Histopathological Evaluation of Middle Cerebral Artery After Percutaneous Intracranial Transluminal Angioplasty

H. Christian Schumacher, MD; Kurenai Tanji, MD, PhD; Sundeep Mangla, MD; Philip Meyers, MD; John Pile-Spellman, MD; Arthur P. Hays, MD; J.P. Mohr, MD, MS

Background—Intracranial atherosclerosis accounts for 8% to 10% of all ischemic strokes, and intracranial angioplasty is increasingly performed to treat stenotic lesions. We report an autopsy case and discuss the effects of intracranial angioplasty for atherosclerotic arteries.

Case Description—A 77-year-old patient died 9 days after angioplasty of the left middle cerebral artery as a result of cardiorespiratory failure. The patient was anticoagulated before, during, and after the procedure with heparin, aspirin, and clopidogrel. At the site of angioplasty, the densely fibrotic eccentric plaque was displaced from the adjacent media into the lumen, distorting it and forming elongated projections. No local thrombosis, plaque compression, or inflammation was observed. Additionally, an intramural hemorrhage extended from the site of angioplasty into the stenotic proximal inferior division of the left middle cerebral artery.

Conclusions—Histopathological findings after intracranial angioplasty parallel those in other arterial territories. The implications of these pathological findings on the medical and endovascular treatment of intracranial atherosclerosis are discussed. ([Stroke. 2003;34:e170-e173.])

Key Words: angioplasty ■ atherosclerosis ■ autopsy

Intracranial atherosclerosis accounts for 8% to 10% of all ischemic strokes, and intracranial angioplasty is increasingly performed to treat stenotic lesions. Pathological descriptions after intracranial angioplasty are rare. We present the autopsy results of a patient who died 9 days after angioplasty of the left middle cerebral artery (MCA).

Case Reports

A 77-year-old, right-handed man presented with recurrent left hemispheric transient ischemic attacks. Over the course of 1 year, he developed progressively worsening symptoms of transient sensory disturbance of first the right arm and then the right leg. Despite medical therapy with warfarin (Coumadin) and with warfarin combined with aspirin, the patient progressed to develop an episodic receptive aphasia, with the attacks increasing in severity and frequency over 4 to 6 weeks. By the time of admission he was experiencing daily aphasic attacks. His neurological examination between attacks remained normal. Intracranial MR angiography confirmed widespread intracranial stenoses involving the M1 segments of both MCAs (worse on the left than on the right), the P1 and P2 segments of the right posterior cerebral artery, and the right distal vertebral artery. MRI of the brain revealed only chronic ischemic changes in the border zone region between the left MCA and posterior cerebral artery, suspicious for distal field or watershed hypoperfusion. Transcranial Doppler studies demonstrated elevated velocities and diminished CO2 reactivity compatible with the symptomatic left MCA M1 stenosis and suspected perfusion failure. Because the patient had progressed symptomatically despite aggressive medical therapeutic regimens, endovascular revascularization was offered.

Intervention

The procedure was performed under general anesthesia and with systemic anticoagulation. The angiogram confirmed a 50% to 75% stenosis of the mid M1 segment of the left MCA, traversing the origin of the anterior temporal branch. In addition, high-grade stenosis with prestenotic aneurysmal dilatation was observed within this anterior temporal branch. Delayed antegrade flow and washout of contrast was noted within the distal MCA branches (Figure 1). Through a 6F guiding catheter, a Prowler 14 microcatheter (Cordis Endovascular) and a 0.014 Transend microguidewire (Target Therapeutics) were navigated cautiously across the stenotic M1 segment into the distal M2-M3 segments of the angular branch. A 0.014 exchange length (300 cm) Luge microguide-wire (Luge, Scimed) was positioned within the distal M2-M3
segments, and a 2×9-mm monorail high-pressure angioplasty balloon (Open Sail, Guidant Vascular Intervention) was exchanged and positioned across the left M1 stenosis. Three serial inflations of the microballoon to pressures of 2, 4, and 6 atm for periods of 30 to 60 seconds were required to improve the stenotic waist to <25% (Figure 1D). After angioplasty, the lumen of the stenosed M1 segment was improved in transverse diameter with more rapid antegrade flow and washout of contrast within the distal left MCA branches (Figure 1E and 1F). The patient was maintained on intravenous anticoagulation with unfractionated heparin (activated partial thromboplastin time, 60 to 80 seconds) for 48 hours, which was changed to subcutaneous heparin after day 2. He received antiplatelet therapy with aspirin (325 mg/d) and clopidogrel (75 mg/d) throughout his course.

Postprocedural Course
In the morning after the procedure, the patient demonstrated a mild anomic aphasia but was otherwise intact. A repeated angiogram remained unchanged. At 36 hours after angioplasty he became agitated, uncooperative, and hypertensive (230/155 mm Hg) and developed a more severe anomic aphasia. A new infarct involving the left caudate head, anterior limb of the internal capsule, and lentiform nucleus was confirmed on CT and MRI. Over the next 24 hours the patient developed an acute delirium. Treatment with haloperidol and diazepam was initiated. However, he remained delirious, developed aspiration pneumonia, and experienced a transfusion as a result of a fall in his hematocrit level. Repeated CT performed on day 4 demonstrated a new infarction in the left anterior temporal lobe in the territory supplied by the stenotic inferior division of the left MCA, which had not been able to be treated as part of the angioplasty. On day 6 he experienced cardiorespiratory arrest. Cardiopulmonary function was restored, but the patient remained deeply comatose after cardiopulmonary resuscitation, consistent with widespread ischemic brain damage. On day 9, life support was withheld following the written living will of the patient, and he died. Permission for an autopsy of the brain was given.

Pathological Findings

Brain Parenchyma
The brain was fixed with 10% formalin. The fixed brain weighed 1410 g. On gross examination, cerebral hemispheres were globally and severely edematous. There was a slight shift of the midline from left to right but no uncal herniation. The brain showed multiple infarcts of different age in the territory of the left MCA. The oldest infarct, measuring 4×3×1 cm and thought to have preceded the angioplasty by several weeks, resided in the left inferior parietal lobule. Histologically, it consisted of cystic cavities containing macrophages and reactive gliosis. The second oldest infarction, measuring 2×1×1 cm, was located in the left caudate nucleus extending into the anterior limb of the internal capsule and superior part of the putamen. Microscopically, pallor and rarefaction of the tissue were observed together with many macrophages, occasional axonal spheroids, and microscopic foci of hemorrhage throughout the necrotic tissue. No significant reactive gliosis was associated. These histological alterations were consistent with ischemic damage roughly 1 to 2 weeks antemortem. A third infarct, measuring 4×4×3 cm, was located in the left anterior temporal lobe including the temporal pole and was estimated to be approximately a few days old. The lesion was characterized histologically by marked tissue pallor, prominent neutrophil infiltration with karyorrhexis, scattered macrophages, sparse microscopic hemorrhages, and endothelial swelling of the vessels. Additionally, acute ischemic change evidenced by the presence of many eosinophilic neurons involved extensive areas of the brain superimposed on the aforementioned infarcts. Eosinophilic neurons were observed in the frontal, temporal, parietal, and occipital cortices, basal ganglia, thalamus, hippocampus, cerebellar cortex, midbrain, pons, medulla, and cervical spinal cord.

Cerebral Arteries
After fixation, the circle of Willis and its branches, including the left MCA, were embedded en bloc in paraffin in the coronal plane along with the neighboring frontal and temporal brain parenchyma. Four-micrometer serial sections were cut from the origin of the left MCA through the proximal segment of inferior and superior divisions (sections 1 through 1523). Selected sections were stained by hematoxylin-eosin, elastic van Gieson, and Masson trichrome. The vessels at the base of the brain revealed a normal adult configuration but exhibited severe atherosclerosis. Sections 401 through 1001, corresponding to the site of the angioplasty, revealed an eccentric, densely fibrotic atheroma that reduced the transverse area of the lumen by roughly one third. One edge of the eccentric atheroma and fragmented internal
elastic lamina appeared to be displaced from the rest of the vessel wall and protruded as 2 elongated structures into the lumen (Figure 2A and 2B). In this segment, the atheroma progressed to reduce the lumen up to approximately 50% of the normal caliber. There were no overt emboli or thrombi obstructing the lumen, evident dissection of the media, or inflammatory reaction. The remaining arterial wall (media) was apparently thinner and more fibrotic (Figure 2C) than the similar area of the right MCA (Figure 2D). At section 401 (M1), a small, focal intramural hemorrhage was first identified within the eccentric atheroma and extended distally into the inferior division, appearing to contribute to its stenosis. At the angioplasty site, a lenticulostriate artery passed through the body of the atheroma but had not been occluded by the angioplasty. The MCA bifurcated at section 1060. The proximal inferior division, not amenable to angioplasty, narrowed abruptly to approximately 10% of the transverse area between sections 1201 and 1401 by an eccentric atheroma and a small mural hemorrhage. The intramural hemorrhage, which extended from the M1 segment of the artery into the inferior division, was seen there to be an enlarged mass of blood along one side of the vessel between the internal elastic lamina and the surface of the lumen. It also extended deep into the atheroma separating it from the internal elastic lamina (Figure 3A). The intramural hematoma showed early organization (Figure 3B) and disappeared at section 1500.

**Discussion**

Pathological studies established that lumen enlargement may be achieved after angioplasty in arteries harboring eccentric plaques. In our case, the lumen enlargement was attributable to stretching and/or disruption of the contralateral media, a process that we inferred occurred because the densely fibrous plaque was not distensible, as has been cited in prior reports.

Intimal splitting of the plaque at its weakest point is also a well-characterized phenomenon after angioplasty, and eccentric plaques offer more accessible media for disruption compared with concentric plaques. In our case, the eccentric stenotic plaque at the site of M1 stenosis was disrupted and separated from the underlying media at its thinnest part, and the contralateral media appeared to be thinned. No compression of the plaque was visible in our patient. These findings suggest that morphological changes after intracranial angioplasty for atherosclerosis parallel those in other arterial territories.
The stenotic plaque in the M1 segment was composed of dense fibrotic tissue, resembling the so-called stable white plaques thought to carry a low risk for acute thrombotic events as opposed to the yellow unstable plaques consisting of a thin fibrous cap and a large necrotic core consisting of a mixture of debris, cholesterol, and inflammatory cells, which are associated with acute vascular events. In symptomatic patients with dense fibrotic intracranial atheromas, as seen in our case, treatment strategies seeking to stabilize the plaque or leading to its regression in a reasonable time are not likely to be successful, and immediate invasive revascularization procedures in the patient at high risk for stroke may prove to be the treatment of choice. Furthermore, the benefit of antithrombotic agents for stroke prevention in overt chronic perfusion failure due to this type of atheroma may be limited. For treatment decisions, improved imaging techniques in intracranial atherosclerosis are needed to distinguish between the 2 plaque types.

Pathologically, one end of the disrupted atheroma was protruding into the arterial lumen (Figure 2). Angiographically, this was not appreciated and may have predisposed to further dissection from the vessel wall, possibly leading to a catastrophic complete vessel occlusion. Stenting may prevent this, and intracranial stents are being developed. “Off-label” compassionate use of coronary devices has been reported but remains difficult within the MCA distribution. In the recently completed nonrandomized feasibility study Stenting for Symptomatic Atherosclerotic Lesions in the Vertebral and Intracranial Arteries (SSYLVIA), stent placement in the MCA was difficult, and only 5 of 60 study patients were treated in that study for an MCA stenosis. Additionally, SSYLVIA documented a high restenosis rate at 6 months. Because of the limited experience with high-grade MCA stenoses, symptomatic patients with perfusion failure may need to await further prospective evaluation of available treatments, including conventional or modified extracranial-intracranial bypass surgery and angioplasty with or without stenting on an individual compassionate basis.

We found a fresh-appearing intramural hemorrhage in the already stenotic proximal inferior division of the left MCA. Luminal stenosis due to angioplasty-induced intraplaque hemorrhage is a known complication after angioplasty. It may be that our intensive antithrombotic treatment plan contributed to the hemorrhage, especially in an area where vessel manipulation has taken place. In our patient, the left temporal infarction developing distal to the stenosis of the inferior division was not observed on the MRI performed on postprocedure day 2. The delayed nature of this inferior division occlusion does not favor a procedural etiology; however, progression of an angioplasty-induced dissection remains plausible. Delayed thromboembolism despite antithrombotic therapy remains as an alternative source.

In summary, our case confirms known pathological findings after angioplasty that have been observed after angioplasty of intracranial atherosclerosis and documents the value of combined detailed clinical and pathological studies in evaluating the effects of therapeutic intervention on cerebrovascular disease.

Acknowledgments

This study was supported by the Horace W. Goldsmith Foundation for Cerebrovascular Research (Dr Schumacher). We thank Trevor Winterbottom for editorial assistance in the preparation of the manuscript.

References

Histopathological Evaluation of Middle Cerebral Artery After Percutaneous Intracranial Transluminal Angioplasty


Stroke. 2003;34:e170-e173; originally published online August 7, 2003;
doi: 10.1161/01.STR.0000086764.86787.9C

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/34/9/e170

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/