

## Treatment of postoperative vasospasm with intraarterial verapamil after removal of intracranial tumor: patient series

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**BACKGROUND** The authors report on four clinical cases with intraarterial verapamil administration to resolve vasospasm in patients who underwent surgery for intracranial tumors. Iatrogenic subarachnoid hemorrhage after tumor resection and subsequent vasospasm (an increase in the systolic linear velocity of blood flow through the M1 segment of the middle cerebral artery of more than 250 cm/sec; Lindegaard index: 4.1) were observed in four patients during the early postoperative period after the removal of intracerebral tumors. Each vasospasm case was confirmed by angiography data, was clinically significant, and manifested as the development of a neurological deficit.

**OBSERVATIONS** Resolution of vasospasm with the intraarterial administration of verapamil was achieved in all four cases as confirmed by angiographic data in all four cases and complete regression of neurological symptoms in two cases. In all four presented cases, vasospasm was resolved; unfortunately, the resolution did not always lead to significant clinical improvement. However, lethal outcomes were avoided in two cases, and almost full recoveries were achieved in the other two.

**LESSONS** The authors believe that the removal of intracranial tumors can cause expected and potential complications, such as cerebral vasospasm, which must be diagnosed and treated in a timely manner.

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**KEYWORDS** tumor; cerebral angiospasm; intraarterial verapamil; iatrogenic subarachnoid hemorrhage

Cerebral vasospasm occurring after aneurysmal subarachnoid hemorrhage (SAH), traumatic SAH, or post-SAH following removal of intracranial tumors is widely described in the literature.<sup>1,2</sup> However, it appears that, for cerebral spasm after the removal of intracranial tumors, no treatment options have been proposed in the literature. We describe our clinical experiences while treating this complication with intraarterial verapamil administration in four patients who underwent surgery for intracranial tumors

During surgery, bleeding from the damaged vessel may visually disappear from the surgical field, and the blood will leak into the subarachnoid space, which will cause an acute swelling of the brain. A thick layer of subarachnoid blood can cause vasospasm and delayed ischemic deficiencies. It is well known that the amount of subarachnoid blood determines the onset of vasospasm and ischemic symptoms. On the basis of our experience, we believe that iatrogenic SAH following

removal of an intracranial tumor can cause cerebral spasm and delayed cerebral ischemia, which determines the need for intraarterial verapamil administration in severe symptomatic cases. Such an SAH can occur after resection of a parenchymal tumor, which is similar to a low-grade glioma, formations of the chiasm-parasellar region, and other intracranial tumors. The first description of vasospasm after removal of an intracranial tumor was published by Krayenbuhl in 1960 and reported on two patients with pituitary adenoma and vestibular schwannoma.<sup>1</sup> In both cases, the patients had symptoms of delayed neurological deficit associated with cerebral vasospasm, which was confirmed by angiography. Since then, several publications on this subject have appeared in the literature.<sup>2-5</sup> Sometimes, the leading cause of vasospasm is not SAH but mechanical trauma to the arteries. The development of vasospasm is accompanied by cerebral and focal neurological symptoms, which

**ABBREVIATIONS** ACA = anterior cerebral artery; CT = computed tomography; DSA = digital subtraction angiography; EVD = external ventricular drain; ICA = internal carotid artery; ICP = intracranial pressure; MCA = middle cerebral artery; MRI = magnetic resonance imaging; mRS = modified Rankin Scale; OD = oculus dextrus; OS = oculus sinister; SAH = subarachnoid hemorrhage; TC = transcranial.

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**TABLE 1. Patient characteristics (clinical, DSA, and ultrasound)**

Case No.	Age (yrs)	Tumor	Vasospasm Severity	Verapamil/Dosage	Improvement after Verapamil Injection	Outcome on mRS
1	62	Craniofacial glial tumor	Severe	3 sessions/45 mg each	+	5
2	65	Craniopharyngioma	Severe	5 sessions/80 mg each	+	4
3	40	Oligodendroglioma	Mild	1 session/25 mg	+	1
4	33	Astrocytoma	Severe	2 sessions/25 mg each	+	2

+ = overall improvement after procedure.

can be quite pronounced and refractory to noninterventional treatment methods.<sup>6–11</sup>

In this study, we describe our experience with the use of intraarterial verapamil administration for resolving vasospasm in four patients with iatrogenic SAH and symptomatic cerebral vasospasm following intracranial tumor removal.

### Study Description

Severe vasospasm (an increase in systolic linear velocity over the M1 segment of the middle cerebral artery [MCA] of more than 250 cm/sec; Lindegaard index: 4.1) was observed in four patients in the early postoperative period (on the 3rd day) after removal of intracranial tumors (Table 1). Each case of vasospasm was confirmed by digital subtraction angiography (DSA), was clinically significant, and manifested as the development of neurological deterioration. To exclude surgical complications, patients underwent contrast-enhanced magnetic resonance imaging (MRI) or computed tomography (CT) scanning on the day of and the day after the intervention to exclude ischemic stroke. The blood flow examination before and after verapamil administration was performed by measuring the linear velocity using transcranial (TC) Doppler. The procedure for verapamil administration involved puncture of the right femoral artery, selective catheterization of the right and left internal carotid arteries (ICAs) and the left vertebral artery, and angiography to evaluate the angiospasm. A diagnostic catheter was then placed above the ICA bifurcation, and 25 to 80 mg of verapamil was administered. The severity of vasospasm was measured by angiographic data as a percentage of the normal caliber of the arteries, averaging 3.2 mm for the MCA.

### Clinical Case 1

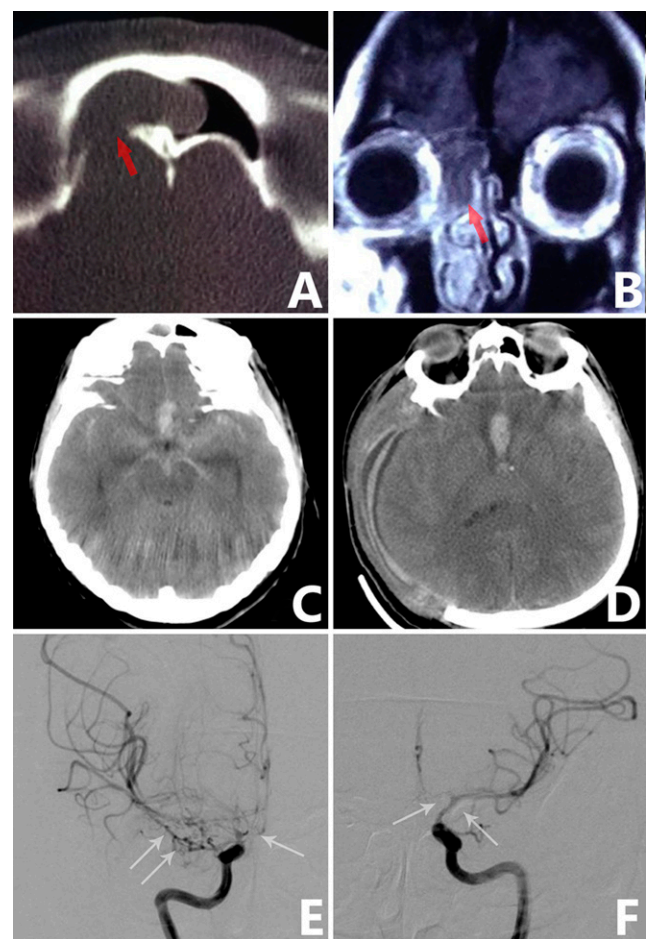
This patient was a 62-year-old female with a diagnosis of a tumor with craniofacial localization. Upon admission, the patient was conscious and cooperative, and no focal neurological symptoms were identified. On CT and MRI, a tumor located in the ethmoid cells and frontal sinus with destruction of the posterior wall of the frontal sinus was noted. Endoscopic endonasal tumor removal was performed. Bleeding was stopped with a hemostatic sponge. Immediately after surgery, the patient became comatose.

A CT study of the brain was performed, and Fisher grade 4 SAH was found, indicating blood in the suprasellar region, in the sylvian fissures, in the interhemispheric fissure, and in the fourth ventricle. Diffuse cerebral edema and signs of intracranial hypertension (Fig. 1) were noted. An external ventricular drain (EVD) with intracranial pressure (ICP) monitoring was placed. On the 2nd day after surgery, decompressive craniotomy of the right frontoparietal region with duraplasty was performed.

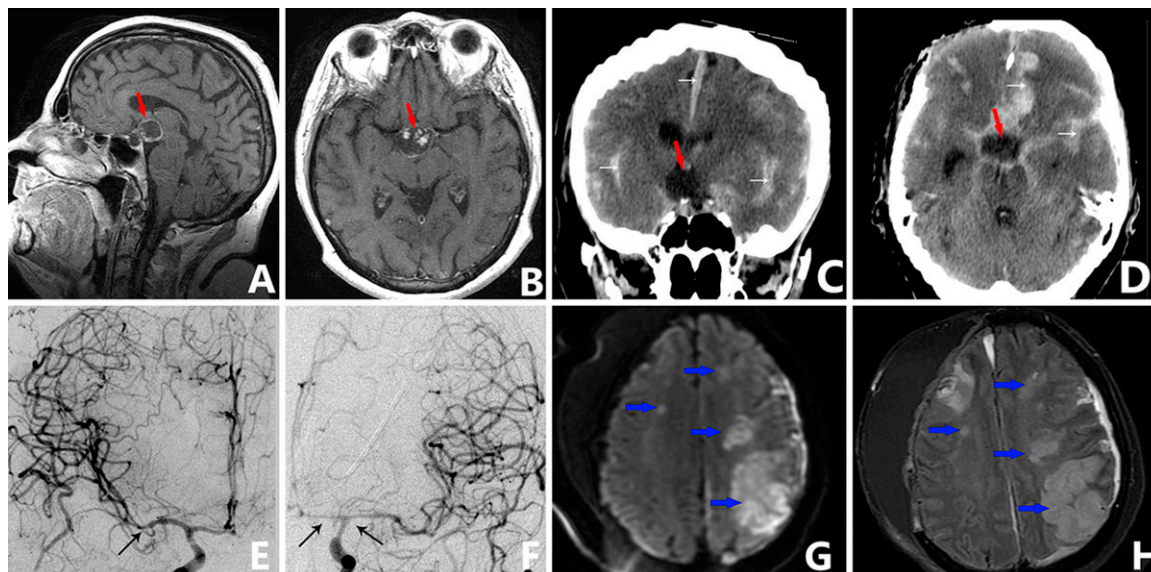
TC Doppler sonography on the 4th day after surgery, showed the development of a pronounced vasospasm with velocities up to 400 cm/sec in the pool of the right MCA, 300 cm/sec in the left MCA, 350 cm/sec in

the right anterior cerebral artery (ACA), and 230 cm/sec in the left ACA.

Catheterization on the 5th day after surgery, of the right femoral artery and selective intraarterial administration of verapamil was done. According to the ultrasound scan, vasospasm regression was observed based on a



**FIG. 1.** Clinical case 1. **A** and **B**: CT and MRI scans show a tumor located in the ethmoid cells and frontal sinus with destruction of the posterior wall of the frontal sinus (red arrows). **C**: The postoperative CT shows the diffuse SAH, Fisher score of 4. **D**: The results of decompressive hemicraniectomy due to refractory intracranial hypertension. **E** and **F**: Appearance of cerebral vasospasm confirmed by DSA. Severe vasospasm of MCA and ACA of both sides is indicated by white arrows.



**FIG. 2.** Clinical case 2. **A** and **B**: The classic MRI appearance of extraventricular craniopharyngioma is present (*red arrows*). **C** and **D**: Postoperative CT scans show diffuse SAH (*white arrows*) and residual tumor (*red arrows*). **E** and **F**: DSA shows severe cerebral vasospasm of left ICA, MCA, ACA, and M2 segments of the right MCA (*black arrows*). **G** and **H**: MRI scan at discharge shows diffuse multiple cerebral infarctions (*blue arrows*) due to the vasospasm on diffusion-weighted magnetic resonance imaging and T2-weighted fluid attenuated inversion recovery.

decrease in dynamics. Ultrasound data on the 6th day after surgery, indicated vasospasm with 105 cm/sec of both MCAs, 200 cm/sec in the pool of the right ACA, and 135 cm/sec in the pool of the left ACA.

After long-term rehabilitation, the modified Rankin Scale (mRS) score was 5. An MRI study of the brainstem showed ischemic changes.

## Clinical Case 2

This patient was a 65-year-old female with a diagnosis of extraventricular craniopharyngioma and visual and hormonal impairment (Fig. 2). Upon admission, the patient was conscious and cooperative. Signs of involvement of the visual pathway were evident. Visual acuity parameters were measured at the oculus dextrus (OD) and oculus sinister (OS) of 0.01 and 0.3, respectively. In the visual fields, OD was preserved in the nasal half with violation of the central vision, and the patient could not distinguish colors. OS color loss was noted in the temporal half. Full eye movement was found. Endocrinological status indicated secondary hypothyroidism.

TC microsurgical removal of the craniopharyngioma was performed. The first stage was resection. The trepanation was complicated by damage to the cortex and cortical vessels, and swelling of the pole of the right frontal lobe. Attempts to access the chiasmatal area were unsuccessful. Duraplasty and removal of the bone flap were performed. After transferring the patient to the intensive care unit, a CT scan was obtained, showing a massive SAH in the chiasmatal region, and an interhemispheric fissure with the spread of blood into the enclosing cistern was noted. A marked shift of the midline to the right had occurred. The lateral ventricles were moderately dilated. It was decided to place an EVD in the right lateral ventricle for monitoring and controlling ICP. Later, decompressive hemicraniectomy was performed. The size of the ventricles decreased during drainage. ICP was 8–9 mm Hg in dynamics. On the 1st day after surgery, no vascular pathology was observed on a CT angiogram.

According to the deterioration of neurological status and the results from the ultrasound of cerebral vessels, the development of a

pronounced vasospasm up to 250 cm/sec in the pool of the right MCA, 280 cm/sec in the left MCA, 180 cm/sec in the right ACA, and 140 cm/sec in the left ACA was noted.

Five sessions of intraarterial verapamil infusion (80 mg each session) were performed. A successful decrease in blood flow velocity was observed. Status at discharge for rehabilitation was an mRS of 4.

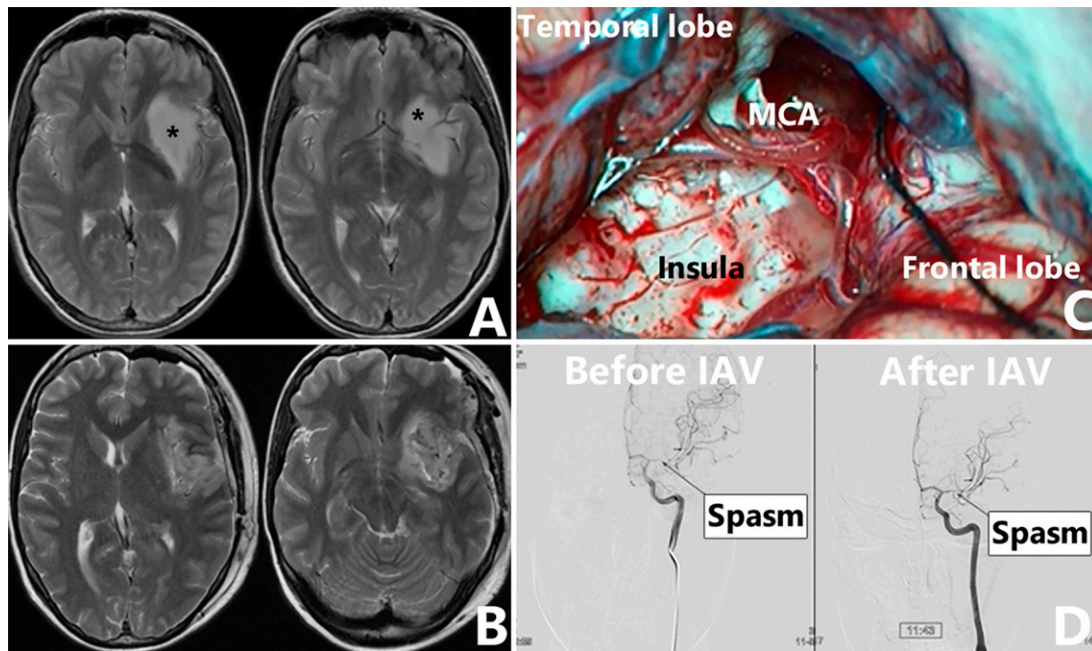
## Clinical Case 4

This patient was a 33-year-old male with a diagnosis of diffuse astrocytoma of the left insular lobe (grade II). Upon admission, the patient was conscious and cooperative, and no focal neurological symptoms were identified. On MRI of the brain, a typical diffuse glial tumor of the islet on the left was observed (Fig. 3A). The tumor was removed. TC motor evoked potentials remained stable without significant dynamics during tumor removal.

In the early postoperative period starting on day 3, the emergence of focal symptoms was observed in the form of a pronounced conductive aphasia and a right-sided severe hemiparesis. Postoperative MRI of the brain revealed a slight accumulation of blood in the bed of the removed tumor without requiring its removal (Fig. 3B and C).

Considering the picture of arterial spasm in the left MCA pool obtained during the surgery (Fig. 3C) and the MRI on which no traces of damage to the inner capsule were found, it was assumed that the vasospasm was the cause of the symptomatology. This assumption was confirmed by the TC Doppler. On the 3rd day after the operation, the linear velocity of blood flow over the M1 segment of the MCA was as high as 300 on the right and 100 cm/sec on the left. The patient was prepared for the endovascular operation of selective administration of verapamil in the left ICC. During the angiography, a diffuse narrowing of the second and third segments of the left MCA branches (up to 70%) occurred, as shown in Fig. 3D. Verapamil (25 mg) was selectively administered into the MCA. Administration of verapamil resulted in a





**FIG. 3.** Clinical case 4. **A:** MRI T2 shows a glial diffuse tumor of the left frontotemporal region and insula (asterisks). **B:** Postoperative 3rd day MRI shows near-total resection of the tumor; no ischemia was diagnosed, but there is some blood collection in the tumor bed. **C:** Intraoperative view, tumor bed is presented. Also, the MCA branches are preserved without vessel damage. **D:** Angiograms before and after intraarterial verapamil (IAV) infusion. DSA shows dilatation of the M1 segment, which correlates with clinical improvement.

decrease in the linear velocity of blood flow over the M1 segment of the MCA, and a distinct regression of neurological symptoms was observed the next day. On the 6th day, in view of the persisting high values of linear velocity of the blood flow, a repeated administration of verapamil was performed. Narrowing of the arteries also amounted to about 70%, and 25 mg of verapamil was selectively administered into the MCA. After treatment, aphasic disorders regressed completely, and movements in the right extremities were restored to mild hemiparesis. The patient was graded as mRS 2.

### Clinical Case 3

This patient was a 40-year-old male who was diagnosed with oligodendroglioma of the left insular and temporal lobe (grade II) as shown in Fig. 4A and B. An islet tumor removal surgery was performed with ultrasound navigation and intraoperative electrophysiological mapping of motor tracts of the left hemisphere. According to the electrophysiological monitoring data, the amplitude of the M-waves after resection was preserved. On the 1st day after the operation, a CT scan of the patient's head was obtained and revealed accumulation of blood in the resected tumor bed that did not require a second surgery (Fig. 4C and D). Starting on the 2nd day, gradual deterioration of the patient's status was observed, as manifested by headaches, disorientation, and a declining level of consciousness. Later, moderate hemiparesis developed, and the TC Doppler revealed a gradual increase in linear velocity values (270 cm/sec) and showed increasing vasospasm.

On the 4th day after tumor removal, endovascular intervention for vasospasm was performed. With selective contrast-enhancement of the left ICA, a distinct segmental spasm of the distal part of the M1

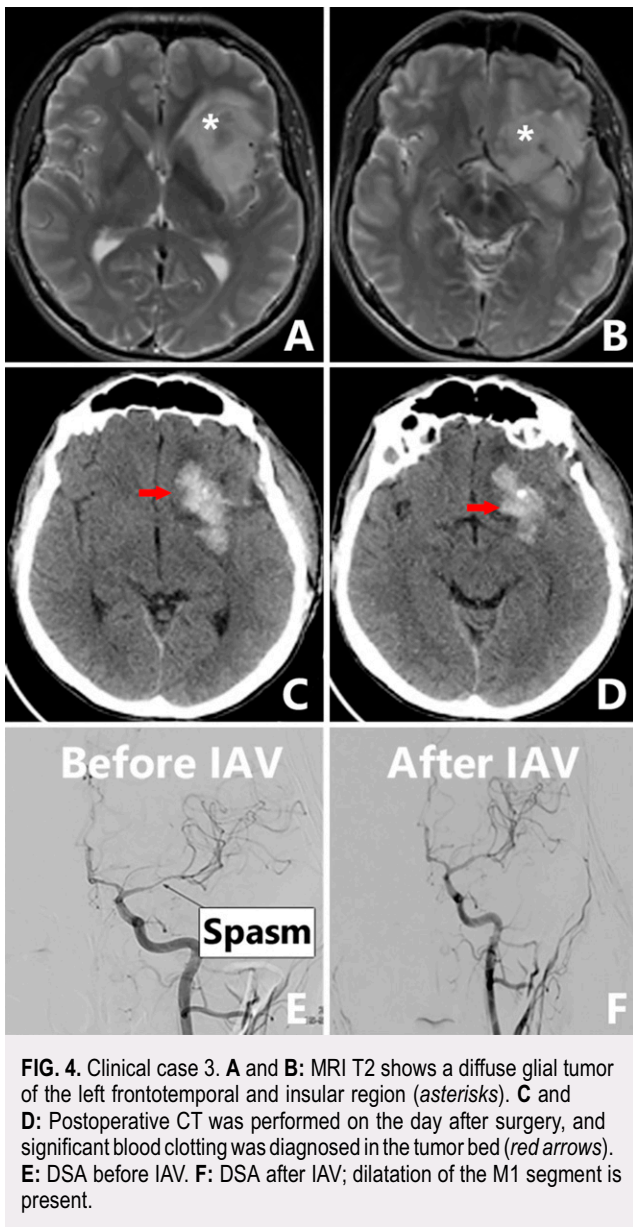
segment of the left MCA of over 70% was identified (Fig. 4E). A diagnostic catheter was placed in the left ICA above the bifurcation, 25 mg of verapamil was administered, and extension of distal segments of the M1 segment of the MCA was recorded (Fig. 4F). After the procedure, clear positive dynamics of the clinical status was observed; gradually, the wakefulness level increased, while the hemiparesis decreased. The TC Doppler monitoring revealed a gradual decrease in the linear velocity. The patient was discharged with a complete regression of neurological symptoms and an mRS of 1.

### Discussion

Cerebral vasospasm is commonly observed after aneurysmal SAH,<sup>5-9,12</sup> after traumatic SAH, or SAH following removal of intracranial tumors. SAH is well described in the literature. However, the treatment options proposed and discussed in the literature are only for vasospasm after aneurysmal and traumatic SAH, leaving treatment of vasospasm after removal of intracranial tumors unaddressed. After surgical intervention for intracranial tumor removal, bleeding and perhaps mechanical damage to blood vessels can contribute to the development of vasospasm and delayed ischemic deficiency. Left untreated, this damage can lead to future severe disability, which could be prevented with timely treatment of cerebral vasospasm.

Intraarterial administration of verapamil<sup>13-16</sup> for treatment of cerebral vasospasm is considered a safe and effective treatment option by many authors. We believe that this treatment must also be used in cases of vasospasm after removal of intracranial tumors.

To avoid future complications resulting from cerebral vasospasm, all operations for intracranial tumor removal should be accompanied by immediate postoperative imaging. Thick postoperative SAH can



**FIG. 4.** Clinical case 3. **A** and **B**: MRI T2 shows a diffuse glial tumor of the left frontotemporal and insular region (*asterisks*). **C** and **D**: Postoperative CT was performed on the day after surgery, and significant blood clotting was diagnosed in the tumor bed (*red arrows*). **E**: DSA before IAV. **F**: DSA after IAV; dilatation of the M1 segment is present.

predispose all major vessels of the circle of Willis to severe vasospasm. Vascular spasm can be serious enough to cause serious delayed neurological deficits. Growing linear velocity over the MCA and the corresponding neurological symptoms are manifested subsequently and can persist up to 2 weeks after the operation. The values of linear velocity are also similar to the values seen in patients after SAH, reaching 250–300 cm/sec. It should be noted that focal symptomatology (hemiparesis) after surgery for tumor removal can be observed due to the damage to the deep cerebral structures or arteries, especially to perforators. Those cases require careful differential diagnosis by analyzing the data of MRI of the brain, TC Doppler, and neurological status of the patient.

### Observations

In all four presented cases, the vasospasm resolved; unfortunately, this resolution did not result in drastic clinical improvement. However,

lethal outcomes were avoided in two cases, and almost full recovery was achieved in the other two.

### Lessons

We believe that after the removal of intracranial tumors, potential complications, such as cerebral vasospasm, can be expected and must be diagnosed and treated in a timely manner.

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### **Disclosures**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

### **Author Contributions**

Conception and design: Mikeladze, Konovalov, Bykanov, Vinogradov. Acquisition of data: Konovalov, Mikeladze, Bykanov, Vinogradov. Analysis and interpretation of data: Mikeladze, Konovalov, Bykanov,

Vinogradov. Drafting the article: Mikeladze, Konovalov. Critically revising the article: Mikeladze. Reviewed submitted version of manuscript: Mikeladze, Konovalov. Approved the final version of the manuscript on behalf of all authors: Konovalov. Statistical analysis: Mikeladze, Konovalov, Vinogradov. Administrative/technical/material support: Mikeladze, Konovalov, Yakovlev. Study supervision: Mikeladze, Konovalov, Yakovlev.

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