

Case Report

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Temporal, spatial, and histopathological heterogeneity of multiple meningiomas associated with neurofibromatosis type 2: An 11-year follow-up case report

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Abstract

Neurofibromatosis type 2 (NF2) is a hereditary tumor predisposition syndrome frequently associated with multiple meningiomas. We report a young woman with NF2 who was followed for more than 11 years and developed multiple cranial and spinal meningiomas requiring seven surgical interventions. Tumors arose in distinct anatomical locations, including the cerebellum, temporal lobe, cerebellopontine angle, posterior corpus callosum region, cervical spine, and fronto-orbital region. Histopathological examination demonstrated marked heterogeneity, including transitional, psammomatous, and fibrous meningioma subtypes (CNS WHO grade 1), as well as atypical meningioma (CNS WHO grade 2). During follow-up, the patient also received temozolomide therapy, during which temporary radiological stabilization was observed before subsequent progression necessitated additional treatment. This case highlights the temporal, spatial, and histopathological heterogeneity of NF2-associated meningiomas and underscores the importance of individualized treatment planning, multidisciplinary follow-up, and long-term surveillance in patients with multifocal disease.

Keywords: neurofibromatosis type 2, meningioma, histopathological heterogeneity, multiple meningiomas, long-term follow-up

1. Introduction

Meningiomas are neoplasms arising from arachnoid cap cells and represent the most common primary intracranial tumors in adults. Although the majority of meningiomas are benign and exhibit slow growth, their clinical presentation varies according to tumor location, size, and involvement of adjacent neurovascular structures, ranging from headache and epileptic seizures to focal neurological deficits and signs of increased intracranial pressure (1).

Neurofibromatosis type 2 (NF2) is an autosomal dominant tumor predisposition syndrome caused by mutations in the tumor suppressor NF2 gene. Although bilateral vestibular schwannomas constitute the hallmark feature of the disease, meningiomas, ependymomas, and spinal tumors are also frequently encountered in affected individuals. Compared with sporadic meningiomas, NF2-associated meningiomas tend to occur at a younger age, present as multiple lesions, develop in different anatomical locations over time, and require repeated surgical interventions. These characteristics make disease management particularly challenging and necessitate long-term multidisciplinary follow-up (2, 3).

The tendency of NF2-associated meningiomas to arise at distinct anatomical sites and exhibit variable histopathological features over time necessitates an individualized treatment strategy. However, reports describing long-term follow-up of NF2-associated multiple meningiomas with repeated surgical

interventions and marked histopathological heterogeneity remain scarce. In this report, we describe the clinical course and management of a young woman with NF2 who developed multiple cranial and spinal meningiomas during more than 11 years of follow-up, underwent seven surgical interventions, and exhibited marked histopathological heterogeneity.

2. Case Report

A 23-year-old woman initially presented to an outside institution in November 2014 with bilateral hearing loss and severe headache. Following neurological and radiological evaluation, including the identification of bilateral vestibular schwannomas and multiple intracranial lesions radiologically suggestive of meningiomas, she was clinically diagnosed with NF2 at the outside institution. During this period, a right cerebellar lesion was surgically resected, and histopathological examination revealed a meningioma, CNS WHO grade 1.

The patient was referred to our institution in June 2021 because of persistent headache. Radiological evaluation demonstrated progression and rapid growth of multiple intracranial lesions; however, there was no new neurological deficit or clinical deterioration warranting immediate surgical intervention. Given the multiplicity and distribution of the intracranial lesions, treatment of all lesions with surgery or radiotherapy was not considered feasible. Following multidisciplinary tumor board discussion, systemic treatment

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with temozolomide was initiated by the Department of Medical Oncology, and the patient received six cycles between June and December 2021. Temporary radiological stabilization was observed; however, follow-up imaging in November 2022

demonstrated renewed tumor progression. The overall clinical course, treatment interventions, and histopathological findings are summarized in Fig. 1.

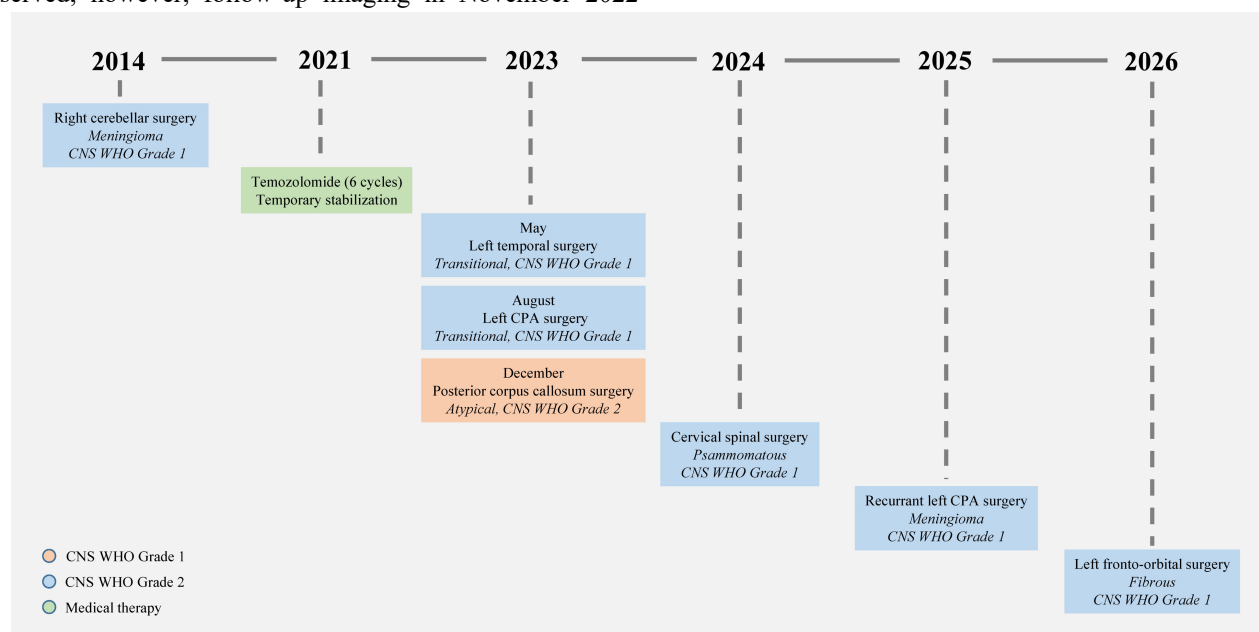


Fig. 1. Timeline of the clinical course, treatment interventions, and histopathological findings during long-term follow-up of a patient with NF2-associated multiple meningiomas. Blue boxes indicate CNS WHO grade 1 meningiomas, the orange box indicates a CNS WHO grade 2 meningioma, and the green box represents temozolomide therapy. Histopathological subtypes are shown in italics.

The left temporal lesion, which had been present on imaging since 2021, demonstrated progressive growth on follow-up imaging in November 2022. Given the progressive growth of the lesion and the development of seizures despite antiepileptic treatment, surgical resection was performed in May 2023. Histopathological examination demonstrated a transitional meningioma, CNS WHO grade 1. Subsequently, in August 2023, a second surgical procedure was performed for a left cerebellopontine angle lesion, and histopathological examination likewise demonstrated a transitional meningioma, CNS WHO grade 1. In December 2023, progression of a lesion located posterior and inferior to the corpus callosum resulted in brainstem compression, prompting surgical resection. Histopathological evaluation revealed an atypical meningioma, CNS WHO grade 2. Representative preoperative and postoperative images from these three surgical interventions are shown in Fig. 2.

As part of neuraxis surveillance, spinal MRI had been performed as early as March 2020. During subsequent follow-up, the patient developed progressive myelopathic symptoms. Spinal MRI demonstrated multiple contrast-enhancing intradural lesions, including a posteriorly located lesion extending from the foramen magnum to C6, with a maximum thickness of approximately 8 mm. The lesion caused spinal

canal narrowing and cord compression, most pronounced at C5–6, with associated myelopathic signal changes extending into the upper thoracic cord. Compared with the March 2020 spinal MRI, the distribution and size of the intradural lesions were largely similar, whereas cord compression at C5–6 and the associated myelopathic signal changes had progressed. The cervical lesion was excised via a posterior cervical approach in June 2024, and histopathological examination revealed a psammomatous meningioma, CNS WHO grade 1. Follow-up imaging performed in July 2025 because of recurrent headache and gait imbalance demonstrated recurrence of the left cerebellopontine angle lesion. The patient subsequently underwent repeat surgical resection, and histopathological examination confirmed a meningioma, CNS WHO grade 1. During continued follow-up, the patient developed progressive visual impairment and was evaluated by the Department of Ophthalmology. Ophthalmological examination demonstrated compression of the left optic disc, and radiological studies revealed progression of a left fronto-orbital meningioma. Surgical resection was performed in January 2026, and histopathological examination revealed a fibrous meningioma, CNS WHO grade 1. Representative preoperative and postoperative images from these three surgical interventions are shown in Fig. 3.

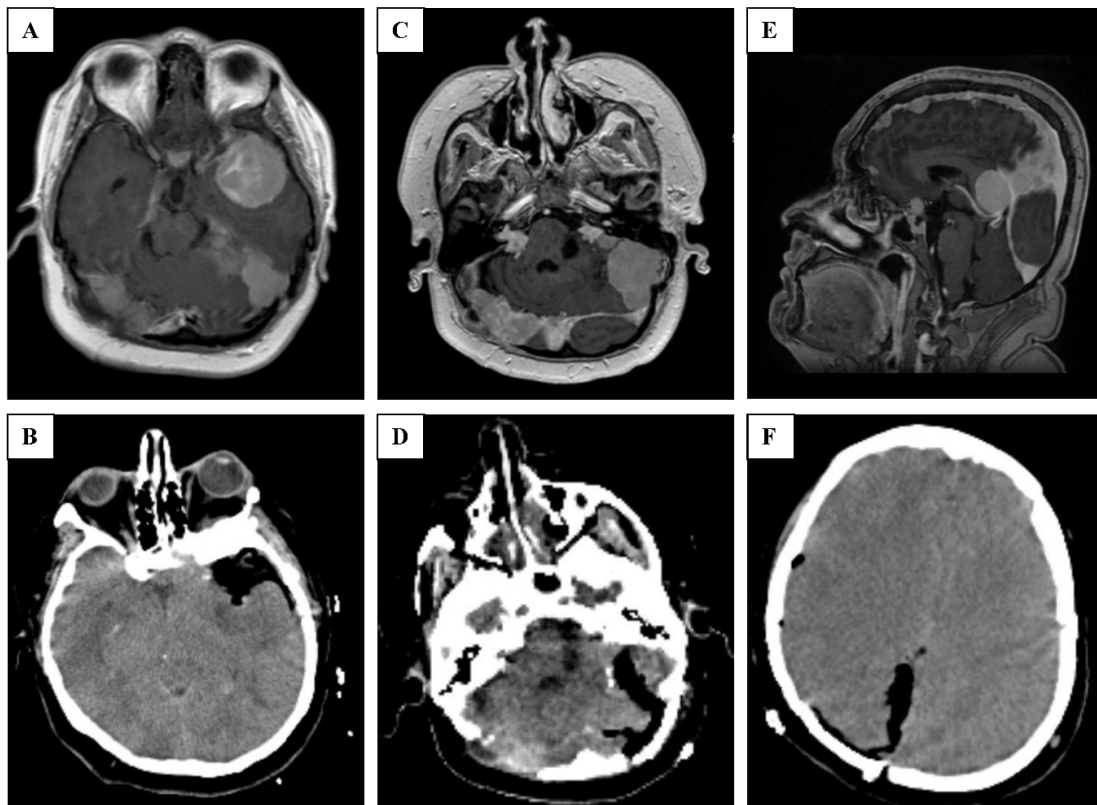


Fig. 2. Representative radiological images of intracranial meningiomas and postoperative findings during the early course of the disease. May 2023 left temporal meningioma resection: (A) preoperative contrast-enhanced MRI demonstrating the lesion and (B) postoperative CT showing the resection cavity. August 2023 left cerebellopontine angle meningioma resection: (C) preoperative contrast-enhanced MRI and (D) postoperative CT. December 2023 resection of the lesion located posterior to the corpus callosum: (E) sagittal preoperative contrast-enhanced MRI and (F) postoperative CT. Preoperative images were obtained with contrast-enhanced MRI, whereas postoperative images were obtained with CT.

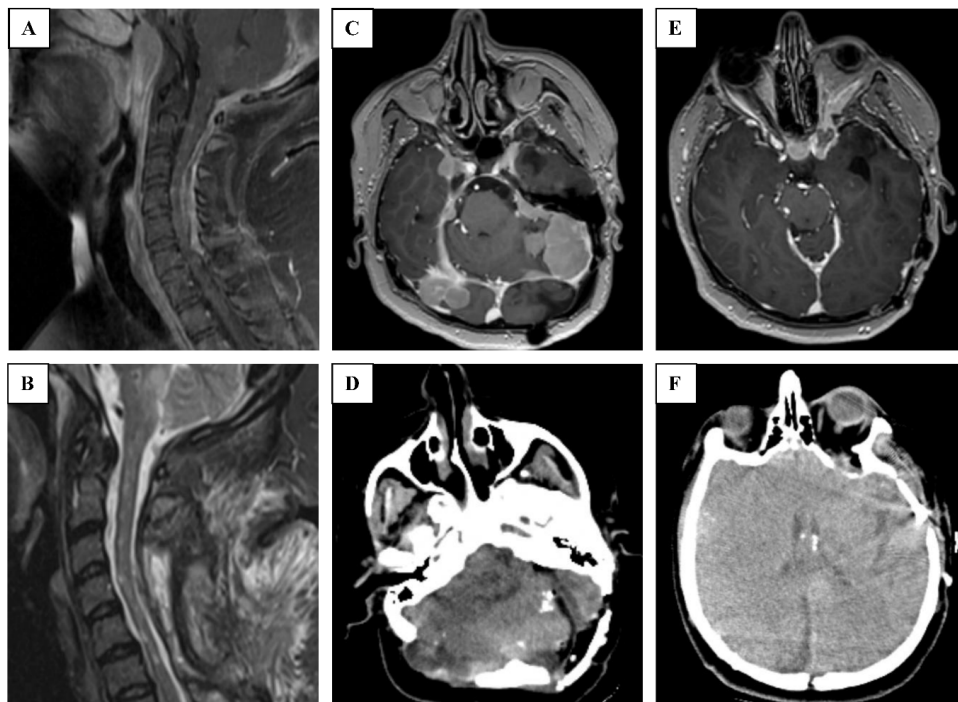


Fig. 3. Representative radiological images obtained during the later course of the disease. June 2024 cervical spinal meningioma resection: (A) preoperative MRI demonstrating the lesion and (B) postoperative MRI showing decompression after surgery. July 2025 resection of recurrent left cerebellopontine angle meningioma: (C) preoperative contrast-enhanced MRI and (D) postoperative CT. January 2026 left fronto-orbital meningioma resection: (E) preoperative contrast-enhanced MRI and (F) postoperative CT. Preoperative images were obtained with MRI, whereas postoperative imaging consisted of MRI or CT depending on the surgical stage and follow-up protocol. Representative images from six of the seven surgical interventions are shown. Imaging studies from the initial surgery performed at an outside institution in 2014 were unavailable for review.

During more than 11 years of follow-up, the patient underwent seven separate surgical interventions for multiple cranial and spinal meningiomas, as summarized in Table 1. Histopathological evaluation demonstrated marked heterogeneity among the tumors, including transitional,

psammomatous, and fibrous meningioma subtypes (CNS WHO grade 1), as well as atypical meningioma (CNS WHO grade 2). The patient remains under regular clinical and radiological surveillance, continues to use a hearing aid, and has no significant motor neurological deficits.

Table 1. Chronological clinical course, management, and histopathological findings

Date	Tumor Location	Clinical Presentation	Management	Histopathological Diagnosis
November 2014	Right cerebellar	Bilateral hearing loss, severe headache	Surgical resection	Meningioma, CNS WHO grade 1
June 2021	Multiple progressive intracranial lesions	Headache and radiological progression	Surveillance and 6 cycles of temozolomide	No tissue diagnosis
May 2023	Left temporal	Seizure despite antiepileptic treatment	Surgical resection	Transitional meningioma, CNS WHO grade 1
August 2023	Left CPA	Radiological progression	Surgical resection	Transitional meningioma, CNS WHO grade 1
December 2023	Posterior corpus callosum	Brainstem compression	Surgical resection	Atypical meningioma, CNS WHO grade 2
June 2024	Cervical spinal	Myelopathic symptoms	Surgical resection	Psammomatous meningioma, CNS WHO grade 1
July 2025	Left CPA (recurrent)	Headache and gait imbalance	Repeat surgical resection	Meningioma, CNS WHO grade 1
January 2026	Left fronto-orbital	Visual impairment and optic disc compression	Surgical resection	Fibrous meningioma, CNS WHO grade 1

CNS WHO: World Health Organization Classification of Tumours of the Central Nervous System.

3. Discussion

The present case highlights three notable features of NF2-associated meningiomas: temporal heterogeneity, spatial heterogeneity, and histopathological heterogeneity. During more than 11 years of follow-up, the patient underwent seven surgical interventions for multiple cranial and spinal meningiomas arising in distinct anatomical locations. In addition to the development of new lesions over time, recurrence occurred in a previously treated cerebellopontine angle lesion, illustrating the dynamic nature of tumor progression in NF2-associated disease (3, 4).

The prolonged clinical course observed in this patient underscores the complexity of managing multifocal NF2-associated tumors. Previous studies have shown that NF2-associated meningiomas may involve both cranial and spinal compartments and often require repeated interventions throughout long-term follow-up (5-7). Consistent with this approach, management in our patient evolved according to tumor location, growth pattern, symptom burden, and functional status. As a result, treatment consisted of repeated surgical interventions performed at different time points rather than a single definitive procedure. To contextualize the present case, table 2 summarizes representative reports selected for their relevance to multifocal cranial and spinal involvement, longitudinal or staged management, and biological or pathological heterogeneity in NF2-associated disease.

Table 2. Representative Reports on Complex NF2-Associated Meningiomas and Comparison with the Present Case

Study	Main Clinical Features	Treatment Strategy	Relevance to Present Case
Aboukais et al., 2018 (7)	Multiple cranial and spinal tumors in NF2 patients	Individualized multidisciplinary management	Demonstrates the complexity of treatment planning in NF2
Sirko et al., 2019 (9)	Multifocal cranial and spinal tumors	Multistage treatment approach	Illustrates successful staged management of multifocal NF2 disease
Pemov et al., 2020 (6)	Cranial and spinal NF2-associated meningiomas	Long-term clinical and pathological evaluation	Demonstrates clinical and genomic diversity of NF2-associated cranial and spinal meningiomas
Present case	Multifocal cranial and spinal meningioma with marked histopathological heterogeneity	Seven surgeries and temozolomide therapy during long-term follow-up	Demonstrates temporal, spatial, and histopathological heterogeneity requiring individualized long-term management

NF2: Neurofibromatosis type 2

The most distinctive feature of the present case was the marked histopathological heterogeneity observed throughout the follow-up period. Histological examination revealed transitional, psammomatous, and fibrous meningioma subtypes (CNS WHO grade 1), as well as atypical meningioma (CNS WHO grade 2), across anatomically distinct tumors. Although NF2-associated meningiomas are known to exhibit considerable biological diversity compared with sporadic meningiomas, reports demonstrating multiple histological subtypes within the same patient over such a prolonged period remain limited (8). Pemov et al. demonstrated clinical and genomic diversity among cranial and spinal NF2-associated meningiomas, while Gregory et al. highlighted the biological heterogeneity of meningiomas arising in patients with NF2-schwannomatosis (4, 6). Our findings further illustrate how this heterogeneity may manifest in routine clinical practice, with distinct histopathological subtypes emerging at different anatomical locations and time points.

Another notable aspect of this case was the need for treatment adaptation throughout the clinical course. Despite radiological progression in 2021, immediate surgical intervention was deferred because there was no new neurological deficit or clinical deterioration warranting surgery. Given the multiplicity and distribution of the intracranial lesions, treatment of all lesions with surgery or radiotherapy was not considered feasible, and temozolomide was initiated following multidisciplinary tumor board evaluation. Importantly, temozolomide is not an established standard systemic therapy for meningiomas, and available evidence has not demonstrated clinically meaningful activity sufficient to support its routine use (10). Although temporary radiological stabilization was observed in our patient, this finding should be interpreted cautiously and cannot establish a therapeutic effect in a single case. Subsequent disease progression was accompanied by seizures, myelopathic symptoms, gait disturbance, and visual deterioration, necessitating further surgical interventions. Similar to the staged treatment strategy reported by Sirko et al., management required repeated reassessment and adaptation according to the evolving clinical course (9).

Preservation of neurological function remains a major objective in the management of NF2-associated tumors. Despite seven surgical procedures during more than 11 years of follow-up, the patient maintained functional independence with the aid of a hearing device and did not develop significant motor neurological deficits. This favorable functional outcome highlights the value of long-term multidisciplinary follow-up and individualized treatment planning in patients with complex NF2-associated disease (3, 10).

The present case demonstrates the temporal, spatial, and histopathological heterogeneity of NF2-associated multiple meningiomas over long-term follow-up. Management should be individualized according to tumor location, growth pattern,

clinical presentation, and functional status, with continuous clinical and radiological surveillance and multidisciplinary reassessment. Beyond tumor control, preservation of neurological function and quality of life should remain a primary therapeutic goal in patients with complex multifocal disease.

Conflict of interest

The authors declared no conflict of interest.

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None to declare.

Authors' contributions

Concept: M.A.E., O.B., Design: M.A.E., O.B., Data Collection or Processing: M.A.E., G.G., Analysis or Interpretation: M.A.E., M.A., Literature Search: M.A.E., Writing: M.A.E., M.A.

Ethical Statement

Ethics committee approval was not required for this case report in accordance with institutional policies.

References

1. Ogasawara C, Philbrick BD, Adamson DC. Meningioma: a review of epidemiology, pathology, diagnosis, treatment, and future directions. *Biomedicines*. 2021;9(3):319. doi:10.3390/biomedicines9030319.
2. Bachir S, Shah S, Shapiro S, Koehler A, Mahammedi A, Samy RN, et al. Neurofibromatosis type 2 (NF2) and the implications for vestibular schwannoma and meningioma pathogenesis. *Int J Mol Sci*. 2021;22(2):690. doi:10.3390/ijms22020690.
3. Evans DG, Mostaccioli S, Pang D, Fadzil OCM, Pittara M, Champollion N, et al. ERN GENTURIS clinical practice guidelines for the diagnosis, treatment, management and surveillance of people with schwannomatosis. *Eur J Hum Genet*. 2022;30(7):812-817. doi:10.1038/s41431-022-01086-x.
4. Gregory GE, Islim AI, Hannan CJ, Jones AP, Hammerbeck-Ward C, Rutherford SA, et al. The clinical, genetic, and immune landscape of meningioma in patients with NF2-schwannomatosis. *Neurooncol Adv*. 2023;5(Suppl 1):i94-i104. doi:10.1093/noajnl/vdac127.
5. Nawabi NLA, Chalif JJ, Renauld S, Mehta NH, Jha R, Gerstl JVE, et al. Presenting characteristics and clinical outcomes of idiopathic versus neurofibromatosis type 2-associated spinal meningiomas: a retrospective institutional experience. *J Neurosurg Spine*. 2025;42(2):238-247. doi:10.3171/2024.7.SPINE24607.
6. Pemov A, Dewan R, Hansen NF, Chandrasekharappa SC, Ray-Chaudhury A, Jones K, et al. Comparative clinical and genomic analysis of neurofibromatosis type 2-associated cranial and spinal meningiomas. *Sci Rep*. 2020;10(1):12563. doi:10.1038/s41598-020-69074-z.
7. Aboukais R, Bonne NX, Baroncini M, Zairi F, Schapira S, Vincent C, et al. Management of multiple tumors in neurofibromatosis type 2 patients. *Neurochirurgie*. 2018;64(5):364-369. doi:10.1016/j.neuchi.2014.11.012.
8. Teranishi Y, Miyawaki S, Nakatochi M, Okano A, Ohara K, Hongo H, et al. Meningiomas in patients with neurofibromatosis type 2 predominantly comprise 'immunogenic subtype' tumours characterised by macrophage infiltration. *Acta Neuropathol*

- Commun. 2023;11(1):156. doi:10.1186/s40478-023-01645-3.
9. Sirko A, Romanukha D, Pilipenko G, Sklyar N. Successful step-by-step treatment of multiple tumours in neurofibromatosis type 2. Interdisciplinary Neurosurgery. 2019;15:101-105. doi:10.1016/j.inat.2018.10.011.
10. Goldbrunner R, Stavrinou P, Jenkinson MD, Sahm F, Mawrin C, Weber DC, et al. EANO guideline on the diagnosis and management of meningiomas. Neuro Oncol. 2021;23(11):1821-1834. doi:10.1093/neuonc/noab150.