The MRI appearance of cavernous malformations (angiomas)

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The angiographic, computerized tomography (CT), and magnetic resonance imaging (MRI) findings were compared in 10 patients with a total of 16 pathologically verified cavernous angiomas. Only three lesions had abnormal vasculature in the form of venous pooling or a capillary blush. The CT scans were positive in seven patients and detected 14 lesions, while high-field strength (1.5 Tesla) MRI was positive in each case and demonstrated 27 distinct lesions. On T2-weighted MRI, the combination of a reticulated core of mixed signal intensity (SI) with a surrounding rim of decreased SI strongly suggests the diagnosis of a cavernous malformation. Smaller lesions appear as areas of decreased SI (black dots). The sensitivity of MRI is based on magnetic susceptibility and possibly diffusion effects related to field heterogeneity that is more conspicuous on high-field imaging and caused by the presence of excessive iron (hemosiderin).

KEY WORDS • cavernous angioma • magnetic resonance imaging • computerized tomography • cavernous malformation • hemosiderin

MAGNETIC resonance imaging (MRI) is emerging as the most effective diagnostic modality for a majority of disorders that affect the central nervous system (CNS). The importance of MRI becomes increasingly apparent when using a high-field strength system to evaluate brain hemorrhage. The present study was undertaken to define the MRI characteristics of a pathologically verified group of cavernous angiomas and to compare the merits of computerized tomography (CT) with those of MRI in delineating this brain abnormality.

Clinical Material and Methods

The neuroradiological findings of 10 patients who underwent surgical removal of a histologically verified cerebral cavernous angioma were reviewed retrospectively. All patients underwent cerebral angiography, CT, and MRI. Selective carotid angiography was performed via the femoral route. The CT scanning was performed with a GE 9800 scanner (with and without the intravenous infusion of iodinated contrast medium), and MRI was performed with a 1.5-Tesla GE Signa system.*

Results

The clinical presentation and neuroradiological findings of the 10 patients in this series are summarized in Table 1. The most common presenting symptoms were seizures (in six patients) and progressive neurological deficits (in five patients). An acute neurological deficit secondary to hemorrhage was present in two cases.

Angiography

Angiography, including delayed imaging during the venous phase and careful subtraction, was negative in four instances. Two studies showed an avascular area.

Three spin-echo pulse sequences in the axial plane were routinely used to achieve T1-weighted images (repetition time (TR) 500, echo delay time (TE) 20 msec), intermediate images (TR 2500 msec, TE 40 msec), and T2-weighted images (TR 2500 msec, TE 80 msec). Routine imaging parameters included a 20- or 24-cm field of view, 128 × 256-pixel acquisition matrix, and 2 excitations (1 average). In each case the diagnosis of a cerebral cavernous malformation was verified by gross microscopic pathological analysis. Perl's staining for ferric iron was performed on one surgical specimen and on one autopsy specimen.

* CT scanner, Model 9800, and Signa MRI system manufactured by General Electric Medical Systems, Milwaukee, Wisconsin.
### Magnetic resonance imaging of cavernous angiomas

**TABLE 1**

Clinical presentation and radiological findings in 10 cases of pathologically verified cerebral cavernous angiomas

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex, Age (yrs)</th>
<th>Presenting Symptoms</th>
<th>Angiography</th>
<th>Contrast-Enhanced CT</th>
<th>MRI (TR 2500 msec/TE 80 msec)</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M, 10</td>
<td>It hemiparesis, 3 yrs</td>
<td>avascular mass, venous pooling</td>
<td>hyperdense enhancing lesion, mass effect</td>
<td>mixed SI core, decreased SI rim, mass effect</td>
<td>verified</td>
</tr>
<tr>
<td>2</td>
<td>M, 17</td>
<td>motor seizures, 8 yrs</td>
<td>negative</td>
<td>calcified lesion, not enhancing</td>
<td>mixed SI core, decreased SI rim</td>
<td>verified</td>
</tr>
<tr>
<td>3</td>
<td>M, 15</td>
<td>complex/partial seizures, 4 yrs; severe headache, 3 wks</td>
<td>avascular mass, capillary blush</td>
<td>hyperdense enhancing lesion with mass effect</td>
<td>mixed SI core, decreased SI rim, mass effect</td>
<td>verified</td>
</tr>
<tr>
<td>4</td>
<td>F, 33</td>
<td>complex/partial seizures, 15 yrs; “rage” attacks, 2 yrs</td>
<td>negative</td>
<td>negative</td>
<td>multiple lesions: mixed SI core, decreased SI rim (1) decreased SI core (2)</td>
<td>verified</td>
</tr>
<tr>
<td>5</td>
<td>F, 54</td>
<td>generalized seizures, 12 yrs; lt-sided numbness, 1 mo</td>
<td>avascular area</td>
<td>calcified enhancing lesions (3)</td>
<td>multiple lesions: mixed SI core, decreased SI rim (4) decreased SI core (2)</td>
<td>verified (2)</td>
</tr>
<tr>
<td>6</td>
<td>F, 23</td>
<td>complex partial seizures, 8 yrs; severe headache, 3 wks</td>
<td>negative</td>
<td>hyperdense enhancing lesion (1)</td>
<td>multiple lesions: mixed SI core, decreased SI rim (2) decreased SI core (1)</td>
<td>verified</td>
</tr>
<tr>
<td>7</td>
<td>F, 14</td>
<td>progressive lt hemiparesis &amp; hemiatrophy, 1 yr</td>
<td>avascular area</td>
<td>negative</td>
<td>mixed SI core, decreased SI rim</td>
<td>verified</td>
</tr>
<tr>
<td>8</td>
<td>M, 45</td>
<td>headache, diplopia, rt hemiparesis, 5 days</td>
<td>pontine avascular mass, frontal capillary blush</td>
<td>hyperdense lesions (5), enhancement (1), mass effect</td>
<td>multiple lesions: mixed SI core, decreased SI rim (5) decreased SI core, mass effect (1)</td>
<td>verified (2)</td>
</tr>
<tr>
<td>9</td>
<td>M, 24</td>
<td>complex partial seizures, 15 yrs</td>
<td>negative</td>
<td>negative</td>
<td>mixed SI core, decreased SI rim</td>
<td>verified</td>
</tr>
<tr>
<td>10</td>
<td>M, 9</td>
<td>nausea, vomiting, lethargy, &amp; gait ataxia, few weeks</td>
<td>avascular mass</td>
<td>hyperdense enhancing lesions (2), mass effect</td>
<td>multiple lesions: mixed SI core, decreased SI rim (2) decreased SI core, mass effect (2)</td>
<td>verified (2)</td>
</tr>
</tbody>
</table>

* Cases 1, 2, 4, 5, and 6 had a positive family history of histologically verified cavernous angioma. CT = computerized tomography; MRI = magnetic resonance imaging; TR = repetition time; TE = echo delay time; SI = signal intensity.

† Data derived from a postmortem magnetic resonance image. The patient died of generalized varicella-zoster virus infection.

The remaining four angiograms depicted a mass lesion with displacement of adjacent vessels; a subtle vascular abnormality was observed in three patients in the form of focal capillary blush (two cases) and venous pooling (one case). Angiography revealed multiple lesions in only one instance (Case 7). Dilated arteries, rapid arteriovenous shunting with enlarged draining veins, or abnormal draining veins suggestive of arteriovenous or venous malformations were not visualized in any case.

**Computerized Tomography**

Computerized tomography was negative both before and after administration of contrast medium in three of the 10 cases (Fig. 1 left). In the remaining seven patients, the CT scan depicted a hyperdense lesion in the precontrast study (Fig. 2 left); faint contrast enhancement was observed in five of these seven patients. In four patients, the CT scan confirmed a mass lesion that had been suggested by vessel displacement on angiography. Multiple lesions were visualized in only three patients. A total of 14 lesions were visualized by CT.

**Magnetic Resonance Imaging**

In every case MRI demonstrated the lesion(s), with a total of 27 separate lesions seen on the T₂-weighted...
D. Rigamonti, et al.

**FIG. 1.** Case 7. *Left:* Computerized tomography scan with contrast enhancement. The medulla is obscured by a transverse artifact. *Center:* Axial magnetic resonance image (TR 600 msec, TE 20 msec) showing a prominent core of increased signal intensity (methemoglobin) surrounded by a rim of decreased signal (hemosiderin). The rim was better seen on the spin-echo sequence (TR 2500 msec, TE 80 msec) T2-weighted images. *Right:* Sagittal magnetic resonance image (TR 600 msec, TE 20 msec) showing the cavernous angioma more clearly localized in the posterior medulla in the sagittal plane.

**FIG. 2.** Case 2. *Left:* Computerized tomography scan with contrast enhancement showing a calcified, minimally enhancing lesion. *Right:* Magnetic resonance image (TR 2500 msec, TE 80 msec) showing the same lesion as a central core of mixed increased and decreased signal intensity (SI) surrounded by a dense black rim of decreased SI due to hemosiderin-laden macrophages. The arrows point to a smaller lesion characterized by a core of predominantly decreased SI (“black dots”).

Images. Eighteen larger lesions appeared on T2-weighted images as areas of mixed signal intensity (SI) with a “reticulated” appearance and a prominent surrounding rim of decreased SI (Figs. 1 center, 2 right, and 5). Eight smaller lesions were seen as punctate areas of decreased SI (“black dots,” Fig. 2 right). Multiple lesions were detected in five patients (Figs. 2 right and 3) and mass effect in four individuals, even without evidence of acute hemorrhage.

The T1-weighted MRI studies were less sensitive than the T2-weighted images and detected only 23 of the 27 lesions. On T1-weighted images, the larger lesions appeared as mixed SI areas and the smaller ones as areas of signal hypointensity. In a patient who underwent both low-field (0.35 Tesla) and high-field (1.5 Tesla) imaging, two lesions were not visualized at the lower field. Intermediate and T2-weighted imaging were most efficient in visualizing lesions with low SI. This is a result of the T2 and magnetic susceptibility effect of iron.

**FIG. 3.** Case 6. Axial magnetic resonance images (TR 2500 msec, TE 40 msec) showing discrete well-circumscribed lesions consisting of a reticulated core of mixed increased and decreased signal intensity surrounded by a black hemosiderin rim.

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Magnetic resonance imaging of cavernous angiomas

Pathological Examination

Sixteen lesions were verified pathologically: 14 were large and on MRI had shown a mixed SI with a surrounding rim of decreased SI; two were small and appeared on MRI as a decreased SI core. All lesions were sharply circumscribed and composed of large thin-walled vascular spaces; generally, no brain tissue intervened. There were no arterialized veins, and a vessel with an elastic membrane or mural smooth muscle was rarely noted. Variable features included the amount and age of thromboses, fibrosis, calcification, ossification, and surrounding gliosis. In all cases, microscopy demonstrated various numbers of hemosiderin-laden macrophages immediately surrounding the angioma (Fig. 4) and iron deposition apparently within glial cells in the adjacent white matter. The Perls stain for ferric iron (Cases 4 and 10) highlighted iron deposition in and around the angioma (Fig. 6).

Discussion

Vascular malformations are commonly divided into four categories: arteriovenous, venous, cavernous mal-

Fig. 4. Photomicrographic appearance of a cavernous angioma showing thin-walled vascular channels with little intervening brain. Several channels have old hyalinized thrombi (asterisks). Hemosiderin-laden macrophages can easily be seen (arrows) in the adjacent gliotic brain. H & E, x 64.

Fig. 5. Case 9. Axial magnetic resonance image (TR 2500 msec, TE 80 msec) showing a reticulated mixture of increased and decreased signal intensity in the right medial temporal lobe with a prominent border of markedly decreased signal (hemosiderin) typical of cavernous angioma.
formations, and capillary telangiectasias. 

The cavernous malformation, or angioma, is characteristic because it contains almost no intervening brain parenchyma among the abnormally enlarged, thin-walled vascular channels. It can vary from a small petechial lesion of a few millimeters to a larger, well-circumscribed, "mulberry-like" hemorrhagic mass many centimeters in size. Previous clinical reports have indicated that the majority of angiomas are single lesions. Pathological studies have demonstrated that multiple lesions may represent more than 25% of the cases. In our series, 50% of patients harbored multiple lesions. This finding may relate either to a special patient population or, more likely, to the enhanced sensitivity of high-field MRI compared to CT scanning and low-field MRI.

A familial incidence, thought to be exceptional, has been documented in only seven previous reports. Surprisingly, a familial incidence occurred in more than 50% of the patients in our series. Whether this represents a peculiar patient population or the increased sensitivity of our diagnostic tools is difficult to determine. Patients with cavernous angioma most commonly present with seizures, progressive neurological deficits, and hemorrhage. Our series corroborated these clinical manifestations: 60% of patients presented with seizures, 50% with progressive neurological deficits, and 20% with intracerebral hemorrhage.

Conventional skull radiographs rarely reveal calcifications, even though microscopic calcifications are common features of this lesion. Only one of our patients (10%) had calcifications on skull film examination. Angiography was normal in about one-third of the reported cases with cavernous malformations. For this reason, cavernous angiomas represent a large proportion of histologically verified, angiographically occult cerebrovascular malformations. At angiography, cavernous angiomas may present as an avascular region in the capillary phase or as an avascular mass with displacement of adjacent vessels. A dense venous pooling pattern and a localized area of capillary staining that persists into the late venous phase have both been described as diagnostic features of cavernous malformations. These features were identified in only three patients in this series (Cases 1, 3, and 8). These findings are too infrequent and nonspecific to be characteristic of this entity.

The ability of CT to detect cavernous malformations has been described as excellent, approximating 100%. In scans obtained before administration of contrast medium, the lesion commonly appears hypodense, but mixed hyperdense and isodense lesions have been described. Contrast administration may improve the delineation of the lesion with faint enhancement. While CT studies may
Magnetic resonance imaging of cavernous angiomas

detect a lesion consistent with a cavernous malformation, the CT findings are not specific for this entity. In a recent CT series, the presumptive diagnosis of cavernous angioma was established preoperatively in only seven (44%) of 16 patients. Chronic hemorrhage does not remain hyperdense on CT; therefore, it is often difficult to differentiate glioma or infarction from angioma by CT criteria alone. In our series, CT studies were negative in three instances and correctly identified only 14 of 27 lesions that were detected by MRI.

The sensitivity of MRI increases the probability of detecting a cavernous malformation. Computerized tomography may occasionally miss even relatively large lesions (Fig. 1) and is not sensitive enough to detect the small lesions that appear as cores of decreased SI on T2-weighted MRI studies. Two lesions characterized by decreased SI were verified pathologically and showed the typically dilated vascular channels. Magnetic resonance imaging is also particularly valuable in terms of specificity because residual macrophages laden with hemosiderin provide an indelible tissue signature (decreased SI on T2-weighted images). In the periphery of an area of mixed SI with a reticulated appearance, this finding characterizes a cavernous angioma.

The detection of hemosiderin (ferric iron) by MRI is related to field heterogeneity. The detection of magnetic susceptibility and diffusion effects in the local environment of heme or nonheme iron is proportional to the square of the magnetic field strength. The magnetic susceptibility effect is further highlighted by employing gradient reversal acquisition techniques in cases of multiple cavernous angiomas. These techniques also distinguish flowing blood in an arteriovenous malformation (increased SI) from the hemosiderin effect (decreased SI) in the cavernous malformation (Fig. 7). Hemosiderin deposition in and around a cavernous malformation is most likely related to repeated subclinical hemorrhages or to slow lysis of red blood cells.

Although residual hemosiderin-laden macrophages are clearly not unique to cavernous malformations, the presence of multiple lesions, a reticulated core of increased and decreased SI, a prominent surrounding rim of decreased SI, and a pertinent family history strongly support the diagnosis of cavernous malformation. This combination of features should improve the diagnostician’s ability to identify the disease entity and will improve the management of patients with these lesions.

References


Fig. 7. Gradient reversal acquisition technique images obtained with TR 300 msec, TE 12 msec, and a 60° flip angle showing some large and many small areas of decreased signal intensity (SI) due to hemosiderin deposition. These images are extremely sensitive to the magnetic susceptibility effects produced by hemosiderin (decreased SI) while blood vessels are seen as linear increased SI’s.

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