Surgical Experience With Cerebral Amyloid Angiopathy

George M. Greene, MD, John C. Godersky, MD, José Biller, MD, Michael N. Hart, MD, and Harold P. Adams Jr., MD

Cerebral amyloid angiopathy can present as lobar intracerebral hemorrhage in an elderly person, presumably due to increased fragility of the vessels affected by amyloid deposition. For this reason, patients presenting with intracerebral hemorrhage and suspected of having cerebral amyloid angiopathy have often been treated nonsurgically. Since 1983 we have evaluated 11 patients with cerebral amyloid angiopathy (nine women and two men, mean age 73 years) who have undergone either intracerebral hematoma evacuation or brain biopsy. Nine of the 11 patients presented with intracerebral hemorrhage, which was unilobar in three patients and multilobar in six and involved the parietal lobes seven times, the frontal lobes four times, the temporal lobes four times, and the occipital lobes twice. These nine patients underwent hematoma removal, with no cases of abnormal intraoperative bleeding or recurrent hemorrhage. Six patients improved neurologically, and two were unchanged after hematoma evacuation; the remaining patient had a fatal cardiopulmonary arrest during the immediate postoperative period. During follow-up in seven patients (median 11 months, range 1 week to 74 months) none experienced a recurrent intracerebral hemorrhage and four continued to improve. Two of the 11 patients had cerebral amyloid angiopathy diagnosed by brain biopsy as part of an evaluation for dementia, also without surgical complications. This series suggests that patients with cerebral amyloid angiopathy may safely undergo operative procedures, and patients presenting with intracerebral hemorrhage may show neurologic improvement following evacuation of the hematoma. (Stroke 1990;21:1545–1549)
cerebrovascular events, anticoagulant or antiplatelet drug use, and dementia. Hypertension was defined as
blood pressure consistently elevated above 140/90
mm Hg, a history of elevated blood pressure treated
with antihypertensive medications at the time of
admission, or left ventricular hypertrophy docu-
mented by electrocardiography or autopsy. Hyper-
cholesterolemia was defined as a serum cholesterol
level of ≥200 mg/dl.

Evidence of coagulation disturbance on hospital
admission, radiographic evaluations, and intraoper-
ative findings were also recorded. The patients’ hos-
pital course, results of neurobehavioral evaluations,
and neurologic status at dismissal were reviewed.
Follow-up evaluations were performed at return
clinic visits and/or by telephone contact.

Results

All 11 patients (mean age 73 [range 62–82] years)
had histologically verified CAA; nine were women
(mean age 73 [range 62–82] years) and the other two
were men (mean age 76 [ages 72 and 80] years).
Presenting symptoms were spontaneous ICH, ICH in
association with trauma, or dementia (Table 1).

Among the nine patients presenting with ICH,
three had a history of arterial hypertension, six had
an elevated serum cholesterol level, and three had
coccurrent coronary artery disease. Three patients
had experienced previous cerebrovascular events
(ischemic stroke in one and spontaneous ICH in
two). One patient was receiving warfarin for recent
depth-vein thrombosis and had an elevated prothrom-
bin time (21 seconds, laboratory normal 10–13 sec-
onds) on admission; no other patient had an abnor-
mal prothrombin time, partial thromboplastin time,
or platelet count. Aspirin was being taken regularly
by one of the patients with a traumatic ICH. Two
patients had a previously diagnosed dementia. Ra-
diographic evaluations included computed tomogra-
phy (CT) in all nine, cerebral angiography in seven,
and magnetic resonance imaging (MRI) in four of
the patients. CT demonstrated ICH in all nine.
Angiography revealed an avascular mass in six (with
associated vasospasm in one) and a sylvian arterio-
venous fistula in one. MRI abnormalities included
white matter changes, consisting of increased signal
intensity on T2-weighted images, in two patients.

Four patients experienced a spontaneous ICH and
the other five had an ICH following a minor fall. Two
of the patients with a spontaneous ICH had suffered
a previous spontaneous ICH (6 weeks and 8 months
earlier, both managed nonsurgically) at a location
separate from the presenting hemorrhage. The ICHs
were unilobar in three patients and multilobar in the
other six and involved the parietal lobe seven times,
the frontal lobe four times, the temporal lobe four
times, and the occipital lobe twice. One of the
patients with a spontaneous ICH presented with
bilateral lobar hematomas and during hospitalization
developed a third spontaneous ICH in a different
location.

No abnormal bleeding was encountered intraop-
eratively, and no patient experienced a recurrent
hemorrhage during the remainder of the hospitaliza-
tion or during follow-up (median 11 months, range 1
week to 74 months, n = 7). Neurobehavioral testing
was performed postoperatively in three patients, all
of whom had deficits attributable to the location of
the ICH, but without evidence of dementia. At
dismissal six of the patients were improved neurolog-
ically and two were unchanged; the remaining patient
had experienced a fatal cardiopulmonary arrest dur-
ing the immediate postoperative period. Following
discharge four of the patients continued to improve
neurologically, two remained unchanged, one died 1
week after dismissal, and the other was lost to follow-
up (Table 2).

In addition to the histologic features of CAA,
seven of the nine patients were found to have neu-
rofibrillary tangles and/or neuritic plaques in the

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Sex</th>
<th>Associated conditions</th>
<th>Previous diagnosis of dementia</th>
<th>Hematoma location (lobe)</th>
<th>Operative procedure</th>
<th>Neurologic outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>62</td>
<td>F</td>
<td>None</td>
<td>No</td>
<td>P</td>
<td>ICH evacuation</td>
<td>Improved*</td>
</tr>
<tr>
<td>77</td>
<td>F</td>
<td>None</td>
<td>Yes</td>
<td>F, P, T</td>
<td>ICH evacuation</td>
<td>Improved</td>
</tr>
<tr>
<td>62</td>
<td>F</td>
<td>Previous ICH</td>
<td>No</td>
<td>T</td>
<td>ICH evacuation</td>
<td>Improved*</td>
</tr>
<tr>
<td>71</td>
<td>F</td>
<td>Previous ICH</td>
<td>No</td>
<td>P, O</td>
<td>ICH evacuation</td>
<td>Unchanged</td>
</tr>
<tr>
<td>80</td>
<td>M</td>
<td>Fall, HTN</td>
<td>No</td>
<td>P, T</td>
<td>ICH evacuation</td>
<td>Died</td>
</tr>
<tr>
<td>82</td>
<td>F</td>
<td>Fall, aspirin</td>
<td>No</td>
<td>F</td>
<td>ICH evacuation</td>
<td>Improved*</td>
</tr>
<tr>
<td>72</td>
<td>F</td>
<td>Fall, HTN</td>
<td>No</td>
<td>F, P</td>
<td>ICH evacuation</td>
<td>Improved*</td>
</tr>
<tr>
<td>78</td>
<td>F</td>
<td>Fall, HTN, warfarin</td>
<td>No</td>
<td>P, T, O (s)</td>
<td>ICH evacuation</td>
<td>Improved</td>
</tr>
<tr>
<td>72</td>
<td>M</td>
<td>Fall</td>
<td>Yes (Alzheimer’s disease)</td>
<td>F, P</td>
<td>ICH evacuation</td>
<td>Unchanged</td>
</tr>
<tr>
<td>80</td>
<td>F</td>
<td>None</td>
<td>Yes (NPH)</td>
<td>None</td>
<td>Brain biopsy, VP shunt</td>
<td>Improved</td>
</tr>
<tr>
<td>72</td>
<td>F</td>
<td>HTN</td>
<td>Yes</td>
<td>None</td>
<td>Brain biopsy</td>
<td>Unchanged</td>
</tr>
</tbody>
</table>

F, female; M, male; ICH, intracerebral hemorrhage; HTN, hypertension; NPH, normal-pressure hydrocephalus; P, parietal; F, frontal; T, temporal; O, occipital; s, separate hematoma; VP, ventriculoperitoneal.

*Continued to improve neurologically after dismissal.
surgical specimens; these tangles and/or plaques were in sufficient numbers to be consistent with Alzheimer’s disease in this age group by suggested criteria.10 In the other two patients there was insufficient viable brain tissue to examine for meaningful numbers of neuritic plaques or tangles. Only two of the nine patients had the premorbid clinical diagnosis of a degenerative dementia.

One patient also had an arteriovenous malformation that was congophilic focally but separate from the other vessels within the brain parenchyma that were amyloid-positive. Two of these nine patients were also used as controls for A4 peptide staining performed in a previously published series of brain vascular malformations.11 In both of these controls congophilic vessels were A4-positive, and in one several vessels negative with Congo red were positive with A4.

Among the two patients presenting with dementia, the diagnosis of CAA without ICH was made in both from brain biopsy specimens obtained during dementia evaluations. One patient presented with a 4-year history of dementia, increasing gait difficulty, and urinary disturbance and was found to have hydrocephalus by CT; MRI also revealed white matter disease. A diagnosis of normal-pressure hydrocephalus was made, and a brain biopsy was performed at the time of ventriculoperitoneal shunt placement. Postoperatively, the patient’s ambulation was improved. The second patient had the recent onset of dementia and evidence of bilateral prefrontal dysfunction on neurobehavioral testing. MRI revealed extensive bilateral abnormalities involving both the gray and the white matter. Brain biopsy specimens from both patients demonstrated CAA with neurofibrillary tangles and neuritic plaques in sufficient numbers to diagnose Alzheimer’s disease. No hemorrhages occurred following these surgical procedures.

**Discussion**

Small and medium-sized leptomeningeal and cortical vessels are predominantly affected by CAA, in which twisted beta-pleated sheet fibrils are deposited in the vessel wall, resulting in the characteristic staining with Congo red and birefringence under polarized light.12 Segmental fibrinoid degeneration in some of the vessels affected by amyloid has also been shown.13 Hemorrhage as the presenting feature of CAA has been attributed to suspected brittleness and fragility of the involved vessels.5,8,14 The widespread nature of these features is also believed to account for the occurrence of both multiple and recurrent hemorrhages, as was seen in one and three of the 11 patients in this series, respectively. Both multiple8,15,16 and recurrent17-21 CAA-related hemorrhages have been reported, and recurrent hemorrhages are now thought to occur in approximately 10% of cases.22 Because of concern regarding difficult-to-control intraoperative bleeding and postoperative hemorrhages, previous authors have recommended nonsurgical therapy for patients with CAA-related hemorrhages.1,8,9,23 Two patients in this series and other patients with recurrent CAA-related hemorrhages18,21 have been managed nonsurgically and showed neurologic improvement. Other authors have recommended biopsy of the adjacent brain if hematoma evacuation is deemed necessary.21

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**TABLE 2. Neurologic Status of Nine Patients Undergoing Evacuation of CAA-Related Hematomas**

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Sex</th>
<th>Preoperative status</th>
<th>Postoperative status</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>62</td>
<td>F</td>
<td>Arousal to noxious stimulation, localization with L arm, R hemiplegia</td>
<td>Speech fluent with few repetition errors, R hemiparesis, ambulates with cane</td>
<td>Lives independently. Last seen in clinic 39 months after surgery</td>
</tr>
<tr>
<td>77</td>
<td>F</td>
<td>R decorticate posturing, L hemiparesis</td>
<td>Alert, mouthing words, purposeful with R arm, L hemiparesis</td>
<td>Died in nursing home 1 week after dismissal</td>
</tr>
<tr>
<td>62</td>
<td>F</td>
<td>Lethargic, L hemiparesis</td>
<td>Normal motor exam</td>
<td>Lives independently. Last seen in clinic 11 months after surgery</td>
</tr>
<tr>
<td>71</td>
<td>F</td>
<td>Mild L hemiparesis</td>
<td>Unchanged</td>
<td>Lives in nursing home, needs assistance with ADLs. Last telephone contact 74 months after surgery</td>
</tr>
<tr>
<td>80</td>
<td>M</td>
<td>L hemiparesis</td>
<td>Unchanged</td>
<td>Fatal cardiopulmonary arrest 4 days after surgery</td>
</tr>
<tr>
<td>82</td>
<td>F</td>
<td>L hemiparesis</td>
<td>Improved L hemiparesis</td>
<td>Lives in nursing home. Last telephone contact 17 months after surgery</td>
</tr>
<tr>
<td>72</td>
<td>F</td>
<td>L hemiparesis</td>
<td>Improved L hemiparesis</td>
<td>Lives independently. Last seen in clinic 5 months after surgery</td>
</tr>
<tr>
<td>78</td>
<td>F</td>
<td>L hemiparesis</td>
<td>Normal motor exam</td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td>72</td>
<td>M</td>
<td>Lethargic, R hemiparesis</td>
<td>Unchanged</td>
<td>Died in nursing home 3 months after dismissal</td>
</tr>
</tbody>
</table>

CAA, cerebral amyloid angiopathy; F, female; M, male; L, left; R, right; ADLs, activities of daily living.
series nine patients underwent surgical evacuation of an ICH and biopsy of the adjacent brain parenchyma, with no instances of abnormal bleeding or recurrent hemorrhage. This finding suggests that patients with ICH in whom CAA is suspected may safely undergo ICH removal.

Two of the nine patients with CAA-related ICH experienced fatal cardiopulmonary arrests postoperatively, one several days after ICH evacuation and the other 1 week following dismissal from the hospital, for a surgical mortality rate of 22%. This mortality rate is lower than that observed by Cosgrove et al., who reported 75% mortality (three of four) in patients undergoing evacuation of CAA-related hematomas. Their overall mortality rate of 94% (15 of 16) is consistent with the 90% mortality rate reported by other authors, whose patients also received either aggressive medical or surgical treatment.17

Patients have also developed ICH following ventriculoperitoneal shunt placement, again attributed to pathologic changes in the vessel wall. One patient in this series underwent brain biopsy and ventriculoperitoneal shunt placement, and another underwent brain biopsy alone, without evidence of abnormal bleeding or postoperative complications.

Six of the nine patients undergoing ICH removal had improved neurologically by the time of dismissal from the hospital, whereas two remained unchanged (Table 2). During follow-up four of the improved patients continued to improve and now live independently or are able to perform their activities of daily living in a care facility. These results indicate that not only may patients safely undergo ICH evacuation, but neurologic improvement may often be seen during both the immediate postoperative period and continued follow-up. The observations of neurologic improvement and lower mortality in this series compared with those reported previously16-17 may reflect the severe neurologic impairment of the other patients at the time of presentation.

Predisposing factors for ICH were reviewed in these patients to identify possible causal relations to CAA. Hypertension was present in three of the nine patients, consistent with the incidence of hypertension in patients of this age25 and in other series of patients with CAA.1,13,14,17,22,26 Other authors have not considered it important in the causation of CAA, although hypertension may contribute to the occurrence, size, or extent of hemorrhages in patients with CAA.8,18 The coagulation status may also have contributed to the ultimate size of the hematoma in the one patient who was treated with warfarin and developed an ICH after a fall. The incidence of hypercholesterolemia (six of nine) and coexistent coronary artery disease (three of nine) appears appropriate for this age group, and autopsy studies have found no correlation between the severity of CAA and that of cerebral or visceral atherosclerosis.3,13 One patient in this series had a history of ischemic stroke, an association that has been reported previously.6,8,13,15,16 Most (seven) of the nine patients with ICH in this series were women, a finding that has been reported by others6,13 but not substantiated from compiled series of patients.7 Also, autopsy studies8,13,26,27 have not shown a sex predilection for CAA. Thus, except for a documented history of head trauma in five of the nine patients, no other factors were clearly identified as causally related to the development of ICH in these patients with CAA. A discrepancy has been noted between the anatomic distribution of the changes of CAA and the sites of hemorrhage. The most severe CAA has been found in the temporal, parietal, and occipital lobes, whereas CAA-related hemorrhages have been reported most often in the frontal and parietal regions.5 In this series most (six) of the nine patients presented with multilobar hemorrhages, which were most commonly (six times) located in the parietal lobe and less frequently in the frontal, temporal, and occipital lobes (three, three, and two times, respectively). The unilobar hemorrhages (three of nine patients) were evenly distributed among the parietal, frontal, and temporal lobes. These findings are consistent with those reported previously, in which ICH infrequently involves the occipital lobe.5

In addition to ICH as a presenting feature of CAA, a history of dementia has also been considered significant. Clinically evident dementia is seen in approximately 30-40% of patients with CAA5,22,26 and was found in four (36%) of the 11 patients in this series, although only two (22%) of the nine patients presenting with ICH had a history of dementia. A disparity exists, however, between the relatively low clinical incidence of dementia and the presence of the pathologic features of Alzheimer's disease reported in the tissue specimens from patients with CAA. Neurofibrillary tangles and/or neuritic plaques were identified in nine of the 11 patients in this series, although only four of the 11 were clinically demented. The high incidence of neurofibrillary tangles and neuritic plaques with CAA has been reported previously,1,7,13,22,26 but no obvious relation has been established between the severity and extent of CAA and that of neurofibrillary tangles and plaques, nor between the presence and severity of these histopathologic changes and dementia.27

References


**KEY WORDS** • amyloid • cerebral hemorrhage • surgery
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