisis
Shams et al. (2002) [6]	54/M	Posterior pons, tectal plate, cerebellar peduncle, thalamus, internal capsule	Nodular enhanced	Ocular myasthenia gravis	DLBCL	Died in 2 months	Steroids used before biopsy
Larner et al. (1999) [7]	73/M	Pons	Circumscribed, homogeneously enhanced	Diplopia, speech disturbance, unsteadiness, hemifacial numbness	DLBCL	Died	Steroids used before biopsy
Campbell et al. (2005) [8]	55/F	Pons	Irregular margin, uniformly enhanced	Hemibody weakness, diplopia, headache	DLBCL	Partial remission after 2 months	
McCue et al. (1993) [9]	60/M	Midbrain, pons, medulla, middle cerebellar peduncle to cerebellar hemisphere	Circumscribed, peripheral enhancing lesion	Dysarthria, dysphagia, vertigo, diplopia, gait instability	T	Died before biopsy on hospital day 6	Diagnosed by autopsy

F: female, M: male, DLBCL: diffuse large B-cell lymphoma, T: T-cell lymphoma.

Table 2. Summary of primary spinal cord lymphomas

Report	Age (yr)/sex	Location	Imaging	Presentation	Diagnosis	Outcome	Remark
Elavarasi et al. (2018) [10]	18/M	CM junction-C7	High SI in T2, not enhanced	Progressive walking difficulty	Lymphoma	Mild weakness on lower limbs remained as a sequelae	Diagnosed by CSF cytology, misdiagnosed initially as tuberculosis
Chida et al. (2017) [11]	79/M	C1	High SI in T2, presyrinx state in medulla oblongata-C5, homogeneously enhanced	Numbness in the left arm, left-sided weakness	DLBCL	Complete remission in 3 months	
Hertlinger et al. (2002) [12]	36/F	C1-6	Inhomogeneous high SI on T2-enhanced imaging	Radiating pain and sensory loss in both upper extremities	Malignant lymphoblastic B-cell lymphoma	Not mentioned	
Lin et al. (2012) [13]	75/F	C1-T5	Enhanced	Ascending paraparesis, stool incontinence	Not mentioned	Not mentioned	Misdiagnosed initially as demyelinating disease
Bini Viotti et al. (2018) [14]	37/M	C2-3	Inhomogeneous ring enhancement	Left-sided weakness	High-grade B-cell lymphoma	Died due to sepsis 115 days after the diagnosis	
Machiya et al. (2007) [15]	60/F	C2-7	Enhanced	Sensory loss and mild weakness in both legs	DLBCL	Not mentioned	
Ezon et al. (2014) [16]	40/M	C2-T1	Enhanced	Right arm weakness, paresthesia, urinary and fecal incontinence	DLBCL	Complete remission in 3.5 months	
Beume et al. (2019) [17]	67/F	C6-T12	Inhomogeneous high SI in T2, high SI in T1, enhanced	Gait disturbance, reduced sensory in lower extremities, bowel and bladder dysfunction	DLBCL	Marked reduction of spinal lesion, but no improvement of neurologic deficit, treatments were terminated	

(Continued to the next page)

Table 2. Continued

Report	Age (yr)/sex	Location	Imaging	Presentation	Diagnosis	Outcome	Remark
Guzik (2018) [18]	44/M	C7-T1	High SI in T2, enhanced, ringomyelia (C2-7, T1-7)	Reduced sensory in the left lower limb, and right shoulder pain	DLBCL	Complete remission for 3 years	Misdiagnosed initially as ependymoma
Sivri et al. (2015) [49]	50/F	T7-8	High SI in T2, isointensity in T1, homogeneously enhanced	Back pain, leg weakness, walking and urinating disorder	DLBCL	Not mentioned	
Guzzetta et al. (2015) [20]	82/M	T7-cauda equina	High SI in T2	Not mentioned	T	Died	Diagnosed by autopsy
Bhushanam et al. (2014) [21]	11/M	T8-1	Iso to high SI in T2, high SI in T1, moderately enhanced	Weakness of both lower limbs	DLBCL	Complete remission for 2 years	
Toshkezi (2010) [22]	71/F	T11-12	Leptomeningeal enhancement in T9 to cauda equina	Low back pain with progressive right leg weakness	Histiocytic sarcoma	Died 5 months after diagnosis	
Teo et al. (2012) [23]	58/M	T11-L4	Minimally enhanced	Progressive back pain, and bilateral leg pain, numbness, and weakness	DLBCL	Symptoms relieved in 2 years	
Sato et al. (2013) [24]	37/M	T spinal cord	High SI in T2, enhanced	Left leg paresis, right paresthesia	DLBCL	Complete remission	
Legéais et al. (2004) [25]	71/F	Conus medullaris	High SI in T2, not enhanced	Gradually progressive sensory loss and weakness in both legs over 2 weeks	Angiotrophic large cell lymphoma	Complete remission after 19 months	Invasion of brain, brain biopsy was done
Morita et al. (2009) [26]	67/M	Cauda equina	Low SI in T2, homogeneous enhancement	Leg pain and weakness, bowel and bladder dysfunction	Natural killer/T	Died in 14 months	
Broen et al. (2014) [27]	75/F	Cauda equina	Thickening of nerve roots, enhanced	Weakness and sensory loss in the left foot	DLBCL	Died in 6 months	Atypical cells found in CSF
Broen et al. (2014) [27]	71/F	Cauda equina	Thickening of nerve roots, enhanced	Paresthesia, dysesthesia, and weakness in the right leg	DLBCL	Complete remission after 8th chemotherapy	Atypical cells found in CSF
Feng et al. (2018) [28]	45/M	Cauda equina	Enhancement in meninges and nerve roots	Progressive tremor in left limbs	DLBCL	Died in 2 weeks	Abundant lymphocytes in CSF

M: male, F: female, CM: cervicomedullary, T: T-cell lymphoma, DLBCL: diffuse large B-cell lymphoma, CSF: cerebrospinal fluid.

the cauda equina (9 cases of cervical spine, 8 cases of thoracic spine, and 6 cases of lumbar spine and cauda equina). The patients developed various myelopathy symptoms depending on the location of the lesions.

In an immunocompetent patient, lymphoma is classically described as a solitary mass with intense homogeneous enhancement. MRI typically reveals low signal intensity on T1-weighted images and an isointense or hypointense signal on T2-weighted images [29]. However, in an immunocompromised patient, the proportion of rim enhancement or hyperintense signal on T2-weighted images is higher than that of an immunocompetent patient [29-31], and lymphomas tend to present as multiple lesions. In the literature, most cases showed typical radiological findings, but there were quite a few different images. For example, no enhancement, inhomogeneous enhancement, and leptomeningeal enhancement were presented and inhomogeneous signal intensity in T2-weighted image, or syringomyelia [18] was reported. Because of these various radiologic findings of brain stem or spinal cord lymphoma and its rarity, misdiagnosis at the initial state is common.

The lesion in our case showed scattered enhancement, diffuse swelling, and enlargement in the lower brain stem and cervical spinal cord. Because the patient had no evidence of human immunodeficiency virus or other immune deficiency, the heterogeneous enhancement was thought not related to lymphoma. In addition, the incidence of intramedullary spinal cord lymphoma is very rare and he did not present with 'B-symptoms' such as sweating, fever, and weight loss; therefore, the first differential diagnosis included glioma rather than lymphoma. When we reviewed several articles of PCNSL, various imaging patterns emerged indicating radiology findings are not typical or specific for differential diagnosis from other central nervous system diseases.

It is important to confirm the diagnosis histologically. In many cases, steroids were used to relieve symptoms without biopsy. Patients using steroids presented with symptom relief initially but deteriorated again for a few days or weeks [6,7,10,15,24]. This can induce disease progression and delay the diagnosis and proper treatment. There have been three reported cases of initial misdiagnosis including ependymoma, tuberculosis, and demyelinating disease [10,13,18]. Lymphocytic pleocytosis in a CSF exam is likely to lead many physicians to consider tuberculosis, and high protein levels in the CSF suggest a demyelinating disease. Malignant cells were only found in 2 cases of the reports we reviewed. In all cases, diagnoses were obtained through biopsy or CSF cytology. In many cases, CSF examination showed inconclusive results, suggesting that the specificity of CSF cytology is low and therefore is of low diagnostic value. Therefore, unless a biopsy is performed and pathologic results are checked, the specific diagnosis for

PCNSL is difficult. Early biopsy should be considered for brain stem or spinal cord lesions that might be primary cancer.

The optimal treatment for PCNSL has not been established. High-dose methotrexate (HD-MTX) and rituximab is used as basic regimen for induction therapy. Combined chemical treatment with vincristine, procarbazine, temozolomide, or cytarabine could be added. Reduced-dose whole brain radiation (WBRT) for minimizing neurologic side effects could be added [32]. For consolidation, radiation and conventional chemotherapy (cytarabine, etoposide) is used. High dose chemotherapy and autologous stem cell transplantation can be considered for the patients who are younger and have no organ failure [32-34].

The median survival of untreated patients with PCNSL is 3 months, and the patient who treated with methotrexate-based chemotherapy and WBRT have a median survival of 36 months to 60 months [33,35]. Prognosis of patients with primary refractory or recurrent PCNSL is poorer with median survival of 2 months without additional treatment. There is no consensus about the optimal treatment of recurrent PCNSL, however WBRT and HD-MTX rechallenge seems to be effective in small studies [32]. The patients who were treated with MTX rechallenge had median overall survival of 41 to 62 months, and the patients with WBRT had median overall survival of 10 to 16 months [32,36,37]. There is a large difference in prognosis between untreated and treated PCNSL patients, and this is another reason why early diagnosis through biopsy is important.

CONCLUSION

For lesions that might be primary cancer, early biopsy can help achieve a correct diagnosis, avoiding progression of the disease, and improving its prognosis.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Jiménez de la Peña MD, Vicente LG, Alonso RC, Cabero SF, Suárez AM, de Vega VM. The multiple faces of nervous system lymphoma. Atypical magnetic resonance imaging features and contribution of the advanced imaging. *Curr Probl Diagn Radiol* 2017;46:136-45
2. Koeller KK, Smirniotopoulos JG, Jones RV. Primary central nervous system lymphoma: radiologic-pathologic correlation. *Ra-*

- diographics 1997;17:1497-526
3. Murray K, Kun L, Cox J. Primary malignant lymphoma of the central nervous system. Results of treatment of 11 cases and review of the literature. *J Neurosurg* 1986;65:600-7
4. O'Neill BP, Illig JJ. Primary central nervous system lymphoma. *Mayo Clin Proc* 1989;64:1005-20
5. Kim J, Kim YZ. A case of primary central nervous system lymphoma located at brain stem in a child. *Brain Tumor Res Treat* 2016;4:155-9
6. Shams PN, Waldman A, Plant GT. B cell lymphoma of the brain stem masquerading as myasthenia. *J Neurol Neurosurg Psychiatry* 2002;72:271-3
7. Larner AJ, D'Arrigo C, Scaravilli F, Howard RS. Bilateral symmetrical enhancing brainstem lesions: an unusual presentation of primary CNS lymphoma. *Eur J Neurol* 1999;6:721-3
8. Campbell PG, Jawahar A, Fowler MR, Delaune A, Nanda A. Primary central nervous system lymphoma of the brain stem responding favorably to radiosurgery: a case report and literature review. *Surg Neurol* 2005;64:400-5; discussion 405
9. McCue MP, Sandrock AW, Lee JM, Harris NL, Hedley-Whyte ET. Primary T-cell lymphoma of the brainstem. *Neurology* 1993;43:377-81
10. Elavarasi A, Dash D, Warriar AR, Bhatia R, Kumar L, Jain D, et al. Spinal cord involvement in primary CNS lymphoma. *J Clin Neurosci* 2018;47:145-8
11. Chida K, Sugawara A, Koji T, Beppu T, Mue Y, Sugai T, et al. Primary intramedullary malignant lymphoma in the cervical cord with a presyrinx state. *Cureus* 2017;9:e2006. doi: 10.7759/cureus.2006
12. Herrlinger U, Weller M, Küker W. Primary CNS lymphoma in the spinal cord: clinical manifestations may precede MRI detectability. *Neuroradiology* 2002;44:239-44
13. Lin YY, Lin CJ, Ho DM, Guo WY, Chang CY. Primary intramedullary spinal cord lymphoma. *Spine J* 2012;12:527-8
14. Bini Viotti J, Doblecki S, Luca CC, Mackrides N, Vega F, Alcaide ML. Primary intramedullary spinal cord lymphoma presenting as a cervical ring-enhancing lesion in an AIDS patient. *Open Forum Infect Dis* 2018;5:ofy128. doi: 10.1093/ofid/ofy128
15. Machiya T, Yoshita M, Iwasa K, Yamada M. Primary spinal intramedullary lymphoma mimicking ependymoma. *Neurology* 2007;68:872. doi: 10.1212/01.wnl.0000257150.31403.61
16. Ezon IC, Barteselli G, Rosenberg J, Freeman WR. Concurrent primary vitreoretinal and spinal cord lymphoma: a unique entity. *JAMA Ophthalmol* 2014;132:902-4
17. Beume LA, Wolf K, Urbach H, Klingler JH, Staszewski O, Marks R, et al. Primary intraspinal non-Hodgkin's lymphoma: case report and review of literature. *J Clin Neurosci* 2019;61:262-4
18. Guzik G. Primary B-cell spinal cord lymphoma of the cervical spine. *Ortop Traumatol Rehabil* 2018;20:219-27
19. Sivri M, Erdoğan H, Allahverdiyev I, Koplay M, Temizöz O. A rare cause of spinal mass: primary intramedullary spinal cord lymphoma. *Spine J* 2015;15:e43-4
20. Guzzetta M, Drexler S, Buonocore B, Donovan V. Primary CNS T-cell lymphoma of the spinal cord: case report and literature review. *Lab Med* 2015;46:159-63
21. Bhushanam TV, Rajesh A, Linga VG, Uppin MS, Malik M. Primary intramedullary non-Hodgkin's lymphoma in an immunocompetent child. *Spinal Cord* 2014;52 Suppl 2:S21-3
22. Toshkezi G, Edalat F, O'Hara C, Delalle I, Chin LS. Primary intramedullary histiocytic sarcoma. *World Neurosurg* 2010;74:523-7
23. Teo MK, Mathieson C, Carruthers R, Stewart W, Alakandy L. Cauda equina lymphoma—a rare presentation of primary central nervous system lymphoma: case report and literature review. *Br J Neurosurg* 2012;26:868-71
24. Sato H, Takahashi Y, Wada M, Shiono Y, Suzuki I, Kohno K, et al. Lymphomatosis cerebri with intramedullary spinal cord involvement. *Intern Med* 2013;52:2561-5
25. Legeais M, Gallas S, Cottier JP, Herbreteau D. Paraplegia and sensory deficit caused by angiotropic large cell lymphoma. *AJNR Am J Neuroradiol* 2004;25:1831-5
26. Morita M, Osawa M, Naruse H, Nakamura H. Primary NK/T-cell lymphoma of the cauda equina: a case report and literature review. *Spine (Phila Pa 1976)* 2009;34:E882-5
27. Broen M, Draak T, Riedl RG, Weber WE. Diffuse large B-cell lymphoma of the cauda equina. *BMJ Case Rep* 2014;2014:bcr2014205950. doi: 10.1136/bcr-2014-205950
28. Feng L, Chen D, Zhou H, Shen C, Wang H, Sun X, et al. Spinal primary central nervous system lymphoma: case report and literature review. *J Clin Neurosci* 2018;50:16-9
29. Erdag N, Bhorade RM, Alberico RA, Yousuf N, Patel MR. Primary lymphoma of the central nervous system: typical and atypical CT and MR imaging appearances. *AJR Am J Roentgenol* 2001;176:1319-26
30. Dina TS. Primary central nervous system lymphoma versus toxoplasmosis in AIDS. *Radiology* 1991;179:823-8
31. Johnson BA, Fram EK, Johnson PC, Jacobowitz R. The variable MR appearance of primary lymphoma of the central nervous system: comparison with histopathologic features. *AJNR Am J Neuroradiol* 1997;18:563-72
32. Grommes C, DeAngelis LM. Primary CNS lymphoma. *J Clin Oncol* 2017;35:2410-8
33. Illerhaus G, Marks R, Ihorst G, Gittenberger R, Ostertag C, Derigs G, et al. High-dose chemotherapy with autologous stem-

- cell transplantation and hyperfractionated radiotherapy as first-line treatment of primary CNS lymphoma. *J Clin Oncol* 2006;24:3865-70
34. Milpied N, Deconinck E, Gaillard F, Delwail V, Foussard C, Berthou C, et al; Groupe Ouest-Est des Leucémies et des Autres Maladies du Sang. Initial treatment of aggressive lymphoma with high-dose chemotherapy and autologous stem-cell support. *N Engl J Med* 2004;350:1287-95
35. DeAngelis LM, Seiferheld W, Schold SC, Fisher B, Schultz CJ; Radiation Therapy Oncology Group Study 93-10. Combination chemotherapy and radiotherapy for primary central nervous system lymphoma: Radiation Therapy Oncology Group Study 93-10. *J Clin Oncol* 2002;20:4643-8
36. Pentsova E, Deangelis LM, Omuro A. Methotrexate re-challenge for recurrent primary central nervous system lymphoma. *J Neurooncol* 2014;117:161-5
37. Plotkin SR, Betensky RA, Hochberg FH, Grossman SA, Lesser GJ, Nabors LB, et al. Treatment of relapsed central nervous system lymphoma with high-dose methotrexate. *Clin Cancer Res* 2004;10:5643-6