Imaging studies of cerebral hyperperfusion after carotid endarterectomy

Case report

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 \checkmark A case is reported of severe unilateral hemispheric edema and localized hemorrhage associated with seizures following endarterectomy of an ipsilateral high-grade carotid stenosis. Imaging studies including angiography, computerized tomography (CT), magnetic resonance imaging/angiography, and xenon-CT, suggested postoperative ipsilateral cerebral hyperperfusion. Cerebral hyperperfusion syndromes caused by a probable failure of vascular autoregulation are rare but potentially serious complications after endarterectomy. The literature on this type of complication is briefly reviewed, and the role of various imaging modalities in identification of the syndrome and in guiding management decisions is emphasized.

KEY WORDS • carotid endarterectomy • carotid stenosis • cerebral hyperperfusion • postoperative seizures • imaging studies

OST complications following carotid endarterectomy are considered to be ischemic in nature, L caused either by embolization or occlusion. However, postoperative neurological dysfunction may also be related to a syndrome of cerebral hyperperfusion. Hyperperfusion is a major increase (> 100%) in ipsilateral cerebral blood flow (CBF) well above the metabolic demands of the tissue after removal of a high-grade carotid stenosis.^{13,28} We report a patient with multiple risk factors for ipsilateral hyperperfusion who developed seizures after undergoing carotid endarterectomy. We have documented this case with the following imaging studies: angiography, computerized tomography (CT), magnetic resonance (MR) imaging/angiography, singlephoton emission computerized tomography (SPECT), and xenon (Xe)-CT. We thus demonstrate both the changes that may be associated with hyperperfusion and the role of imaging studies in the diagnosis and management of this unusual syndrome.

Case Report

This 53-year-old woman had a long history of carotid disease, including bilateral endarterectomy at 24 years of age, and subsequent left subclavian to left common carotid artery (CCA) saphenous vein grafting with a vein

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patch graft of the left internal carotid artery (ICA) at 25 years of age. She presented to a community hospital in 1993 with right-sided hemisensory disturbance and expressive aphasia. Her symptoms resolved within 24 hours; however, despite heparin anticoagulation therapy and continuation of her routine aspirin antiplatelet therapy, she had a second transient ischemic attack (TIA) consisting of tingling of her right shoulder. A cerebral angiogram demonstrated occlusion of the left CCA at its origin. A saphenous vein graft with end-to-side anastomosis to the left subclavian artery several centimeters distal to the vertebral artery origin, and end-to-end anastomosis to the left CCA bifurcation were identified. A severe (> 95%) circumferential stenosis was present near the distal anastomosis site, with poststenotic dilation of the left ICA (vein patch) (Fig. 1). Occlusion of the right CCA origin with distal reconstitution via muscular collaterals from the right vertebral artery was present. Patency of the left vertebral artery was also demonstrated.

The patient's medical history was remarkable for the prior cerebrovascular procedures noted above, with intermittent TIAs since those surgeries, but no permanent neurological deficits. She also had chronic obstructive pulmonary disease, coronary artery disease, hyperlipidemia; and she smoked heavily.



FIG. 1. Left subclavian artery angiogram showing a lateral view of the saphenous vein graft to the common carotid artery and revealing a high-grade ($\geq 95\%$) stenosis at the site of the previous anastomosis (*arrow*), with poststenotic dilation of the vein patched internal carotid artery.

Examination. The patient was transferred to Stanford Medical Center, where examination revealed a loud left carotid bruit. She was neurologically normal except for poor recent memory and a mild right pronator drift. Collateral flow to the left hemisphere was poor, with the fetal origin of the left posterior cerebral artery limiting important collateral contribution from the posterior circulation (Fig. 2A). Right carotid occlusive disease was also demonstrated, with filling of the middle cerebral artery (MCA) territory via collateralization primarily from a large right posterior communicating artery. Also in evidence were reverse flow through the right ophthalmic artery, as well as reconstitution of the right ICA via collateral vessels (Fig. 2A). An MR image/angiogram obtained just prior to surgery showed a small left hemisphere watershed infarction in the centrum semiovale (Fig. 2B, arrow).

Operative and Postoperative Course. The patient received intravenously administered heparin until surgery (partial thromboplastin time, 50–70 seconds). A left carotid endarterectomy was performed and revealed a high-grade stenosis (> 95%) of the left CCA at the anastomosis site between the saphenous vein graft and the CCA, but minimal plaque elsewhere. A shunt was used, and total cross-clamp time was 2 minutes for shunt placement and 4.5 minutes for shunt removal. Heparin antico-



FIG. 2. Magnetic resonance (MR) angiograms/images. A: A direction-sensitive three-dimensional phase-contrast MR angiogram through the circle of Willis revealing relatively poor flow to the left hemisphere with development of leptomeningeal collateralization. Velocity encoding during image acquisition allows for flow direction analysis. High signal (white) depicts anteroposterior flow. Retrograde (anteroposterior) flow seen in the right ophthalmic artery (OA) (arrow) suggests that this vessel serves as a collateral from the right external to the internal carotid artery (ICA). Flow in the right posterior communicating artery is also reversed (posteroanterior), suggesting that it serves as a collateral from the posterior circulation (noncomposite data not shown). The left hemisphere cannot develop these additional collateral sources because the left posterior cerebral artery has a fetal origin from the ICA and the external carotid artery is occluded preventing recruitment of the OA. Flow to the left hemisphere is therefore greatly impaired. B: Selected T₂-weighted (TR 2000 msec, TE 80 msec) conventional spin-echo MR image of the brain demonstrating a focal area of signal hyperintensity (arrow) in the deep white matter of the left hemisphere, compatible with a watershed infarct.

agulation therapy was continued throughout surgery and an additional 5000 U was administered prior to crossclamping. Heparin was not reversed. Blood pressure was tightly controlled postoperatively, keeping the mean arterial pressure between 70 and 90 mm Hg for the 1st day, then keeping systolic blood pressure less than 120 mm Hg and less than 140 mm Hg for the 2nd and 3rd days, respectively. Her immediate postoperative recovery was uneventful and her right pronator drift resolved.

After discharge on the 4th postoperative day, she had a witnessed focal motor seizure with secondary generalization. She presented to the community hospital in an unresponsive condition and was treated with dilantin and decadron. A CT scan revealed severe left hemisphere white matter hypodensity with vasogenic edema and a small hemorrhage in the left temporal region (Fig. 3A and B). Emergency carotid ultrasound and a carotid angiogram revealed a widely patent endarterectomy site and excellent flow through her left CCA and ICA graft (Fig. 4). A SPECT study indicated delayed filling and hypoperfusion of the right cerebral hemisphere relative to the left and a region of increased radionucleotide uptake in the left temporal region (Fig. 5). Her neurological status returned to baseline the following day and no further seizures were

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FIG. 3. Postoperative computerized tomography (CT). Axial CT scan of the brain at the level of the ventricles (A), and centrum semiovale (B) obtained to investigate postoperative seizures revealing extensive vasogenic edema in the left hemisphere and a small focal hemorrhage in the left posterior temporal region (*arrow*). Similar views obtained 2 months later (C and D), revealing complete resolution of these findings.

noted. An episode of hypertension was noted during this hospitalization, and when she was discharged she was receiving antihypertensive medications as well as dilantin and aspirin. She was well until 2 months later when she had another TIA causing right upper-extremity weakness. A CT scan revealed resolution of the earlier edema with no acute infarction or hemorrhage (Fig. 3C and D). Coumadin therapy was initiated and she has since remained stable. A Xe-CT scan obtained 3 months after the seizures showed asymmetrical blood flow to the two hemispheres, with normal blood flow to the left hemisphere, low normal flow to the right hemisphere, and good flow reserves bilaterally.

Discussion

The incidence of hyperperfusion syndromes after carotid endarterectomy is reported to be between 0.3% and 1.2%.^{6,15,21,23,28} The symptoms cover a wide spectrum from benign to fatal, and include ipsilateral headaches, seizures, and intracerebral hemorrhage. Risk factors include: a high-grade stenosis (> 70%); a large pressure



FIG. 4. Postoperative and postseizure cerebral angiogram. Postoperative angiography in the frontal plane demonstrating wide patency of the endarterectomy site and high flow in the supraclinoid portion of the left internal carotid artery and its branches. The middle cerebral artery and anterior cerebral artery territories fill briskly.

gradient across the stenosis; poor collateral flow; contralateral carotid occlusion; evidence of chronic ipsilateral hypoperfusion; pre- and postoperative hypertension; and perioperative anticoagulation or antiplatelet therapy.^{2,6,15,21–23,28} Our patient's preoperative risk factors and her postoperative imaging studies support the hypothesis that a mechanism of hyperperfusion led to her seizures. The angiographic studies indicate an elevated risk due to the high-grade stenosis and contralateral carotid occlusion. Evidence obtained by MR imaging/angiography of poor hemispheric collateral flow and the fetal origin of the posterior communicating artery, in association with a watershed infarct, suggest chronic hypoperfusion (lack of collateralization from the posterior circulation has recently been identified as strongly correlated with evidence of hypoperfusion).¹⁸ Postoperatively, the extensive left hemisphere vasogenic edema seen after the seizure, and the SPECT study, which shows an increased level of technetium 99m-Ceretec uptake in the left hemisphere, support the mechanism of hyperperfusion.

The incidence of seizures following all carotid endarterectomy is 0.4% to 1.0%.^{15,28,30} Sundt²⁷ initially reported five patients with seizures early in the postoperative period following carotid endarterectomy, and, in large-scale reviews, documented that patients with post-



FIG. 5. Single-photon emission computerized tomography (SPECT). Rotational SPECT was performed 5 days after the episode of postoperative seizure using intravenous ^{99m}Tc-Ceretec contrast. A large focus of increased radionucleotide uptake is seen in the left temporal lobe (*arrow*). A relative hyperperfusion of the left hemisphere over the right hemisphere was observed in the SPECT series. A ^{99m}Tc-glucoheptonate cerebral blood flow study also demonstrated left hemisphere hyperperfusion with a 3 to 4 second delay in filling of the right hemisphere (data not shown).

operative seizures had preoperative ipsilateral CBFs that were 75% of normal, with a postoperative increase to approximately 170%.²⁸ In 1.3% of postcarotid endarterectomy patients, an electroencephalogram demonstrated periodic lateral epileptiform discharges, and 30% of these patients had clinical seizures associated with an ipsilateral increase in CBF of up to four times baseline.¹⁵ The hyperperfusion-related seizures usually occur within the first 10 postoperative days.^{1,9,11,15,28} They are often preceded by severe, ipsilateral frontotemporal or periorbital headaches: the most common symptom of hyperperfusion.5,15,26,28-30 Most often, they are focal motor seizures with secondary generalization, frequently followed by a postictal Todd's paralysis.^{5,15,28–30} Whereas the seizures may initially be very difficult to control, patients generally make a full recovery. However, progression to hemorrhage occurs in more than 40% of such patients9,15,26 and carries a mortality rate of greater than $50\%.^{67,13,21-23}$ Overall, the risk of postendarterectomy hemorrhage is elevated 10-fold in patients with hyperperfusion.¹³ Postoperative hypertension and pre- and postoperative anticoagulation or antiplatelet therapy have been identified as significant risk factors for progression to hemorrhage, 6,13,22,23,26 and postcarotid endarterectomy seizures have been considered a significant contraindication for anticoagulation therapy.^{13,26}

Hyperperfusion is thought to result from an impairment of autoregulation. Long-standing decreased flow across a stenosis leads to inappropriate vasodilation, development of cerebral edema, breakdown of the blood-brain barrier, and possible hemorrhage when normal perfusion is re-

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established.^{3,12,13,23,24} Eighty percent carotid stenosis²¹ has been associated with postoperative hyperperfusion, and a stenosis of 95% to 99% carries the highest risk.^{6,13,15,23} Severe stenosis may induce maximum dilation of cerebral arterioles, with cerebral autoregulation being reset to a low CBF.^{12,13,15,22,23,28} Episodes of acute ischemia may also impair vascular reactivity. After endarterectomy, the vasculature is unable to respond immediately to increased perfusion pressures, and edema or hemorrhage may result. Autopsy studies of postcarotid endarterectomy hemorrhage patients have demonstrated changes resembling malignant hypertension, including fibrinoid necrosis of arterioles, and red blood cell extravasation into cerebral parenchyma associated with severe edema.³ These histological changes may occur specifically in the presence of perioperative hypertension or acute ischemic insult.¹⁶ The mechanism of postendarterectomy hyperperfusion parallels Spetzler's normoperfusion pressure breakthrough theory,²⁴ and cases such as ours suggest that this mechanism may produce seizures and hemorrhage.

Imaging studies are crucial in identifying hyperperfusion in postendarterectomy patients with seizures. Magnetic resonance imaging/angiography may provide a method for identifying those at high risk for hyperperfusion due to poor collateral vessels and chronic preoperative hypoperfusion, and, although it cannot be recommended in the assessment of all carotid endarterectomy patients, it is warranted in selected patients with highgrade stenoses. Once hyperperfusion syndrome is suspected, there are a variety of studies that may aid in its diagnosis. The subcortical hypodensity seen on our patient's postseizure CT scan is characteristic of vasogenic edema and is unlikely to be due directly to the seizures or to acute infarct, as neither has been reported to cause this striking generalized pattern of edema. Although emboli could contribute to this picture, progression to hemorrhage, seen focally in our patient, is extremely rare in seizure patients without evidence of hyperperfusion. The literature reports a number of different radiological findings in hyperperfusion cases: no radiological changes, patchy edema, and two cases similar to ours in which an ipsilateral region of subcortical hypodensity was seen after an episode of seizures.^{5,7,15,29,30} Severe ipsilateral hypodensity after carotid endarterectomy has also been reported in a case of temporary neurological deterioration unaccompanied by seizures.²

Because the symptoms and radiological signs of hyperperfusion are variable, it may be beneficial to assess CBF using SPECT/radionucleotide or other methods. Xenon-CT flow studies have the advantage of assessing the CBF reserve capacity and indicating quantitative increases in flow. It is the best method for demonstrating hyperperfusion; however, it is costly and often unavailable. The use of the simple, inexpensive method of transcranial Doppler (TCD) to evaluate postoperative MCA velocities is also under investigation.^{4,8,14,17} Elevated ipsilateral CBF in at least the 1st postoperative week has been shown by bedside ¹³³Xe monitoring²² and TCD measurements of MCA velocity.⁴ Furthermore, patients who have little increase in MCA velocity with preoperative vasodilator challenges, as shown by TCD, have abnormally elevated MCA velocities postoperatively^{8,17} and may have symptoms of hyperperfusion, including seizures.8

Hyperperfusion after endarterectomy

Management to reduce the threat of hyperperfusion is essential in high-risk patients. It is prudent to diligently control blood pressure not only in patients with symptoms of hyperperfusion, but in patients at increased risk of such syndromes. It has been suggested that equalization of ipsiand contralateral TCDs could be used to optimize blood pressure control.8 It has also been suggested that antihypertensive medications that increase CBF, such as hydralazine, may be inappropriate in these patients.^{19,20} To reduce the risk of catastrophic hemorrhage, anticoagulation therapy must be carefully considered and may be best avoided. The use of prophylactic anticonvulsant drugs in high-risk patients has been recommended,¹¹ but remains controversial. Future interventions may be aimed at pharmacological prevention of reperfusion hyperemia, by agents that attenuate this phenomenon,^{10,25} and such interventions may be particularly valuable in high-risk patients.

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