Spontaneous resolution of multiple hemangiomas of the brain

Case report


Departments of Neurosurgery, Radiology, and Pathology, Saga Medical School, Saga, Japan

A case of multiple intracerebral hemangiomas is reported. The lesions were angiographically hypervascular and accompanied by marked perifocal brain edema. After removal of the main lesion and postoperative steroid administration, the rest of the lesions resolved spontaneously. Histologically, the lesion was composed of capillaries and fibromyxoid stroma. The distinctive clinical, radiological and histological features of this lesion are discussed in contrast to several other types of intracranial vascular tumors.

KEY WORDS • hemangioma • cavernous angioma • brain edema • steroid • multiple tumors

Intracranial hemangiomas are generally considered to be malformations or hamartomas. Unless they bleed, they are not normally associated with brain edema and rarely do they resolve spontaneously. We report the case of an unusual type of hemangioma with clinical and radiological features quite different from those previously documented.

Case Report

This 20-year-old man was well until 2 months before admission when he started to have retro-orbital and frontal headache, occasionally preceded by scintillating scotoma. One week prior to admission, he was observed to turn his head to the right and stretch his limbs; he then fell unconscious for a short time. He was placed on an anticonvulsant medication. Computerized tomography (CT) disclosed abnormalities, and he was transferred to us for further evaluation and treatment.

Examination. No cutaneous or mucosal vascular lesions were noted. Neurological examination of the patient’s mental status and cranial nerves was normal. No papilledema, weakness, sensory changes, or alteration of reflexes in the extremities was detected.

An electroencephalogram showed paroxysmal slow waves over the left frontal and right frontotemporal lobes. A plain CT scan on the day of admission revealed a slightly hyperdense area in the right frontal lobe and widespread areas of hypodensity bilaterally in the frontoparietal lobes. A postcontrast CT scan showed marked enhancement of the lesion in the right frontal lobe and some smaller lesions bilaterally in the frontoparietal lobes (Fig. 1 upper). Hypodense areas were slightly more prominent compared with those in the study performed 1 week before admission. A carotid angiogram in the arterial and capillary phases demonstrated multiple hypervascular lesions with mass effect corresponding to the enhanced areas on the contrast CT scan (Fig. 1 lower).

Magnetic resonance (MR) imaging disclosed no areas of signal characteristic of methemoglobin. From these studies, a preliminary diagnosis of metastatic brain tumors was made; however, an extensive survey for a primary lesion was negative.

Operation. A right frontoparietal craniotomy was performed to remove the largest lesion in the right frontal lobe. When the dura was incised, a thickened arachnoid membrane and a red vein were observed. An echogram disclosed a mass lesion 1 cm below the cortical surface. After a small corticotomy was carried out, a well-encapsulated dumbbell-shaped tumor, 1.5 x 1 x 1 cm in size and surrounded by edematous white matter, was found. It was firm and vascular. The tumor was dissected away from the veins and a few small arteries supplying the mass and was extirpated.

Postoperative Course. The patient received steroid therapy postoperatively, beginning with 12 mg of be-
Spontaneous resolution of multiple hemangiomas

Tamethasone on the day of operation. This was tapered and discontinued in 1 week. A contrast-enhanced CT scan obtained at 2 weeks after surgery disclosed a decrease in the size of the remaining lesions with diminution in the size of the perifocal hypodense areas. A contrast-enhanced CT scan 5 months postoperatively demonstrated only a small defect at the operative site; the rest of the lesions were not visible. Magnetic resonance imaging 9 months after surgery showed only a small area of cerebrospinal fluid intensity at the operative site. There were no areas of hyperintense signal suggestive of thrombi. The patient has been doing quite well in the follow-up period and is without symptoms or neurological deficits. Follow-up CT scans 1 and 2 years after surgery showed no signs of recurrence.

Pathological Study. When studied under a light microscope, the lesion contained numerous blood vessels, which varied widely in size from small lumina lined by plump endothelial cells to large dilated vessels lined by flattened endothelium. Some vessels had thin walls composed of a layer of endothelial cells, and others had walls composed of a compactly arranged periendothelial layer of spindle cells. There was fibromyxoid stroma (positive on Alcian blue staining) between the blood vessels (Fig. 2). Thrombosed blood vessels were scattered throughout the specimen. The interface with the white matter showed glial tissue closely apposed to the periphery of the vascular mass and rare areas pigmented with hemosiderin. Glomeruloid capillaries, which consisted of markedly proliferated capillaries, were occasionally seen at the periphery of the lesion. At no point was atypical cell proliferation observed. Elastic van Gieson stain failed to demonstrate any regular arrangement of elastic laminae inside the lesion. Small muscular arteries were found in some parts of the lesion periphery. Factor VIII-associated protein was identified by immunohistochemical staining only in the flattened cells lining the blood vessels.

Electron microscopic examination of the specimen revealed endothelial cells surrounding the vascular lamina, subendothelial cells, and abundant extracellular matrix. The subendothelial cells were surrounded by a basal lamina of varying thickness. These cells had ir-
FIG. 2. Photomicrograph of the lesion showing an abundance of capillaries and fibromyxoid stroma. H & E, × 140.

regularly shaped nuclei with margined chromatin. A prominent feature was the presence of abundant dilated cisterns of rough endoplasmic reticulum. In addition, the cytoplasm contained other organelles, such as scattered mitochondria and bundles of microfilaments. Weibel-Palade bodies were often seen (Fig. 3), resembling plump endothelial cells surrounding small vascular lumina.

These findings led to the diagnosis of a hemangioma. This particular tumor was different from the intracranial hemangiomas previously described.

**Discussion**

The radiological, clinical, and histological features of this case were quite unique. Multiple hypervascular mass lesions associated with perifocal edema usually suggest metastatic brain tumors. After removal of the main tumor, however, the remaining lesions (probably four lesions in all) resolved completely on CT and MR imaging. Follow-up monitoring with high-resolution CT and MR imaging has not detected any changes suggestive of recurrence for 2 years. The pathological picture showed abundant dilated capillaries and fibromyxoid stroma. Most capillaries had a periendothelial layer of spindle cells which had a structure similar to that of immature endothelial cells.

**Vascular Tumors and Malformations**

We compared the pathological findings of the tumor in our case to those of intracranial vascular tumors and tumor-like lesions. Arteriovenous malformation, venous malformation, and capillary telangiectasis are regarded as vascular malformations and can be differentiated because the individual blood vessels are separated by neural tissues in those malformations. Hemangioblastomas, which can be multiple and located in the cerebrum, always have stroma cells. According to the World Health Organization classification, angiomatous meningiomas comprise subgroups of hemangioblastic meningiomas, hemangiopericytomas, and angiomatous meningiomas. Hemangioblastic meningiomas have structures similar to hemangioblastomas; hemangiopericytomas have a distinct cellular arrangement around capillaries, demonstrated by reticulin stain; and angiomatous meningiomas have a meningotheliomatous component. The tumor removed in this case was well encapsulated like a meningioma; however, it was not attached to dura and was devoid of any of these histological features.

**Cavernous Hemangiomas**

Cavernous hemangiomas are composed of large dilated blood vessels with walls consisting wholly of collagen. There is no cellular stroma. Thrombosis and organization may create superficial variation, however, which sometimes makes the diagnosis difficult. The histological features of this case have some resemblance to cavernous hemangiomas. The lesion in this case might be diagnosed as cavernous hemangioma solely on histological grounds; however, its radiological features and clinical course were against it. Intracerebral cavernous hemangiomas are angiographically occult in most cases, or only slightly stained in the venous phase. A CT scan usually shows a mild-to-moderately enhancing lesion without perifocal edema if not accompanied by a hematoma; however, there is one report of an exceptional case with multiple cavernous hemangiomas associated with multiple perifocal edema.

**Hemangioendotheliomas**

Other intracranial vascular tumors or tumor-like lesions may include hemangioendothelioma and vegetant intravascular hemangioendothelioma, which are both quite rare. Hemangioendotheliomas are usually attached to dura like meningiomas but have some tendency to infiltrate the brain. These are composed of immature capillaries and aggregates of endothelial cells and pericytes. A vegetant intravascular hemangioendothelioma is regarded as an unusual form of organizing thrombus, which follows a benign clinical course. Some reported features of these rare vascular lesions are summarized in Table 1 for comparison with cavernous hemangiomas and the lesion in our case.

**Features of the Present Case**

**Histological Findings.** The histological features of the lesion in our case resemble those of pyogenic granulomas, which have not been reported in intracranial sites. This lesion, which was once regarded as an inflammatory lesion, is a polypoid form of capillary hemangioma. Pyogenic granulomas occur most commonly on the skin and mucosal surfaces, but also arise from a
Spontaneous resolution of multiple hemangiomas

FIG. 3. Electron micrographs showing a capillary (C) and subendothelial cells. The subendothelial cells have abundant dilated cisterns of rough endoplasmic reticulum and occasional Weibel-Palade bodies (arrow). × 4000. Inset: Higher magnification of a Weibel-Palade body. × 40,000.

vein wall. They often represent a secondary inflammatory change from ulceration; however, the basic lesion is a lobulated cellular hemangioma set in a fibromyxoid matrix. They are sometimes accompanied by multiple small satellite nodules, and in some instances regress spontaneously. Since we have no evidence that the hemangioma in our case arose from a vein wall, further verification of the hemangioma is pending.

Radiological Findings. The unique radiological features of our case are well correlated with the pathological findings. Feeding arteries and a tumor stain were demonstrated on angiography. Pathological studies revealed small arteries at the periphery of the lesion and abundant capillaries inside. Angiographic opacification of even smaller lesions may suggest that the lesion is closely related to the preexisting cerebrovascular tree. A marked perifocal hypodense area on the preoperative CT scans was interpreted as brain edema from findings at surgery and on the postoperative CT scans. Markedly proliferated capillaries located at the periphery of the lesion must have been the source of the edema fluid, which then spread into surrounding brain tissue.

Table 1

Features of intracranial hemangiomas and hemangioendotheliomas

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Multiplicity</th>
<th>Angiographic Findings</th>
<th>Computerized Tomography Findings</th>
<th>Histological Findings</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavernous hemangioma</td>
<td>yes (25%)</td>
<td>avascular or slightly hypervascular in venous phase</td>
<td>mass effect equivocal</td>
<td>large dilated vessels</td>
<td>benign tumor, no tendency to regress</td>
</tr>
<tr>
<td>Vegetant intravascular hemangioendothelioma</td>
<td>yes</td>
<td>avascular</td>
<td>mass effect equivocal</td>
<td>Fibroendothelial papillae in vascular space</td>
<td>Reactive vascular proliferation</td>
</tr>
<tr>
<td>Hemangioendothelioma</td>
<td>no</td>
<td>hypervascular</td>
<td>mass effect</td>
<td>Small vascular channels with endothelial aggregates capillaries &amp; fibromyxoid stroma</td>
<td>Infiltrative neoplasm</td>
</tr>
<tr>
<td>Present case</td>
<td>yes</td>
<td>hypervascular</td>
<td>marked perifocal edema</td>
<td>Large dilated vessels</td>
<td>Benign tumor, spontaneous regression</td>
</tr>
</tbody>
</table>

J. Neurosurg. / Volume 73 / September, 1990
Spontaneous Resolution. The spontaneous resolution of the multiple lesions after removal of the main tumor and steroid treatment is another interesting aspect of this case. A juvenile soft-tissue hemangioma usually appears within a few weeks after birth and rapidly enlarges over a period of several months, then regresses over a period of a few years.\(^2\) Thus, one probable mechanism of resolution might be the very nature of hemangiomas. Another mechanism in this case might have been the effect of the corticosteroids. Immature and rapidly proliferating vessels of hemangiomas may be particularly susceptible to corticosteroids. Earlier resolution of juvenile hemangiomas than in the natural course of the lesion by the use of steroid therapy has been noted.\(^3\),\(^15\) Angiographic resolution of a hemangioma in the middle cranial fossa after steroid treatment has also been reported.\(^11\) A third possible mechanism is that the main tumor was producing an angiogenesis factor which was eliminated by tumor removal.

Acknowledgments

We thank Dr. L. J. Rubinstein and Dr. T. Watanabe for reviewing the pathological material, and Ms. R. M. Moffet and Ms. Y. Mukai for assistance in the preparation of this manuscript.

References


Manuscript received June 26, 1989.
Accepted in final form February 15, 1990.
Address reprint requests to: Masamitsu Abe, M.D., D.Sc., Department of Neurosurgery, Saga Medical School, Saga 840-01, Japan.