Fatal Cerebral Reperfusion Hemorrhage
After Carotid Stenting
Dominick J.H. McCabe, MRCPI; Martin M. Brown, FRCP; Andrew Clifton, FRCR

Background—The hyperperfusion syndrome is a recognized complication of carotid endarterectomy. Reports of cerebral hyperperfusion injury following internal carotid artery (ICA) angioplasty are few, and this complication has never been reported following internal carotid stenting.

Case Description—A 68-year-old normotensive man was referred to our hospital for assessment 5 months after experiencing a left hemispheric ischemic stroke. Angiography confirmed 95% stenosis of the left ICA. Left carotid percutaneous transluminal stenting was performed without any initial complications. Color Doppler ultrasound of the ICA immediately after stenting revealed an elevated peak systolic velocity of 2.3 m/s, in the absence of significant vessel stenosis or spasm on angiography. Seven hours after the procedure, the patient suddenly deteriorated. CT of the brain revealed extensive intracerebral hemorrhage (ICH), and he subsequently died 18 days later. There was no history of headache or seizure activity, and his blood pressure was only mildly elevated at the time of the deterioration. This is the first report of ICH after internal carotid stenting.

Conclusions—ICH may occur as a hyperperfusion phenomenon after internal carotid stenting, in the presence of mild to moderate arterial hypertension, without being heralded by any of the typical symptoms of the hyperperfusion syndrome. Patients with increased velocities on color Doppler ultrasound of the ICA after angioplasty should be monitored closely for features of cerebral hyperperfusion injury. Further studies are warranted to determine whether more aggressive treatment of mild to moderate hypertension after carotid stenting would reduce the likelihood of this potentially fatal complication. (Stroke. 1999;30:2483-2486.)

Key Words: hypertension ■ intracerebral hemorrhage ■ stents ■ ultrasonography, Doppler

In 1981, Sundt et al1 used the term “hyperperfusion syndrome” to describe a triad of complications that included atypical migrainous phenomena, transient focal seizure activity, and intracerebral hemorrhage (ICH) after carotid endarterectomy. Symptoms usually developed 5 to 7 days postoperatively and were often preceded by unilateral headaches; the triad was not complete in all patients. The features were attributed to elevated ipsilateral cerebral blood flow without a significant change in systemic blood pressure. Breen et al2 reported that the frequency of the hyperperfusion syndrome was 2.7% in their series, and in a recent review of the literature the frequency of ICH after carotid endarterectomy ranged from 0.3% to 1.2%. However, these authors noted that the blood pressure was elevated in the majority of patients at the time of presentation with the hyperperfusion syndrome. Percutaneous transluminal angioplasty (PTA) and angioplasty with stenting are increasingly being used as an alternative to carotid surgery in patients with carotid stenosis,3–7 but as experience with this novel technique accrues the true complication rate has not yet been established.

Case Report
A 68-year-old right-handed man was referred for treatment of carotid stenosis after an ischemic stroke in which he developed a sudden onset of expressive dysphasia and right-sided facial and limb weakness. In the distant past, he had smoked heavily and had a history of excess alcohol intake, but had stopped both 24 years previously. There was no history of hypertension or other vascular risk factors. He had been initially treated with 75 mg aspirin daily and 20 mg paroxetine daily for depression. When assessed in our hospital 5 months later, his blood pressure was 142/85 mm Hg and he had mild dyscalculia, dysgraphia, and expressive dysphasia. There was a residual right upper motor neuron facial weakness and a mild right hemiparesis. All hematological and biochemical tests were normal, with a normal platelet count and coagulation screen. Brain CT revealed moderate leukoaraisis with no evidence of hemorrhage (Figure 1). The aspirin dose was increased to 300 mg daily, and 200 mg dipyridamole (sustained release) twice daily was commenced. The patient underwent left carotid stenting the next day via a perfemoral approach under local anesthesia. Intra-arterial
Digital subtraction angiography confirmed 95% stenosis of the left internal carotid artery (ICA), 20 to 30 mm distal to its origin (Figure 2), and 50% stenosis of the right ICA. Transcranial Doppler (TCD) monitoring was unsuccessful due to failure to maintain an adequate acoustic window. The patient was given 5000 IU heparin IV, and the stenosis was crossed with a V18 angioplasty wire. Glycopyrrolate and 0.6 mg atropine IV was administered, and the stenosis was predilated with a Savvy 4-mm balloon and stented with a 21-mm-long Jomed stent mounted on a 5 x 40-mm balloon. The blood pressure varied between 160/90 mm Hg and 175/105 mm Hg during the procedure, but there were no residual adverse neurological sequelae, and a postprocedural angiogram showed no significant stenosis or dissection (Figure 3). Color Doppler ultrasound of the ICA immediately after the procedure revealed a visibly patent vessel, but the peak systolic velocity was elevated at 2.3 m/s, with an end diastolic velocity of 1.2 m/s. Over the next 7 hours, the patient was treated with 1000 IU/h unfractionated heparin IV, the blood pressure varied between 140 to 160/95 mm Hg, and the patient was clinically stable.

The patient then suddenly vomited and developed a complete expressive aphasia and increased right-sided weakness. He then became unresponsive, with no witnessed seizure activity or other ictal features, but his blood pressure remained at 150/85 mm Hg. He became more alert after 5 to 10 minutes, and within an hour he opened and closed his eyes to command, nodded appropriately in response to questioning, and did not complain of pain or headache. Examination revealed right-sided neglect, a left Horner’s syndrome, and more pronounced right facial weakness but no papilledema.

He had a dense right hemiplegia with variable movements otherwise. There was generalized hyperreflexia and the plantar responses were extensor bilaterally.

An urgent full blood count was normal, and the activated partial thromboplastin time (APTT) was 29 seconds (normal range 33 to 47 seconds) despite intravenous heparin. Heparin was stopped immediately, but an urgent brain CT revealed extensive hemorrhage with mass effect in the left basal ganglia, extending into the ventricles and posterior frontal and parietal regions (Figure 4). Due to the extent and location of the hemorrhage, surgical evacuation was not performed and the patient was managed conservatively. His conscious level deteriorated over the next 7 days, and he subsequently developed pneumonia and died 18 days after the procedure. The blood pressure varied between 125/70 and 195/95 mm Hg (average 160/90 mm Hg) during this period. An autopsy was not performed.

**Discussion**

Despite the increasing use of PTA and stenting for the treatment of extracranial carotid artery stenosis, there are only 4 reports of “hyperperfusion injury” following PTA/stenting in the literature to date. Two of these patients had ICA PTA, I had common carotid stenting for recurrent stenosis
after carotid endarterectomy, and 1 had PTA of the ICA and both vertebral arteries and stenting of the right subclavian artery. Headache, seizures, ICH, and hypertension were noted in 2 patients (1 developed diffuse basal subarachnoid hemorrhage), headache and ICH (without reference to the blood pressure or seizures) in 1, and the clinical details were not specified in the fourth patient. This is the first report of ICH after carotid stenting that was not heralded by or associated with any of the typical symptoms of the hyperperfusion syndrome. Despite the absence of EEG monitoring, there was no witnessed seizure activity. In addition, although blood pressure was intermittently elevated during the procedure, it did not exceed 160/95 mm Hg for the 7-hour period before the clinical presentation with extensive ICH. Cerebral hyperperfusion injury may occur in the presence of normal or elevated blood pressure after carotid endarterectomy, but it has been associated with severe hypertension (240/100 mm Hg) after carotid angioplasty in the 2 cases in which it has been documented to date.

Color Doppler ultrasound demonstrated increased velocity measurements in the visibly patent stented ICA immediately after the procedure in this case. These findings could be interpreted as indicating residual ICA stenosis of 70% to 79% or perhaps arterial spasm, but both of these possibilities were excluded on the postprocedural angiogram; therefore, the elevated velocities indicated increased flow through the treated ICA. It is reasonable to include patients with isolated ICH and elevated ipsilateral carotid velocities in the definition of cerebral hyperperfusion injury, once significant ipsilateral carotid stenosis and contralateral carotid occlusion are excluded. It is possible that carotid sinus baroreceptors responded to the increased carotid blood flow by appropriately lowering systemic blood pressure but that high cerebral perfusion pressures overwhelmed arteriolar vasoconstriction ability and led to ICH. One cannot completely exclude the possibility of embolism and silent cerebral infarction at the time of stenting, with subsequent hemorrhagic transformation in response to hyperperfusion, but the CT scan appearances do not suggest this mechanism. ICH secondary to anticoagulation is not likely in view of the shortened APTT despite intravenous heparin, although the combination of antiplatelet therapy and heparin could increase the risk of hyperperfusion hemorrhage after carotid stenting. In the original description of the hyperperfusion syndrome after carotid endarterectomy, patients were receiving heparin and 2 were on aspirin at the time of their ICH. Leukoaraiosis, indicative of small-vessel disease, was classified as moderate on brain CT in our patient but may have been more extensive if MRI brain had been performed. It is possible that leukoaraiosis is a risk factor for reperfusion hemorrhage after carotid stenting and further studies should investigate this potential association. TCD was performed in 3 of the cases reported to date, but immediate postangioplasty velocities were reported in only 1 patient, in whom it was elevated. It was suggested that this was secondary to severe vessel spasm, but it may have been indicative of hyperperfusion through the middle cerebral artery.
Because fatal hyperperfusion ICH has now been described after ICA stenting in addition to PTA without primary stenting, one must be aware of this potential complication in both treatment groups.

In conclusion, ICH, with or without associated symptoms, may occur as a hyperperfusion phenomenon after carotid PTA or stenting in the presence of mild to moderate arterial hypertension. Patients with increased velocities on color Doppler ultrasound of the ICA or TCD after angioplasty should be monitored closely for features of cerebral hyperperfusion injury. Further studies are warranted to determine whether more aggressive antihypertensive treatment for mild to moderate hypertension after carotid angioplasty, especially in the presence of leukoaraiosis, would reduce the likelihood of this potentially fatal complication.

Acknowledgment

Dr McCabe is funded by a grant from the NHS Research and Development Programme in the United Kingdom. The ultrasound laboratory was funded by a grant from The Wellcome Trust and the British Heart Foundation. We thank Diana Colquhoun for her assistance with the ultrasound measurements.

References

Fatal Cerebral Reperfusion Hemorrhage After Carotid Stenting
Dominick J. H. McCabe, Martin M. Brown and Andrew Clifton

Stroke. 1999;30:2483-2486
doi: 10.1161/01.STR.30.11.2483

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/30/11/2483

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/