Case report and review of the literature of primary central nervous system lymphoma of the fourth ventricle

Yuichiro Kojima, Kosuke Nakajo, Tsutomu Ichinose, Yoichiro Morikawa, Masahiko Osawa, Takeo Goto

1Department of Neurosurgery, Osaka Metropolitan University, 2Department of Hematology, Sumitomo Hospital, 3Department of Pathology, Osaka Metropolitan University, Osaka, Japan.

E-mail: Yuichiro Kojima - yuichiro_igaiga@yahoo.co.jp; *Kosuke Nakajo - kousuke19841984@yahoo.co.jp; Tsutomu Ichinose - e21043p@omu.ac.jp; Yoichiro Morikawa - morikawa-yoichi@sumitomo-hp.or.jp; Masahiko Osawa - m-ohsawa@med.osaka-cu.ac.jp; Takeo Goto - gotot@omu.ac.jp

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is a rare variant of extranodal non-Hodgkin’s lymphoma. The incidence rate has recently increased to 0.43 cases/100,000 people/year.[22] Most PCNSLs arise in the cerebral parenchyma, but rarely in the fourth ventricle. The gold standard treatment for PCNSL, and for diffuse large B-cell lymphoma (DLBCL) in particular, is chemoradiation therapy including high-dose methotrexate. Most PCNSLs are highly responsive to steroids, which are often used before the definitive diagnosis of PCNSL; however, some PCNSLs are refractory to steroids. In these cases, PCNSLs accompanied by obstructive hydrocephalus sometimes require drainage or shunting. Here, we report a rare case of PCNSL arising in the fourth ventricle, in which hydrocephalus was difficult to control after biopsy. We also review the literature regarding PCNSLs arising in the fourth ventricle [Table 1].
Table 1: Literature review of 18 cases of PCNSL originating from the fourth ventricle.

| Series                  | Age/sex | Immunodeficiency | Pathology                  | Presenting symptom                        | Imaging feature                      | Hydrocephalus | Extent of resection | Drainage/shunt | Result                        |
|-------------------------|---------|------------------|-----------------------------|-------------------------------------------|---------------------------------------|---------------|---------------------|----------------|------------------------------|
| Haegelen et al., 2001   | 33/F    | —                | High-grade BCL              | Headache, vertigo, ataxia                | Homogeneous enhancement               | NA            | Total resection      | NA             | No recurrence at 7 months    |
| Browning et al., 2008   | 51/F    | NA               | DLBCL within ganglioglioma  | Headache, diplopia, facial palsy, facial numbness, hearing loss | Homogeneous enhancement               | NA            | Subtotal resection   | NA             | No recurrence at 3 months    |
| Hill et al., 2009       | 69/M    | NA               | BCL                         | Nausea, anorexia                          | Homogeneous enhancement               | NA            | Biopsy              | NA             | No recurrence at 2 months    |
| Fear et al., 2012       | 65/F    | —                | High-grade BCL              | Headache, nausea                         | Homogeneous enhancement               | NA            | Biopsy              | NA             | No recurrence at 2 months    |
| Bokhari et al., 2013    | 50/M    | —                | High-grade BCL              | Headache, nausea, consciousness disturbance | Homogeneous enhancement               | —             | Total resection      | NA             | No recurrence at 6 months    |
| Rao et al., 2013        | 59/M    | NA               | BCL                         | Nausea, vertigo, tremor, gait disturbance | Contrast-enhancing mass                | NA            | Near-total resection | NA             | No recurrence at 9 months    |
| Alabdulsalam et al., 2014 | 18/M  | —                | Burkitt lymphoma            | Ataxia, diplopia, facial palsy, tinnitus, dysphasia | Homogeneous enhancement               | NA            | Gross total resection | NA             | No recurrence at 18 months   |
| Fabiano et al., 2014    | 60/F    | —                | DLBCL                       | Diplopia                                 | Homogeneous enhancement               | NA            | Resection           | NA             | No recurrence at 6 months    |
| Liao et al., 2014       | 77/M    | —                | DLBCL                       | Nausea, vertigo, tremor, gait disturbance | Homogeneous enhancement               | —             | Gross total resection | NA             | No recurrence at 9 months    |
| Grossman et al., 2014   | 66/M    | —                | DLBCL                       | Diplopia, gait disturbance                | Homogeneous enhancement               | NA            | Biopsy              | NA             | No recurrence at 6 months    |
| Zhu et al., 2015        | 66/M    | NA               | DLBCL                       | Diplopia, facial palsy, dizziness         | Homogeneous enhancement               | —             | Biopsy              | NA             | No recurrence at 3 months    |
| Hsu et al., 2015        | 61/M    | —                | DLBCL                       | Ataxia                                    | Homogeneous enhancement               | —             | Total resection      | —/—            | No recurrence at 2 weeks     |
| Suri et al., 2015       | 15/M    | NA               | DLBCL                       | Headache, nausea, ataxia, facial palsy, lower cranial nerve palsy, Weight loss, headache, consciousness disturbance, motor weakness | Homogeneous enhancement               | +             | Biopsy              | —/—            | No recurrence at 2 weeks     |
| Cellina et al., 2015    | 65/M    | —                | DLBCL                       | Ataxia                                    | Homogeneous enhancement               | —             | Biopsy              | NA             | No recurrence at 6 months    |
| Liu et al., 2016        | 6/M     | —                | Burkitt lymphoma            | Headache                                  | Homogeneous enhancement               | —             | Resection           | NA             | No recurrence at 6 months    |
| Brozovich et al., 2019  | 65/M    | —                | DLBCL                       | Diplopia, vertigo, nausea, dysmetria      | Homogeneous enhancement               | —             | Biopsy              | NA             | No recurrence at 10 months   |
| Wang et al., 2020       | 51/F    | NA               | DLBCL                       | Gait disturbance, memory loss             | Multiple lesion                       | —             | Biopsy              | NA             | No recurrence at 14 months   |
| Present case            | 54/M    | —                | DLBCL                       | Headache, nausea, ataxia, abducens nerve palsy, facial palsy | Homogeneous enhancement               | +             | Biopsy              | NA             | No recurrence at 14 months   |

PCNSL: Primary central nervous system lymphoma, BCL: B-cell lymphoma, DLBCL: Diffuse large B-cell lymphoma, NA: Not available
CASE DESCRIPTION

A 54-year-old man with no relevant previous medical or family history presented to our hospital complaining of headache, nausea, diplopia, and dizziness. Neurological examination revealed bilateral abducens nerve palsy and left facial nerve palsy and ataxia. Computed tomography (CT) showed a slightly high-density tumor [Figure 1a] that was seen in the fourth ventricle on magnetic resonance imaging (MRI), along with obstructive hydrocephalus. The tumor extended into the foramen of Magendie and bilateral foramen of Luschka. The tumor was slightly hypointense on T1-weighted imaging [Figure 1b] and iso- to slightly hyperintense on T2-weighted imaging [Figure 1c]. The tumor was uniformly hyperintense on diffusion-weighted imaging [Figure 1d] and iso- to slightly hyperintense on apparent diffusion coefficient. After injection of gadolinium-based contrast medium, the tumor showed uniform contrast enhancement [Figures 1e-g]. We suspected malignant lymphoma accompanied by obstructive hydrocephalus, but could not exclude metastasis, ependymoma, or glioma. Tumor markers such as squamous cell carcinoma antigen, carcinoembryonic antigen, CA19-9, and soluble interleukin-2 receptor were negative. Torso CT revealed no obvious malignant neoplasm.

Biopsy was performed by the transmedullary fissure approach. Histopathological examination revealed diffusely growing tumor cells with a high nucleocytoplasmic ratio and differently sized nuclei, some of which had mucus and multiple mitotic figures [Figure 2a]. The tumor was negative for CD3, CD5, CD10, Keratin7, and Keratin20 and was positive for CD20, CD79a, Bcl-2, Bcl-6, and MUM-1 [Figures 2b-f]. The final pathological diagnosis was non-germinal center B-cell-like type diffuse large B-cell lymphoma with a Ki-67 proliferation index of 90%. Steroids administered after tumor biopsy were largely ineffective. With the definitive diagnosis of diffuse large B-cell lymphoma, chemotherapy with rituximab, methotrexate, procarbazine, and vincristine (R-MPV regimen) was administered. After 5 cycles of R-MPV regimen, the tumor decreased in size but the obstructive hydrocephalus remained [Figures 3a and b]. Thus, repeated ventricular drainage was required. Finally, ventriculoperitoneal shunting was performed. The patient was then transferred to another hospital for additional chemotherapy. Autologous

Figure 1: The tumor showed slightly high density on CT (a), slightly hypointensity on T1-weighted image (b), iso- to slightly high intensity on a T2-weighted image (c), uniformly high intensity on diffusion-weighted image (d), and heterogeneous enhancement with gadolinium (e: axial, f: sagittal, and g: coronal).
Kojima, et al.: Primary central nervous system lymphoma of the fourth ventricle

Peripheral blood stem cell transplantation was performed after 2 cycles of high-dose cytarabine chemotherapy. Tumor was disappeared after chemotherapy with autologous blood stem cell transplantation. There was no sign of recurrence at 20 months after biopsy [Figures 3c and d].

DISCUSSION

The incidence rate of PCNSLs has increased recently and is currently 0.43/100,000 people/year.[22] Most PCNSLs arise in the cerebral parenchyma, and to the best of our knowledge, only 18 cases of PCNSL originating from the fourth ventricle (including the present case) have been reported [Table 1].[1-6,8,12-14,16-18,23,25,26,28]

Our literature review of PCNSL originating from fourth ventricle [Table 1] revealed that this tumor occurs most frequently in the 50s and 60s (range, 6–77 years; mean age, 51.7 years) and shows male predominance (males: females = 14:4). Although lymphoma has sometimes been associated with immunodeficiency, we found no history of immunodeficiency in any patient in our review. Patients presented with headache (44.4%), nausea or vomiting (44.4%), diplopia (38.9%), ataxia (33.3%), vertigo or dizziness (27.8%), facial palsy (27.8%), and gait disturbance (22.2%). Almost all single or multiple mass lesions showed homogeneous gadolinium enhancement. B-cell lymphoma constituted the majority of PCNSLs originating from the fourth ventricle (88.9%) followed by Burkitt lymphoma (11.1%).

The treatment for PCNSL has traditionally been whole-brain radiation therapy alone; however, median survival has been reported as 8–12 months and the 5-year survival rate as 6%.[20] Due to the limited efficacy of radiation therapy alone,
chemoradiotherapy has also been developed. The combination of whole-brain radiation and high-dose methotrexate has improved survival, with reported median survival of 33–36 months and a 5-year survival rate of 37%. However, the synergistic effect of high-dose methotrexate and whole-brain radiation causes neurotoxicity. As a new treatment, rituximab is an anti-CD20 monoclonal antibody that has been used in combination with high-dose methotrexate to enhance chemotherapy and reduce radiation dose. Holdhoff et al. reported complete remission rates of 36% among patients using high-dose methotrexate and 73% in those using high-dose methotrexate with rituximab; and median progression-free survival was 4.5 months among patients using high-dose methotrexate and 26.7 months in those using high-dose methotrexate with rituximab. Moreover, the effectiveness of high-dose chemotherapy followed by autologous stem cell transplantation has been reported for avoiding whole-brain radiation therapy. In the present case, we added autologous stem cell transplantation after 5 cycles of R-MPV chemotherapy and 2 cycles of cytarabine, to avoid radiation therapy.

PCNSLs are often highly responsive to steroids, with an efficacy rate of 40%, because steroid glucocorticoid is a strong inducer of apoptosis of lymphoid cells. In the present case, however, steroids did not decrease the tumor size or improve the obstructive hydrocephalus. Moreover, the obstructive hydrocephalus did not disappear after 5 cycles of R-MPV chemotherapy, although complete response of the tumor was finally achieved. Thus, the patient required repeated ventricular drainage before ventriculoperitoneal shunting was finally performed. In our literature review, Suri et al. reported a similar case of DLBCL originating from the fourth ventricle, in which the patient experienced hydrocephalus before tumor removal and finally required ventriculoperitoneal shunting. In addition, Weller et al. reported that the extent of resection was related to prognosis, although biopsy followed by chemoradiation therapy is the gold standard treatment because PCNSL tends to occur in multiple locations and the tumors are highly invasive into the subarachnoid space, perivascular space, and brain parenchyma. As drainage or shunting may be required when these tumors are accompanied by obstructive hydrocephalus, it is important to consider relatively radical removal of PCNSL originating from the fourth ventricle. However, there is a risk after radical resection/radiotherapy of PCNSL originating from the fourth ventricle. Thus, morbidity arising due to radical resection/radiotherapy of resistant PCNSL could be prevented by ventriculoperitoneal shunting with chemotherapy and autologous blood stem cell transplantation.

CONCLUSION

We report an extremely rare case of PCNSL originating from the fourth ventricle. Morbidity arising due to radical resection/radiotherapy of resistant PCNSL originating from the fourth ventricle could be prevented by ventriculoperitoneal shunting with chemotherapy and autologous blood stem cell transplantation.

Declarations of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Alabdulsalam A, Zaidi SZ, Tailor I, Orz Y, Al-Dandan S. Primary burkitt lymphoma of the fourth ventricle in an immunocompetent young patient. Case Rep Pathol 2014;2014:630954.
2. Bokhari R, Ghanem A, Alahwal M, Baeesa S. Primary isolated lymphoma of the fourth ventricle in an immunocompetent patient. Case Rep Oncol Med 2013;2013:614658.
3. Brar R, Prasad A, Sharma T, Vermani N. Multifocal lateral and fourth ventricular B-cell primary CNS lymphoma. Clin Neurol Neurosurg 2012;114:281-3.
4. Browning L, Leach J, Watts C, Kuker W, Stacey R. 51-year-old woman with double vision. Brain Pathol 2008;18:295-9.
5. Brozovich A, Ewing D, Burns E, Hatcher C, Acosta G, Khan U, et al. Primary CNS lymphoma arising from the 4th ventricle: A case report and review of the literature. Case Rep Oncol Med 2019;2019:2671794.
6. Cellina M, Fetoni V, Baron P, Orsi M, Oliva G. Unusual primary central nervous system lymphoma location involving the fourth ventricle and hypothalamus. Neuroradiol J 2015;28:120-5.
7. DeAngelis LM, Yahalom J, Heinemann MH, Cirrincione C, Thaler HT, Krol G. Primary CNS lymphoma: Combined treatment with chemotherapy and radiotherapy. Neurology 1990;40:80-6.
8. Fabiano AJ, Syrac S, Fenstermaker RA, Qiu J. Primary fourth ventricular B-cell lymphoma in an immunocompetent patient. Clin Neuropathol 2014;33:94-7.
9. Gavrilovic IT, Hormigo A, Yahalom J, DeAngelis LM, Abrey LE. Long-term follow-up of high-dose methotrexate-based therapy with and without whole brain irradiation for newly diagnosed primary CNS lymphoma. J Clin Oncol 2006;24:4570-4.
10. Glass J, Gruber ML, Cher L, Hochberg FH. Preirradiation methotrexate chemotherapy of primary central nervous system lymphoma: Long-term outcome. J Neurosurg 1994;81:188-95.
11. Gritsch D, Mrugala MM, Marks LA, Mangipudi K, Neal M, Wingerchuk DM, et al. Is autologous stem cell transplantation a safe and effective alternative to whole brain radiation as consolidation therapy in patients with primary central nervous system lymphoma?: A critically appraised topic. Neurologist 2021;26:137-42.

12. Grossman R, Nossek E, Shimony N, Raz M, Ram Z. Intraoperative 5-aminolevulinic acid-induced fluorescence in primary central nervous system lymphoma. J Neurosurg 2014;120:67-9.

13. Haegelen C, Riffaud L, Bernard M, Morandi X. Primary isolated lymphoma of the fourth ventricle: Case report. J Neurooncol 2009;93:261-2.

14. Holdhoff M, Ambady P, Abdelaziz A, Sarai G, Bonekamp D, Blakeley J, et al. High-dose methotrexate with or without rituximab in newly diagnosed primary CNS lymphoma. Neurology 2014;83:235-9.

15. Hsu HI, Lai PH, Tseng HH, Hsu SS. Primary solitary lymphoma of the fourth ventricle. Int J Surg Case Rep 2015;14:23-5.

16. Hsu HI, Lai PH, Tseng HH, Hsu SS. Primary solitary lymphoma of the fourth ventricle. Int J Surg Case Rep 2015;14:23-5.

17. Liao CH, Lin SC, Hung SC, Hsu SP, Ho DM, Shih YH. Primary large B-cell lymphoma of the fourth ventricle. J Clin Neurorad 2014;21:180-3.

18. Liu H, Hou H, Cheng J. Primary Burkitt lymphoma of the fourth ventricle mimicking a medulloblastoma in a child. J Neurooncol 2016;127:205-7.

19. Morris PG, Correa DD, Yahalom J, Raizer JJ, Schiff D, Grant B, et al. Rituximab, methotrexate, procarbazine, and vincristine followed by consolidation reduced-dose whole-brain radiotherapy and cytarabine in newly diagnosed primary CNS lymphoma: Final results and long-term outcome. J Clin Oncol 2013;31:3971-9.

20. Nelson DE, Martz KL, Bonner H, Nelson JS, Newall J, Kerman HD, et al. Non-Hodgkin’s lymphoma of the brain: Can high dose, large volume radiation therapy improve survival? Report on a prospective trial by the radiation therapy oncology group (RTOG): RTOG 8315. Int J Radiat Oncol Biol Phys 1992;23:9-17.

21. O’Brien PC, Roos DE, Pratt G, Liew KH, Barton MB, Poulsen MG, et al. Combined-modality therapy for primary central nervous system lymphoma: Long-term data from a Phase II multicenter study (Trans-tasman radiation oncology group). Int J Radiat Oncol Biol Phys 2006;64:408-13.

22. Ostrom QT, Gittleman H, Xu J, Kromer C, Wolinsky Y, Kruchko C, et al. CBTRUS statistical report: Primary brain and other central nervous system tumors diagnosed in the United States in 2009-2013. Neuro Oncol 2016;18:v1-75.

23. Rao RN, Mishra D, Agrawal P, Kumar R. Primary B-cell central nervous system lymphoma involving fourth ventricle: A rare case report with review of literature. Neuro Ind 2013;61:450-3.

24. Reni M, Ferreri AJ, Garancini MP, Villa E. Therapeutic management of primary central nervous system lymphoma in immunocompetent patients: Results of a critical review of the literature. Ann Oncol 1997;8:227-34.

25. Suri V, Mittapalli V, Kulkrestha M, Premiani K, Sogani SK, Suri K. Primary intraventricular central nervous system lymphoma in an immunocompetent patient. J Pediatr Neurosci 2015;10:393-5.

26. Wang D, Su M, Xiao J. A rare case of primary ventricular lymphoma presented on FDG PET/CT. Clin Nucl Med 2020;45:156-8.

27. Weller M, Martus P, Roth P, Thiell E, Korfel A, German PCNSL Study Group. Surgery for primary CNS lymphoma?: Challenging a paradigm. Neuro Oncol 2012;14:1481-4.

28. Zhu Y, Ye K, Zhan R, Tong Y. Multifocal lateral and fourth ventricular primary central nervous system lymphoma: Case report and literature review. Turk Neurosurg 2015;25:493-5.

How to cite this article: Kojima Y, Nakajo K, Ichinose T, Morikawa Y, Osawa M, Goto T. Case report and review of the literature of primary central nervous system lymphoma of the fourth ventricle. Surg Neurol Int 2022;13:529.