

# GIANT CAVERNOUS MALFORMATIONS IN YOUNG ADULTS: REPORT OF TWO CASES, RADIOLOGICAL FINDINGS AND SURGICAL CONSEQUENCES

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**Cerebral cavernous malformations, also known as cavernous angioma or cavernoma, are a type of vascular disorder. They consist of abnormally large vascular cavities or sinusoid channels of varying size. The majority of cavernous malformations in the brain are small and do not always present with symptoms. A minority of large cavernous malformations, known as giant cavernous malformations (GCM), can cause neurological symptoms (such as headaches, focal neurologic deficits and seizures), which are probably related to hemorrhage and mass effect. GCM grow steadily in size over time, due to repetitive episodes of bleeding.**

**The purpose of this paper is to document two case reports of patients with GCM, illustrate the radiological appearance, discuss the neurosurgical consequences, and to provide a literature analysis.**

**Key-words:** Cerebral blood vessels, abnormalities – Cerebral blood vessels, MR.

Cerebral cavernous malformations represent a special subtype of low-flow vascular disorder. Histopathologically, these lesions consist of sinusoid-like capillary channels of varying sizes, containing slowly flowing blood. These lesions are located inside the brain, but do not invade the adjacent brain parenchyma, and are usually not surrounded by perilesional edema (1). The cavernous malformation is also known as cavernous angioma or cavernoma,

The majority of cavernous malformations in the brain are small, with a mean size of 14.2 mm in diameter (2). Often these lesions are asymptomatic and are discovered on imaging studies as incidental findings. A minority of cavernous malformations may increase in size, due to repeated episodes of hemorrhage; these larger lesions cause neurological symptoms such as headaches, focal neurologic deficits and seizures (3). A clinically important subgroup is the so-called "giant" cavernous malformation (GCM). The size criterion for GCM is not sharply defined; some authors use a minimum diameter of 6 cm as threshold (4), while most other authors use a diameter of 4 cm as cut-off (3). GCM are rare tumor-like lesions, which are characterized by a typical layered appearance on MR imaging studies.

In this paper we report on two patients with GCM, describe the radiological characteristic, discuss the neurosurgical consequences, and provide a literature analysis.

## Case reports

### Patient 1

This 16-year-old high-school student presented with recurrent head-

aches, intermittent nausea, and sensory disturbances involving the left hand and fingers. Over the past year, his school performance had steadily deteriorated, without specific explanation. Three months prior to admission, he had been involved in a road-traffic accident when a car hit his motorcycle, but he did not sustain any neurological injury. Previous medical history was otherwise unremarkable, and the young man was generally in good health. Clinical neurological examination showed a mild paresis in the lower left leg, but was otherwise normal.

The patient was referred for an MR examination of the brain. Before contrast administration, the following sequences were obtained: axial fluid attenuated inversion recovery (FLAIR), axial T2-weighted images, axial diffusion-weighted images, axial gradient echo T2\*, axial susceptibility-weighted (SWI) images, axial T1-weighted images. After intravenous injection of a gadolinium-chelate, axial, coronal and sagittal T1-weighted sequences were obtained. The MR examination revealed a large mass, in the deep right frontal-parietal region (Fig. 1). The largest diameters of the mass were 43 mm antero-posteriorly, 31 mm left-right, and 38 mm head-feet. The lesion was sharply circumscribed, but contained markedly heterogeneous signal intensities, suggestive of recent as well as old blood degradation products. The mass was surrounded by perilesional edema in the white matter of the right centrum semiovale. The lesion caused mass effect on the right lateral ventricle and displaced and compressed the corpus callosum. Imaging findings were consistent with a giant cavernous malformation.

The patient underwent a under neurosurgical intervention. A right-sided parafrontal craniotomy was performed. Via a paramedical approach, along the falx, the mass was resected using microsurgical techniques. The giant cavernous malformation could be removed completely, as well as an old and liquefied hematoma next to the large mass. Deposits of hemosiderin and reactive gliosis were observed. The layer of hemosiderin was carefully removed by microsurgical suction.

The post-operative course was uneventful (with the exception of a pneumothorax caused by placement of a subclavian catheter). Neurologically the patient was intact. A post-operative CT scan one day after surgery of the brain showed a resection cavity with no further abnormalities (Fig. 2). Pathological examination confirmed the diagnosis of a giant cavernous malformation (Fig. 3).

Follow-up visits confirmed that this young man is clinically doing well, without any neurological deficit, at 15 months post operatively. Follow-up MR examination showed a small resection cavity, partially lined with hemosiderin, but no other abnormalities.

### Patient 2

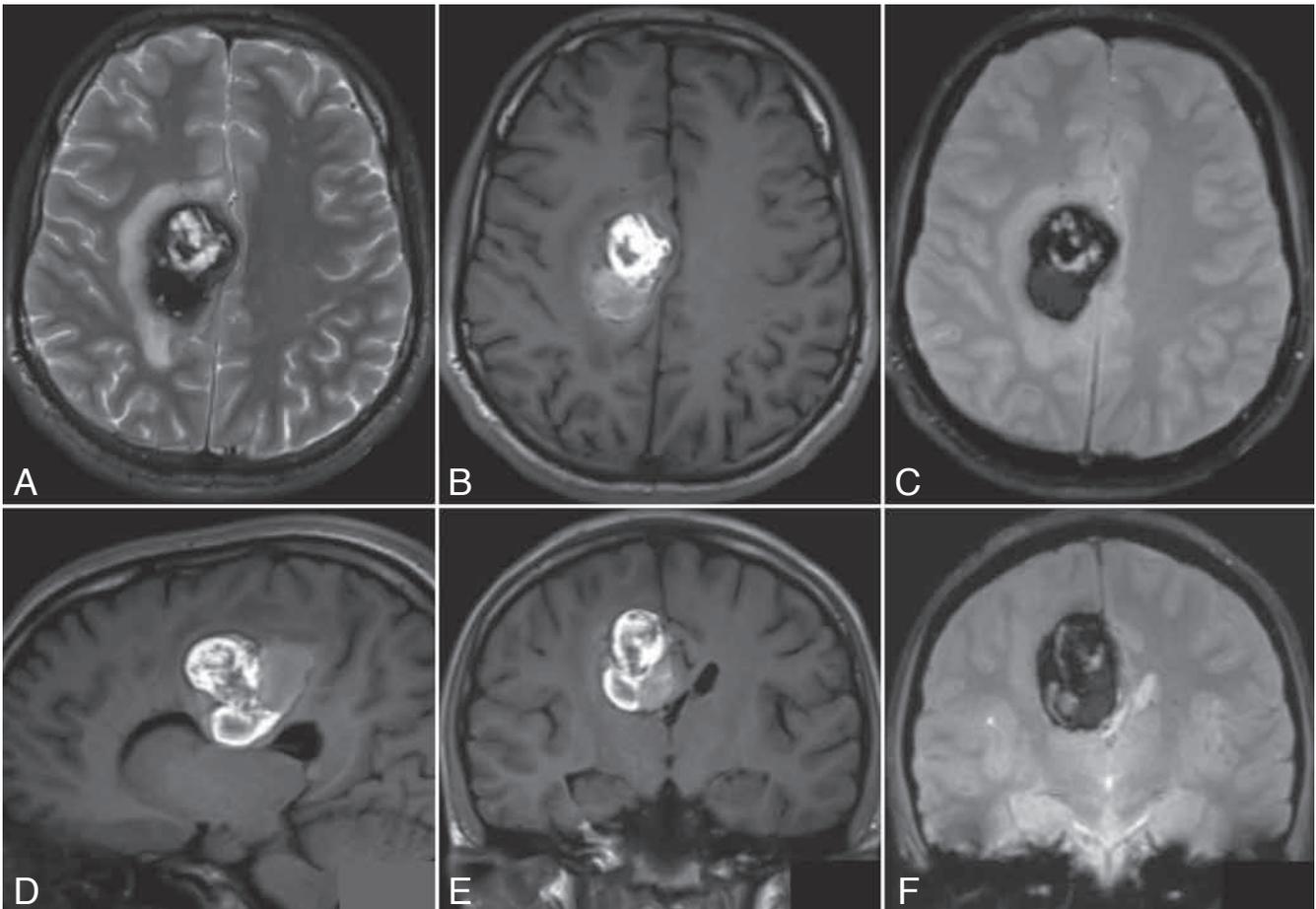
This 25-year-old woman was admitted with complaints of gradually worsening nausea and vomiting, headache and anorexia. She had experienced a weight loss of 9 kg during the 5 weeks prior to admission. At the age of 19, she had been treated for syringomyelia, with placement of a syringo-dural shunt and posterior cervical decompression surgery. Previous medical history reveals chronic fatigue syndrome and fibromyalgia.

Clinical examination revealed a lethargic woman. There were no neurological deficits.

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*Fig. 1.* — Patient 1, pre-operative MRI of the brain with axial TSE T2-WI (A), axial TSE T1-WI (B), axial gradient echo T2\* (C), sagittal TSE T1-WI (D), coronal TSE T1-WI (E) and coronal gradient echo T2\* (F). A sharply marginated mass lesion is identified in the deep right frontal-parietal lobes. The mass presents with a heterogeneously layered appearance with blood degradation products of varying age. The hyperintense signal intensity components represent extracellular methemoglobin, while the hypointense portions indicate the presence of hemosiderin. Behind the giant cavernous malformation, there is a liquefied hematoma.

MR examination of the brain (Fig. 4) was performed including axial T2-weighted images, axial FLAIR, axial diffusion-weighted images, axial gradient echo T2\*, axial susceptibility-weighted (SWI) images, axial T1-weighted images; after intravenous injection of a gadolinium-chelate, additional axial, coronal and sagittal T1-weighted sequences were obtained. The MR examination revealed a large left frontal mass lesion, with heterogeneous signal architecture, involving the head of the left caudate nucleus and the lentiform nucleus, and extending across the midline in the suprasellar region. In the axial plane, the largest diameter of the mass is 43 mm. The lesion was partially surrounded by a halo of vasogenic edema, and compressed and displaced the frontal horn of the right lateral ventricle; the midline structures were shifted to the right. Imaging findings were highly suggestive for a giant cavernous malformation, after recent episode of hemorrhage.

A neurosurgical intervention was performed and consisted of a left frontal craniotomy, with a left-sided transcallosal approach. The mass was completely removed using microsurgical techniques. Adjacent to the giant cavernous malformation, an old and liquefied hematoma was found; this was evacuated together with a layer of hemosiderin and reactive gliosis.

The post-operative course was free of complications. A CT examination one day post-operatively revealed a sharply defined resection cavity, with a limited amount of intracranial air, consistent with a recent status post surgery (Fig. 5). The patient was discharged in good clinical condition on day 4 after the surgical procedure.

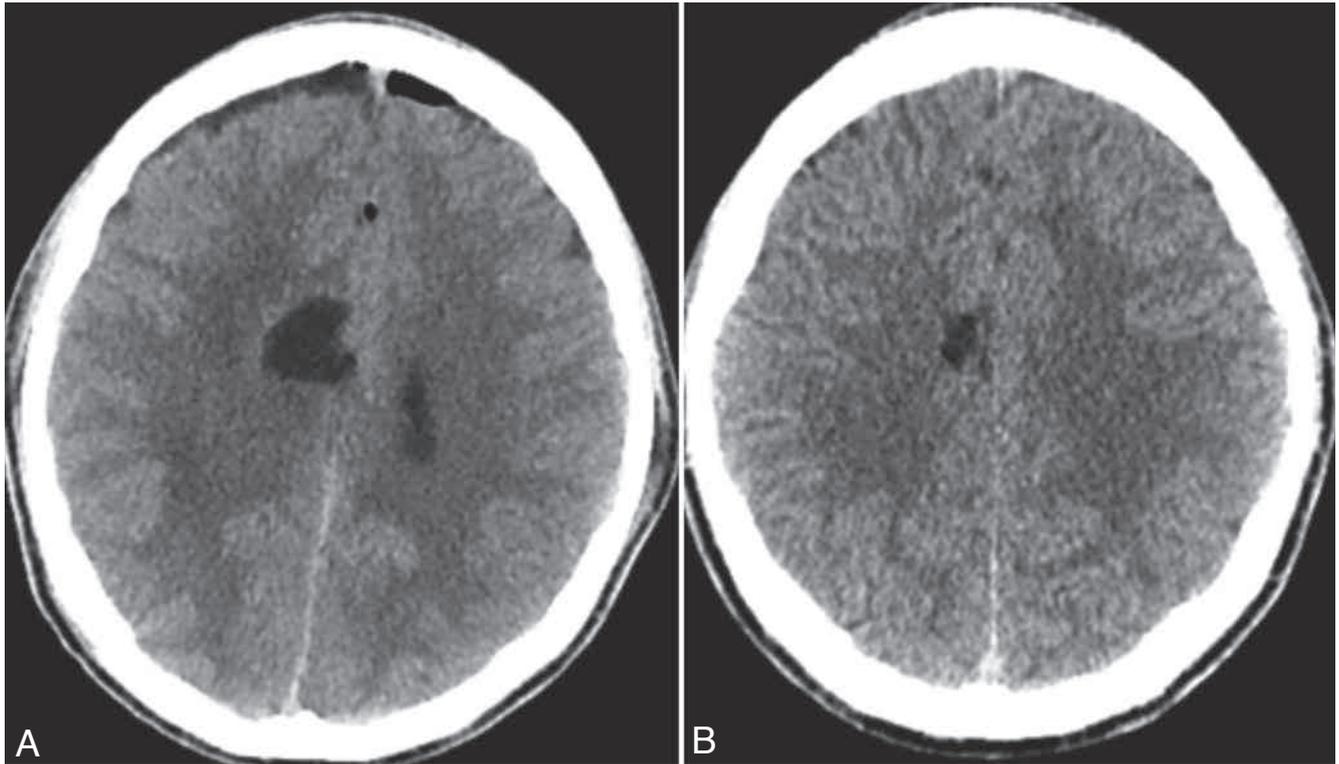
The patient is clinically doing well without any neurological deficit at 14 months post operatively.

#### Discussion

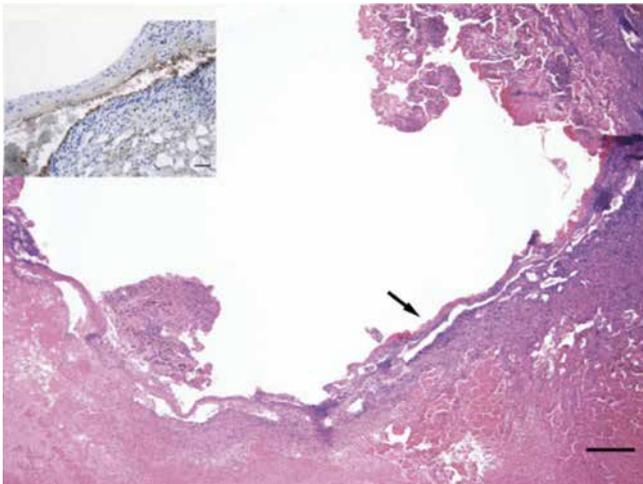
Cavernous malformations also known as cavernous angioma or

cavernoma, are a type of vascular disorder, consisting of abnormally large vascular cavities or sinusoid channels of varying size. These lesions have alternately been classified as neoplastic or hamartomatous. Cavernous malformations can occur in mostly any organ.

In the brain, cavernous malformations account for 5-10% of all vascular malformations (5). They occur with an incidence of approximately 0,5-1% in the general population. Most lesions are small and do not always cause neurological symptoms; it is estimated that only 1 in 3 cavernous malformations causes clinical symptoms, mostly seizures, progressive neurologic deficits and hemorrhage. Although almost all of the cases have micro-bleedings, bleeding leading to clinical symptoms is a rare entity in cavernomas (0,25-6%) (6). Symptoms are reported to occur when the lesion diameter is greater than 1,75 cm (7). Cavernous malformations are found in the cerebral hemispheres (66%), brainstem



**Fig. 2.** — Patient 1, post-operative follow-up. Axial non-contrast CT examinations, 24 hours after surgery (A) and 4 months later (B). In the immediate postoperative period (A), the surgical cavity is sharply defined and dry; four months after surgery (B), the resection cavity has further decreased in size.



**Fig. 3.** — Giant cavernous malformation (haematoxylin/eosin stained paraffin section, bar: 500  $\mu$ m). The wall of the lesion is covered by fibrinous material (arrow). Inset, left (CD34 immunohistochemical staining, bar: 100  $\mu$ m) shows that the vessel wall is lined by a single-layered endothelium.

(18%), basal ganglia or thalamus (8%), cerebellum (6%), and other locations (2.5% [combined supra- and infratentorial, callosal or insular] (8).

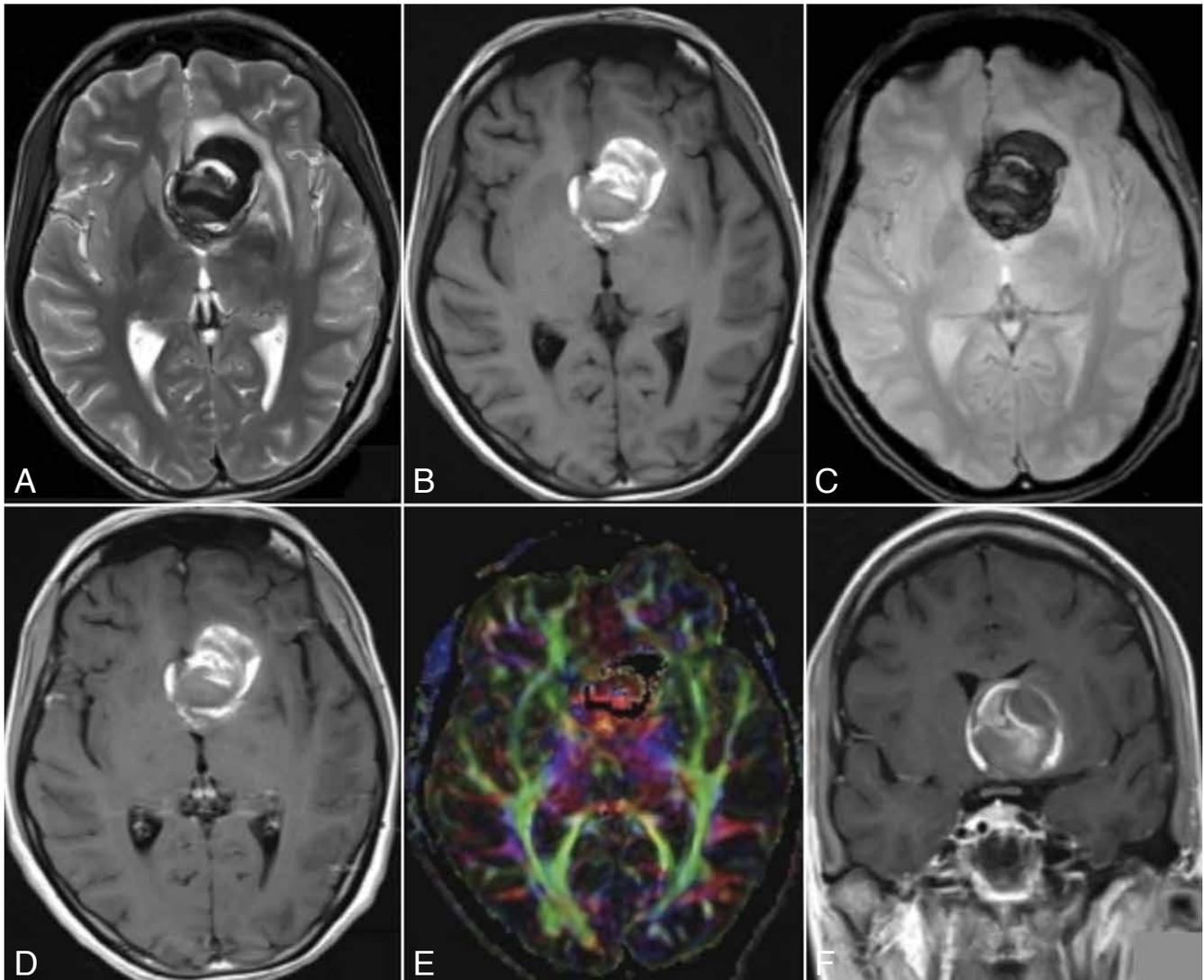
The natural history of cavernous malformations is to increase in size due to repeated episodes of hemorrhage (9). This leads to their markedly heterogeneous internal architecture on MR imaging, with blood degradation products of varying age.

The presence of vasogenic edema in the surrounding brain tissue, as seen in our patients, indicates a recent episode of bleeding. The hemorrhage of the cavernoma can increase the edema. The increase in size of the cavernoma can be explained by re-endothelialisation of the hemorrhagic cavity, formation of new blood vessels and proliferation of granulation tissue. New bleedings

from this hemorrhagic cavity may further increase the size in time. This is analogue to the growth of a subdural hematoma (10). The rate of bleeding is higher when the size of the lesion is greater than 10 mm and when the patient is aged 35 years or younger (11).

There is a small, but clinically important, subgroup of so-called giant cavernous malformations (GCM). Unlike giant aneurysms, defined as having a diameter of at least 25 mm, no real threshold dimension has been agreed upon for giant cavernous malformation. Some authors define GCM as having a diameter of greater than 6 cm (4), while others use 4 cm as a cut-off (3). Because of their slow development and size, GCM present with subtle symptoms, that can mimic depression or brain tumor. Their clinical presentation depends on size and location, and is affected by recent episodes of bleeding. GCM occur more often in children and adolescents (12). In children they are frequently associated with intractable epilepsy (13, 14).

The MRI characteristics of GCM are variable, depending on the presence of hemorrhage breakdown products and calcifications. The typical MR appearance of a GCM is that of a heterogeneous “popcorn-like” mass lesion (15, 16). We compare



*Fig. 4.* — Patient 2, pre-operative MRI of the brain with axial TSE T2-WI (A), axial TSE T1-WI (B), axial gradient echo T2\* (C), axial susceptibility WI (D), axial first eigenvector fractional anisotropy map (E), sagittal TSE T1-WI (F). There is a large heterogeneous mass in the suprasellar region involving the left caudate and lentiform nuclei. The mass presents a layered appearance, with mixed signal intensity components indicating various stages of blood degradation products. On the T2\* and SWI sequences, the lesion is predominantly hypointense due to susceptibility effects caused by hemosiderin. Adjacent to the giant cavernous angioma, there is a layer of liquefied blood. The lesion is surrounded by vasogenic edema in the deep frontal white matter.

the appearance of the GCM in our two patients to a freshly cracked “walnut” with a heterogeneously mixed signal core and a hypointense hemosiderin rim. This heterogeneous signal architecture, with high and low signal intensity components, is explained by the presence of old and fresh blood breakdown products. The mottled appearance is best appreciated on T2\* gradient echo or susceptibility weighted images (SWI); in these sequences, old blood degradation products (hemosiderin) appear hypointense (black) whereas fresh blood is hyperintense (white). These lesions are more conspicuous on high-field MR systems, because of their greater sensitivity to susceptibility artifacts. Diffusion-weighted images may show throm-

bosed blood clots as areas of diffusion restriction. Innovative imaging techniques, such as diffusion tensor imaging and functional MR imaging, have been applied to the preoperative and intra-operative management of these lesions.

Histopathologically, cavernous malformations are well-circumscribed, lobulated, red to purple, raspberry-like lesions. They consist of thin hyalinized vascular channels without interposed brain tissue. Their size varies from punctate to several centimeters. On microscopic examination, cavernous malformations are shown to be composed of dilated, thin-walled capillaries that have one layer of endothelial lining and a variable layer of fibrous adventitia. Elastic fibers are absent in the

walls of these vascular caverns. There is usually evidence of previous hemorrhage on pathological examination. Thrombosis may be present within some of the lumens. Although not present in these two cases, literature describes that cavernous malformations may be associated with venous malformations (17). There is growing evidence that cavernous malformations and venous developmental anomaly (DVA) co-exist, and may even be different manifestations of the same disease spectrum (18-20). When these patients present with hemorrhage, it is often the cavernous malformation that has bled and not the venous developmental anomaly. In fact, it is exceedingly rare for a venous anomaly alone to hemorrhage.

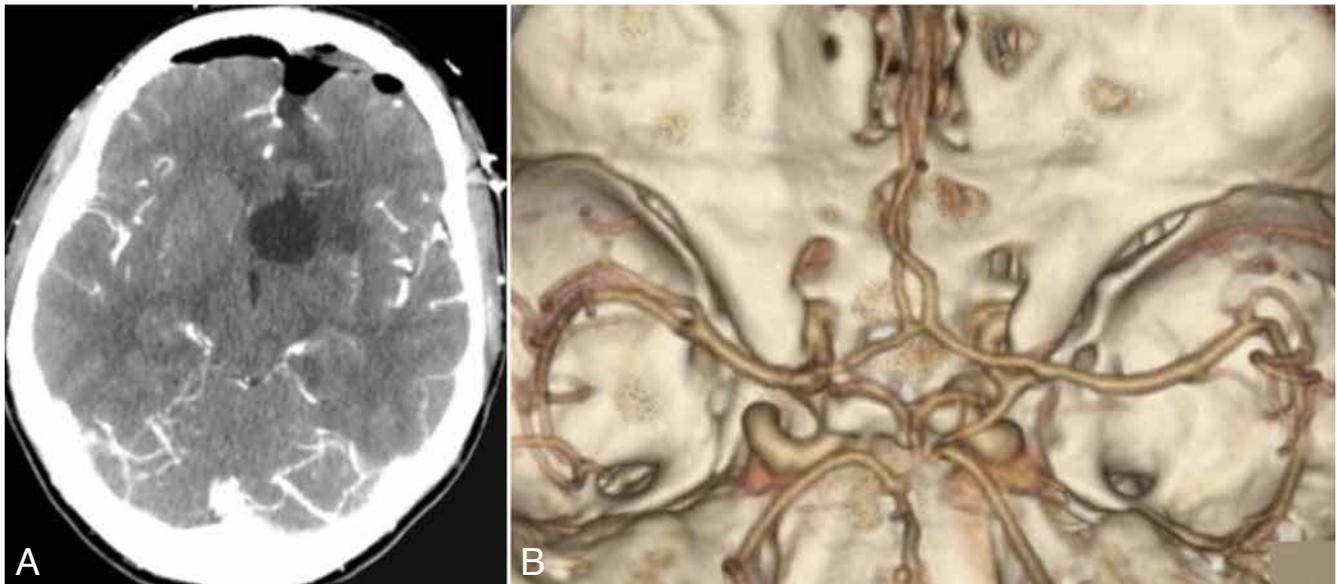


Fig. 5. — Patient 2, post-operative contrast enhanced CT scan (A) and CT angiography (B) on day 1 after surgery. There is a sharply defined, non-enhancing post-operative resection cavity in the suprasellar and left caudato-lenticular region; note the presence of intracranial air, consistent with a recent post-operative status. CT-angiography with volume rendering shows that the blood vessels of the circle of Willis are intact.

The subgroup of giant cavernous malformations constitutes a formidable challenge to the neurosurgeon. These lesions need to be removed by circumferential dissection of the malformation. In both our patients, evacuation of the liquefied hematoma created space to facilitate surgical removal. Incomplete removal increases the risk of a post-operative hemorrhage or recurrence of the cavernous malformation.

In conclusion, we have documented two patients with giant cavernous malformations. Clinical presentation may be insidious. The diagnosis is made with MR imaging, and both of our patients presented with a typical “walnut” appearance on T2\* and SWI sequences. The neurosurgical approach consists of circumferential dissection with complete removal of the lesion.

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