

Meningioma-associated parkinsonism related to basal ganglia and cerebellar motor circuits: A case report and literature review

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Abstract. Parkinsonism can be caused by a variety of factors, such as drugs, vascular disease, toxicity, infection, and autoimmune, neoplastic, metabolic and functional diseases. Parkinsonism is associated with both motor and nonmotor clinical symptoms. Notably, the accurate diagnosis of Parkinson's disease and parkinsonism remains challenging. Meningioma is the most common type of extraparenchymal brain tumor, which typically presents with headaches, focal symptoms and cranial nerve symptoms. Parkinsonism is a rare initial symptom of meningioma. The present report describes an unusual case of a 70-year-old man who presented with tremors, pill-rolling tremors and left-sided rigidity. In addition, the patient exhibited asymmetrical bradykinesia (left > right) and mild postural instability. Magnetic resonance imaging (MRI) revealed a homogeneously enhanced cerebral falx meningioma and dilated tortuous veins. Dopamine transporter single-photon emission computed tomography revealed decreased ¹²³I-ioflupane uptake in the right striatum. The patient underwent two surgical interventions due to tumor growth and symptom deterioration. Pathological examination revealed transitional meningioma. Postoperatively, the symptoms of the patient improved, and MRI revealed a residual tumor without basal ganglia mechanical compression or venous congestion. It was hypothesized that involuntary movements, including parkinsonism in the present case, were associated with the disruption of the cortico-cerebellar-cortical

and the dentato-rubro-olivary pathways (the Guillain-Mollaret triangle) due to tumor mechanical compression and venous congestion. Meningioma, which is a type of extraparenchymal tumor, is more likely to cause mechanical compression and venous congestion than the infiltration of the basal ganglia circuit, leading to symptom improvement after surgical removal. This case highlights the importance of considering meningioma as a rare cause of lateral parkinsonism and its potential for symptom improvement after surgical intervention.

Introduction

Parkinsonism is a neurological syndrome and is divided into primary and secondary parkinsonism. Primary parkinsonism is caused by neurodegenerative disease and secondary parkinsonism can be caused by a variety of factors, such as drugs, vascular disease, toxicity, infection, and autoimmune, neoplastic, metabolic, and functional diseases (1). The clinical symptoms are motor and nonmotor. It is characterized by motor symptoms, including tremors, rigidity, bradykinesia, gait disorders, and akinesia, and nonmotor symptoms, such as cognitive decline, depression, anxiety, sleep disturbance, and dysautonomia (2,3). Accurate diagnosis of Parkinson's disease (PD) and parkinsonism remains challenging. Clinical symptoms and levodopa challenge tests are important for differentiation. PD typically responds better to levodopa than parkinsonism (4).

Among adults, meningiomas occur most frequently in individuals aged 65 and above. Overall, these tumors are observed 2.3 times more often in women than in men. Meningiomas are usually benign and develop slowly. They are the most prevalent type of extraparenchymal brain tumors, accounting for approximately 40% of all brain tumors (5). The initial symptoms of meningiomas typically include headaches, focal symptoms, and cranial nerve symptoms. Some patients are diagnosed without clinical symptoms during routine medical examinations. The occurrence of meningiomas becomes more frequent as people get older (5). Although meningiomas can exhibit a range of clinical symptoms, parkinsonism is an unusual initial symptom. Tumoral parkinsonism is rare and is defined as parkinsonism that develops as a direct or indirect result of tumors, such as infiltration or compression (6).

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Abbreviations: MRI, magnetic resonance imaging; CE-T1WI, contrast-enhanced T1-weighted image; DAT SPECT, dopamine transporter single-photon emission computed tomography; PD, Parkinson's disease; ION, inferior olivary nucleus

Key words: meningioma, parkinsonism, cortico-cerebellar-cortical pathway, dentato-rubro-olivary pathway, basal ganglia, DAT SPECT

In this report, we present an unusual case of meningioma in which parkinsonism manifested as the primary clinical symptom. We describe the patient's clinical course of treatment, explore the underlying mechanism responsible for this occurrence, and predict symptom improvement based on preoperative imaging findings.

Case report

A 70-year-old man without a family history was referred in November 2020 to the University of Occupational and Environmental Health Hospital in Kitakyushu, Japan because of involuntary movement 3 years prior to presentation. Examination revealed resting tremors, pill-rolling tremors, and muscle rigidity on the left side. Asymmetrical bradykinesia (left > right) and mild postural instability were also observed. His eyeballs showed no saccadic slowing or eye-movement limitations. Deep tendon reflexes of the upper and lower extremities were normal. He did not experienced paralysis and non-motor symptoms such as sensory disorder, urinary incontinence, or cognitive decline (Fig. 1). Magnetic resonance imaging (MRI) with T2-weighted images revealed dilated tortuous veins (Fig. 2A), and contrast-enhanced T1-weighted imaging (CE-T1WI) revealed homogeneous enhancement of a frontal lobe extra-axial giant lesion suggestive of a falx meningioma (Fig. 2B and C). Dopamine transporter single-photon emission computed tomography (DAT-SPECT) revealed decreased ^{123}I -ioflupane uptake in the right striatum (Fig. 2D). Considering the diagnosis of PD based on the DAT-SPECT findings, he was started on oral levodopa/carbidopa. The patient refused surgery and was discharged for frequent follow-up visits.

One year later, the patient continued to take medication; however, his symptoms did not improve. Additionally, his condition deteriorated, and he presented with urinary incontinence, cognitive decline, and focal behavioral arrest seizures. MRI with CE-T1WI revealed a growing tumor. The patient subsequently underwent surgery. The tumor was removed using an interhemispheric approach; however, it persisted due to intraoperative blood loss. Pathological examination revealed the proliferation of spindle or oval meningothelial cells, including components arranged in fascicles or whorls, corresponding to a transitional meningioma. The patient's symptoms did not improve because the residual tumor compressed the right basal ganglia and caused venous congestion. After 14 months, the residual tumor enlarged. The Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part I score was 24. In brief, the patient experienced non-motor symptoms of PD such as cognitive decline, urinary incontinence, depression, and constipation. Parts II and III had Hoehn and Yahr (H&Y) stage 5 scores of 31 and 53, respectively. MRI with CE-T1WI revealed a homogeneously enhanced tumor (Fig. 3A and B). The patient then underwent surgery again. The tumor was resected via an interhemispheric approach. The interhemispheric fissure was identified by opening the dura mater and the tumor, which was covered with a hard capsule. Although the tumor was attached to the surrounding brain, the arachnoid membrane was preserved in some areas (Fig. 3C). The pathology was similar to that observed after the initial surgery,

and the intraoperative findings showed no tumor invasion of the brain. The patient did not develop any complications. Eight months later, the residual tumor had grown slightly, and the patient underwent radiation therapy. The MDS-UPDRS Part I score improved from 24 to 5. Overall, the non-motor symptoms showed improvement, with the exception of minor urinary incontinence and constipation. Parts II and III scored 9 and 23, respectively, as functions of H&Y stage 1. The patient discontinued oral levodopa/carbidopa. Eight months later, an MRI revealed a residual tumor; however, the basal ganglia were no longer compressed (Fig. 4A and B). The tumor was stable, and the patient's symptoms did not change.

Discussion

Focal brain lesions can induce involuntary movement disorders, such as hemichorea, hemiballism, dystonia, tremor, myoclonus, parkinsonism, and asterixis (7). Cerebrovascular disease and stroke are the major causes of this condition; however, other factors include tumors, trauma, anoxia, and multiple sclerosis (7,8). Parkinsonism has been observed in approximately 0.3% of patients with supratentorial tumors, particularly those located in the sphenoidal ridge or the frontal or parietal lobes (9). Brain tumors in the basal ganglia, corpus callosum, periventricular white matter, midbrain, and hypothalamus cause parkinsonism. Intraparenchymal tumors, such as primary central nervous system lymphomas and gliomas, are associated with parkinsonism (10,11). Previous reports have described basal ganglia lymphoma-induced parkinsonism, suggesting that tumor cell infiltration and damage to neuronal membranes contribute to its development (11). Conversely, tumors with extraparenchymal locations, such as meningiomas, may disrupt neuronal circuits, including presynaptic dopaminergic neuronal axons and the output pathway from the postsynaptic cells of the basal ganglia circuit to the cortex. This disruption can result from the mass effect of the tumor, leading to parkinsonism (1). In tumor-associated parkinsonism, DAT-SPECT may show decreased uptake due to tumor invasion or compression (12,13). In the present case, DAT SPECT revealed decreased ^{123}I -ioflupane uptake in the right striatum. Levodopa/carbidopa was administered for 1 year; however, symptoms did not improve. Therefore, the patient was diagnosed with meningioma-associated parkinsonism.

We hypothesized that involuntary movements, including parkinsonism, are associated with the following two parallel pathways: the cortico-cerebellar-cortical pathway and the dentato-rubro-olivary pathway (Guillain-Mollaret triangle) (8). The cortico-cerebellar-cortical pathway comprises major afferent and efferent fibers. Afferent fibers extend from the frontal lobe to the cerebellar cortex via the pons. In contrast, efferent fibers extend from the dentate nucleus to the motor cortex via the red nucleus and thalamus. The dentato-rubro-olivary pathway comprises the inferior olivary nucleus (ION). Efferent fibers from the dentate nucleus to the contralateral red nucleus, red nucleus to the ipsilateral ION, and ION to the contralateral cerebellum form a triangular circuit that governs motor activity. Both basal ganglia and cerebellar circuits function as subcortical loops that receive and return cortical information. Brain tumors can influence

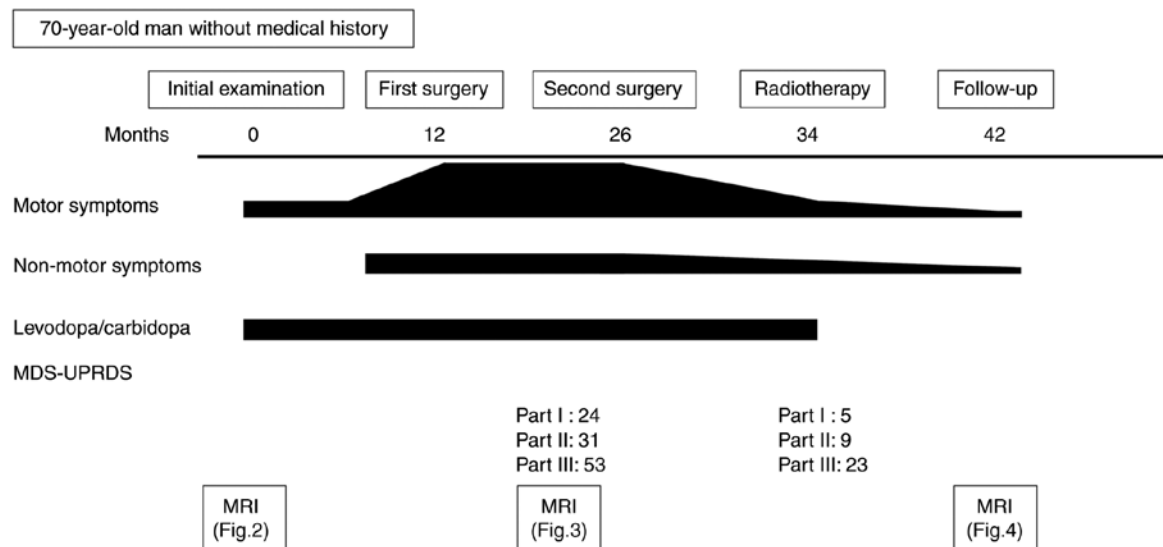


Figure 1. Timeline of the patient's clinical course. MRI, magnetic resonance imaging; MDS-UPRDS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale.

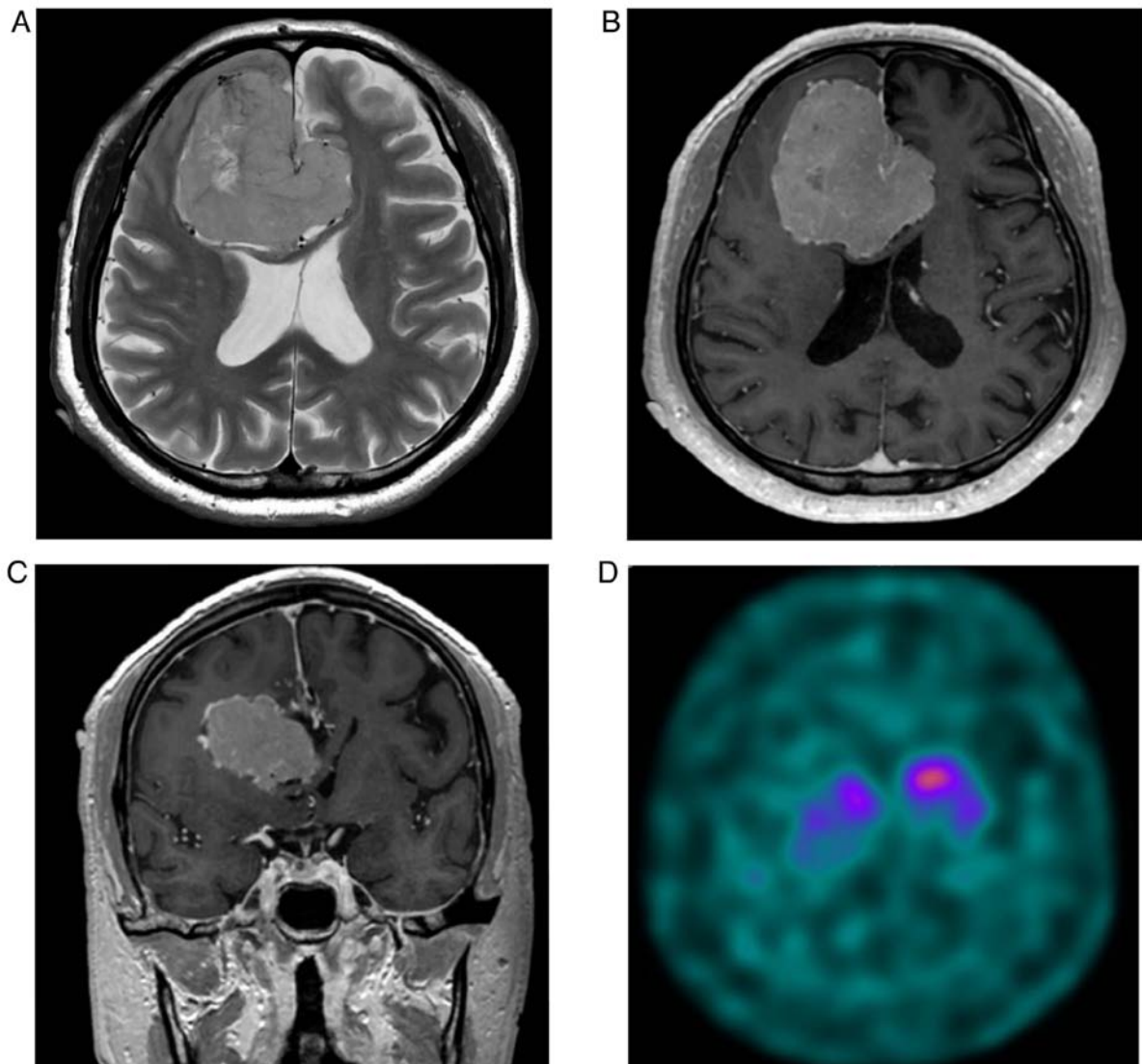


Figure 2. Preoperative magnetic resonance imaging showing homogenous enhancement of the tumor. (A) Axial T2-weighted images revealed dilated tortuous veins. (B) Axial and (C) coronal contrast-enhanced T1-weighted images revealing compression of the right basal ganglia. (D) Dopamine transporter single-photon emission computed tomography showing decreased ^{123}I -ioflupane uptake in the right striatum.

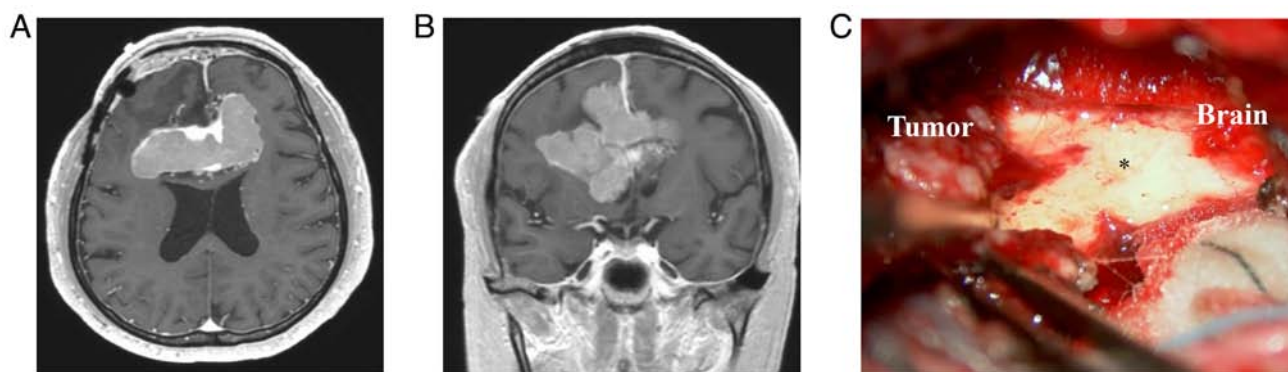


Figure 3. Postoperative magnetic resonance imaging showing homogenous enhancement of the tumor. (A) Axial and (B) coronal contrast-enhanced T1-weighted images after the initial surgery revealing compression of the right basal ganglia. (C) Intraoperative findings. The tumor does not invade the brain and shows a clear borderline (*).

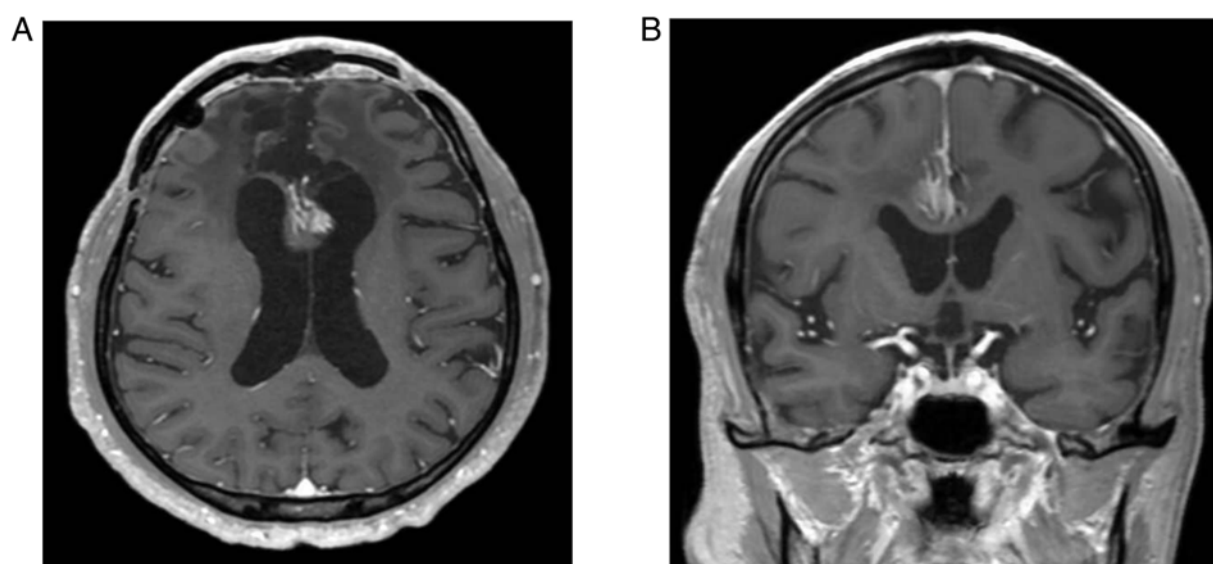


Figure 4. After the second surgery, (A) axial and (B) coronal magnetic resonance imaging reveal that the tumor no longer compresses the right basal ganglia.

the output pathway of the basal ganglia circuit from the post-synaptic cells to the cortex. These pathways may be infiltrated and compressed by tumors (8). It is often difficult to alleviate symptoms when tumor infiltration is involved; however, meningiomas are more prone to mechanical compression than infiltration into the basal ganglia circuit and show improvement after surgery. Involuntary movements in meningioma are rare. Since 2010, to our knowledge, involuntary movements in seven meningioma cases improved after surgery (Table I) (1,14-19). The mean age at diagnosis was 54.9 years (range, 41-67 years), and all patients were female. Several clinical symptoms have been reported previously. Six patients presented with tremors, followed by parkinsonism in five patients. Two of the five patients received levodopa but responded poorly. All patients demonstrated laterality of clinical symptoms as opposed to tumor location; however, only one patient had a tumor located in the bifrontal region. Four tumors were located in the sphenoid ridge, followed by the frontal lobe and midbrain. The meningiomas were removed in all patients, and the symptoms included involuntary movements due to compression, which improved postoperatively. Only seven cases of involuntary

movement in meningiomas have been reported in the literature. Involuntary movements in patients with tumors may mimic these symptoms, leading to misdiagnosis. Clinical features are not well known; however, for tremors and parkinsonism, especially when there are laterality symptoms and opposite to tumor location, clinicians should suspect the risk of tumor-associated involuntary movements.

In our cases, the patient showed laterality of parkinsonism. The first surgery slightly improved the mechanical compression but did not improve the parkinsonism because the venous congestion did not improve; however, the second surgery improved symptoms by relieving the compression of the basal ganglia and venous congestion. Previous reports have focused on mechanical compression caused by meningiomas, and the fact that the symptoms did not improve after the first surgery, even though the mechanical compression was relieved, may be due to cortical damage from venous congestion. Considering tumors associated with parkinsonism is important when clinicians suspect the laterality of parkinsonism. Tumor removal decompresses the basal ganglia, resulting in the improvement of parkinsonism, especially in meningiomas.

Table I. Summary of involuntary movements in patients treated for meningioma since 2010.

First author, year	Case	Age, years/ sex	Clinical symptoms	Tumor location	Laterality	Treatment	Prognosis	(Refs.)
Diyora, 2014	1	50/F	Headache, dystonic head tremor, resting tremor	Lt. sphenoid ridge	Right	Surgery	Improved	(14)
Kim, 2014	2	58/F	Resting tremor, bradykinesia, gait disorder	Lt. sphenoid ridge	Right	Surgery	Improved	(1)
Kleib, 2016	3	41/F	Resting tremor, bradykinesia, rigidity, paralysis	Lt. sphenoid ridge	Right	Surgery	Improved	(15)
Fong, 2016	4	58/F	Hypomimic face, hypophonic speech, gait disorder, resting pill-rolling tremor, rigidity, bradykinesia	Lt. frontal tumor	Right	Surgery	Improved	(16)
Labate, 2018	5	67/F	Ataxia, hypotension, urinary incontinence, hyperreflexia, gait disorder, bradykinesia, rigidity, postural and resting tremor	Lt. midbrain	Both	Surgery	Improved	(17)
Al-Janabi, 2019	6	65/F	Resting tremor, bradykinesia, rigidity	Bil. anterior cranial fossa	Right	Surgery	Improved	(18)
Inoue, 2021	7	45/F	Hemichorea	Rt. sphenoid ridge	Left	Surgery	Improved	(19)
Present study	8	70/M	Tremor, pill-rolling tremor, rigidity, bradykinesia, postural instability	Bil. anterior cranial fossa	Left	Surgery	Improved	-

F, female; M, male; lt, left; bil, bilateral; rt, right.

In conclusion, various pathogeneses, including trauma, drug-induced cerebrovascular disorders, and brain tumors can cause parkinsonism. This report presents a rare case of meningioma presenting with parkinsonism as an initial manifestation in an older adult. Parkinsonism is related to the cortico-cerebellar-cortical pathway and the Guillain-Mollaret triangle. Therefore, parkinsonism is rare in both intraparenchymal and extraparenchymal tumors, however, parkinsonism caused by tumor compression or venous congestion is more easily ameliorated than that caused by tumor cell infiltration. Parkinsonism in patients with brain tumors, particularly meningiomas, can be reversed with surgical treatment.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

ST and SN drafted the manuscript and wrote the final draft. KS, KF and JY revised the manuscript and provided constructive feedback. SN and JY performed the surgeries. ST, KF, KS and SN analyzed all the images. SN, KF and JY confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of the case details and associated images.

Competing interests

The authors declare that they have no competing interests.

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