Vascular pressures and cortical blood flow in cavernous angioma of the brain

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This study was designed to investigate the hemodynamic characteristics of cavernous angiomas of the brain. Five adult patients with a cavernous angioma underwent local cortical blood flow studies and vascular pressure measurements during surgery for the excision of the cavernous angioma. Clinical presentation included headache in four patients, seizures in four patients, and recurring diplopia in one patient. Magnetic resonance imaging demonstrated the cavernous angiomas in all patients and revealed an associated small hematoma in two. Four patients with a cerebral cavernous angioma were operated on in the supine position and the remaining patient, whose lesion involved the brain stem, was operated on in the sitting position. Mean local cortical blood flow (± standard error of the mean) in the cerebral cortex adjacent to the lesion was 60.5 ± 8.3 ml/100 gm/min at a mean PaCO₂ of 35.0 ± 0.6 torr. Mean CO₂ reactivity was 1.1 ± 0.2 ml/100 gm/min/torr. The local cortical blood flow results were similar to established normal control findings. Mean pressure within the lesion in the patients undergoing surgery while supine was 38.2 ± 0.5 mm Hg; a slight decline in cavernous angioma pressure occurred with a drop in mean systemic arterial blood pressure and PaCO₂. Mean pressure in the cavernous angioma in the patient operated on in the sitting position was 7 mm Hg. Jugular compression resulted in a 9-mm Hg rise in cavernous angioma pressure in one supine patient but no change in the patient in the sitting position. Direct microscopic observation revealed slow circulation within the lesions. The hemodynamic features demonstrated in this study indicate that cavernous angiomas are relatively passive vascular anomalies that are unlikely to produce ischemia in adjacent brain. Frank hemorrhage would be expected to be self-limiting because of relatively low driving pressures.

KEY WORDS · cavernous angioma · hemangioma · cerebral blood flow · hemorrhage · seizure · hemodynamics

VASCULAR malformations of the brain have been categorized as arteriovenous malformation (AVM), venous malformation, cavernous angioma, and capillary telangiectasia. For many years, most clinical attention was directed toward AVM's, whereas cavernous angiomas were thought to be of little clinical importance. Recent experience suggests that cavernous angiomas are more common and have greater clinical relevance than was previously believed. This change in thinking has been largely the result of improved diagnosis of cavernous angiomas with the advent of magnetic resonance (MR) imaging.8,9

There is no information available regarding the vascular pressures within a cavernous angioma and the effects on blood flow in the surrounding brain. The objective of the current investigation was to study and characterize the vascular pressures and circulatory changes in cavernous angiomas.

Clinical Material and Methods

Clinical Presentation

Five adult patients with a cavernous angioma of the brain underwent local cortical blood flow studies and vascular pressure measurements during surgery for the excision of the cavernous angioma. All five were women and ranged in age from 23 to 43 years (mean 31 years). Clinical presentation included recent (< 1 month) headache in four patients, recent simple partial seizures in two, recent generalized seizure in one, intractable complex partial seizures in one, transient dysphasia in one, and recurring diplopia in one. The neu-
rological examination was normal in four patients. The patient with diplopia was found to have bilateral sixth cranial nerve palsies and a very mild left facial palsy.

Preoperative Investigations

Computerized tomography (CT) scans of the head, with and without intravenously administered contrast medium, were obtained in all patients. One patient presenting with acute headache and transient dysphasia had a subcortical hematoma 3 cm in diameter in the left frontal lobe adjacent to the junction of the gray and white matter. The patient with acute headache and recurring diplopia was found to have a 2-cm hematoma in the brain stem at the junction of the pons and medulla. Three patients had areas of punctate calcification in the region of the cavernous angiomas (Fig. 1 left). In one patient, a plain CT scan was considered to be normal. Enhancement of the cavernous angioma following the intravenous administration of contrast medium was seen in two patients.

All patients underwent MR imaging of the head. In three patients, a 2- to 3-cm, round, slightly lobulated lesion was identified at the junction of the cerebral gray and white matter (Fig. 1 center and right). Three of these were located in the frontal lobe and one was in the right mesial temporal lobe. These lesions were demarcated by a thin rim of decreased signal intensity. The core consisted of punctate areas of slightly increased or decreased signal intensity. One patient had a recent hematoma, 2 to 3 cm in diameter, adjacent to a 2-cm, round, lobulated lesion. The fifth patient had a large, multilobulated lesion in the brain stem at the junction of the pons and medulla (Fig. 2). The appearance of the lesion was similar to the cerebral lesions in the other four patients. Additionally, a 2-cm acute hematoma lay adjacent to the lesion. The hematoma and lesion appeared to bulge into the fourth ventricle.

Gadolinium was administered intravenously to one of the patients with a cerebral lesion, and slight uptake of the contrast medium was observed.

All patients underwent complete four-vessel angiography using the transfemoral catheter technique. No abnormalities were detected in the region of the lesions identified on the CT scans and MR images.

Intraoperative Studies

Induction of general anesthesia was achieved using thiopental, fentanyl, sufentanil, and pancuronium. Anesthesia was maintained by use of these agents as well

FIG. 1. Left: Computerized tomography scan showing calcification (arrow) in the right frontal lobe. Center: Magnetic resonance $T_1$-weighted image showing the cavernous angioma (arrow) in the right frontal lobe. Right: Magnetic resonance image following the intravenous administration of gadolinium showing enhancement of the cavernous angioma. A draining vein (arrow) is also demonstrated.

FIG. 2. Magnetic resonance $T_1$-weighted image showing a cavernous angioma (arrow) in the brain stem.
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as nitrous oxide and isoflurane. Throughout each operative procedure, the mean systemic arterial blood pressure (MABP) was measured continuously using a brachial artery catheter hydrostatically coupled to a pressure transducer.* The transducer was kept level with the right atrium of the heart. A central venous catheter was placed in the internal jugular vein. This catheter was hydrostatically coupled to a pressure transducer and was used to measure the central venous pressure (CVP).

The craniotomies for cavernous angioma removal were performed using standard neurosurgical techniques. The four patients with a cerebral cavernous angioma were positioned supine and the patient with the lesion involving the brain stem was placed in a sitting position.

Cortical Blood Flow Measurements. Local cortical blood flow measurements were performed in three patients undergoing craniotomy for removal of a cerebral cavernous angioma. After dural opening and microsurgical exposure of a small portion of the cavernous angioma, Peltier stack probes† were applied to the cortical surface 2 to 4 cm from the cavernous angioma.12 The local cortical blood flow was measured continuously as the MABP was allowed to shift over at least a 10-mm Hg range. At the high and low MABP levels, the CO2 reactivity was tested while changing the PaCO2 levels by manipulating the mechanical ventilation. The PaCO2 was changed through a range of at least 8 torr. The baseline PaCO2 was maintained in the 35-torr range.

Angioma Pressure Measurements. Pressure within the cavernous angiomas was measured in all patients. After the microsurgical exposure of a small portion of the angioma, a No. 25 needle was inserted into one of the large chambers of the lesion itself, typically appearing as bright red.23 Care was taken not to insert the needle into a thrombosed region of the angioma, which is often darker in appearance. The needle was stabilized on the blade of a self-retaining retractor, and was coupled to a pressure transducer by semi-rigid tubing filled with normal saline. In the four patients in the supine position, the pressure transducer was kept at the level of the right atrium. In the patient operated on in the sitting position, the transducer was kept at the same level as the cavernous angioma. After insertion of the needle, the MABP and PaCO2 were measured in the same fashion as the local cortical blood flow studies. In the last two patients studied, bilateral jugular venous compression for 1-minute periods was also performed during pressure measurement. In three patients, measurements were repeated in another segment of the cavernous angioma.

Results

Intraoperative Findings

Two patients with a frontal lobe cavernous angioma had evidence of previous hemorrhage adjacent to the lesion. The hematomas in both these patients were known to be 3 months old; the other appeared to be older. The hematomas in both patients were less than 2 cm in diameter. The patient with the brain-stem cavernous angioma was found to have a 3-mm perforation in the floor of the fourth ventricle through which bleeding from the lesion had extended into the ventricular system and subarachnoid space. The subacute clot, approximately 2.0 cm in diameter, was found adjacent to the cavernous angioma.

The cavernous angiomas in all patients had a similar appearance. They ranged in size from 2 to 3 cm and had a multilobulated exterior surface. The walls of the vascular channels were very thin but not particularly friable. Most channels contained dark venous blood although a few compartments were seen to contain thin laminae of arterialized blood flowing slowly within the thin-walled lesion. The "supply" arteries were very small (< 250 mm) and were relatively few in number (two or three). A small but discrete draining vein was observed in the five patients. The angiomas were easily removed in one piece. Bleeding from the lesion or the surrounding brain was minimal and not difficult to control. A CO2 laser was particularly helpful in the removal of the lesion affecting the brain stem. The patient with intractable complex partial seizures and a cavernous angioma in the mesial right temporal lobe underwent a standard temporal lobectomy to eliminate a previously localized epileptogenic focus.

Cortical Blood Flow Measurements

Mean baseline local cortical blood flow (± standard error of the mean) was 60.5 ± 8.3 ml/100 gm/min at a mean PaCO2 of 35.0 ± 0.6 torr. No change in local cortical blood flow was noted with a mean 11-mm Hg shift of MABP. The mean CO2 reactivity was 1.1 ± 0.2 ml/100 gm/min/torr. Overall, the local cortical blood flow findings were similar to previously established results in normal control individuals obtained with this measurement technique.1,2,4

Angioma Pressure Measurements

Mean pressure within the cavernous angiomas in the patients undergoing surgery in the supine position was 38.2 ± 0.5 mm Hg at a mean MABP of 99.6 ± 15.1 mm Hg, a mean CVP of 5.0 ± 1.0 mm Hg, and a mean PaCO2 of 36.6 ± 1.0 torr. Clear-cut pulse-related changes in baseline angioma pressures were not observed. With a mean reduction of 14.7 ± 2.1 mm Hg in MABP, there was a mean 7.0 ± 0.5-mm Hg drop in angioma pressure. A mean reduction in angioma pressure of 6.5 ± 0.5 mm Hg was observed when a PaCO2 was reduced by a mean of 8.0 ± 0.6 torr.

Mean pressure within the cavernous angioma in the
patient operated on in the sitting position was 7.0 mm Hg. A 10-mm Hg reduction of MABP resulted in a drop in cavernous angioma pressure to 2 mm Hg. No change in angioma pressure was observed with changes in PaCO₂.

Jugular compression was performed in one supine patient and in the patient operated on in the sitting position. In the supine patient, jugular compression resulted in a 9.0-mm Hg rise in cavernous angioma pressure, whereas no difference was observed in the sitting patient.

Pathological Examination

Microscopic examination of frozen and permanent sections of the lesions confirmed the diagnosis of cavernous angioma in all patients. Some of the chambers of the cavernous angiomas were found to contain thrombus.

Clinical Course

The four patients undergoing excision of a cerebral cavernous angioma had an uneventful postoperative recovery. One patient subsequently had a single generalized convulsion 1 week after surgery, which was attributed to an inadequate dose of anticonvulsant medication; she recovered from the seizure without side effects. The patient with the brain-stem cavernous angioma exhibited improvement in extracranial movements during the early postoperative period; however, 5 days following surgery the left facial palsy worsened. Repeat MR and CT studies, as well as cerebrospinal fluid examination, failed to demonstrate recurrent hemorrhage. Fortunately, the facial palsy resolved over a 10-day period. The patient with intractable complex partial seizures despite maximal medical therapy has been seizure-free for 1 year since surgery.

Discussion

The clinical presentation and findings of the patients in our series were similar to those described in previous reports. Seizure disorder and headache were the most frequent presenting symptoms. Neurological deficit, when present, was associated with evidence of hemorrhage on neuroradiological studies.

Neuroradiographic Studies

Magnetic resonance imaging was the most sensitive and most specific technique for the demonstration of the cavernous angiomas in our patients. This confirmed the findings of previous studies that MR imaging is the best diagnostic technique available for demonstrating a cavernous angioma. The MR findings in our patients were similar to those previously described, and the pathological examination of the surgically obtained specimens confirmed the diagnosis. In contrast, CT scans were considered normal in one patient and the information derived was less specific than from the MR images. Previous studies have indicated that many cavernous angiomas will go unrecognized when CT scanning is the only imaging modality used. Cerebral angiography has been shown to be very insensitive for identifying the presence of a cavernous angioma; in accordance with this, no abnormalities were seen on angiography in our five patients.

Pathophysiology

The findings of the study provide some insight into the pathophysiology of cavernous angiomas. Measurement of pressure within the compartments of the lesions revealed pressures that were less than MABP and greater than CVP in the supine patients. In this group, the cavernous angioma pressures were midway between the MABP and CVP. These pressure findings differ from those seen in patients with a saccular aneurysm or AVM. Pressures in cortical arteries and in intracranial saccular aneurysms have been shown to be similar to MABP. This has been attributed to the high-flow shunt that exists with AVM's. In cavernous angiomas, the pressure levels cannot be attributed to a similar high-flow shunt, as these lesions are supplied by relatively small arteries with high resistance. Also, flow within the cavernous angiomas appeared to be quite slow on direct microscopic observation.

Hemodynamic Findings

Alteration of the MABP was associated with small changes in cavernous angioma pressure, and a slight reduction in cavernous angioma pressure was associated with a reduction in PaCO₂. These findings do not indicate the presence of pressure regulation and CO₂ reactivity within the angioma but are more likely related to pressure changes within the cerebral white matter itself.

Much lower cavernous angioma pressures were observed in the sitting patient. This was thought to reflect enhanced venous drainage of the angioma when the patient's head was well above the heart level as compared with the supine patients whose heads were at or only slightly above heart level. A rise in angioma pressure was not seen in the sitting patient during jugular compression but was clearly demonstrated in the supine patient tested. These findings were interpreted to support the concept that the cavernous angiomas communicate freely with the venous circulation.

Clinical Implications

Clinical studies have demonstrated the propensity of a cavernous angioma to produce discrete hematomas in adjacent brain. Studies have also consistently demonstrated hemosiderin deposits around cavernous angiomas not previously known to have bled. The latter findings suggest that a small amount of blood might seep from a cavernous angioma in the absence of clinical findings of hemorrhage. The cause of these
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two forms of bleeding is unclear. The pressure within
the thin-walled vascular channels constituting a cavern-
ous angioma appears to be substantially higher than
venous pressure and is position-dependent. It is possible
that sudden increases in CVP may be transmitted di-
rectly to a cavernous angioma. The relatively large
radius of the chambers would also act to increase
tension on the thin walls of the cavernous angioma. A
rapid increase in CVP, possibly associated with a de-
pendent-head position, could be important factors in
producing either microscopic or gross hemorrhage.

The circulation in the adjacent cerebral cortex ap-
peared unaffected by the presence of a cavernous an-
gioma. The local cortical blood flow and CO₂ reactivity
in patients with cerebral cavernous angioma were sim-
ilar to those in previously reported normal control
groups.¹² These findings are consistent with the low-
flow nature of cavernous angiomas.

The clinical importance of cavernous angiomas has
yet to be determined. The hemodynamic features dem-
onstrated in this study indicate that cavernous angiomas
are unlikely to produce ischemia in adjacent brain.
Frank hemorrhage, when it occurs, would be expected
to be self-limiting because of the relatively low driving
pressures. Those pressures are likely to be rapidly neu-
ralized by the increased tissue pressure produced by
the hematoma itself. The seepage of blood into the
surrounding brain tissue (with or without frank hem-
orrhage) and the consequent deposition of iron and
other breakdown products could be an important factor
in the generation of a seizure focus.

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