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)

Cerebral amyloid angiopathy (CAA) is a well-recognized cause of spontaneous lobar intracerebral hemorrhage (ICH) in the elderly. Current estimates attribute 2–10% of all nontraumatic ICHs to CAA. Because the incidence of CAA-related changes within the brain increases with age, CAA may be responsible for a greater proportion of spontaneous ICHs among older patients. While understanding of the pathogenesis and associations of CAA have broadened, the treatment of patients with CAA-related ICH has remained controversial. Many authors recommend nonsurgical management of these patients because of concern regarding fragility of the vessel walls involved with CAA, difficulty in controlling intraoperative hemorrhage, and the possibility of recurrent postoperative hemorrhages. We report 11 patients with histologically confirmed CAA who underwent surgical procedures. No instances of abnormal intraoperative bleeding or recurrent hemorrhage were observed.

Subjects and Methods
We reviewed 11 patients with CAA who were evaluated and treated between May 1983 and January 1989. Nine patients presented with lobar ICH (four spontaneous and five traumatic) and the other two were diagnosed by brain biopsy during evaluations for dementia. Tissue specimens were obtained at the time of hematoma evacuation or brain biopsy. In the nine patients with ICH, biopsy specimens of the adjacent brain parenchyma were taken following hematoma removal. CAA was confirmed by vessel staining with Congo red and birefringence under polarized light. In addition, specimens were examined for the presence of neurofibrillary tangles and neuritic plaques.

Patient records were reviewed for pertinent medical history, including arterial hypertension, hypercholesterolemia, coronary artery disease, previous
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 documented by electrocardiography or autopsy. Hypercholesterolemia was defined as a serum cholesterol level of ≥200 mg/dl.

Evidence of coagulation disturbance on hospital admission, radiographic evaluations, and intraoperative findings were also recorded. The patients' hospital 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).

Table 1. Clinical Features of 11 Patients With Cerebral Amyloid Angiopathy Undergoing Operative Procedures

<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>
</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.

No abnormal bleeding was encountered intraoperatively, and no patient experienced a recurrent hemorrhage during the remainder of the hospitalization 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 neurologically, two were unchanged; the remaining patient had experienced a fatal cardiopulmonary arrest during 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 neurofibrillary tangles and/or neuritic plaques in the
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.

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. Segmental fibrinoid degeneration in some of the vessels affected by amyloid has also been shown. Hemorrhage as the presenting feature of CAA has been attributed to suspected brittleness and fragility of the involved vessels. 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 multiple and recurrent CAA-related hemorrhages have been reported, and recurrent hemorrhages are now thought to occur in approximately 10% of cases. Because of concern regarding difficult-to-control intraoperative bleeding and postoperative hemorrhages, previous authors have recommended nonsurgical therapy for patients with CAA-related hemorrhages. Two patients in this series and other patients with recurrent CAA-related hemorrhages have been managed nonsurgically and showed neurologic improvement. Other authors have recommended biopsy of the adjacent brain if hematoma evacuation is deemed necessary.
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.

Patients have also developed ICH following ventricular 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 previously 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 age and in other series of patients with CAA. 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. The coagulation status may not be considered it important in the causation of CAA, although hypertension may contribute to the occurrence, size, or extent of hemorrhages in patients with CAA. The coagulation status may not be considered it important in the causation of CAA, although hypertension may contribute to the occurrence, size, or extent of hemorrhages in patients with CAA.

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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. In this series most (six) of the nine patients presented with multilobar hemorrhages, which were most commonly located in the parietal lobe and less frequently in the frontal, temporal, and occipital lobes. 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.

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 CAA 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 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 age and in other series of patients with CAA. 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.

References

KEY WORDS • amyloid • cerebral hemorrhage • surgery
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