Parenchymal central nervous system involvement in aggressive B-cell lymphoma: retrospective analysis of clinical and MRI features in a Chinese population

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Abstract

Introduction

Secondary central nervous system lymphoma (SCNSL) was defined as secondary central nervous system (CNS) involvement in patients with systemic lymphoma. Parenchymal involvement of the CNS in aggressive B-cell lymphoma was rare and remains a diagnostic dilemma.

Materials and Methods

In our study, we retrospectively analyzed the clinical and magnetic resonance imaging (MRI) features of 26 parenchymal SCNSL patients. In addition, we compared MRI features between SCNSL and primary CNS lymphoma (PCNSL) patients after 1:1 propensity score matching.

Results

Among SCNSL patients, the median CNS relapse time was 3 months, and multiple lesions were found in 76.9% of the cases. In PCNSL, this percentage was 34.8% (p=0.023). None of the SCNSL patients and 11.5% of the PCNSL patients had solitary infratentorial lesions (p=0.011).

Conclusions

the majority of parenchymal involvement occurred within the first year of systemic lymphoma, in which mostly cases presenting with multiple and supratentorial locations, unlike what was found in PCNSL.

Background

CNS lymphoma (CNSL) is an aggressive and rare brain neoplasm that can involve the brain, meninges, spinal cord, and eyes. Secondary CNS lymphoma is defined as secondary CNS involvement in patients with systemic lymphoma[1],[Scott, 2013 #1] Diffuse large B-cell lymphomas (DLBCLs) are the most common lymphoid neoplasms in adults, in which they account for approximately 32.5% of NHLs diagnosed annually. Secondary CNS involvement, which affects approximately 5% of patients with DLBCL, is considered a profoundly adverse complication with a median post-SCNSL overall survival of only 3.9-7.2 months[2, 3].

SCNSL can be generally divided into three conditions: systemic lymphoma combined with CNS involvement at presentation (combined disease), CNS involvement at the time of systemic relapse or
progression (CNS with disease progression) and isolated CNS relapse despite systemic remission (isolated CNS disease)[4, 5]. The patterns of CNS involvement can be categorized as leptomeningeal, parenchymal, eye or combined. Spinal cord, peripheral nerve, or systemic involvement is uncommon as an initial manifestation of CNS lymphoma[6]. Despite intrathecal injection and intravenous application of methotrexate for CNS prophylaxis, 5% of systematic DLBCL patients eventually present with involvement of the central nervous system[7].

A diagnosis of SCNSL is usually made based on a combination of clinical presentation, radiological manifestations (enhanced MRI), and cerebral spinal fluid tests (conventional cytology and flow cytometry)[1]. Enhanced MRI of parenchymal SCNSL in symptomatic patients was highly informative[8]. However, patients with systematic DLBCL usually received corticosteroids included chemotherapy, and imaging features and differential diagnostic considerations may be altered by exposure to corticosteroids or in a setting involving immunosuppression[1]. The clinical presentations and neuroimaging characteristics of affected patients may mimic those of other progressive neurologic disorders, including primary brain tumor, demyelinating disease, autoimmune or paraneoplastic syndromes, or CNS infection. SCNSL is challenging to detect, especially in the early stage, due to its diversity of magnetic resonance imaging (MRI) patterns and the complicated immune status of patients[9, 10].

No current report describes the clinical and MRI features of parenchymal involvement of aggressive B-cell lymphoma in the Chinese population. This study aims to summarize the clinical information of parenchymal CNS involvement in DLBCL and compare the magnetic resonance (MR) imaging features of primary and secondary CNS lymphomas to provide a clinical and imaging overview of this rare and fatal disease.

Methods

Patients Clinical data were retrospectively reviewed at the Department of Hematology, Beijing Tiantan Hospital, Capital Medical University (Beijing, China) and the Department of Neurosurgery, Navy General Hospital (Beijing, China) between 2012 and 2019. There were a total of 26 SCNSL and 26 PCNSL patients. All of them were HIV-negative. The present study protocol was approved by the
Ethics Committees of Beijing Tiantan Hospital and Navy General Hospital. All patients gave written informed consent to participate in this study.

**Diagnosis of CNS lymphoma** The diagnosis of CNS relapse was based on the combination of clinical CNS features, radiological findings and histological findings of tumors. All PCNSL patients had histologically confirmed systemic lymphoma, 24 (92.3%) received stereotactic biopsy and 2 (7.7%) underwent intracranial tumor resection. Among SCNSL patients, 24 (92.3%) received stereotactic biopsy or intracranial tumor resection, and 2 (7.7%) were diagnosed by enhanced MRI. The immune-histochemical markers CD20, CD10, BCL-6, BCL-2, MUM1, CD138, EBER and Ki-67 were analyzed, and immunophenotype classification was based on Hans’ method.

**Statistical analysis** The distributions of the characteristics of the patients were examined using the \( \chi^2 \) test. All statistical analyses were performed using SPSS 17.0 (SPSS, Inc., Chicago, IL, USA). \( P<0.05 \) was considered to indicate a statistically significant difference.

**Results**

**Characteristics of SCNSL patients at initial systemic disease diagnosis**

Clinical findings are shown in Table 1. Half of the SCNSL patients (n=13) were older than 60 years old when diagnosed with systematic aggressive B cell lymphoma. Extranodal involvement was observed in 14 (53.8%) patients, breast involvement in 15.4% (n=4), testicular involvement in 11.5% (n=3), and involvement of the intestines, parotid gland, oral cavity, rhino, orbit and spleen in 26.9% (n=7). The histological findings were DLBCL in 92.3% (n=24) of the patients, mantle-cell lymphoma in 3.5% (n=1), and follicular lymphoma in 3.5% (n=1). For the initial treatment, 42.3% (n=11) of the patients used Rituximab-containing therapy. Only 7.7% (n=2) of the patients received intravenous HD-MTX for CNS prophylaxis.

**Clinical and physiological findings, relapse site, pathological findings, and treatment at CNS relapse.**

All patients presented with brain parenchymal lesions, and one patient also had spinal cord compression. The symptoms of CNS relapse varied with location; the most common symptom was headache, and no epilepsy was observed in our study. Eye symptoms, such as blurred vision, were
observed in 26.9% (n=7) of the patients. The time from clinical presentation to a definite diagnosis ranged from 4 to 180 days (median 30 days). One patient died of post-operation intracranial hemorrhage. Three patients presented to our center initially as PCNSL but were later detected as having systemic disease and were distributed to SCNSL.

In this study, 80.8% (n=21) of the patients were categorized as having isolated CNS relapse, 19.2% (n=6) had concurrent CNS and systematic disease, and those in whom CNS involvement was found after the first year of systemic disease were more likely to have isolated CNS relapse (p=0.034) (Table 2). Regarding the time of relapse, 73.1% (n=19) had CNS relapse within the first five years after diagnosis with systemic disease with a median CNS relapse time of 3 years (Fig. 1). Twenty-two patients underwent biopsy or surgery, and two of these were diagnosed with enhanced MRI.

Pathological results showed that all were DLBCL, and of these, 92.3% (n=24) were ABC subtypes, while others were GCB. BCL2 and BCL6 expression was detected in 75% (n=18) of the patients, MYC was positive in 15 out of 16 (93.7%) of the SCNSL patients, and 93.75% presented with Ki-67 higher than 90%.

**MRI findings in SCNSL and PCNSL patients (Table 3).**

**Multiplicity and localization** Parenchymal involvement was present in all SCNSL patients, with multiple lesions found in 76.9% (n=20) of the cases; in PCNSL, this proportion was 42.3% (n=11) (p=0.023). The SCNSL lesions were located in the deep gray matter in 68% (n=17) and in the white matter in 84% (n=21) of the patients; in PCNSL, these ratios were 46.2% (n=12) and 65.4% (n=17). Brainstem involvement was detected in only 12% (n=3) of SCNSL cases but was observed in 34.6% (n=9) of PCNSL patients (p=0.097). In SCNSL, supratentorial lesions were seen in 64% (n=16) of the cases and concomitant supratentorial and infratentorial lesions in 36% (n=9), and none of them had solitary infratentorial lesions. Among the PCNSL patients, 23.1% (n=6) had solitary infratentorial lesions (p=0.017).

**Signal characteristics** The signal characteristics of SCNSL and PCNSL were quite similar. On T1-weighted (T1W) images, lesions were hypointense in 76% (n=19), hyperintense in 4% (n=1), and isointense in 12% (n=3) of SCNSLs. The T2-weighted (T2W) signal of the lesions was hyperintense in
65.2% (n=15) of SCNSL and 92.3% (n=24) of PCNSL patients. T2 Flair hyperintensity was detected in 83.3% (n=10) of the patients. Diffusion-weighted imaging (DWI) hyperintensity was found in 80% (n=12) of the SCNSL patients, while all of the PCNSL patients presented with hyperintensity on DWI (p=0.043).

**Enhancement pattern** In the SCNSL group, the enhancement pattern was homogenous nodular in 64% (n=16), patchy in 24% (n=6) and ring-like in 4% (n=1) of the cases. Notably, 8% (n=2) of the patients presented with lesions without enhancement (Fig. 2). One SCNSL patient initially had no enhancement on MRI and was diagnosed with anti-NMDA-receptor encephalitis, but eventually, with the progression of the disease, the tumor developed enhancement, and stereotactic biopsy confirmed DLBCL with CNS involvement (Fig. 3).

**Discussion**

In the Rituximab era, the rate of CNS relapse of DLCBL in the form of parenchymal disease is increasing[11]. This condition accounts for high mortality[2] and shortened overall survival of less than 6 months[3]. Early diagnosis of CNS events is critical for successful treatment and improved prognosis. Some patients with typical MRI features, conventional cerebrospinal fluid (CSF) cytology and CSF flow cytometry tests could allow a definite diagnosis of SCNSL. However, in some patients, MRI features could be untypical at the initial of CNS relapse, making it difficult to confirm diagnosis. Stereotactic biopsy is a standard procedure in PCNSL diagnosis but is not routinely observed in SCNSL due to its invasion and its relatively limited sensitivity (20%–65% in immunocompetent patients). We observed that PCNSL and SCNSL share some common MRI manifestations; moreover, SCNSL had some unique characteristics when compared with PCNSL.

CNS relapse in DLBCL is reported to mainly occur within the first year after diagnosis (median, 6 months)[12]. In our study, the median CNS relapse time was 3 months, which corresponds to previous reports. The distribution of CNS involvement times also indicates that early relapse or concurrent disease is not rare in SCNSL groups, suggesting that affected patients harbor occult malignant cells in the CNS at diagnosis[13-15]. The incidence of CNS relapse decreased after the introduction of rituximab following a change in the pattern of CNS relapse, with a predominance of parenchymal over
leptomeningeal relapse and of isolated over combined (systemic plus CNS) relapse[2]. Increasing reports indicate that SCNSL presents as a parenchymal disease[14, 16-18]. Hana Malikova et al recently presented a series of SCNSL cases in which parenchymal lesions occurred in 18 out of 21 cases, indicating that SCNSL presents as a parenchymal disease.

Efsun Senocak reported that SCNSL predominantly presents as multiple lesions, while deep gray matter and infratentorial involvement were scarce but not statistically significant, perhaps because of a relatively small sample size[19]. In our study, the sample size was larger, and SCNSL presented with multiple lesions, in contrast to PCNSL (p=0.016), and infratentorial and brainstem involvement were significantly rarer in SCNSL patients. Thus, there was a statistically significant difference in the investigated MR features between the two groups.

Two patients with SCNSL presented with lesions showing hyperintensity on T2 Flair without enhancement, although the mechanism remains unknown. In PCNSL, Tabouret E et al found that nonenhancing FLAIR abnormalities may add to the overall tumor burden, and they suggested that response criteria should be refined to incorporate the evaluation of T2-weighted/FLAIR sequences[20]. Thus, we postulated that this pattern of nonenhanced lymphoma may be due to the alternated immune state related to corticosteroid-containing chemotherapy as both patients were receiving standard treatment for systemic DLBCL when the CNS lesions occurred. Koubska et al found that there were statistically significant differences in morphological MRI findings between immunocompromised and immunocompetent patients with CNSL. The authors speculated that the enhancement differences between immunocompromised and immunocompetent patients may be related to corticosteroid therapy[21]. Hana Malikova et al also introduced varied MR performance in SCNSL in their study, which showed that SCNSL can mimic progressive multifocal leukoencephalopathy and multiple ischemic lesions. Moreover, this could be a unique manifestation of SCNSL, and further research should explore the correlation between MRI features and biological characteristics.

Conclusions
Due to the rarity of parenchymal SCNSL, very few studies have summarized its characteristics on MRI.
This study provides an overview of the characteristics of both clinical and MRI presentations in SCNSL patients. Additionally, we compared SCNSL and PCNSL to further identify their unique radiological findings. The majority of parenchymal involvement occurred within the first year of systemic lymphoma, and those in whom CNS involvement was found after the first year of systemic disease were more likely to have isolated CNS relapse. For MRI features, SCNSL mostly presented at multiple and supratentorial locations and was significantly different from PCNSL in this regard. Moreover, nonenhancement MRI could not rule out the possibility of SCNSL, T2 Flair may provide more information, and dynamic monitoring on MRI could help in patient diagnosis.

**Abbreviations**

SCNSL: secondary central nervous system lymphoma; CNS: central nervous system; PCNSL: primary central nervous system lymphoma; HD-MTX: High-dose methotrexate; PFS: progression free survival; CSF: cerebrospinal fluid; WBRT: whole brain radiotherapy; DWI: diffusion weighted imaging; T2W : T2-weighted imaging; FLAIR: fluid-attenuated inversion recovery;

**Declarations**

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**Availability of data and materials**

All data generated or analyzed during this study are included in this published article.

**Authors’ contributions**

LYB and WYM designed the study; WYM and JN provided the patient samples; SSJ revised neuroimaging; WYM and WYC analyzed the data and wrote the manuscript; SXF, CQ, ZH and QJ performed the experiments; BXY, XRX, CYD and GJY collected and analyzed the data; and all the authors have read the manuscript and approved its submission.

**Ethics approval and consent to participate**
Ethics approval and consent to participate was approved by Beijing Tiantan Hospital Ethics Committee, Capital medical university. Ethical approval reference number: KYSB2016-170.

**Consent for publication**

All patients involved in this study gave consent for the publication of the clinical data.

**Competing interests**

The authors declare that they have no competing interests.

**References**

1. Scott BJ, Douglas VC, Tihan T, Rubenstein JL, Josephson SA. A systematic approach to the diagnosis of suspected central nervous system lymphoma. JAMA neurology. 2013;70 3:311-9; doi: 10.1001/jamaneurol.2013.606.

2. Zhang J, Chen B, Xu X. Impact of rituximab on incidence of and risk factors for central nervous system relapse in patients with diffuse large B-cell lymphoma: a systematic review and meta-analysis. Leukemia & lymphoma. 2014;55 3:509-14; doi: 10.3109/10428194.2013.811239.

3. Fletcher CD, Kahl BS. Central nervous system involvement in diffuse large B-cell lymphoma: an analysis of risks and prevention strategies in the post-rituximab era. Leukemia & lymphoma. 2014;55 10:2228-40; doi: 10.3109/10428194.2013.869326.

4. Haioun C, Besson C, Lepage E, Thieblemont C, Simon D, Rose C, et al. Incidence and risk factors of central nervous system relapse in histologically aggressive non-Hodgkin's lymphoma uniformly treated and receiving intrathecal central nervous system prophylaxis: a GELA study on 974 patients. Groupe d'Etudes des Lymphomes de l'Adulte. Annals of oncology : official journal of the European Society for Medical Oncology. 2000;11 6:685-90.

5. Tomita N, Kodama F, Kanamori H, Motomura S, Ishigatsubo Y. Secondary central nervous system lymphoma. International journal of hematology. 2006;84 2:128-35; doi: 10.1532/ijh97.06091.
6. Tomita N, Kodama F, Sakai R, Koharasawa H, Hattori M, Taguchi J, et al. Predictive factors for central nervous system involvement in non-Hodgkin's lymphoma: significance of very high serum LDH concentrations. Leukemia & lymphoma. 2000;38 3-4:335-43; doi: 10.3109/10428190009087024.

7. Peñalver FJ, Sancho JM, De IFA, Olave MT, Martin A, Panizo C, et al. 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. 2017;102 2:235.

8. Abrey LE, Batchelor TT, Ferreri AJ, Gospodarowicz M, Pulczynski EJ, Zucca E, et al. Report of an international workshop to standardize baseline evaluation and response criteria for primary CNS lymphoma. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2005;23 22:5034-43; doi: 10.1200/jco.2005.13.524.

9. Burgetova A, Seidl Z, Vaneckova M, Jakoubkova M. Concurrent occurrence of multiple sclerosis and primary CNS lymphoma: a case report. Neuro endocrinology letters. 2008;29 6:867-70.

10. Hunt MA, Jahnke K, Murillo TP, Neuwelt EA. Distinguishing primary central nervous system lymphoma from other central nervous system diseases: a neurosurgical perspective on diagnostic dilemmas and approaches. Neurosurgical focus. 2006;21 5:E3.

11. Malikova H, Burghardtova M, Koub ska E, Mandys V, Kozak T, Weichet J. Secondary central nervous system lymphoma: spectrum of morphological MRI appearances. Neuropsychiatric Disease & Treatment. 2018;14:733-40.

12. Qualls D, Abramson JS. Advances in risk assessment and prophylaxis for central nervous system relapse in diffuse large B-cell lymphoma. Haematologica. 2019;104
van Besien K, Ha CS, Murphy S, McLaughlin P, Rodriguez A, Amin K, et al. Risk factors, treatment, and outcome of central nervous system recurrence in adults with intermediate-grade and immunoblastic lymphoma. Blood. 1998;91 4:1178-84.

Chihara D, Oki Y, Matsuo K, Onoda H, Taji H, Yamamoto K, et al. Incidence and risk factors for central nervous system relapse in patients with diffuse large B-cell lymphoma: analyses with competing risk regression model. Leukemia & lymphoma. 2011;52 12:2270-5; doi: 10.3109/10428194.2011.596966.

Siegal T, Goldschmidt N. CNS prophylaxis in diffuse large B-cell lymphoma: if, when, how and for whom? Blood Rev. 2012;26 3:97-106; doi: 10.1016/j.blre.2011.12.001.

Malikova H, Burghardtova M, Koubksa E, Mandys V, Kozak T, Weichet J. Secondary central nervous system lymphoma: spectrum of morphological MRI appearances. Neuropsychiatric disease and treatment. 2018;14:733-40; doi: 10.2147/ndt.s157959.

Villa D, Connors JM, Shenkier TN, Gascoyne RD, Sehn LH, Savage KJ. Incidence and risk factors for central nervous system relapse in patients with diffuse large B-cell lymphoma: the impact of the addition of rituximab to CHOP chemotherapy. Annals of Oncology Official Journal of the European Society for Medical Oncology. 2010;21 5:1046.

Volkmar B, Norbert S, Samira Z, Markus L, Michael P. CNS events in elderly patients with aggressive lymphoma treated with modern chemotherapy (CHOP-14) with or without rituximab: an analysis of patients treated in the RICOVER-60 trial of the German High-Grade Non-Hodgkin Lymphoma Study Group (DSHNHL). Blood. 2009;113 17:3896-902.

Senocak E, Oguz KK, Ozgen B, Mut M, Ayhan S, Berker M, et al. Parenchymal lymphoma of the brain on initial MR imaging: a comparative study between primary
and secondary brain lymphoma. European journal of radiology. 2011;79 2:288-94; doi: 10.1016/j.ejrad.2010.01.017.

20. Tabouret E, Houillier C, Martin-Duverneuil N, Blonski M, Soussain C, Ghesquieres H, et al. Patterns of response and relapse in primary CNS lymphomas after first-line chemotherapy: imaging analysis of the ANOCEF-GOELAMS prospective randomized trial. Neuro-oncology. 2017;19 3:422-9; doi: 10.1093/neuonc/now238.

21. Koubska E, Weichet J, Malikova H. Central nervous system lymphoma: a morphological MRI study. Neuroendocrinology letters. 2016;37 4:318.

Tables
Table 1 Clinical characteristics of SCNSL patients.
| Characteristics                        | N   | %   |
|---------------------------------------|-----|-----|
| Age at initial disease                | 20-76 | 59±13.0 |
| ≤60                                   | 13  | 50  |
| >60                                   | 13  | 50  |
| Gender                                |     |     |
| Male                                  | 14  | 53.8|
| Female                                | 12  | 46.2|
| Primary site                          |     |     |
| Lymph node                            | 12  | 46.2|
| Extranodal                            | 14  | 53.8|
| Breast                                | 4   | 15.4|
| Testicular                            | 3   | 11.5|
| Others                                | 7   | 26.9|
| CNS Relapse Type                      |     |     |
| Isolated disease                      | 21  | 80.8|
| CNS with disease progression          | 1   | 3.8 |
| Combined disease                      | 5   | 15.4|
| CNS relapse time (range, median)      | (0-10,3) |     |
| <5 years                              | 19  | 73.1|
| ≥5 years                              | 7   | 26.9|
| Performance Status at CNS relapse     |     |     |
| 0-1                                   | 18  | 69.2|
| 2-4                                   | 8   | 30.8|
| Diagnosis approaches                  |     |     |
| Biopsy or surgery                     | 24  | 92.3|
| Enhanced MRI                          | 2   | 7.7 |

Table 2 Clinical characteristics and CNS relapse types.
| Characteristics          | Isolated CNS | Synchronic CNS and systemic disease | P value |
|--------------------------|--------------|-------------------------------------|---------|
| Age                      |              |                                     |         |
| ≤60                      | 10(47.6%)    | 3(60%)                              | 1.000   |
| >60                      | 11(52.4%)    | 2(40%)                              |         |
| Relapse time             |              |                                     |         |
| ≤1year                   | 5(23.8%)     | 4(80%)                              | 0.034   |
| >1year                   | 16(76.2%)    | 1(20%)                              |         |
| Primary site             |              |                                     |         |
| Lymph node               | 9[42.9%]     | 3[60%]                              | 0.635   |
| Extra node               | 12[57.1%]    | 2[40%]                              |         |
| Intravenous MTX          |              |                                     |         |
| Yes                      | 2[9.5%]      | 0                                   | 1.000   |
| No                       | 19[90.5%]    | 5[100%]                             |         |
| Rituximab                |              |                                     |         |
| Yes                      | 10[47.6%]    | 1[20%]                              | 0.356   |
| No                       | 11[52.4%]    | 4[80%]                              |         |

Methotrexate, MTX;

Table 3 Results of statistical analyses of radiological evaluation regarding location, enhancement pattern, multiplicity of the lesions between PCNSL and SCNSL.

|                      | PCNSL group n(%) | SCNSL group n(%) | P value |
|----------------------|------------------|------------------|---------|
| Gender               |                  |                  | 1.000   |
| Male                 | 14[53.8%]        | 14[53.8%]        |         |
| Female               | 12[56.2%]        | 12[53.8%]        |         |
| Age                  |                  |                  | 0.577   |
| ≤60                  | 16[61.5%]        | 13[50%]          |         |
| >60                  | 10[38.5%]        | 13[50%]          |         |
| Performance Status   |                  |                  | 0.067   |
| 0-1                  | 10[38.5%]        | 18[69.2%]        |         |
| 2-4                  | 15[57.7%]        | 8[30.8%]         |         |
| Multiplicity         |                  |                  | 0.023   |
| Single               | 15[57.7%]        | 6[23.1%]         |         |
| Multiple             | 11[42.3%]        | 20[76.9%]        |         |
| Butterfly pattern    |                  |                  | 1.000   |
| Yes                  | 2[7.7%]          | 3[11.5%]         |         |
| No                   | 24[92.3%]        | 23[88.5%]        |         |
| T1W                  |                  |                  | 0.754   |
| Hypo                 | 21[80.8%]        | 18[78.3%]        |         |
| Iso                  | 4[15.4%]         | 3[13%]           |         |
| Hypo-Iso             | 0                | 1[4.3%]          |         |
| Hyper                | 1[3.8%]          | 1[4.3%]          |         |
| T2W                  |                  |                  | 0.086   |
| Hyper                | 24[92.3%]        | 15[65.2%]        |         |
Iso 2(7.7%) 4(17.4%)  
Hyper-Iso 0 1(4.3%)  
Hypo 0 3(13%)  
T2 Flair 0.229  
Hyper 25(96.2%) 10(83.3%)  
Iso or Hypo 1(3.8) 2(16.7%)  
DWI 0.043  
Hyper 26(100%) 12(80%)  
Non-hyper 0 3(20%)  
Enhancement 0.457  
Homogeneous 16(61.5%) 16(64%)  
Patchy 8(30.8%) 6(24%)  
Ringlike 2(7.7%) 1(4%)  
No enhancement 0 2(8%)  
Location of Lesion(s)  
Deep grey matter 12(46.2%) 17(68.0%) 0.160  
White matter 17(65.4%) 21(84.0%) 0.199  
Cerebellum 6(23.1%) 5(20.0%) 1.000  
Brainstem 9(34.6%) 3(12.0%) 0.097  
Supra or Infra 0.011  
Supratentorial 17(65.4%) 16(64.0%)  
Infratentorial 6(23.1%) 0  
Both 3(11.5%) 9(36.0%)  

Diffusion weighted imaging, DWI; T2 fluid-attenuated inversion-recovery, T2 Flair; T1 weighted imaging, T1W; T2 weighted imaging, T2W

Figures
Figure 1

Distribution of relapse times from initial diagnosis of systemic disease in SCNSL patients.
Multiple patchy hyperintensity on T2 Flair (A and B: arrows) were found in the right cerebellar hemisphere, bilateral cerebral peduncle, bilateral basal ganglia, thalamus, but enhancement was not observed (C and D). Re-examinations one month later via T2 Flair revealed some enlarged lesions without enhancement (E and F: arrows) and some still without enhancement (G and H), and stereotactic biopsy confirmed DLBCL.
Multiple lesions in the brain parenchyma showed hyperintensity on T2 Flair images (A and B: arrows). No enhancement was observed on MRI (C and D). Two months later, with the progression of the disease, the volume of lesions was observed on T2 Flair (E and F: arrows), strong enhancement was present after gadolinium injection in T1-weighted images (E and H: arrows), and stereotactic biopsy confirmed DLBCL CNS involvement.