Clinical implications of associated venous drainage in patients with cavernous malformation

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Object. The authors reviewed angiograms obtained in patients with cavernous malformations to identify and characterize coexisting venous drainage.

Methods. Fifty-seven patients with cavernous malformations treated at the authors’ institutions between 1994 and 2002 were classified into three groups according to the venous system adjacent to the malformation on angiography studies. In Group A patients (23 patients) the malformations had no venous drainage; in Group B patients (14 patients) the lesions were associated with typical venous malformations; and in Group C patients (20 patients) the lesions had atypical venous drainage (AVD). The risk of hemorrhage based on the type of associated venous drainage was analyzed, and the usefulness of magnetic resonance (MR) imaging compared with digital subtraction (DS) angiography in demonstrating associated AVD was determined.

Fifty-seven patients harbored 67 cavernous malformations: Group A patients had 29 cavernous malformations with no associated venous drainage; Group B patients had 17 lesions associated with venous malformations; and Group C patients harbored 21 lesions, 20 of which manifested AVD. Symptomatic hemorrhage was present in 10 (43.5%) of 23 Group A patients and in 28 (82.4%) of 34 Groups B and C patients. Although high-resolution MR imaging revealed the presence of associated venous malformations in 11 (78.6%) of 14 Group B patients, such studies demonstrated AVD in only two (10%) of 20 Group C patients.

Conclusions. Patients harboring cavernous malformations plus venous malformations or AVD are more likely to present with symptomatic hemorrhage than are patients with cavernous malformation alone. The actual incidence of associated venous drainage may be underestimated when MR imaging alone is used rather than combined with DS angiography.

KEY WORDS • cavernous malformation • venous drainage • venous malformation • magnetic resonance imaging • digital subtraction angiography

O bservations that cavernous and venous malformations occasionally coexist proximally were initially accepted as interesting, unusual coincidences. Over time, however, the phenomenon acquired clinical importance because it was recognized that in symptomatic patients with this combination of vascular anomalies, particularly those who presented with hemorrhage, the cavernous malformation was the culprit. Abdulrauf, et al., clearly demonstrated remarkable, important differences in the clinical profiles of patients harboring cavernous malformations either with or without associated venous malformations. Note that these authors based their definition of venous malformations on MR imaging studies and published criteria. Porter, et al., reported that among the patients in whom they had performed surgery, all 86 had venous anomalies intimately associated with a cavernous malformation of the brainstem, although preoperative MR imaging studies had revealed classic venous malformations in only 23 (31.5%) of 73 patients. This outcome led us to suspect that the association between cavernous malformations and venous malformations may be more common than previously thought.

To elucidate the clinical implications of associated venous drainage in patients with cavernous malformations, we performed a detailed retrospective analysis in 57 patients harboring cavernous malformations who had undergone high-resolution MR imaging and DS angiography studies. Furthermore, we characterized venous drainage as classic venous malformations and AVD based on the results of DS angiography studies. As defined here, AVD consists of small venous structures with no connection to the transcortical venous system.

Clinical Material and Methods

Thirty male and 27 female patients made up the group of 57 harboring 67 cavernous malformations treated between 1994 and 2002 at our institutions. The mean age among this group was 29.6 years. All patients had undergone both high-resolution MR imaging and DS angiography studies at approximately the same time. The DS angiography study had been performed in the usual manner. The catheter tip was
advanced into the internal carotid or vertebral artery, 4 to 6 ml contrast medium was delivered at 1.2 to 2 ml/second via an automatic pressure injector, and 30 frames/second were acquired for 10 seconds. The cavernous malformations were defined based on their appearance on T2-weighted MR images as a central core of reticulated mixed signals surrounded by a low signal intensity rim. The DS angiograms were carefully inspected for the presence of associated venous anomalies adjacent to the cavernous malformations. The lesions were categorized as follows: Group A (23 patients), no venous drainage associated with the lesion (Fig. 1); and Group B (14 patients), lesion associated with a typical venous malformation. A collection of dilated medullary veins, the so-called caput medusae, converged in an enlarged transcortical collector draining vein with subependymal drainage and/or drainage into the superficial venous system (Fig. 2). Group C consisted of 20 patients with cavernous malformations manifesting AVD different from typical venous malformations. Several tiny vessels drained into a slightly dilated vein without a connection to the transcortical venous system. These venous structures appeared primarily during the late venous phase. There was no associated arteriovenous malformation or arteriovenous fistula. (Fig. 3).

Each patient’s clinical data, including age at initial presentation, sex, personal and family medical histories, condition at clinical presentation, and neuroimaging studies, were reviewed and characterized. Initial clinical presentation was classified as incidental, symptomatic hemorrhage, seizure, or focal neurological deficits. Symptomatic hemorrhage was defined as a clinical history of acute neurological deterioration and MR imaging evidence of associated acute bleeding. The MR imaging studies were used to determine the location, size, and multiplicity of the cavernous malformations. In Group C patients, these studies were also reviewed to determine whether the images displayed AVD. The location of each lesion was categorized as supratentorial and as deep or superficial. Deep locations included the thalamus, basal ganglia, brainstem, or cerebellar nuclei. The size of each lesion was measured on serial MR

Cavernous malformation with venous drainage

Fig. 1. Images obtained in a patient in Group A; that is, one harboring a cavernous malformation with no coexisting venous drainage. Left: Axial T2-weighted MR image demonstrating a cavernous malformation without associated venous drainage. Right: A DS angiogram revealing no coexisting venous drainage.

Fig. 2. Images obtained in a patient in Group B; that is, one harboring a cavernous malformation together with a venous malformation. Left: A Gd-enhanced T1-weighted MR image displaying a cavernous malformation with an associated typical venous malformation. Right: A DS angiogram demonstrating a collection of dilated medullary veins, the so-called caput medusae, converging in an enlarged transcortical collector draining vein.

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images, and the maximal lesion diameter was used for size calculations.

Statistical comparisons were made using the Fisher exact test, chi-square test, or Kruskal–Wallis test. A probability value less than 0.05 was considered statistically significant.

Results

Patient Demographics

The 57 patients harbored 67 cavernous malformations: Group A (23 patients) had 29 lesions with no associated venous drainage; Group B (14 patients) had 17 lesions that were associated with typical venous malformations; and Group C (20 patients) had 21 lesions, 20 of which manifested AVD. No patient with multiple cavernous malformations had a drainage pattern other than venous malformation or AVD.

The mean age at initial clinical presentation for patients in Group A (11 male and 12 female patients) was 31.2 years (range 7–54 years), and for those in Groups B (eight male and six female patients) and C (11 male and nine female patients) 32 years (range 6–52 years) and 26.4 years (range 10–49 years), respectively. There was no significant difference regarding the mean patient age on initial presentation and the sex ratio among the three groups. Of the 23 Group A patients, three (13%) had a family history of cavernous malformations; this was not the case in any Group B or C patients. Regarding a family history of cavernous malformations, note that the difference between Group A patients and those in the other two groups was not statistically significant.

Comparison of Group A With Groups B and C

Of the 29 cavernous malformations in Group A, 18 (62.1%) were supratentorial and 11 (37.9%) were infratentorial (Table 1). Of the 38 lesions associated with venous drainage (Groups B and C), 15 (39.5%) were supratentorial and 23 (60.5%) were infratentorial. Although Group A patients tended to harbor supratentorial lesions and those in Groups B and C tended to have infratentorial lesions, this difference was not significant. Of the 29 cavernous malformations in Group A, 17 (58.6%) were superficial and 12 (41.4%) were in a deep location. Of the 38 lesions in Groups B and C, 18 (47.4%) were superficial and 20 (52.6%) were in a deep location. Again, the difference in lesion location in Group A compared with that in the other two groups was not significant. There was also no apparent difference in the mean maximal lesion size between Group A (2.32 ± 0.43 cm³) and Groups B and C (2.64 ± 0.26 cm³).

None of the 67 lesions were diagnosed incidentally. Symptomatic hemorrhage was present in 10 (43.5%) of 23 patients without associated venous drainage (Group A) and in 28 (82.4%) of 34 patients with associated venous drainage (Groups B and C; Fisher exact test, p = 0.0028). Seizure was the initial clinical presentation in six (26.1%) Group A and three (8.8%) Group B and C patients. Seven (30.4%) of 23 Group A and three (8.8%) of 34 Groups B and C patients manifested a focal neurological deficit on initial presentation. There was no significant difference in the incidence of seizures and focal neurological deficits as the initial presenting symptom in a comparison between Group A and Groups B and C.

Comparison of Group B With Group C

Of the 17 cavernous malformations in Group B, seven (41.2%) were supratentorial and 10 (58.8%) were infratentorial (Table 2). Of the 21 lesions in Group C, eight (38.1%) were supratentorial and 13 (61.9%) were infratentorial. Nine (52.9%) of 17 lesions in Group B were superficial and eight (47.1%) were in a deep location. Nine (42.9%) of 21 lesions in Group C were superficial and 12 (57.1%) were in a deep location. There was no significant difference between the two groups regarding the lesion location. Among 14 Group B patients, 10 (71.4%) had venous malformations located in the infratentorial compartment. In 13 (65%) of 20 Group C patients, the AVD was also located in the infratentorial compartment. The deep compartment was the location of venous malformations in eight (57.1%) of 14 Group B patients. Twelve (60%) of 20 Group C patients had AVD located in the deep compartment. The difference regarding the lesion depth was not significant. There was also no apparent difference in the mean maximal lesion size between Group B (2.26 ± 0.23 cm³) and Group C (2.91 ± 0.40 cm³).
Cavernous malformation with venous drainage

TABLE 1
Clinical features of patients harboring cavernous malformations with (Groups B and C) and without (Group A) AVD*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A</th>
<th>Groups B &amp; C</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>23</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>sex (M/F)</td>
<td>11/12</td>
<td>19/15</td>
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<tr>
<td>age in yrs (mean ± SEM)</td>
<td>31.2 ± 5.0</td>
<td>28.7 ± 4.1</td>
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<tr>
<td>no. of CMs</td>
<td>29</td>
<td>38</td>
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<td>family history of CM</td>
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<td>0 (0.0)</td>
<td>0.0605</td>
</tr>
<tr>
<td>CM location</td>
<td>18/11</td>
<td>15/23</td>
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<td>VM or AVD location</td>
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<tr>
<td>supra-/infratentorial</td>
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<td>NA</td>
<td></td>
</tr>
<tr>
<td>superficial/deep</td>
<td>17/12</td>
<td>18/20</td>
<td>0.2527</td>
</tr>
<tr>
<td>CM size in cm³ (mean ± SEM)</td>
<td>2.32 ± 0.43</td>
<td>2.64 ± 0.26</td>
<td>0.2101</td>
</tr>
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<td>initial presentation of patients</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>symptomatic hemorrhage</td>
<td>10 (43.5)</td>
<td>28 (82.4)</td>
<td>0.0028</td>
</tr>
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<td>seizure</td>
<td>6 (26.1)</td>
<td>3 (8.8)</td>
<td>0.0843</td>
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<tr>
<td>focal neurological deficits</td>
<td>7 (30.4)</td>
<td>3 (8.8)</td>
<td>0.0801</td>
</tr>
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</table>

* Values in parentheses are percentages. Abbreviations: CM = cavernous malformation; NA = not applicable; SEM = standard error of the mean; VM = venous malformation.

Symptomatic hemorrhage was present in 11 (78.6%) of 14 Group B and 17 (85%) of 20 Group C patients. Seizure was the initial presenting symptom in two (14.3%) Group B and three (15%) Group C patients. Only one patient (7.1%) in Group B and none in Group C manifested focal neurological deficits on initial presentation. There was no significant difference with respect to the initial clinical presentation between the two groups. Although vascular malformations were detected on high-resolution MR imaging in 11 (78.6%) of 14 Group B patients, this same method revealed AVDs in only two (10%) of 20 Group C patients. There was a statistically significant difference between the two groups regarding the detection rate by MR imaging (Fisher exact test, p = 0.0003).

Discussion

Although there is a well-documented relationship between cavernous malformations and venous malformations, the rate of association has remained unclear. Awad, et al., who reviewed the clinical, radiological, surgical, and pathological records of 280 patients, found that six (2.1%) had associated venous malformations. Based on MR imaging studies, Abdulrauf, et al., reported that 13 (23.6%) of 55 patients with lesions also had associated venous malformations. This same outcome occurred in 22 (23.6%) of 173 patients examined using MR imaging and pathological studies in the report by Porter, et al. In a later account of intraoperative findings, they documented that all 86 patients with cavernous malformations in the brainstem also had intimately associated venous anomalies. These anomalies were classic venous malformations on 23 (31.5%) of 73 preoperative MR images and on seven (14%) of 50 angiographic studies. Porter, et al., posited that the true incidence of associated venous malformations may be underestimated, even when MR images are carefully inspected, because the venous anomalies may be too small to be detected on these images. Therefore, the reported venous anomalies other than the classic ones may be the same as the AVDs in our study or may be lesions occult on imaging, which are discovered only intraoperatively. Their observation that all of the cavernous malformations in the brainstem were associated with venous anomalies represents significant new findings regarding the pathophysiology of these lesions. In our series, analysis of angiographic studies revealed that in 34 (59.6%) of 57 patients with cavernous malformations there was an association between the lesion and typical venous malformations or AVD. Atypical venous drainage in our study may be identical to the small venous anomalies Porter and colleagues encountered at surgery. Thus, the actual incidence of associated venous drainage may be underestimated when MR imaging alone without DS angiography is used on preoperative examination of patients with cavernous malformations.

Others have estimated that 8 to 37% of cavernous malformations occur with overt hemorrhages and that most are intraparenchymal within the area of the lesion. Subarachnoid hemorrhage or intraventricular hemorrhage is rare. Although hemorrhage is caused by the cavernous malformations and the risk of bleeding from lesions occurring with associated venous malformations is unclear. Abdulrauf, et al., reported that 16 (38.1%) of 42 patients harboring lesions without and eight (61.5%) of 13 patients with venous malformations presented with symptomatic hemorrhage and that patients with a lesion plus venous malformation were more likely to present with associated symptomatic hemorrhage. Although our study population is small, 10 (43.5%) of 23 patients harboring lesions without and eight (62.5%) of 34 patients (82.4%) with associated venous drainage also manifested symptomatic hemorrhage on initial presentation. There was no significant difference with respect to the incidence of symptomatic hemorrhage of lesions associated with venous malformation or AVD. Although the findings in our study regarding the risk of hemorrhage in patients harboring lesions with no associated venous drainage coincide with the results of others, the
patients with associated venous drainage in our study manifested a significantly higher incidence of bleeding. This discrepancy regarding the risk of symptomatic hemorrhage may be explained by the fact that we subjected all patients to angiographic studies to discern the presence of coexisting venous drainage, including venous malformations and AVD. Although there may be selection bias in our results—many of our patients were referred to our institutions after the detection of hemorrhage—we propose that patients with lesions plus venous malformations or AVD are more likely to present with symptomatic hemorrhage than are patients with cavernous malformation alone.

Vascular malformations and AVD are considered to represent a variant of normal venous drainage. In patients with cavernous malformations associated with venous drainage, drainage usually occurs via the venous malformations or AVD and there is a paucity of other venous structures. Although the origin(s) of bleeding and the precise mechanism(s) underlying hemorrhage from cavernous malformations with associated drainage are unknown, we posit that latent venous hypertension may induce bleeding from lesions that communicate freely with the venous circulation. Atypical venous drainage may also indicate the presence of regional venous hypertension, which in turn may lead to hemorrhage from the lesion. Surgical or radiosurgical obliteration of venous malformations or AVD results in venous infarction because these means of drainage replace the normal venous drainage for that region.

Associated venous malformations were detected on MR imaging studies in 11 (78.6%) of 14 Group B patients. On the other hand, associated AVD was detected in only two (10%) of 20 Group C patients despite angiographic evidence of its presence. The difference in the detection rate by using MR imaging was statistically significant. Note, however, that although MR imaging was more accurate in the study of venous malformations, it performed poorly in the detection of AVD because these lesions consist of many tiny vessels. In our series, three (21.4%) of 14 venous malformations were missed on MR imaging studies, probably because they were small. On the other hand, DS angiography studies revealed all venous malformations. Although MR imaging is a noninvasive procedure with a lower risk of complications, DS angiography yields superior information regarding venous drainage in patients with cavernous malformations. Magnetic resonance imaging continues to be important in the diagnosis of cavernous malformations; however, this method is suboptimal in the evaluation of AVD in patients with these lesions.

Conclusions

We found that patients with cavernous malformations and associated venous drainage (venous malformation or AVD) were more likely to present with symptomatic hemorrhage than were patients with cavernous malformation alone. Additionally, DS angiography was far superior to MR imaging in the detection of AVD. Studies with larger populations are underway to strengthen our preliminary findings and to provide guidelines for treatment decisions.

References