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Von Hippel-Lindau disease with intracranial hemorrhage due to arteriovenous anastomosis via multiple spinal hemangioblastomas: illustrative case

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BACKGROUND Some spinal hemangioblastomas (HBLs) resemble spinal vascular malformations. Intracranial subarachnoid hemorrhage (SAH) secondary to spinal HBL has rarely been reported.

OBSERVATIONS A 67-year-old man with a prolonged von Hippel-Lindau disease (VHL) history presented with sudden headache and vomiting. Cranial and cervical computed tomography (CT) revealed severe infratentorial, supratentorial, and cervical SAH. Cranial CT angiography and magnetic resonance imaging revealed a mismatch in hemorrhage and intracranial tumor localization, with no vascular lesions that could lead to intracranial SAH. Cervical CT angiography revealed abnormal blood vessels originating from 5 spinal tumors suspected to be HBLs. We considered that the SAH was caused by venous reflex from vascular malformation–like spinal HBLs. Transarterial embolization (TAE) of the feeding artery of HBLs was performed to improve symptoms and reduce rebleeding risk. Nine months after TAE, angiography showed no venous reflux into the intracranial space. Ten months later, the authors excised the T1–2 tumor because the patient complained of progressive paralysis of the right upper extremity.

LESSONS In HBL with prolonged VHL, intracranial hemorrhage due to venous regurgitation via a mimicked vascular malformation may occur. Reducing venous reflux with TAE may improve symptoms and prevent rebleeding.

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KEYWORDS von Hippel-Lindau disease; arteriovenous anastomosis; spinal hemangioblastoma

Spinal hemangioblastomas (HBLs) are rare, benign, vascular-rich tumors that are closely associated with a diagnosis of von Hippel-Lindau disease (VHL).[1] Spontaneous subarachnoid hemorrhage (SAH) secondary to spinal HBL is extremely rare, and only a few reports have been published.[1,2] Kalyvas and Change[3] reported the first case of multiple intramedullary spinal HBLs and VHL that mimicked a spinal vascular malformation on radiological imaging. We report a rare case of spinal HBLs and VHL that mimicked a spinal vascular malformation presenting clinically with intracranial SAH. We also aimed to illustrate related diagnostic difficulties in this report.

Illustrative Case

History and Examination

A 67-year-old man with pancreatic neuroendocrine tumors, renal tumors, and spinal HBLs was diagnosed with VHL at 31 years of age. Since he had spinal cord hemorrhage in his 50s, he presented with paraplegia and paresis of the right upper limb. He had undergone surgery for cerebellar HBL 3 years before SAH presentation and resection of the brainstem and cerebellar HBL 1 year before SAH presentation. Multiple spinal HBLs were already diagnosed at levels C4–5, C6–7, C8, T1, and L1–2; however, these tumors were asymptomatic (Fig. 1). He had a family history of VHL, and his 2 sons also had multiple HBLs due to VHL. Three months before, he had experienced headache and vomiting after bathing. Subsequently, he presented to our hospital with a sudden onset of severe headache and vomiting.

Cranial and cervical computed tomography (CT) revealed severe infratentorial, supratentorial, and cervical SAHs at level C1–2 (Fig. 2). Cranial CT angiography and magnetic resonance imaging (MRI) revealed a mismatch in hemorrhage and intracranial tumor

ABBREVIATIONS CT = computed tomography; HBL = hemangioblastoma; JCS = Japan Coma Scale; MRI = magnetic resonance imaging; SAH = subarachnoid hemorrhage; TAE = transarterial embolization; VA = vertebral artery; VHL = von Hippel-Lindau disease.

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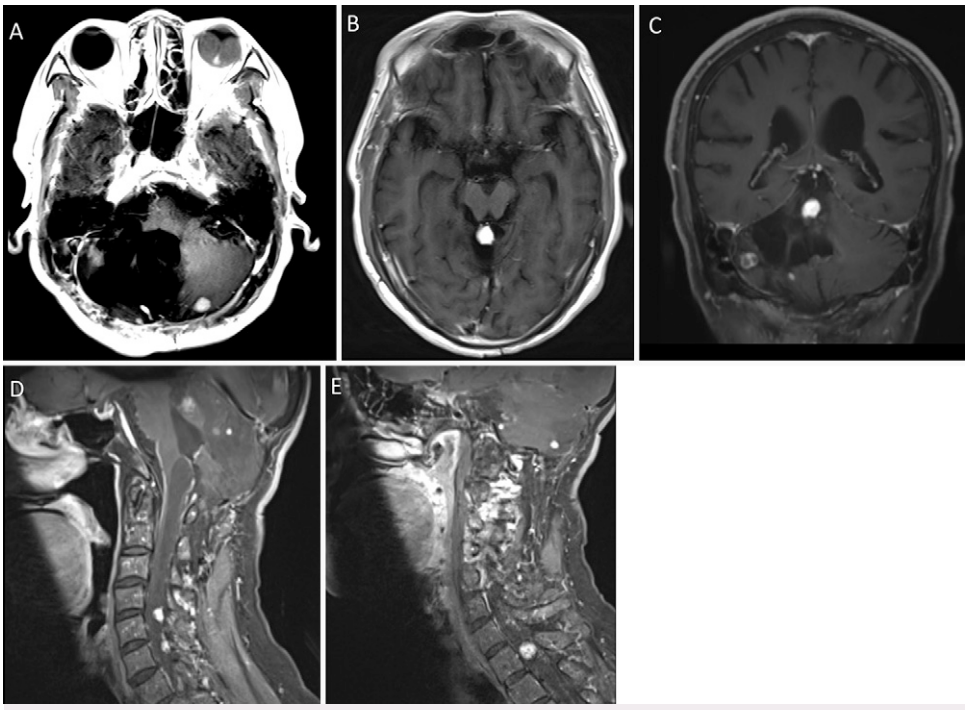

FIG. 1. Cranial gadolinium (Gd)-enhanced MRI (**A**–**C**) performed 3 months before the onset of SAH, showing multiple HBLs in the posterior fossa. Cervical Gd-enhanced MRI (**D and E**) performed 3 months before the onset of SAH, revealing multiple spinal HBLs at levels C4–5, C6–7, C8, and T1.

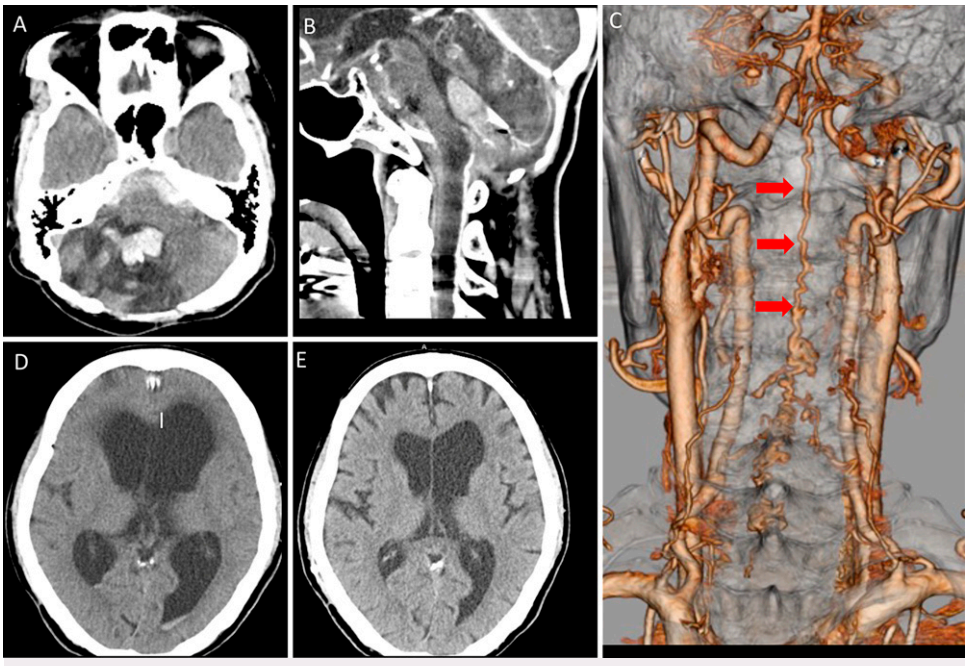

FIG. 2. Cranial and cervical CT (**A and B**) showing severe infratentorial, supratentorial, and cervical SAHs at level C1–2. Cervical CT angiography (**C**) revealing abnormal blood vessels (*red arrows*) that originated from cervical HBLs, meandered on the dorsal side of the cervical cord, and flowed into the intracranial space in the arterial phase. Cranial CT (**D**) obtained 20 days after admission, revealing an enlarged ventricle. CT obtained after ventricular peritoneal shunt surgery and TAE (**E**), showing the size of the ventricles had decreased.

localization, with no vascular lesions that could lead to SAH in the intracranial space. Conversely, cervical CT angiography revealed abnormal blood vessels that initiated from cervical HBLs, meandered on the dorsal side of the cervical cord, and flowed into the intracranial space in the arterial phase (Fig. 2C). Cerebral angiography was performed 1 and 12 days after admission. No cerebral vasospasm was detected on either scan. Right vertebral angiography revealed a dilated venous reflux into the intracranial space from a strongly enhanced HBL in C3–4, C5–6, and C7–T1, fed by the radiculomedullary artery originating from the right vertebral artery (VA) (Fig. 3).

Treatment and Post-Treatment Course

Twenty days after admission, ventricular peritoneal shunt surgery was performed with a variable pressure shunt because of severe headache and progression of consciousness disorder (Japan Coma Scale [JCS] 30)[4] due to secondary hydrocephalus (Fig. 2D). The cerebrospinal fluid pressure during surgery was 18 cm H_2O. To avoid rebleeding due to a decrease in cerebrospinal pressure, the shunt pressure was set to 18 cm H_2O. After surgery, the patient's state of consciousness improved (from JCS 30 to JCS 3); however, the headache remained unchanged.

Twenty-three days after admission, we considered that SAH occurred by venous reflex due to vascular malformation–like spinal

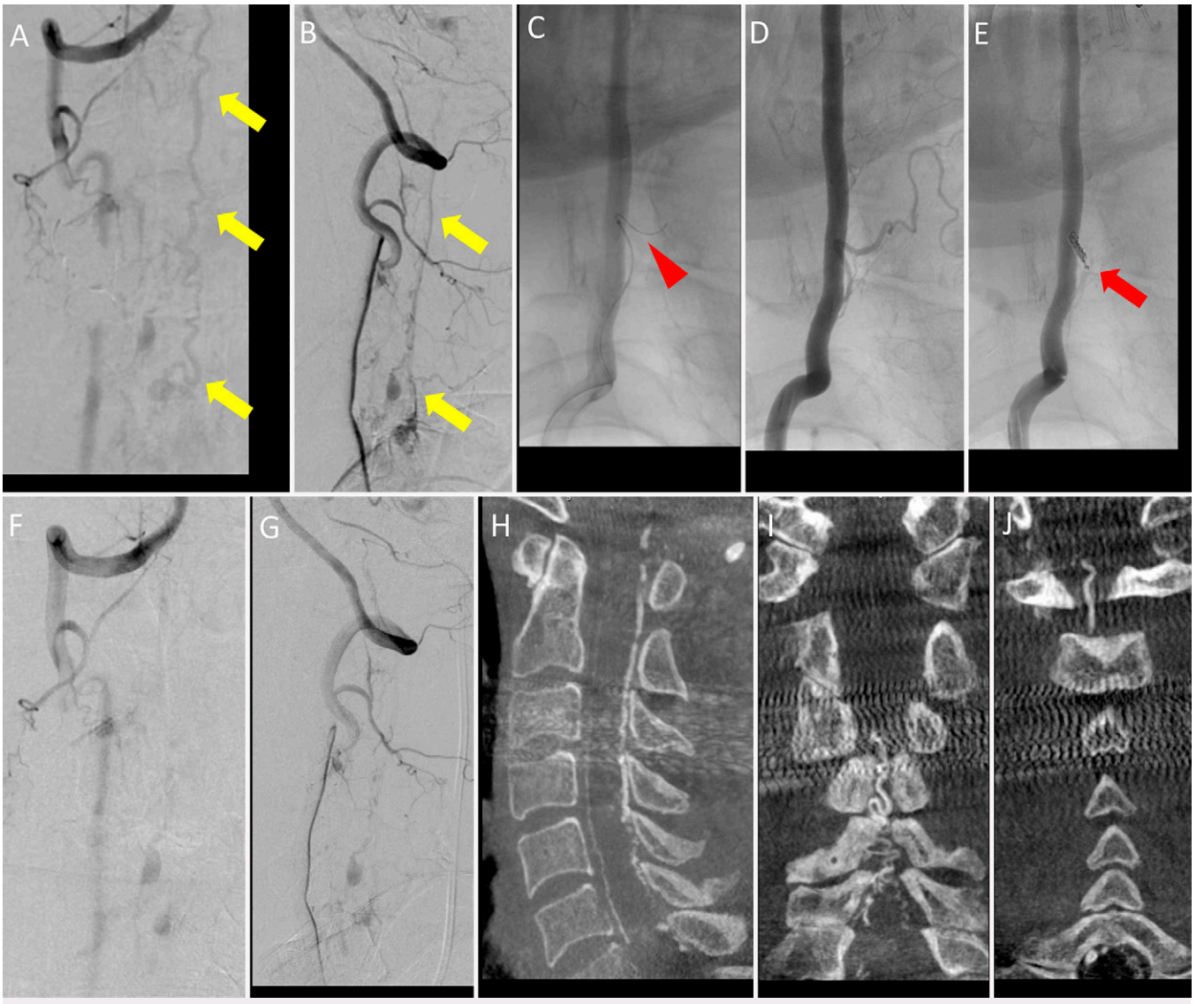

FIG. 3. Right vertebral angiography performed 12 days after admission (frontal, **A**; lateral, **B**), revealing dilated venous reflux (*yellow arrows*) into the intracranial space from a strongly enhanced HBL at C3–4, C5–6, and C7–T1, fed by the radiculomedullary artery originating from the right VA. TAE was performed 23 days after admission (**C**–**E**). A microcatheter (*red arrowhead*, **C**) was placed in the distal portion of the feeding artery and wedged to block blood flow. Detachable coils (*red arrow*, **E**) were inserted one after another into the artery through the microcatheter. After the embolization, VA angiography revealed obstruction of the feeding artery, reduction of the contrast area of the HBLs, and a marked reduction of venous reflux into the intracranial space (frontal, **F**; lateral, **G**). Cone-beam CT via a microcatheter revealed a tortuous vein flowing into the intracranial space (sagittal, **H**; coronal, **I and J**).

HBLs. Therefore, transarterial embolization (TAE) of the feeding artery of cervical HBLs was performed to reduce the risk of rebleeding. With the patient under local anesthesia, a 5-Fr introducer sheath was placed in the right femoral artery. A 5-Fr Chaperon guiding catheter (MP2, 95 cm; Boston Scientific) was inserted into the right VA. A microcatheter (Excelsior SL10-STR, 150 cm; Balt) was placed in the distal portion of the feeding artery and wedged to block blood flow. No new neurological findings were confirmed, even after blocking blood flow for 10 minutes. Cone-beam CT via a microcatheter revealed a tortuous vein flowing into the intracranial space (Fig. 3G–I). Detachable coils (Target, Stryker ED COIL10; Stryker) were inserted one after another into the artery through the microcatheter (Fig. 3C and D). After embolization, VA angiography revealed obstruction of the feeding artery, reduction of contrast area of the HBLs, and marked reduction of venous reflux into the intracranial space (Fig. 3E and F).

After TAE, without changing the shunt valve pressure, the patient's headache completely disappeared, his level of consciousness markedly improved (JCS 1), and the size of his ventricles decreased (Fig. 2E). Cervical CT angiography 3 months after TAE showed no venous reflux into the intracranial space via spinal HBLs (Fig. 4). Angiography 9 months after TAE showed no venous reflux into the intracranial space. Recurrence of intracranial hemorrhage and symptoms, such as headache or vomiting, was not observed.

Ten months later, he complained of progressive paralysis of the right upper extremity without worsening headaches. Because the T1–2 tumor continued to grow despite reducing the feeding artery by TAE, we surgically excised it and obtained a pathological diagnosis of HBL.

Nine months later, he died of pulmonary embolism due to deep vein thrombosis. There was no worsening of his neurological symptoms or rebleeding during the period until his death.

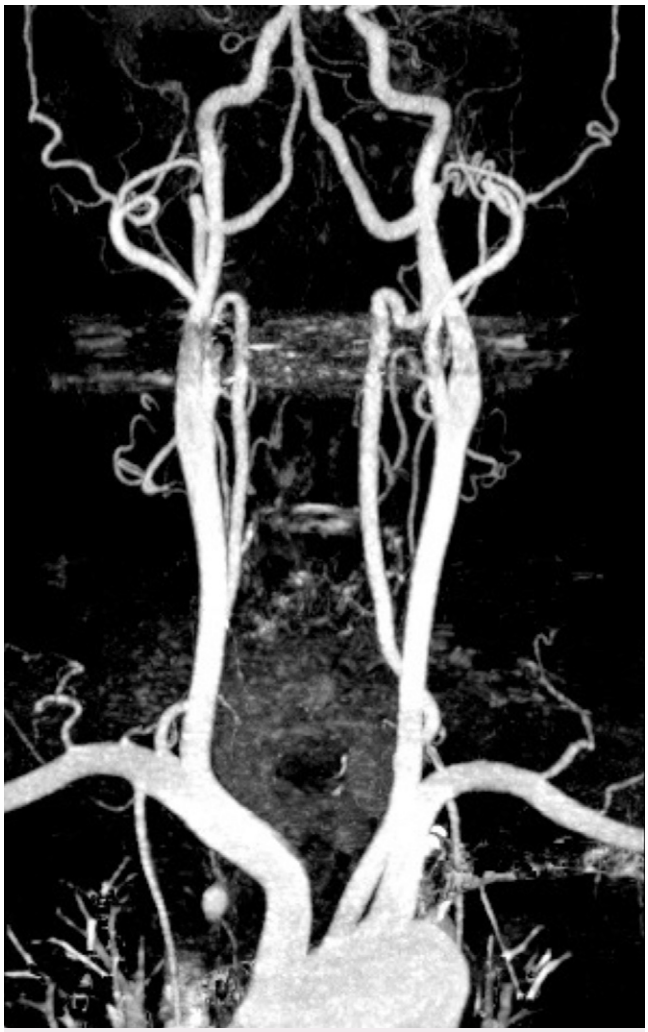

FIG. 4. Cervical CT angiography 3 months after TAE showing disappearance of venous reflux through the spinal HBLs.

Discussion

Observations

Some spinal HBLs can be difficult to differentiate from spinal vascular malformation because they may have massive arteriovenous shunting and dilation of draining veins tracking the spinal cord.[5] Spinal HBLs with hemorrhage in the central nervous system are extremely rare, with currently only a few cases being reported.[1]

Our patient with a 36-year history of VHL developed intracranial hemorrhage, and the cause was assumed to be venous reflux into the intracranial space due to mimicked vascular malformation by multiple spinal HBLs. The cause of intracranial hemorrhage in our case cannot be completely determined, and other possible causes include SAH of unknown etiology, bleeding from the intracranial tumor itself, and bleeding from the spinal cord tumor itself. However, the following findings support intracranial hemorrhage due to the mimicked vascular malformation caused by multiple spinal HBLs. First, SAHs of unknown etiology tend to localize around the midbrain; however, in this case, massive hemorrhage had markedly spread into the posterior cranial fossa and cervical cord.[6] Second, for bleeding from the intracranial or cervical cord tumor itself, there was a notable distance between the bleeding site on the image and the tumor. Third, there were no intracranial tumors with thick hematomas that would indicate the bleeding site.

We performed TAE with good results to prevent bleeding and improve venous reflux. TAE was initially performed because the cause of neurological symptoms was not mass effect but instead venous reflux. An advantage of TAE is that it is possible to immediately and effectively reduce blood flow in a less invasive procedure and can be immediately confirmed by angiography. Because HBLs are tumors, cutting off blood supply encourages additional recruitment, so TAE may not be a long-term treatment. Resection was considered before TAE; however, because the resection is more invasive, we decided to perform TAE first, followed by surgery if additional symptoms appeared. TAE improved the venous reflux, but 10 months later, the mass effect of the tumor caused neurological symptoms; therefore, the tumor was excised.

Lessons

In our patient, we observed enlarged draining veins flowing from multiple spinal HBLs to the cranial side, similar to vascular malformations. Some studies report that spinal HBLs appear similar to spinal vascular malformations that often cause intracranial hemorrhage.[3] Glasker and Van Velthoven reported that hemorrhage due to HBL can occur by mechanisms similar to vascular malformation occurring in pathophysiological mechanisms; the partial transmission of the arterial pressure to the venous side eventually causes

TABLE 1. Literature review of patients with spinal HBLs with intracranial SAH

Authors & Year	Age (yrs), Sex	Symptoms & Signs	Tumor Location	Hemorrhage Type	MRI/DSA Findings	VHL	Treatment	Outcome
Kormos et al., 1980[8]	31, F	3 mos of paresthesia, HA, nuchal rigidity, vomiting	C2	SAH	Tumor-like aneurysm	Sporadic	Laminectomy	Good recovery
Minami et al., 1998[9]	48, M	12 yrs earlier unknown SAH, severe HA	C1	SAH	Tumor strongly fed by radicular artery	Sporadic	Craniectomy & laminectomy	Good recovery
Irie et al., 1998[10]	41, M	Numbness of upper extremities, severe nuchal pain	C5–6	SAH	Tumor enhanced by rt radiculomedullary artery	Sporadic	Laminectomy	Good recovery
Berlis et al., 2003[11]	47, F	Severe HA, slightly progressive rt paresis	C1–2, C4–6	SAH	Rt VA w/ intense tumor stain, lt VA w/ tumor stain	VHL	Laminectomy	Good recovery
Nishimura et al., 2012[12]	56, M	Sudden onset of lumbago, neck pain, HA, transient paraparesis	L2–3	SAH, IVH	Tumor strongly enhanced, fed by radicular arteries w/ varix, massive flow-void signals around tumor	VHL	Embolization & laminectomy	Slight hypesthesia
Present case	67, M	3 mos of mild HA, sudden onset of severe HA & vomiting	C4–5, C6–7, C8, T1, L1–2	SAH, IVH	Tumor strongly enhanced, fed by radiculomedullary artery, dilated venous reflux into intracranial space from tumor	VHL	Embolization & laminectomy	Good recovery

DSA = digital subtraction angiography; HA = headache; IVH = intraventricular hemorrhage.

structural changes that lead to vascular vulnerability.[7] The mechanism of intracranial hemorrhage in our case is considered to be venous reflux due to a rare tumor.

We reviewed previous reports of spinal HBLs with intracranial hemorrhage that included vascular structures on MRI or angiography. The clinical characteristics and outcomes of these patients are presented in Table 1.[1,8–12] Among these cases, only the one reported by Nishimura et al.[12] had a massive arteriovenous shunting or dilation of draining veins tracking the spinal cord, similar to spinal vascular malformation. In previous reports, headache was the most common symptom, and tumors were often found in the cervical spinal cord. Although the prognosis was often favorable in the reports, there is a possibility of publication bias.

TAE was performed with good postoperative results. Significant improvement in symptoms, such as headache and impaired consciousness, by TAE may paradoxically suggest that this patient had venous circulatory disturbance. To improve venous reflux, TAE was performed, and then tumor removal was performed to reduce the mass effect. TAE could effectively treat tumor-feeding arteries at once. Tumors in which blood flow could not be decreased with TAE and that grew postoperatively were surgically resected. There was no rebleeding during the 9-month period until death caused by pulmonary embolism. The long-term results of the same disease and treatment are unknown, and it is necessary to repeat the case and investigation in the future.

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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: Ikeuchi, Nishihara, Ashida. Acquisition of data: Ikeuchi, Nishihara. Analysis and interpretation of data: Ikeuchi, Nishihara. Drafting the article: Ikeuchi. Critically revising the article: Nishihara, Ashida, Hosoda. Reviewed submitted version of manuscript: Ikeuchi. Approved the final version of the manuscript on behalf of all authors: Ikeuchi. Statistical analysis: Ikeuchi. Administrative/technical/material support: Ashida, Hosoda. Study supervision: Hosoda.

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