



Case Report

Primary intracranial marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue arising in the lateral ventricle: Case report and review of pathogenesis

Sabastian Hajtovic¹, Edward Yu², Alexander Bershadskiy³, Raphael Sacho¹, Ronit Gilad¹

Departments of ¹Neurosurgery, ²Neurology and ³Hematology/Oncology, Staten Island University Hospital, Staten Island, New York, United States.

E-mail: *Sabastian Hajtovic - shajtov000@citymail.cuny.edu; Edward Yu - eyu@northwell.edu; Alexander Bershadskiy - abershadsk@northwell.edu, Raphael Sacho - rsacho@northwell.edu; Ronit Gilad - rgilad@northwell.edu



*Corresponding author:

Sabastian Hajtovic,
Department of Neurosurgery,
Staten Island University
Hospital, Staten Island,
New York, United States.

shajtov000@citymail.cuny.edu

Received : 14 January 2022

Accepted : 14 April 2022

Published : 29 April 2022

DOI

10.25259/SNI_54_2022

Quick Response Code:



ABSTRACT

Background: Primary central nervous system lymphoma (PCNSL) is an aggressive extranodal subtype of non-Hodgkin's lymphoma. Ventricle-predominant PCNSL, arising in the CNS ventricular system, is a rare entity. In over 90% of cases, PCNSL is classified as diffuse large B-cell lymphoma. Rarely, PCNSL may be classified as marginal zone B-cell lymphoma (MZBCL) of mucosa-associated lymphoid tissue (MALT). Taken together, a primary MALT-type MZBCL arising in a cerebral ventricle is an extremely rare presentation.

Case Description: A 69-year-old female presented with a persistent left frontal headache for 1 year. Magnetic resonance imaging revealed an enhancing soft-tissue lesion within the left lateral ventricle, with associated periventricular edema. We performed an excisional biopsy of the tumor, which grossly had the appearance of a meningioma. Histopathology of the tumor was consistent with MZBCL of the MALT type. The patient was treated with Rituximab and Ibrutinib. Six months after surgery, she remained neurologically intact and free of disease.

Conclusion: We report the case of a primary MALT-type MZBCL arising in the CNS ventricular system, with characteristics mimicking meningioma. This lymphoma involved the lateral ventricle and likely originated from the choroid plexus. Meningothelial cells and epithelial cells in the choroid plexus may acquire MALT in response to chronic inflammatory stimuli, such as infection or autoimmune disease. In rare cases, MALT lymphoma may develop as part of this pathogenesis.

Keywords: Cerebral ventricle, Choroid plexus, CNS lymphoma, MALT lymphoma, Marginal zone B-cell lymphoma

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is an aggressive extranodal subtype of non-Hodgkin lymphoma (NHL) arising in the brain, spinal cord, eyes, or leptomeninges.^[4] PCNSL parenchymal lesions are often periventricular,^[4] contacting the ependyma in 18% of cases,^[2] and extending into the ventricles in up to 10.6% of cases.^[1] However, an isolated or predominantly intraventricular mass is rare.^[1]

PCNSL is classified as diffuse large B-cell lymphoma in 90% of cases.^[4] Rarely, pathology may show Burkitt, low-grade, or T-cell lymphoma.^[4] Marginal zone B-cell lymphoma (MZBCL) is a

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2022 Published by Scientific Scholar on behalf of Surgical Neurology International

low-grade subtype of NHL that includes mucosa-associated lymphoid tissue (MALT) lymphoma.^[15] MALT-type MZBCL, representing 7.6% of NHLs, most commonly arises in the gastrointestinal tract but can also arise in tissues without a mucosa.^[15] Primary MALT-type MZBCL of the CNS is a very rare entity that, when present, most often involves the dura and can mimic meningioma.^[8,10,15]

Primary MALT-type MZBCL arising in an intraventricular location of the CNS is an extremely rare presentation. To the best of our knowledge, this has only been reported in three cases.^[7,8,13] Here, we present the fourth case of primary MALT-type MZBCL arising in the left lateral ventricle of a 69-year-old female. We characterize the tumor on neuroimaging and histopathologic examination and review its potential pathogenesis.

CASE PRESENTATION

A 69-year-old right-handed female with a medical history of migraines presented with a persistent left frontal headache for 1 year. She characterized the headache as morning onset, non-radiating, and lasting several minutes with spontaneous resolution. It was not associated with visual changes, nausea, vomiting, altered mental status, or constitutional symptoms. Neurologic examination showed no focal deficits.

Magnetic resonance imaging (MRI) revealed an enhancing soft-tissue lesion within the atrium of the left lateral ventricle [Figure 1a-c]. The lesion was associated with mild periventricular edema in the periatrinal region, extending along the temporal region. Diffusion-weighted imaging showed no diffusion restriction. There was no evidence of hydrocephalus or midline shift. There were two incidental small enhancing lesions in noncontiguous areas of the brain parenchyma, without surrounding edema. One lesion was noted within the left corona radiata [Figure 2a-c] while the second was noted along the left parasagittal frontoparietal region [Figure 2d-f].

Five months earlier, the patient presented to the hospital with similar complaints. Complete workup, including computed tomography (CT) scan of the chest, abdomen, and pelvis, and lumbar puncture to evaluate for infectious, inflammatory, and neoplastic causes, was negative. MRI showed the same intraventricular lesion coinciding with the choroid plexus, in addition to the two enhancing lesions in the parenchyma. However, at this time, postinfectious inflammation from COVID-19 infection 4 months before the onset of headaches was considered a potential etiology of the lesions and symptoms. Thus, no treatment was initiated, and surgery was not considered, at this time. Follow-up MRI 5 months later [Figure 1a-c] demonstrated a mild increase in the size of the intraventricular lesion. Differential diagnosis included meningioma or choroid plexus lesion. The two additional incidental lesions remained stable.

We decided to perform an excisional biopsy of the tumor under general anesthesia, with the intent of using direct vision to control potential intraventricular bleeding. A 3 cm × 3 cm left parietal craniotomy was performed. A tubular retractor was guided to the left atrium of the lateral ventricle using neuronavigation. An operating microscope was used for visualization. Once the ventricle was entered, the lesion was firm and encapsulated, in a distinct plane relative to surrounding structures. It was separated from the choroid plexus and removed *en bloc* to avoid spilling its contents into the ventricular system. Grossly, the tumor had the appearance of a meningioma.

Postoperatively, systemic steroid therapy was initiated. MRI on postoperative day 9 demonstrated gross total resection (GTR) of the tumor [Figure 3a-c]. The two additional incidental lesions remained stable. The patient remained neurologically intact.

Pathology of the tumor was consistent with MZBCL of the MALT type. Histologic examination revealed a dense diffuse infiltrate of small lymphoid cells with dark nuclei and scant to moderate amounts of pale cytoplasm, with

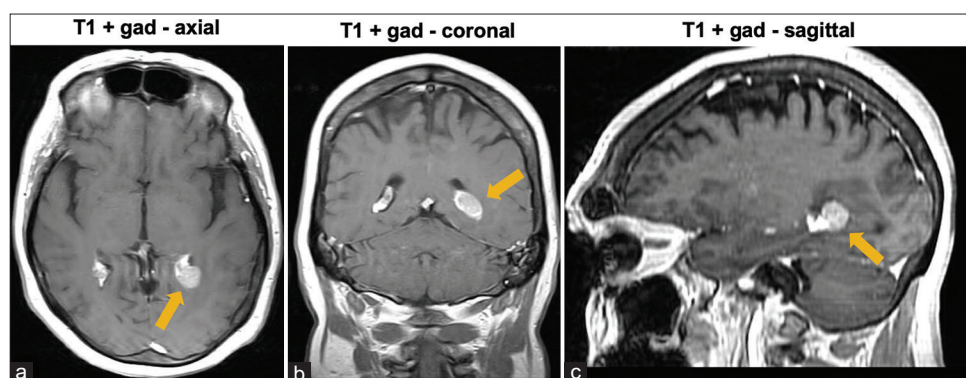


Figure 1: (a-c) Preoperative T1-weighted MRI images enhanced with gadolinium show the homogeneously enhancing tumor (arrow) in the left lateral ventricle.

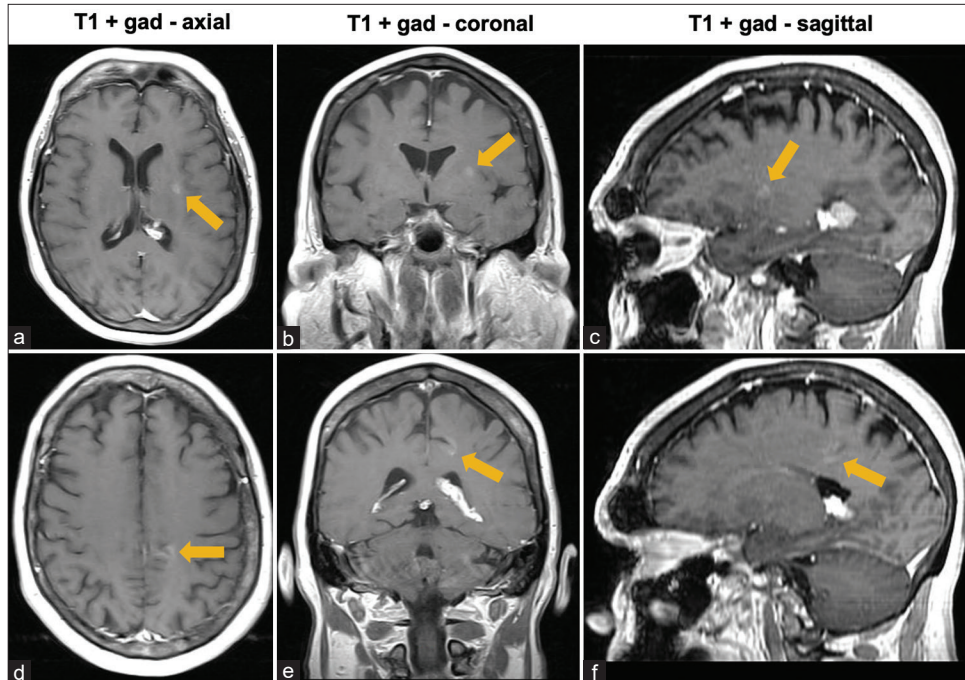


Figure 2: T1-weighted MRI images enhanced with gadolinium show the small enhancing lesions (arrow) in both the left corona radiata (a-c) and the left parasagittal frontoparietal region (d-f).

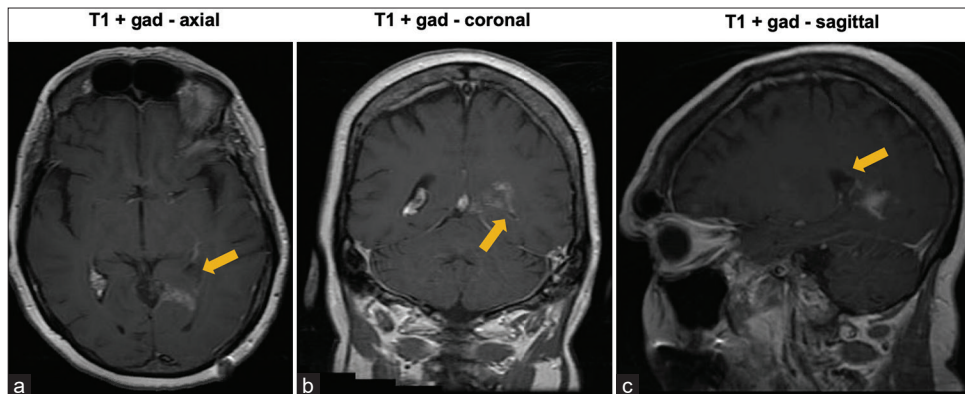


Figure 3: (a-c) T1-weighted MRI images with gadolinium enhancement on postoperative day 9 shows gross total resection (arrow) of the enhancing mass.

occasional aggregates resembling germinal centers. Scattered psammomatous calcification was seen. Most tumor cells were CD20 and PAX5 positive B-cells negative for cyclin D1, CD5, CD10, CD43, and MYC. A subset of B-cells was BCL6 and Ki-67 positive in irregular aggregates, consistent with germinal centers. Kappa light chain restriction was present. Tumor cells were negative for Epstein-Barr virus-encoded small RNAs by *in situ* hybridization. The Ki-67 proliferation index outside germinal centers was 20%.

Additional workup was performed to rule out peripheral involvement. Bone marrow biopsy demonstrated involvement by CD10 and CD5 negative B-cell lymphoma in 10–20% of cells by immunostaining, consistent with the

patient's MZBCL. Fluorodeoxyglucose (FDG) positron emission tomography scan showed no evidence of pathologic FDG uptake.

She is receiving adjuvant treatment with Rituximab, planned for 9 months, and Ibrutinib maintenance therapy planned for 2 years. At 6 months after surgery, she was neurologically intact and free of disease, demonstrated by lumbar puncture and complete neuraxis MRI.

DISCUSSION

We present a rare case of PCNSL of the MALT type of MZBCL originating in the left lateral ventricle of a 69-year-

old woman. To the best of our knowledge, only three other cases have been reported in the literature.^[7,8,13]

PCNSLs of the MALT type, not limited to intraventricular locations, most commonly present in middle-aged or older women with seizures, headaches, or visual disturbances.^[8] The majority of these tumors are dural-based,^[8,15] in line with the 2016 World Health Organization classification of CNS tumors which describes MALT lymphoma of the dura.^[10] In addition to mimicking meningiomas,^[1,15] MALT-type PCNSLs are most often indolent and have a good prognosis,^[8,15] with an overall 5-year survival rate of 81%.^[15]

In a recent review encompassing 45 cases, ventricle-predominant PCNSL (VP-PCNSL) was defined as occurring almost exclusively within the CNS ventricular system, with little or no adjacent parenchymal involvement and no separate intraparenchymal lesions.^[11] Our case meets these criteria as a solitary intraventricular lymphoma in the left lateral ventricle. Although our patient had two additional enhancing lesions, these were noncontiguous with, and likely unrelated to, the intraventricular tumor. While the tumor displayed mild interval growth on MRI, these lesions were stable over the course of 5 months and postoperatively. They may represent incidental vascular malformations or persistent postinfectious inflammatory changes from COVID-19 infection.

VP-PCNSLs present with a median age of 60.5 years, rapid clinical progression, multifocal disease, edema in adjacent brain tissue, and avid enhancement and restricted diffusion on MRI.^[11] Our patient's presentation is not in line with all these features, as her clinical progression was not rapid and diffusion restriction not present on MRI. Our patient's lymphoma progressed over the course of a year, causing indolent symptoms, as would be expected for an intraventricular tumor not obstructing CSF flow or compressing brain parenchyma. Aside from the primary

tumor, our patient also had a positive bone marrow biopsy consistent with MZBCL. This finding is significant, as bone marrow involvement in MALT-type MZBCL is rare.^[15]

VP-PCNSLs involve the lateral ventricles in 56% of cases,^[11] as in our case. [Table 1] provides a comparison of our case to the MALT VP-PCNSLs reported in the literature thus far. All three previously reported MALT VP-PCNSLs arose in the lateral ventricle and appeared to follow the choroid plexus.^[1,7,8,13] As seen on MRI, our patient's lymphoma also appears to follow, and likely originated from, the choroid plexus. In fact, in our patient, this close association with the choroid plexus contributed to contrast-enhanced CT of the head being non-diagnostic months before the first MRI. At that time, the lateral ventricles displayed bilateral hyperdensity of both the choroid plexus and tumor. Enlargement of the tumor relative to the choroid plexus was subtle and indistinguishable on CT. Hyperdensity on CT is, in fact, a characteristic feature of VP-PCNSLs.^[11] On histology, no choroid plexus tissue was identified in our patient's resected mass, confirming a distinct tumor lesion. In one case of MALT VP-PCNSL, pathology showed engorgement of the choroid plexus papillae due to lymphoid infiltrates.^[13]

Few plausible hypotheses exist regarding the potential pathogenesis of MALT lymphomas in the CNS, which contains no native mucosal tissue. In one hypothesis, meningeothelial cells (MECs) of the CNS serve as a substitute for a mucosal surface.^[6] MECs are present in the arachnoid membrane and in arachnoid villi within dural venous sinuses,^[6] which could explain MALT PCNSL reported in the cavernous sinus.^[12] Similarly, arachnoid cell nests are known to be associated with the choroid plexus in the lateral ventricles, which may account for intraventricular meningiomas.^[8] Thus, the pathogenesis of intraventricular MALT lymphoma and meningioma shares similarities, both potentially arising from meningeal cells in the same locations, such as the choroid plexus. This, coupled with

Table 1: Clinical characteristics of reported MALT VP-PCNSLs.

Case	Year	Author	Age	Sex	Tumor Location	Symptoms	Clinical Diagnosis	Treatment	Clinical Outcome
1	2014	Sebastian <i>et al.</i> ^[13]	65	F	Atrium, L lateral ventricle	Incidental finding	Asymmetric choroid glomus	GTR	Not reported
2	2006	Jung <i>et al.</i> ^[7]	63	M	Atrium, R lateral ventricle	Seizures, transient L leg monoparesis	Meningioma	GTR, adjuvant MTX	Not reported
3	2005	Kelley <i>et al.</i> ^[8]	53	M	Atrium, R lateral ventricle	Headaches, seizure	Meningioma	GTR, adjuvant Liposomal Ara-C	No recurrence at 14 months
4	Present report	Present report	69	F	Atrium, L lateral ventricle	Headaches	Meningioma	GTR, adjuvant Rituximab and Ibrutinib	No recurrence at 6 months

MALT: Mucosa-associated lymphoid tissue, VP-PCNSLs: Ventricle-predominant primary central nervous system lymphomas, GTR: Gross total resection, L: Left, R: Right

MALT lymphomas being radiographically indistinguishable from meningiomas,^[15] explains why the preoperative clinical diagnosis of MALT lymphomas is often meningioma.

Psammoma bodies present in MALT-lymphomas may be an indicator of the presence of meningothelial cells.^[8] Psammomatous calcifications were seen in our patient's tumor, as well as in two of the three other cases of intraventricular MALT lymphoma.^[7,8] All four cases of intraventricular MALT lymphoma, including our case, involved the atrium of the lateral ventricle.^[7,8,13] The atrium contains the choroid glomus, a bulky enlargement of choroid plexus often presenting with calcifications or cysts.^[9] MALT lymphomas or meningiomas arising from the choroid glomus can be misdiagnosed as asymmetric enlargements of the choroid glomus.^[13]

While MECs may serve as a substitute for a mucosal surface, allowing MALT PCNSLs to grow, recruitment of peripheral B lymphocytes to the site of MECs may be an important part of the pathogenesis.^[6,7] In fact, MALT lymphoma growth is known to be associated with chronic antigenic stimulation and inflammation due to infectious or autoimmune causes.^[6,7,15] The potential role of this mechanism in the CNS is further supported when considering that MECs are known to provide a protective and immunologic role within meninges, clearing CSF of bacteria and apoptotic cells and secreting both pro- and anti-inflammatory cytokines.^[5] Choroidal epithelial cells have similarly been found to be involved in leukocyte recruitment to the choroid plexus through secretion of cytokines and expression of surface adhesion molecules.^[14] These findings, taken together, suggest that MECs and epithelial cells in the choroid plexus may have a robust response to chronic inflammatory stimuli, eventually acquiring MALT and, in rare cases, developing MALT lymphoma.

Infections such as *Helicobacter pylori*, *Borrelia burgdorferi*, *Campylobacter jejuni*, and *Chlamydia psittaci*, and autoimmune diseases such as Hashimoto's disease and Sjogren's syndrome, have been implicated in CNS MZBCLs.^[15] However, the majority of MALT PCNSL cases in the literature report no identifiable inflammatory condition.^[8] Despite this, consideration should be given to lesser-known potential inflammatory etiologies of MALT lymphomas, including viruses. Hepatitis C, for instance, has been implicated in CNS MZBCLs.^[3] The choroid plexus is known to undergo a robust inflammatory reaction to pathogens, including viruses.^[14] More recently, the COVID-19 virus has been shown to infect and damage choroid plexus epithelium.^[11] We may speculate regarding whether our patient's intraventricular MALT lymphoma arose through the mechanisms described previously, given that she reported COVID-19 infection about 4 months before the onset of her symptoms.

The standard of care in PCNSL treatment includes high dose methotrexate and rituximab as first-line induction therapy.^[4] In addition to GTR/near-GTR (24%), VP-PCNSLs are commonly treated with systemic chemotherapy including methotrexate (38%), steroids (13%), radiation (29%), and intrathecal chemotherapy (9%).^[1] Our patient underwent GTR of her tumor followed by a planned current regimen of Rituximab for 9 months and Ibrutinib for 2 years, with a good clinical outcome and no recurrence at 6 months postoperatively.

CONCLUSION

We report the case of a primary MALT-type MZBCL arising in the CNS ventricular system, with characteristics mimicking meningioma. This lymphoma involved the lateral ventricle and likely originated from the choroid plexus. Meningothelial cells and epithelial cells in the choroid plexus may acquire MALT in response to chronic inflammatory stimuli, such as infection or autoimmune disease. In rare cases, MALT lymphoma may develop as part of this pathogenesis.

Declaration 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. Ball MK, Morris JM, Wood AJ, Meyer FB, Kaszuba MC, Raghunathan A. Ventricle-predominant primary CNS lymphomas: Clinical, radiological and pathological evaluation of five cases and review of the literature. *Brain Tumor Pathol* 2020;37:22-30.
2. Bataille B, Delwail V, Menet E, Vandermarcq P, Ingrand P, Wager M, et al. Primary intracerebral malignant lymphoma: Report of 248 cases. *J Neurosurg* 2000;92:261-6.
3. Estevez M, Chu C, Pless M. Small B-cell lymphoma presenting as diffuse dural thickening with cranial neuropathies. *J Neurooncol* 2002;59:243-7.
4. Grommes C, Rubenstein JL, DeAngelis LM, Ferreri AJ, Batchelor TT. Comprehensive approach to diagnosis and treatment of newly diagnosed primary CNS lymphoma. *Neuro Oncol* 2019;21:296-305.
5. Hemion C, Li J, Kohler C, Scholl HP, Meyer P, Killer HE, et al. Clearance of neurotoxic peptides and proteins by

- meningothelial cells. *Exp Cell Res* 2020;396:112322.
6. Itoh T, Shimizu M, Kitami K, Kamata K, Mitsumori K, Fujita M, *et al.* Primary extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue type in the CNS. *Neuropathology* 2001;21:174-80.
 7. Jung TY, Jung S, Lee MC, Lee KH. Extranodal marginal zone B-cell lymphoma mimicking meningioma in lateral ventricle: A case report and possible pathogenesis. *J Neurooncol* 2006;80:63-7.
 8. Kelley TW, Prayson RA, Barnett GH, Stevens GH, Cook JR, Hsi ED. Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue arising in the lateral ventricle. *Leuk Lymphoma* 2005;46:1423-7.
 9. Le Gars D, Lejeune JP, Peltier J. Surgical anatomy and surgical approaches to the lateral ventricles. *Adv Tech Stand Neurosurg* 2009;34:147-87.
 10. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, *et al.* The 2016 World Health Organization classification of tumors of the central nervous system: A summary. *Acta Neuropathol* 2016;131:803-20.
 11. Pellegrini L, Albecka A, Mallery DL, Kellner MJ, Paul D, Carter AP, *et al.* SARS-CoV-2 infects the brain choroid plexus and disrupts the blood-CSF barrier in human brain organoids. *Cell Stem Cell* 2020;27:951-61.e5.
 12. Sanjeevi A, Krishnan J, Bailey PR, Catlett J. Extranodal marginal zone B-cell lymphoma of malt type involving the cavernous sinus. *Leuk Lymphoma* 2001;42:1133-7.
 13. Sebastian C, Vela AC, Figueroa R, Marin MA, Alfaro J. Primary intracranial mucosa-associated lymphoid tissue lymphoma. A report of two cases and literature review. *Neuroradiol J* 2014;27:425-30.
 14. Strazielle N, Gherzi-Egea JF. Choroid plexus in the central nervous system: Biology and physiopathology. *J Neuropathol Exp Neurol* 2000;59:561-74.
 15. Tu PH, Giannini C, Judkins AR, Schwalb JM, Burack R, O'Neill BP, *et al.* Clinicopathologic and genetic profile of intracranial marginal zone lymphoma: A primary low-grade CNS lymphoma that mimics meningioma. *J Clin Oncol* 2005;23:5718-27.

How to cite this article: Hajtovic S, Yu E, Bershadiy A, Sacho R, Gilad R. Primary intracranial marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue arising in the lateral ventricle: Case report and review of pathogenesis. *Surg Neurol Int* 2022;13:181.