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Case Report

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

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ABSTRACT

Background: Primary central nervous system lymphoma of the fourth ventricle is very rare. We present a case of primary central nervous system lymphoma originating from the fourth ventricle and review cases reported in the literature.

Case Description: A 54-year-old man with no previous medical history presented with headache and nausea. Magnetic resonance imaging showed a homogeneously enhancing tumor in the fourth ventricle and obstructive hydrocephalus. We performed biopsy of the tumor, which was diagnosed pathologically as diffuse large B-cell lymphoma. Although the tumor disappeared after 5 cycles of R-MPV regimen, the patient required repeated ventricular drainage and finally received a ventriculoperitoneal shunt. Complete response was achieved after 2 cycles of high-dose cytarabine chemotherapy with an autologous peripheral blood stem cell transplant. There was no sign of recurrence at 20 months after biopsy.

Conclusion: Morbidity arising due to radical resection/radiotherapy of resistant primary central nervous system lymphoma originating from the fourth ventricle could be prevented by ventriculoperitoneal shunting with chemotherapy and autologous blood stem cell transplantation.

Keywords: Fourth ventricle, Lymphoma, Hydrocephalus

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[13]	33/F	—	High-grade BCL	Headache, vertigo, ataxia	Homogeneous enhancement	NA	Total resection	—/—	No recurrence at 7 months
Browning *et al.*, 2008[4]	51/F	NA	DLBCL within ganglioglioma	Headache, diplopia, facial palsy, facial numbness, hearing loss	Homogeneous enhancement	NA	Subtotal resection	NA	NA
Hill *et al.*, 2009[14]	69/M	NA	BCL	Nausea, anorexia	Homogeneous enhancement	NA	Biopsy	—/—	No recurrence at 3 months
Brar *et al.*, 2012[3]	65/F	—	High-grade BCL	Headache, nausea	Multiple lesion homogeneous enhancement	—	Biopsy	—/—	No recurrence at 2 months
Bokhari *et al.*, 2013[2]	50/M	—	High-grade BCL	Headache, nausea, consciousness disturbance	Homogeneous enhancement	—	Total resection	—/—	No recurrence at 18 months
Rao *et al.*, 2013[23]	59/M	NA	BCL	Nausea, vertigo, tremor, gait disturbance	Contrast-enhancing mass	NA	Near-total resection	—/—	NA
Alabdulsalam *et al.*, 2014[1]	18/M	—	Burkitt lymphoma	Ataxia, diplopia, facial palsy, tinnitus, dysphasia	Homogeneous enhancement	NA	Gross total resection	—/—	No recurrence at 18 months
Fabiano *et al.*, 2014[8]	60/F	—	DLBCL	Diplopia	Homogeneous enhancement	NA	Resection	NA	No recurrence at 6 months
Liao *et al.*, 2014[17]	77/M	—	DLBCL	Nausea, vertigo, tremor, gait disturbance	Homogeneous enhancement	—	Gross total resection	—/—	No recurrence at 9 months
Grossman *et al.*, 2014[12]	66/M	—	DLBCL	Diplopia, gait disturbance	Homogeneous enhancement	NA	NA	NA	NA
Zhu *et al.*, 2015[28]	66/M	NA	DLBCL	Diplopia, facial palsy, dizziness	Multiple lesion homogeneous enhancement	—	Biopsy	NA	No recurrence at 6 months
Hsu *et al.*, 2015[16]	61/M	—	DLBCL	Ataxia	Homogeneous enhancement	—	Total resection	—/—	No recurrence at 3 months
Suri *et al.*, 2015[25]	15/M	NA	DLBCL	Headache, nausea, ataxia, facial palsy, lower cranial nerve palsy	Multiple lesion homogeneous enhancement	+	Biopsy	—/+	NA
Cellina *et al.*, 2015[6]	65/M	—	DLBCL	Weight loss, headache, consciousness disturbance, motor weakness	Dissemination homogeneous enhancement	—	Biopsy	—/—	No recurrence at 2 weeks
Liu *et al.*, 2016[18]	6/M	—	Burkitt lymphoma	Headache	Homogeneous enhancement	—	Resection	NA	No recurrence at 6 months
Brozovich *et al.*, 2019[5]	65/M	—	DLBCL	Diplopia, vertigo, nausea, dysmetria	Homogeneous enhancement	—	Biopsy	NA	No recurrence at 10 months
Wang *et al.*, 2020[26]	51/F	NA	DLBCL	Gait disturbance, memory loss	Multiple lesion	—	Biopsy	NA	NA
Present case	54/M	—	DLBCL	Headache, nausea, ataxia, abducens nerve palsy, facial palsy	Homogeneous enhancement	+	Biopsy	+/+	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 nongerminal 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

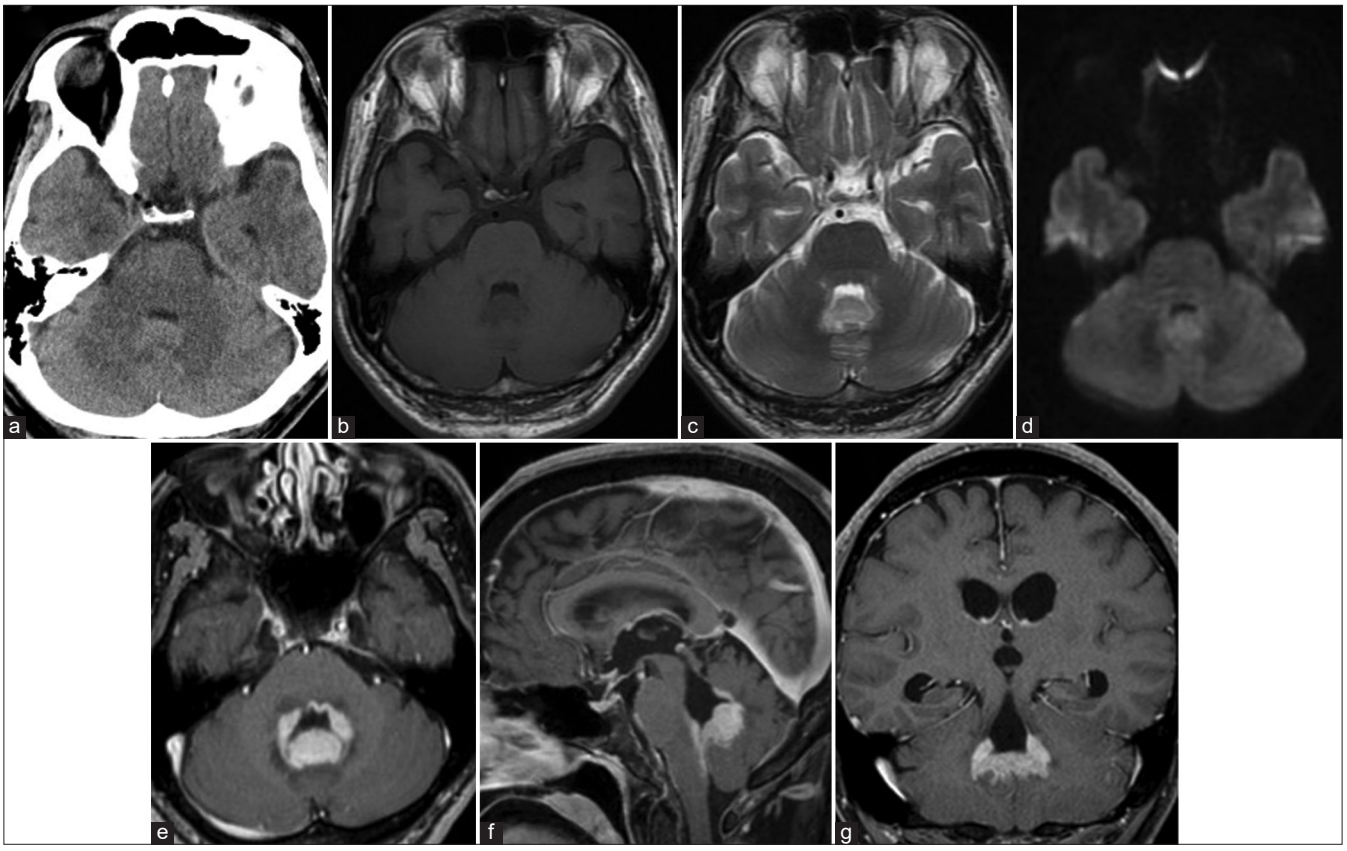

Figure 1: The tumor showed slightly high density on CT (a), slightly hypointensity on T1-weighted image (b), iso- to slightly high intensity on a T2-weighted image (c), uniformly high intensity on diffusion-weighted image (d), and heterogeneous enhancement with gadolinium (e: axial, f: sagittal, and g: coronal).

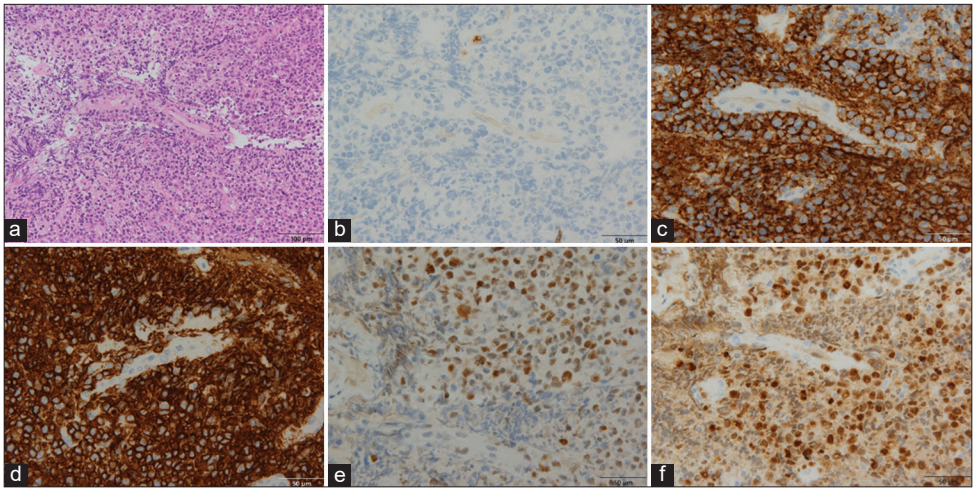

Figure 2: Histopathological examination revealed diffusely growing tumor cells with a high nucleocytoplasmic ratio and differently sized nuclei, some of which had mucus, and multiple mitotic figures (a). The tumor was negative for CD10 (b) and was positive for CD20 (c), CD79a (d), Bcl-6 (e), and MUM-1 (f). a: Hematoxylin-eosin staining, ×200, b: CD10, ×400, c: CD20, ×400, d: CD79a, ×400, e: Bcl-6, ×400, and f: MUM-1, ×400.

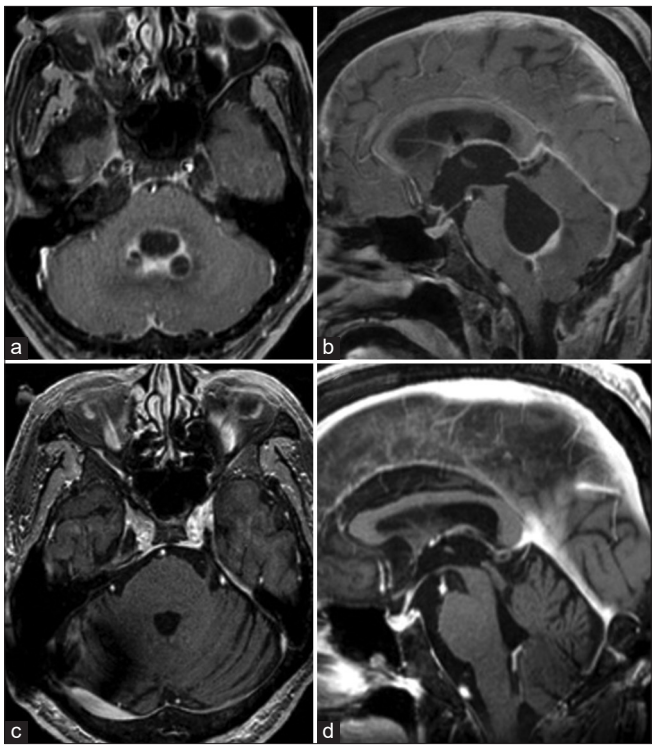

Figure 3: The tumor decreased in size but the obstructive hydrocephalus remained after 5 cycles of R-MPV regimen (a: axial and b: sagittal). The patient achieved complete response after chemotherapy with autologous peripheral blood stem cell transplantation. There was no sign of recurrence at 20 months after biopsy (c: axial and d: sagittal).

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%.[10,21] However, the synergistic effect of high-dose methotrexate and whole-brain radiation causes neurotoxicity.[9] 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.[15,19] 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.[15] Morris *et al*. reported that low-dose whole-brain irradiation of about 23.4 Gy followed by 2 cycles of cytarabine after R-MPV regimen had an objective response rate of 78% and median progression-free survival of 7.7 years.[19] Moreover, the effectiveness of high-dose chemotherapy followed by autologous stem cell transplantation has been reported for avoiding whole-brain radiation therapy.[11] 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.[7] 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.[25] In addition, Weller *et al*. reported that the extent of resection was related to prognosis,[27] 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.[24] 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.

Declaration of patient consent

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

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Nil.

Conflicts of interest

There are no conflicts of interest.

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