ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Professor of Clinical Neurosurgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Neuro-oncology

Editor
Mitsutoshi Nakada, MD
Kanazawa University, Ishikawa, Japan

SNI
Open Access

Case Report

Primary diffuse leptomeningeal glioblastoma: Report of two cases

Jung Saehee[1], Satoshi Tsutsumi[1], Akane Hashizume[2], Satoru Tan[1], Kohei Yoshida[1], Natsuki Sugiyama[1], Hideaki Ueno[1], Hisato Ishii[1]

Departments of [1]Neurological Surgery and [2]Pathology, Juntendo University Urayasu Hospital, Urayasu, Chiba, Japan.

E-mail: Jung Saehee - s.jungu.ar@juntendo.ac.jp; *Satoshi Tsutsumi - shotaro@juntendo-urayasu.jp; Akane Hashizume - akane@juntendo-urayasu.jp; Satoru Tan - s.tan.pn@juntendo.ac.jp; Kohei Yoshida - k.yoshida.rv@juntendo.ac.jp; Natsuki Sugiyama - natsuking0602@yahoo.co.jp; Hideaki Ueno - hideakiueno1229@gmail.com; Hisato Ishii - hisato-i@juntendo.ac.jp

***Corresponding author:**
Satoshi Tsutsumi,
Department of Neurological Surgery, Juntendo University Urayasu Hospital, Urayasu, Chiba, Japan.

shotaro@juntendo-urayasu.jp

Received: 08 February 2026
Accepted: 08 April 2026
Published: 08 May 2026

DOI
10.25259/SNI_180_2026

Quick Response Code:

ABSTRACT

Background: Primary leptomeningeal glioblastoma (PLGBM) is rare and not well understood.

Case Description: Case 1: A 26-year-old woman with neurofibromatosis type 1 (NF1) sustained a headache. At presentation, the patient had unilateral abducens nerve palsy. Cerebral magnetic resonance imaging (MRI) detected subtle leptomeningeal enhancements along the brainstem and fourth ventricle, lacking an identifiable intraparenchymal mass. However, an MRI performed 2 months later revealed extensive leptomeningeal lesions over the cerebrospinal axes. Biopsy through a T9 hemilaminectomy led to the diagnosis of glioblastoma (GBM). The patient underwent chemoradiation therapy but died of disease progression 2 years after diagnosis. Case 2: A 78-year-old man presented with somnolence. The patient did not exhibit any focal neurological deficits. Cerebral MRI revealed diffuse leptomeningeal enhancement over the cerebrospinal axes. No intraparenchymal tumor was identified. Biopsy through craniotomy diagnosed GBM. Despite the commencement of chemoradiation therapy, the patient died of disease progression 45 days after diagnosis.

Conclusion: PLGBM presents a diagnostic challenge for nonspecific clinical findings. For PLGBM patients complicated by NF1, an aggressive treatment strategy may be recommended for longer survival.

Keywords: Biopsy, Chemoradiation therapy, Neurofibromatosis type 1, Primary leptomeningeal glioblastoma

INTRODUCTION

Glioblastoma (GBM) is one of the most critical malignancies, with a 5-year survival rate of 5%.[2] It commonly develops as a parenchymal lesion in the brain and spinal cord. However, in extremely rare instances, GBM shows an extensive, diffuse growth along the leptomeninges of the cerebrospinal axis without forming an intraparenchymal mass. Such GBM is referred to as primary leptomeningeal GBM (PLGBM). To the best of our knowledge, only seven adult patients with such GBMs have been documented.[3,5,7-12]

Herein, we present two patients with PLGBMs, one with familial neurofibromatosis type 1 (NF1) and the other without, with a brief review of reported PLGBMs.

CASE PRESENTATION

Case 1

A 26-year-old woman with NF1 sustained a headache that had worsened over 1 month. No central nervous system tumors had been identified in her. At presentation, the patient had right abducens nerve palsy but did not show any other neurological impairments. Cerebral magnetic resonance imaging (MRI) revealed mild tetraventriculomegaly with a patent aqueduct [Figure 1a-c]. Contrast examination revealed subtle leptomeningeal enhancements along the brainstem and fourth ventricle; however, an intraparenchymal mass was not identified. Spinal MRI revealed an asymptomatic small nodular lesion at T8/T9 on the dorsal surface of the spinal cord [Figure 1d]. At the time, contrast examination was not performed for unknown reasons. A lumbar cerebrospinal fluid (CSF) tap confirmed a markedly elevated intrathecal pressure of 65 cmH_2O. The cell count of CSF was 11/μL, while protein and glucose levels were 400 mg/dL and 50 mg/dL, respectively. CSF cytology revealed only a few lymphocytes with cell atypia. Although continuous lumbar CSF drainage was performed for the following 2 weeks, the communicating hydrocephalus did not resolve. Subsequently, the patient underwent ventriculoperitoneal shunting, which resulted in symptomatic resolution. However, surveillance MRI performed 2 months after the initial examination revealed diffuse leptomeningeal enhancement along the cerebrospinal axes, with massive tumors considerably compressing the dorsal cord [Figure 2]. Intraparenchymal mass lesions were not identified in the brain or spinal cord. A biopsy was performed through a T9 hemilaminectomy, which identified a subdural tumor grayish in color, elastic hard, and moderately vascular [Figure 3]. Microscopically, the tumor comprised highly atypical cells with prominent pleomorphism. Necrotic foci and pseudopalisading were also noted. Immunohistochemically, tumor cells were diffusely positive for glial fibrillary acidic protein (GFAP) [Figure 4]. The mindbomb homolog 1 (MIB-1) index was 40%. Methylation of the O^6-methylguanine-DNA methyltransferase (MGMT) promoter was present, whereas mutations in isocitrate dehydrogenase 1 (IDH1) and isocitrate dehydrogenase 2 (IDH2) were absent. These were analyzed using the polymerase chain reaction method. These results were consistent with an IDH-wild type GBM. Postoperatively, the patient underwent chemotherapy with temozolomide synchronously with radiotherapy to the entire craniospinal axis that resulted in a symptomatic resolution. After discharge from the hospital, the patient did not visit

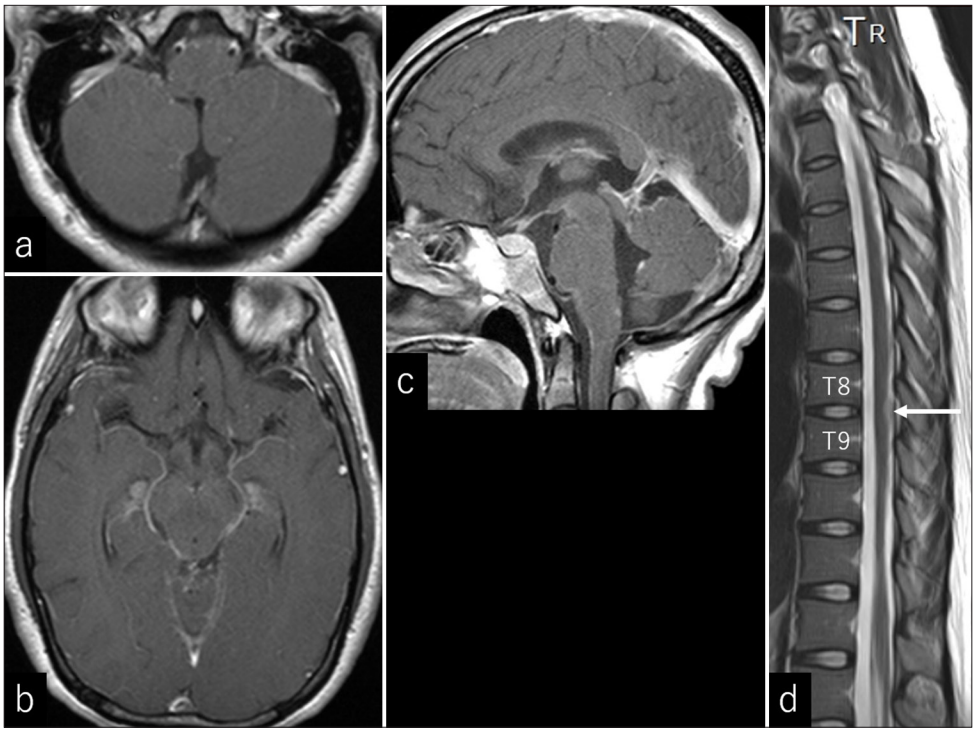

Figure 1: (a and b) Postcontrast axial magnetic resonance imaging at the levels of the medulla oblongata (a) and upper midbrain (b), showing no abnormal enhancements in the cranial cavity. (c) Postcontrast sagittal cerebral magnetic resonance image showing subtle leptomeningeal enhancements along the brainstem and fourth ventricle. (d) Sagittal T2-weighted spinal magnetic resonance image showing a small nodular lesion at T8/T9, on the dorsal surface of the cord (arrow).

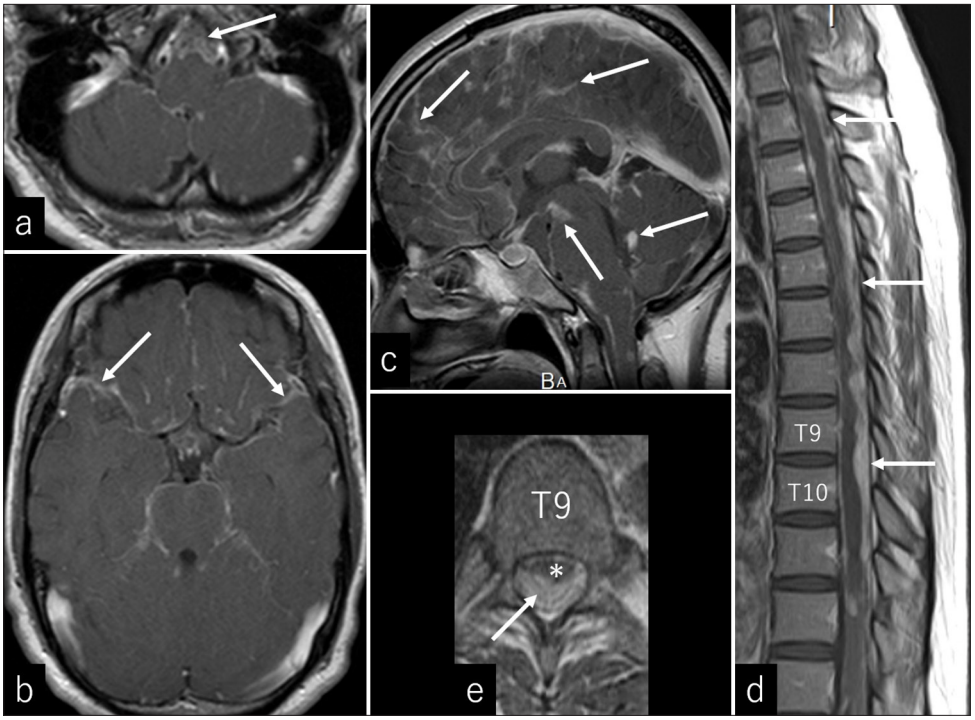

Figure 2: (a-c) Postcontrast (a and b) and (c) sagittal cerebral magnetic resonance images performed 2 months later, at the levels of (a) the medulla oblongata and (b) upper midbrain, showing diffuse leptomeningeal enhancements along the cerebral cisterns, sulci, and fourth ventricle (arrows). (d and e) Postcontrast (d) sagittal and (e) axial magnetic resonance image of the spine showing diffuse leptomeningeal enhancements along the spinal cord, with massive tumors considerably compressing the dorsal cord (arrows). Asterisk: Spinal cord.

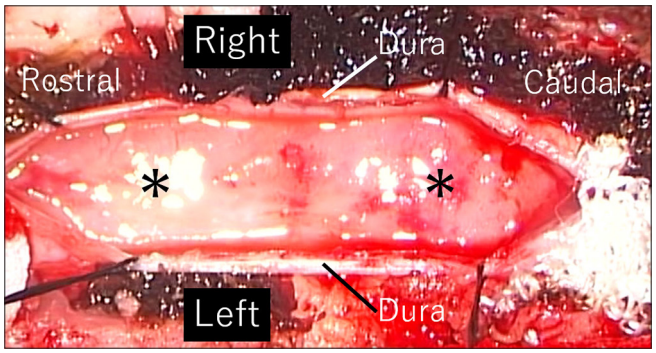

Figure 3: Intraoperative photograph, at the completion of the T9 hemilaminectomy and midline incision in the dura mater, showing tumor tissue located in the subarachnoid space (asterisks).

the outpatient clinic. After 21 months, she was taken to the hospital in a coma. Her poor physical condition did not allow examination of the cerebrospinal axis or salvage therapy. The patient died of disease progression 2 years after diagnosis.

Case 2

A 78-year-old man presented with somnolence worsening for 1 month. The patient was non-NF and his medical history was unremarkable. At presentation, the patient did not exhibit any focal neurological deficits. Cerebral MRI revealed rim-like leptomeningeal enhancements along the cerebral cisterns and spinal cord, in addition to triventricular dilation [Figure 5]. A lumbar CSF tap revealed a cell count of 12/μL, while protein and glucose levels were 183 mg/dL and 34 mg/dL, respectively. CSF cytology revealed only a few lymphocytes with cell atypia. A biopsy was performed through a right frontotemporal craniotomy, which identified a gelatinous tumor tissue located in the subarachnoid space, beneath the opacified arachnoid membranes [Figure 6]. Microscopically, the tumor comprised highly atypical cells with prominent pleomorphism. Necrotic foci were also noted. These cells were diffusely positive for GFAP [Figure 7]. The MIB-1 index was 20%. MGMT promoter methylation was absent, in addition to the absence of mutations in IDH1 or IDH2. These results are consistent with an IDH-wild type GBM. The patient underwent ventriculoperitoneal shunting on postoperative day 19 to treat hydrocephalus. Despite commencing chemotherapy synchronously with whole craniospinal irradiation, the patient died of disease progression 45 days after diagnosis. Thus, chemoradiation therapy was not completed. The family did not consent to an autopsy.

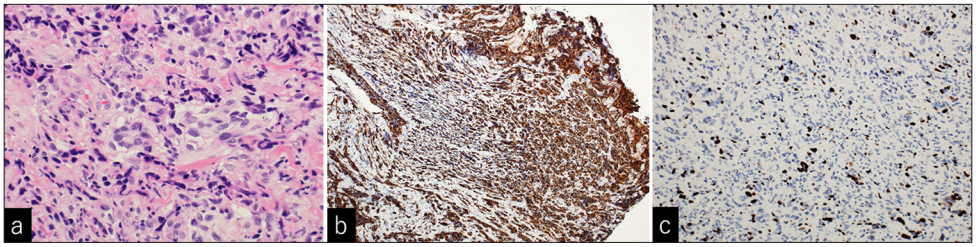

Figure 4: (a) Photomicrograph of the resected specimens showing sheet-like proliferation of highly atypical cells with prominent pleomorphism. Hematoxylin and eosin staining, ×40. (b and c) Immunohistochemical stains showing diffuse positive staining for (b) glial fibrillary acidic protein, with (c) a mindbimb homolog 1 index of 40%. b and c, ×20.

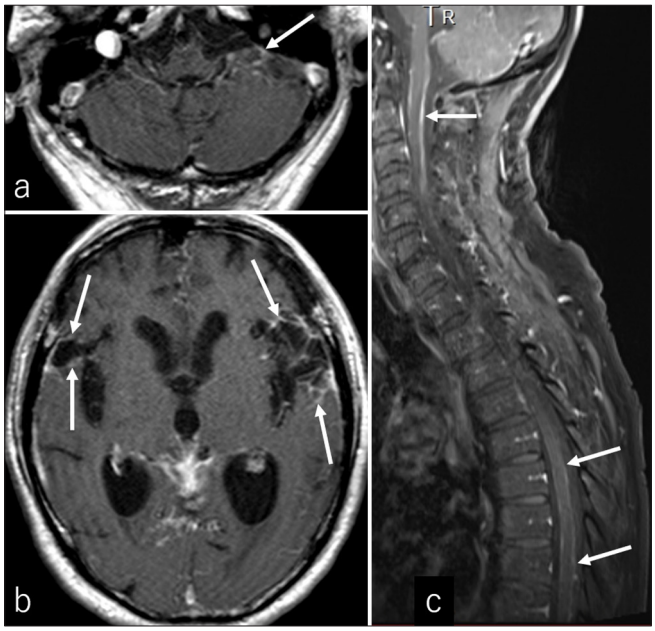

Figure 5: Postcontrast (a and b) axial and (c) coronal magnetic resonance images showing rim-like leptomeningeal enhancements along the cerebral cisterns and spinal cord (arrows).

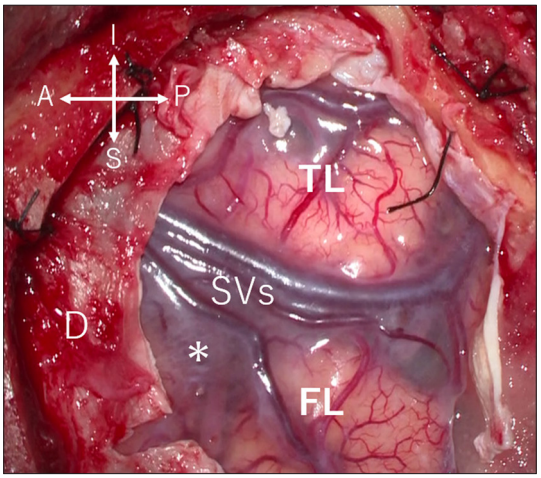

Figure 6: Intraoperative photograph showing tumor tissue located in the subarachnoid space, beneath the opacified arachnoid membrane (asterisk). A: Anterior, D: Dura mater, FL: Frontal lobe, I: Inferior, P: Posterior, S: Superior, SVs: Sylvian veins, TL: Temporal lobe.

DISCUSSION

PLGBMs are a diagnostic challenge because they typically do not show characteristic clinical symptoms, instead presenting with nonspecific clinical and radiological appearances that can result in a diagnostic delay. A recent study has reported the CSF-mediated biology of PLGBM and the development of hydrocephalus in the early stage of the disease.[4] Here, in case 1, PLGBM developed with communicating hydrocephalus followed by a marked progression in 2 months. In case 2, the PLGBM developed somnolence with a marked tumor extension on MRI. Furthermore, in either patient, CSF findings at a lumbar tap were not conclusive.

A recent investigation has suggested that the molecular profile of PLGBM typically aligns with that of IDH-wild type GBM,[13] while comprehensive profiling was often incomplete in reported cases. To date, seven patients with PLGBM have been reported. All of them were adults, including 5 men and 2 women, with a mean age of 52.4 years (range, 23–72 years). Likewise, 5 of 7 patients were managed with chemoradiation therapy [Table 1]. Except for one patient who survived for 23 months, the survival times of the other 5 were <7 months, suggesting a common dismal prognosis of PLGBM. At this time, prompt initiation of chemoradiation therapy after histological diagnosis may be a recommended treatment strategy for PLGBM. Furthermore, hypofractionated craniospinal irradiation may be recommended with the aim of improving quality of life and reducing radiation toxicity.

Although the underlying pathological mechanism remains elusive, patients with GBM complicated by NF1 have been reported to have a longer survival time, both in children and adults, than those without NF1.[1,3,6] Al-Romaihi *et al.* and Basindwah *et al.* documented distinct cerebral GBM cases

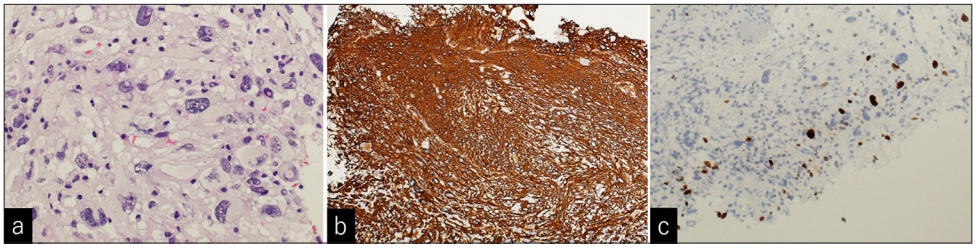

Figure 7: (a) Photomicrograph of the resected specimens showing sheet-like proliferation of highly atypical cells with prominent pleomorphism. Hematoxylin and eosin staining, ×40. (b and c) Immunohistochemical stains showing diffuse positive staining for (b) glial fibrillary acidic protein, with (c) a mindbomb homolog 1 index of 20% (c). b and c, ×20.

Table 1: Summary of reported primary diffuse leptomeningeal glioblastomas with the present cases.

Reported cases	Age (years)	Sex	Treatment	Period between diagnosis and death	NF
Gonda *et al.*[5]	35	Male	CRT	23 months	(-)
Mondia *et al.*[7]	72	Female	Palliative care	Shortly after diagnosis	(-)
Nadkarni *et al.*[8]	50	Male	CRT	6 months	(-)
Nomura *et al.*[9]	75	Female	CRT	2 months	(-)
Shuangshoti *et al.*[10]	23	Male	Unknown	Unknown	Unknown
Yamasaki *et al.*[11]	60	Male	CRT	7 months	(-)
Yomo *et al.*[12]	52	Male	CRT	3 months	(-)
Present case 1	26	Female	CRT	2 years	NF1
Present case 2	78	Male	CRT	1.5 months	(-)

CRT: Chemoradiation therapy, NF: Neurofibromatosis, NF1: Neurofibromatosis type 1

with NF1 who survived for more than 10 years.[1,3] Despite pathologically IDH-wild-type GBM, one of our patients who had complications with NF1 survived for 2 years. NF1 may be an independent prognostic factor for longer survival, although requiring further data accumulation and careful validation, excluding the influence of confounding by age and MGMT promoter methylation. Diffuse leptomeningeal enhancement, as a radiological hallmark, indicates the possibility of PLGBM. For PLGBM complicated by NF1, an aggressive treatment strategy involving prompt neurosurgical intervention may be recommended for a longer survival time.

CONCLUSION

PLGBM is a diagnostic challenge owing to its nonspecific clinical findings. For PLGBM patients complicated by NF1, an aggressive treatment strategy involving prompt neurosurgical intervention may be recommended for an expected longer survival time.

Ethical approval: Institutional review board approval is not required.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given consent for their images and other clinical information to be reported in the journal. The patient understands that the patient's names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Al-Romaihi N, Awadh M, Albalooshi M, Ahmed M, Darwish A. Clinicopathological and immunohistochemistry study of a long survivor of giant cell glioblastoma in a patient with neurofibromatosis 1: Case report. Cureus 2023;15:e39014.
2. Alexander BM, Cloughesy TF. Adult glioblastoma. J Clin Oncol 2017;35:2402-9.
3. Basindwah S, Alkhalidi H, Abdelwarith A, Elwatidy S. Ten-year survival in glioblastoma patient with neurofibromatosis type 1: Illustrative case. J Neurosurg Case Lessens 2022;3:CASE21630.
4. De Liyis BG, Oswari S, Kusdiansah M, Keswani R, Arifianto MR, Perkasa SA, *et al.* Long-term outcomes of ventricular entry in high grade glioma resection: A meta-Analysis and meta regression. Neurosurg Rev 2026;49:184.
5. Gonda T, Wakabayashi K, Haraguchi K, Arai Y, Oyama H.

Primary leptomeningeal gliomatosis treated with temozolomide: A case report. Rinsho Shinkeigaku 2021;61:862-8.
6. Huttner A, Kieran MW, Yao X, Cruz L, Ladner J, Quayle K, *et al*. Clinicopathologic study of glioblastoma in children with neurofibromatosis type 1. Pediatr Blood Cancer 2010;54:890-6.
7. Mondia MW, Hooks RE, Maragkos GA, Smith VL, McCord MR, Donahue JH, *et al*. Primary diffuse leptomeningeal glioblastoma: A case report and literature review. J Neurooncol 2025;172:265-72.
8. Nadkarni T, Hamilton K, Niazi F, Ward M, Okakpu U, Castellani RJ, *et al*. Histone-mutant glioma presenting as diffuse leptomeningeal disease. CNS Oncol 2021;10:CNS75.
9. Nomura N, Nagasaka S, Suzuki K, Yamamoto J. Imaging-tracked progression of primary leptomeningeal gliomatosis: A case report. Surg Neurol Int 2024;15:411.
10. Shuangshoti S, Shuangshoti S. Primary diffuse leptomeningeal glioblastoma multiforme of brainstem and spinal cord clinically mimicking meningitis: Case report and review of literature. J Med Assoc Thai 1996;79:403-8.
11. Yamasaki K, Yokogami K, Ohta H, Yamashita S, Uehara H, Sato Y, *et al*. Case of primary diffuse leptomeningeal gliomatosis. Brain Tumor Pathol 2014;31:177-81.
12. Yomo S, Tada T, Hirayama S, Tachibana N, Otani M, Tanaka Y, *et al*. A case report and review of the literature. J Neurooncol 2007;81:209-16.
13. Zhu Y, Carabenciov DD, Johnson DR, Trejo-Lopez JA, Nguyen AT, Raghunathan A, *et al*. Molecular profile of adult primary leptomeningeal gliomatosis aligns with glioblastoma, IDH-wildtype. Brain Pathol 2025;35:e13326.

How to cite this article: Saehee J, Tsutsumi S, Hashizume A, Tan S, Yoshida K, Sugiyama N, *et al*. Primary diffuse leptomeningeal glioblastoma: Report of two cases. Surg Neurol Int. 2026;17:272. doi: 10.25259/SNI_180_2026