Early elective surgical exploration of spontaneous intracerebral hematomas of unknown origin

Clinical article

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Object. The management of non–life threatening spontaneous intraparenchymal hemorrhage with no obvious medical etiology in patients and the lack of findings on images has not been clearly defined. In general, the current practice is to treat these patients conservatively and repeat studies to rule out a treatable cause 6 weeks to 3 months later; more often than not these repeated studies fail to reveal any findings, and the patient is treated conservatively. For years, the senior author (R.C.H.) has treated these patients with early surgical exploration. This study was undertaken prospectively to ascertain the frequency of positive findings during surgical exploration.

Methods. Between 2000 and 2007, the authors prospectively collected data from 9 cases (4 cerebellar, 4 lobar, and 1 caudate head) of unexplained intraparenchymal hemorrhages. The patient age ranged from 18 to 45 years (mean 31.2 years). All patients were normotensive, had no underlying medical problems explaining such a hemorrhage, and failed to exhibit findings on cerebral angiograms. Magnetic resonance images with contrast showed no abnormal vasculature or enhancement. Eight patients underwent elective surgical exploration in the subacute stage, and urgent decompression of the clot was necessary in 1.

Results. In 7 (77.8%) of the 9 cases, histopathological examination revealed a cause for the hemorrhage (3 “cryptic” arteriovenous malformations, 3 cavernomas, and 1 neoplasm). A good outcome was achieved in all 8 patients who underwent elective surgery.

Conclusions. The authors recommend elective surgical exploration of intracerebral hematomas of unknown etiology provided that the hematoma is surgically accessible and the patient is relatively young and healthy. Early exploration and resection can provide a cure and eliminate the risk of rebleeding when a vascular lesion is found or guide further treatment in cases of tumor. (DOI: 10.3171/JNS.2008.109.12.1005)

Key Words • angiographically occult malformation • early elective exploration • unexplained intraparenchymal hemorrhage

A treatment protocol has not been clearly defined for patients who do not require hematoma evacuation and are in stable condition with non–life threatening spontaneous intraparenchymal hemorrhage of unknown etiology, and negative findings on MR images and angiography. In general, current practice is to treat these patients conservatively and repeat the studies 6 weeks to 3 months later to rule out a treatable cause; more often than not these repeated studies still fail to reveal any findings, and the patient is treated conservatively. For years, the senior author (R.C.H.) has treated many of these patients with early elective surgical exploration and has been rewarded by finding a pathological process as the cause of the hemorrhage in the majority; however, no careful systematic recording of these cases has been undertaken. This study was undertaken prospectively to ascertain the frequency of positive findings at surgical exploration of such patients.

Methods

Patient Population

We prospectively collected data from 9 patients with unexplained non–life threatening intraparenchymal hemmorhages who were selected between 2000 and 2007 for early elective surgical exploration by the senior author.
Our criteria for early surgical exploration will be discussed later. During this time, the senior author was responsible for the care of ~ 50 patients with spontaneous ICH. All patients in the senior author's service who met these criteria during this time were included in this series. The clinical features are presented in Table 1. There were 5 women and 4 men who ranged in age from 18 to 45 years (mean 31.2 years). The presenting symptom usually included a sudden onset of headache with or without nausea, vomiting, and a focal neurological deficit. The location of the hemorrhages included 4 cerebellar, 4 lobar, and 1 in the head of the caudate nucleus. All patients were normotensive on admission and had no underlying medical problems that could explain such a hemorrhage. Computed tomography and MR imaging with Gd was performed in all patients and showed no abnormal vasculature or enhancement. Diagnostic cerebral angiograms were obtained in all patients and failed to demonstrate any tumor blush or vascular malformations. Eight patients underwent elective surgical exploration in the subacute stage, whereas urgent decompression of the clot was necessary in 1 patient (Case 3) due to neurological deterioration while awaiting elective surgery (Table 2).

**Criteria Used to Recommend Early Elective Surgical Exploration**

Empirically, we have used the following criteria to recommend early elective surgical exploration in patients with spontaneous intracerebral hematomas of unknown origin, even when they are stable neurologically and would normally not require evacuation of the hematoma to relieve mass effect. 1) Patients are relatively young and healthy without serious comorbidities. The oldest patient who underwent surgery in this series was 45 years old, and although this is not necessarily a cutoff age, we are generally more conservative in terms of treatment for older patients. 2) There is no known possible cause for the hemorrhage such as hypertension, bleeding diathesis, trauma, drug abuse, cerebral vasculitis, anticoagulation, known or suspected tumor, and so on. 3) The hematoma is in a location where surgical exploration would be very unlikely to lead to a significant neurological deficit.

**Results**

The hematomas were evacuated using microsurgical techniques and careful inspection of the wall of the cavity for abnormal vasculature or evidence of tumor. Intraoperatively, a cavernous angioma was clearly found in 3 patients, a cluster of abnormal fragile vessels typical of a cryptic AVM was encountered in 3, and a hemorrhagic tumor was found in 1. In 2 patients, we found only blood clot. Histopathological examination revealed a cause for the hemorrhage in 7 (77.8%) of the 9 cases. There were 3 “cryptic” AVMs, 3 cavernous malformations, and 1 neoplasm. A good outcome was achieved in all 8 patients who underwent elective surgery. Table 2 summarizes our results.

**Illustrative Cases**

**Case 7**

This 36-year-old previously healthy man presented with a sudden onset of headache, nausea, and vomiting. On physical examination he was normotensive and had horizontal nystagmus, right-sided dysmetria, and truncal ataxia. A CT scan demonstrated a right cerebellar hematoma. An MR image with and without Gd did not reveal any abnormal vasculature or enhancement within the hematoma. A diagnostic cerebral angiogram did not reveal any tumor blush or vascular malformations. In view of the negative workup and the accessible location, we elected to surgically explore the hematoma. The patient underwent an elective retrosigmoid craniotomy 16 days after presentation. Histopathological examination of the cavity wall revealed a medulloblastoma (Fig. 1).

**Case 1**

This 26-year-old previously healthy woman presented with a sudden onset of retroorbital pain and progressive visual deterioration. On examination she had a right inferior temporal quadrant anopia. A CT scan revealed a left inferior temporal quadrant anopia. A CT scan revealed a left posterior parietal hematoma. An MR image and cerebral angiogram failed to demonstrate any tumor or vascular lesion. The patient underwent elective surgical

**TABLE 1**

*Summary of 9 patients with intracerebral hematomas of unknown origin*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Location</th>
<th>Presentation</th>
<th>Examination Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26, F</td>
<td>lt posterior parietal</td>
<td>sudden-onset retroorbital pain, progressive visual loss</td>
<td>rt inferior temporal quadrant anopia</td>
</tr>
<tr>
<td>2</td>
<td>18, F</td>
<td>lt caudate</td>
<td>HA, N/V</td>
<td>intact</td>
</tr>
<tr>
<td>3</td>
<td>35, M</td>
<td>cerebellar vermis</td>
<td>HA, drowsiness</td>
<td>lt lateral gaze palsy</td>
</tr>
<tr>
<td>4</td>
<td>45, F</td>
<td>rt cerebellar</td>
<td>4-mo history of balance difficulty</td>
<td>diminished finger to nose, positive Romberg, dysarthria</td>
</tr>
<tr>
<td>5</td>
<td>22, F</td>
<td>lt cerebellar</td>
<td>HA</td>
<td>intact</td>
</tr>
<tr>
<td>6</td>
<td>24, F</td>
<td>lt temporal</td>
<td>HA, N/V, blurring of vision, lt-sided weakness</td>
<td>intact</td>
</tr>
<tr>
<td>7</td>
<td>36, M</td>
<td>rt cerebellar</td>
<td>HA, N/V</td>
<td>lt nystagmus, rt dysmetria, truncal ataxia</td>
</tr>
<tr>
<td>8</td>
<td>35, M</td>
<td>lt occipital</td>
<td>HA</td>
<td>intact</td>
</tr>
<tr>
<td>9</td>
<td>40, M</td>
<td>lt frontal</td>
<td>HA</td>
<td>intact</td>
</tr>
</tbody>
</table>

* HA = headache; N/V = nausea/vomiting.
exploration 1 week after presentation. Intraoperatively, small fragile pathologically appearing vasculature was seen; however, histopathological analysis failed to demonstrate a lesion (Fig. 2).

**Case 9**

This 40-year-old man with no significant medical history presented with a sudden onset of headache. He was neurologically intact on examination. Computed tomography revealed a left frontal hematoma. Magnetic resonance imaging and cerebral angiography did not reveal any abnormalities. Elective surgical exploration of the hematoma was performed 5 weeks after presentation. Intraoperatively 2 arterialized cortical veins and an abnormal cluster of subpial vessels were seen. Histopathological analysis confirmed the diagnosis of an AVM (Fig. 3).

**Case 2**

This previously healthy 18-year-old woman presented with a sudden onset of headache, nausea, and vomiting.

**TABLE 2**

*Summary of operative results*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Op Timing After Presentation*</th>
<th>Op Findings</th>
<th>Pathology</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7 days</td>
<td>yellowish cavity, soft tissue, small fragile pathological-looking vasculature</td>
<td>blood clot</td>
<td>good, w/ slight field cut</td>
</tr>
<tr>
<td>2</td>
<td>14 days</td>
<td>cavernous angioma w/ venous angioma</td>
<td>cavernous angioma</td>
<td>good</td>
</tr>
<tr>
<td>3</td>
<td>1 day</td>
<td>abnormal vessels</td>
<td>cavernous angioma</td>
<td>poor</td>
</tr>
<tr>
<td>4</td>
<td>3 days</td>
<td>AVM</td>
<td>vascular malformation w/ evidence of old blood</td>
<td>good</td>
</tr>
<tr>
<td>5</td>
<td>1 day</td>
<td>AVM</td>
<td>AVM</td>
<td>good</td>
</tr>
<tr>
<td>6</td>
<td>3 wks</td>
<td>small abnormal vessels abutting a larger deep vessel</td>
<td>blood clot</td>
<td>good</td>
</tr>
<tr>
<td>7</td>
<td>16 days</td>
<td>hemorrhagic tumor</td>
<td>medulloblastoma</td>
<td>ataxia, dysmetria</td>
</tr>
<tr>
<td>8</td>
<td>4 wks</td>
<td>cavernous angioma</td>
<td>cavernous angioma</td>
<td>good</td>
</tr>
<tr>
<td>9</td>
<td>5 wks</td>
<td>2 arterialized cortical veins &amp; abnormal tangle of subpial vessels</td>
<td>AVM</td>
<td>good</td>
</tr>
</tbody>
</table>

* All operations except that in Case 3 were elective.

**Fig. 1.** Case 7. A: Noncontrast CT scan demonstrating a left cerebellar hematoma. B: An MR image with Gd revealing no abnormal enhancement. C: Left vertebral artery angiogram showing no evidence of vascular blush or early draining veins. D: Photomicrograph revealing a medulloblastoma. H & E, original magnification × 200.
She was neurologically intact. Computed tomography revealed a left caudate hematoma. Magnetic resonance imaging with contrast and a cerebral angiogram revealed inconclusive findings. Elective exploration was undertaken 2 weeks after initial presentation. Intraoperatively a cavernous malformation was found (Fig. 4).

Discussion

Intracerebral hemorrhages are known to have a variety of causes including trauma, hypertension, hemorrhagic infarction, anticoagulant use, drug abuse, amyloid angiopathy, cerebral vasculitis, vascular malformations, and primary or metastatic tumors. Trauma is by far the most common cause of ICH. On the other hand, nontraumatic or spontaneous ICHs are most commonly due to chronic arterial hypertension, which accounts for ~50% of cases.13 When presented with a non–life threatening spontaneous ICH, it is necessary to narrow the differential diagnosis with careful history taking and examination. Further assessments include laboratory investigations (coagulation parameters and platelet count) and imaging. Computed tomography is important in localizing and evaluating the extent of the hematoma. Hypertensive hemorrhages are typically seen in the putamen, thalamus, pons, and cerebellum. If the clinical history and CT findings are highly suggestive of a hypertensive hemorrhage, further imaging is rarely indicated. Hemorrhages, especially lobar ones, in patients who are young, normotensive, and previously healthy warrant further workup. Computed tomography with contrast may suggest an underlying pathological condition especially in cases of subcortical hemorrhages7 or hematomas that are rounded, well defined, or show evidence of nodular enhancement.20 However, more often than not, the CT findings are inconclusive. Magnetic resonance imaging with and without the administration of Gd is helpful in demonstrating abnormal vasculature or contrast enhancement suggesting the presence of an underlying vascular or neoplastic lesion. However, MR imaging in the setting of acute hemorrhage is not always capable of depicting an underlying pathological condition.4,19 Signal intensities vary depending on the age of the hematoma, and thus interpretation may be difficult.19 Further imaging with cerebral angiography is necessary to search for abnormal vessels, early draining veins, or a vascular blush. When all imaging studies fail to demonstrate an abnormality, the hemorrhage in these patients is often classified as being of unknown cause.

The management of non–life threatening unexplained intraparenchymal hemorrhage in patients who are stable neurologically has not been clearly defined. In general, the current practice is to treat these patients conservatively and repeat the studies 6 weeks to 3 months later. These patients, however, may harbor an underlying occult vascular malformation or neoplasm and are at risk of rebleeding or tumor progression secondary to delay in diagnosis and treatment.

The first description of small vascular malformations

Fig. 2. Case 1. Noncontrast CT scan demonstrating a left posterior parietal hematoma (A). An MR image with contrast showing no enhancement (B). Left internal carotid artery (C) and left vertebral artery (D) angiograms showing no evidence of a vascular lesion. Photomicrographs revealing a hematoma (E) and surrounding inflammatory cells (F). H & E, original magnification ×400.
as a cause of idiopathic ICH was made during an autopsy study by Margolis et al. in 1951. In 1956, Crawford and Russell proposed the term “cryptic” to describe these small vascular malformations that caused spontaneous cerebral hemorrhages. Currently, the term “cryptic” or “occult” has been used to describe any vascular lesion that cannot be detected angiographically. Pathologically, these lesions have included capillary telangiectasias, cavernous angiomas, venous angiomas, and AVMs as well as mixed or transitional histological forms. However, similarities in their clinical and radiological characteristics have suggested that such histological classifications provide little practical value. The lack of angiographic visualization has been thought to be due to ≥ 1 of the following: 1) small size, 2) thrombosis, 3) destruction following hemorrhage, 4) compression by a hematoma, 5) posthemorrhagic vasospasm, or 6) slow blood flow through the lesion. The term “angiographically occult vascular malformation” has been suggested to encompass these different types of vascular malformations that cannot be visualized angiographically. Previous studies have estimated that between 27 and 53% of patients with lobar hemorrhage have AOVMS.

In 1985 Wakai et al. reported 17 cases of spontaneous intraparenchymal hemorrhages (15 lobar and 2 cerebellar) with no abnormalities on cerebral angiograms. An AOVMS was found in 9 cases and a hemangioblastoma in 5. Unlike our current series, many of these patients were hypertensive, and no mention of MR imaging findings was made. The authors stressed the importance of careful inspection of the wall of the hematoma cavity. They described their microsurgical technique, which consisted of making a small corticotomy over the thinnest portion of the cortex overlaying the hematoma. The brain was then retracted and the hematoma evacuated gradually in layers to separate the clot from the wall of the cavity, which was then inspected for abnormal vasculature with the aid of the microscope. Later in 1992, the same group reported 29 cases of lobar hemorrhages and no findings on cerebral angiograms. Nine patients were hypertensive and 6 patients had suffered previous bleeding. Most of the patients underwent surgery in the subacute setting (< 2 weeks). Vascular malformations were identified in 9 cases (6 AVMs and 3 cavernous angiomas) and tumors in 2 cases. Computed tomography scanning with contrast was performed in 26 patients and revealed enhancement in 10 cases suggestive of an underlying pathological condition. Magnetic resonance imaging was performed in only 9 cases; however, the details were not mentioned.

The natural history of AOVMs and the actual risk of massive hemorrhage is not well defined. Of the vascular malformations that cause intraparenchymal hemorrhages, AVMs and cavernous angiomas are the most common. In a comparative study of 133 cases of angiographically visible AVMs and 55 cases of AOVMs, Lobato et al. reported similarities in presentation by hemorrhage among both lesions. Although bleeding was more severe in patients with AVMs, AOVMs bled subsequently more
frequently than AVMs before they were diagnosed and treated, resulting in a higher nonoperative morbidity rate. Similarly, Tung et al.\textsuperscript{18} reported 13 cases of AOVMs and found that these patients were prone to recurrent hemorrhages and persistent neurological deficits. However, most of these lesions were deep-seated brainstem cavernous malformations and thus even small hemorrhages may have resulted in severe morbidity. The risk of rebleeding from cavernous angioma has been estimated at between 0.7 and 4.5%.\textsuperscript{5,6,11,15} The risk of rebleeding from AOVMs may be similar to that of high-flow angiographically apparent AVMs, although definitive prospective data on this issue are lacking. The annual hemorrhage rate in a patient with an AVM has been reported at ~ 3–4% per year.\textsuperscript{2,3,14} The rebleeding rate is ~ 6% during the 1st year following hemorrhage, after which the annual risk of hemorrhage is similar to that of an AVM that has not bled.\textsuperscript{3}

The presence of an acute ICH in a young and healthy adult in the absence of an obvious cause is highly suggestive of an underlying pathological condition.\textsuperscript{4} Although the risk of rebleeding is not well known, we would recommend early exploration of accessible hematomas in these patients given the high diagnostic yield and low surgical morbidity rate. From the technical point of view, the optimal time for surgery is 2–4 weeks after presentation at which time the hematoma is semiliquified and can be easily evacuated without inducing further bleeding. This facilitates careful inspection of the wall of the hematoma cavity for abnormal vasculature or evidence of tumor. However, in cases of small superficial hematomas in noneloquent areas of the brain, earlier exploration should be considered. Early exploration and resection can provide a cure and eliminate the risk of rebleeding when a vascular lesion is found or guide further treatment in cases of tumor.

In comparison with other patients cared for by the senior author during the study period who did not undergo elective surgical exploration, the 9 patients included in this report were younger (< 45 years of age), healthier, normotensive, had no other known risk factor for hemorrhage, and their hematoma was in an accessible region of the brain where exploration would be unlikely to result in neurological deficit.

Conclusions

Findings in this study suggest that early elective surgical exploration of spontaneous intracerebral hematomas of unknown cause should be considered even in patients who are stable neurologically, have no obvious cause of bleeding on MR imaging and angiography, and have an intracerebral hematoma in an accessible area of the brain where surgery is very unlikely to lead to a neurological deficit. In our small prospective series where this criterion was used for exploration, 7 of 9 patients were found to have definite pathological entities. However, it must be clearly stated that our small anecdotal series should only suggest an alternative to current common practice as an option and only a prospective controlled study where patients that meet the criteria we outlined are randomized to conservative treatment or to elective surgical explora-

Fig. 4. Case 2. A and B: Magnetic resonance images obtained before (A) and after (B) addition of contrast, demonstrating a left caudate hematoma with no abnormal enhancement. C: Left internal carotid artery angiogram with no evidence of abnormal vasculature. D: Photomicrograph revealing a cavernous angioma. H & E, original magnification × 100.
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tion could provide definitive evidence on which treatment paradigm is preferable.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References


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