

Reversible cerebral vasoconstriction syndrome is a rare cause of stroke after carotid endarterectomy

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Neurologic events after carotid endarterectomy (CEA) require prompt diagnosis and management to avoid potentially catastrophic sequelae. This report describes a 69-year-old gentleman who underwent a left CEA for a high-grade asymptomatic carotid stenosis with concomitant contralateral carotid occlusion. He had transient and crescendo neurologic events in the first 3 postoperative weeks that culminated in right hand weakness and paresthesia, despite dual antiplatelet therapy, maximal anticoagulation, and undergoing stenting of the endarterectomy site. Neurologic events recurred despite these measures and subsequent angiography showed reversible cerebral vasoconstriction syndrome that was successfully managed without further events. Reversible cerebral vasoconstriction syndrome is an unusual but important cause of neurologic events after CEA that requires aggressive and directed medical therapy. (*J Vasc Surg* 2016;■:1-4.)

Carotid endarterectomy (CEA) is often used for treatment of carotid stenosis to reduce future stroke risk.^{1,2} Postoperative increased cerebral perfusion can result in intrinsic arterial vasomotor dysregulation leading to two uncommon postoperative complications. The more common of these cerebrovascular dysregulation syndromes is cerebral edema or hemorrhage (reperfusion or hyperperfusion syndrome) and is thought to occur secondary to impaired intracranial vascular autoregulation due to prior chronic cerebral hypoperfusion.³ The other rare complication is intracranial cerebral vasoconstriction, a subtype of reversible cerebral vasoconstriction syndrome (RCVS), which is thought to also occur because of endothelial vascular dysregulation.⁴ This report describes RCVS after a routine CEA and we report on the diagnostic workup and treatment strategies, and discuss the possible pathophysiologic mechanisms. The patient consented to publication of this report.

CASE REPORT

A 69-year-old asymptomatic left-handed man was referred after his primary care physician noted a left carotid bruit. Carotid duplex ultrasound imaging demonstrated an occluded right internal carotid artery (ICA) with a high-grade stenosis of his proximal left ICA (velocity, 229/108; ICA/common carotid artery ratio, 4:1). His medical history was significant only for well controlled hypertension and remote atrial fibrillation in sinus rhythm with medical therapy. He had no history of migraine headaches,

antiphospholipid syndrome, or drug usage. Computed tomography angiography, obtained by the referring provider, showed an 80% to 90% stenosis of the proximal left ICA (*Fig 1, left*), occlusion of the right ICA, an intact circle of Willis, and no intracranial abnormalities. After careful counseling and in light of his good physiologic state, he underwent a left CEA. The endarterectomy, performed using a shunt and bovine pericardial patch, proceeded routinely including a normal completion Duplex ultrasound examination, well maintained perioperative and intraoperative hemodynamics, and he was discharged the following day. On postoperative day four, he experienced a very transient episode of right hand ataxia. Ten days later, he had another focal neurologic episode that manifested as transient right hand weakness and paresthesia, prompting admission. Computed tomography angiography and carotid duplex ultrasound imaging showed findings consistent with changes normal after CEA with no evidence of intracranial arterial pathology, subarachnoid hemorrhage, or vasospasm. After 2 days of hospitalized observation, neurology consultation, and without further symptoms he was discharged with dual antiplatelet therapy (aspirin and clopidogrel). Two days later, he experienced two similar episodes occurring 2 hours apart, manifested by the return of the same transient neurologic deficits in the right upper extremity. He again received systemic anticoagulation using intravenous heparin. Brain imaging revealed small punctate areas of infarction in the left caudate head on magnetic resonance imaging, and computed tomography angiography showed only postsurgical changes at the CEA site from the surgical clamps (*Fig 2, A*). Over the next several hours, the neurologic symptoms increased in frequency and severity (manifesting as arm weakness), despite therapeutic anticoagulation. Emergent cerebral angiography showed an area of focal irregularity at the proximal and distal extent of the CEA likely secondary to clamping (*Fig 2, B and C*). Within the intracranial circulation there was extensive left hemispheric vasculopathy noted, characterized by alternating regions of vessel narrowing and dilatation involving the middle cerebral and anterior cerebral artery branches as well as the very unusual involvement of the ophthalmic artery (unusual because it is rarely involved in cerebral vasculopathy because it is not in the subarachnoid space). Because of the repetitive clinical events despite maximal

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

Published by Elsevier Inc. on behalf of the Society for Vascular Surgery.

<http://dx.doi.org/10.1016/j.jvs.2016.01.020>

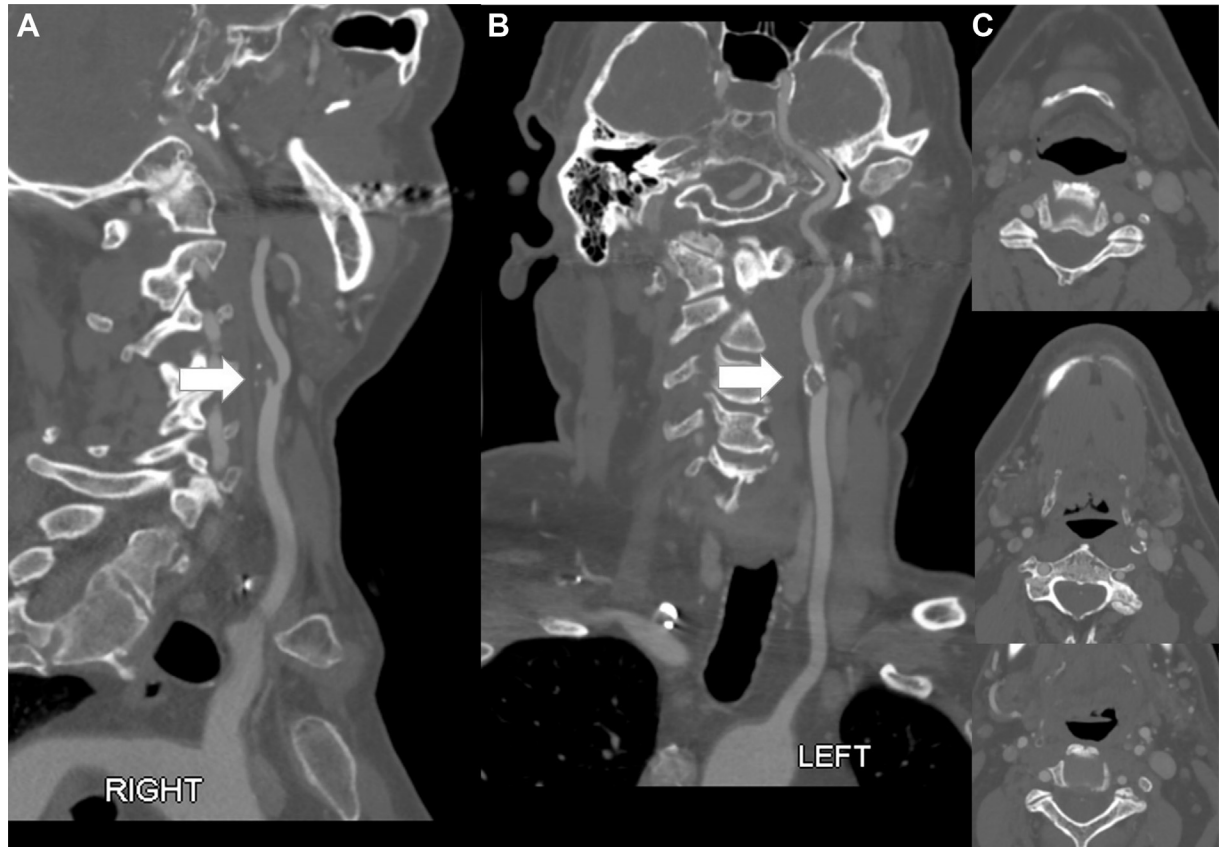


Fig 1. Preoperative computed tomography angiography showing **A**, an occlusion of the right internal carotid artery (ICA; *white arrow*), and **B**, 80% to 90% stenosis of the proximal left ICA (*white arrow*). **C**, The cross-sectional imaging at the level of the carotid bulb and proximal ICA.

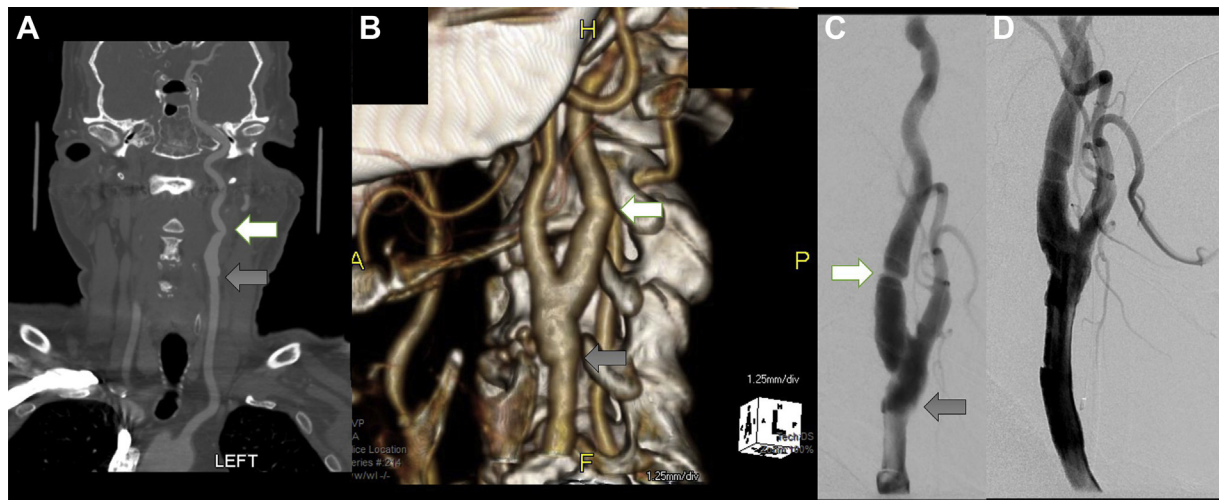


Fig 2. After the patient had repeated neurologic events, he underwent noninvasive imaging with ultrasound (not shown). **A** and **B**, Computed tomography angiography; and magnetic resonance angiography (not shown) (proximal endpoint depicted with the *gray arrow* and the distal endpoint noted with the *white arrows*). **C** and **D**, Subsequent cerebral angiography showed similar findings with a caliber change at the proximal endarterectomy site (*gray arrow*) and a possible kink/clamp site at the distal endpoint (*white arrow*). Because of the concern for these as possible embolic sources despite dual antiplatelet therapy, the carotid artery was stented using an uncovered 7- to 10-mm tapered stent.

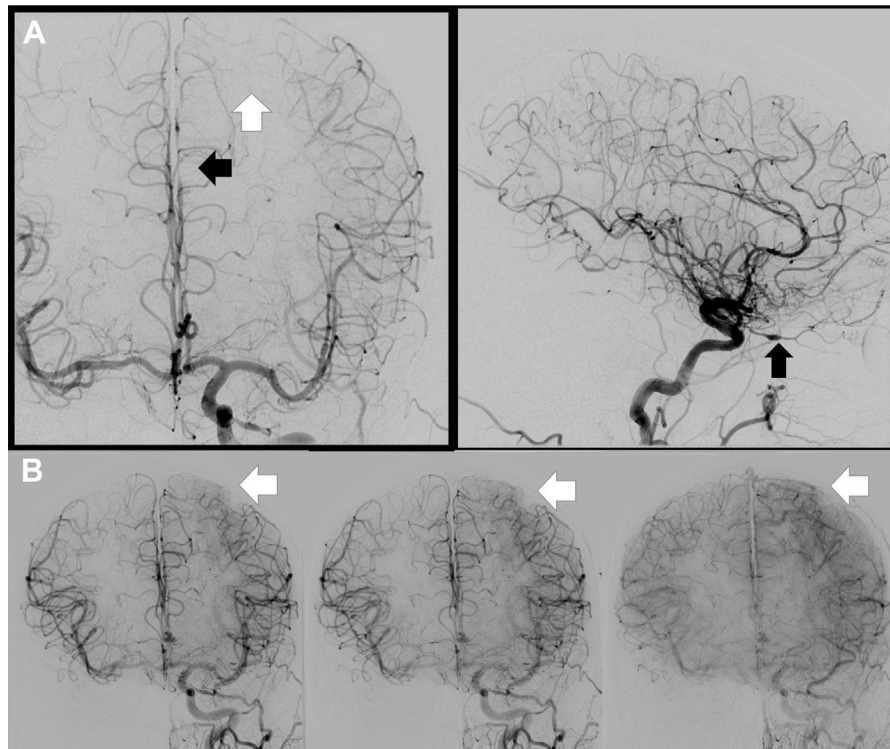


Fig 3. Despite carotid stenting of the concerning areas, the patient had another neurologic event in the same neurologic territory. **A**, Intracranial angiography showed a narrowing and dilation of the ophthalmic artery and distal anterior cerebral artery (*black arrows*) with a lack of parenchymal filling in the motor cortex (*white arrow*). This was far more pronounced than the findings of the previous angiogram. **B**, Intra-arterial administration of 15 mg of verapamil showed much less pronounced vasoconstriction with rapid and full filling of the motor cortex (*white arrows*).

anticoagulation, he underwent carotid artery stenting (CAS) to eliminate any concern over embolization from the endarterectomy site and vessel caliber irregularities (Fig 2, D). The CAS was performed using two 7- to 10-mm tapered carotid stents and distal embolic protection with a large filter element and designed for a vessel sized 4 to 7 mm.

After CAS, his postprocedural management consisted of permission and augmented hypertension without resolution of his hand weakness. Approximately 36 hours after his angiogram and CAS he sustained an episode of transient right facial droop with paresthesia, indicative of a new neurologic event. Urgent repeat angiography showed worsened beading and narrowing of the ophthalmic artery but now also prominently noted in the anterior cerebral artery and its branches (Fig 3, A). Flow in the left anterior circulation was slower than flow in the right anterior circulation indicative of the hemodynamic significance of these lesions. Given these findings, 15 mg of intra-arterial verapamil was injected for diagnostic confirmation as well as therapeutic intervention.⁵ This showed profound and rapid dilation of the affected arterial segments with filling occurring more rapidly in the left hemisphere than the right (Fig 3, B). This confirmed the diagnosis of RCVS, and he underwent medical management of his vasospasm with oral nimodipine (30 mg every 4 hours) for 4 days in the intensive care unit. Medical therapy was then continued for 21 days using short-acting oral verapamil (80 mg every 8 hours)

that was transitioned to oral long-acting verapamil (180 mg daily for 21 days) at discharge, along with dual antiplatelet therapy. This strategy was successful in eliminating any further neurologic events and he remained with permanent mild right hand weakness and paresthesias.

DISCUSSION

Intracranial vasospasm after CEA is a rare but potentially catastrophic complication, with an unknown incidence because the literature is limited to case reports.^{6,7} The larger diagnostic entity known as RCVS has several distinct clinical features in the postoperative state, in contrast to other causes of the same syndrome; namely that there might be no thunderclap headache.⁴ When neurologic deficits are present, they are typically focal and transient and last from 1 minute to 4 hours; however, the manifestations might be so profound as to cause a stroke and permanent disability, as seen in this case report.^{8,9} The greatest period for vasoconstriction occurs within 1 month of the presumed precipitating cause, in this case the CEA.^{10,11} The pathophysiologic mechanism is thought to be secondary to a transient failure of cerebral arterial regulatory control, likely related to endothelial dysfunction, with some component of sympathetic overactivity.¹² The loss of cerebral arterial tone regulation is

thought to be greatest in the 1 to 2 weeks after a significant blood flow change (eg, CEA) affecting predominantly the first and second segments of the large cerebral arteries with resolution generally occurring after 4 weeks.^{4,13}

The treatment goals of RCVS are largely on the basis of the tenets of treatment of intracranial vasospasm that is seen after intracranial hemorrhage and “management is guided only by observational data and expert opinion.”⁴ The mainstay of RCVS treatment is symptom management and identification of the precipitating cause.⁵ When this diagnosis is suspected, patients should be hospitalized, advised to rest, and avoid any known potential vasoconstriction triggers such as physical exertion, Valsalva maneuvers, and invasive procedures. Medical treatment should consist of liberal analgesia (because pain might be a precipitant), antiepileptics (if confounded by seizures), and treatment of hypertension in accordance with stroke management guidelines. Hypotension is potentially catastrophic and should be aggressively avoided because the blood flow to the parenchyma distal to the vasoconstriction is already reduced. Benzodiazepines have been advocated in the management because stress and anxiety might be precipitants; glucocorticoids have no benefit and could possibly worsen the clinical course.⁴

Diagnosis is confirmed, in the manner similar to this case, using cerebral angiography because noninvasive intracranial imaging modalities might lack the small artery resolution necessary to make the diagnosis. The characteristic finding is a segmental narrowing and dilation (string of beads) in the cerebral vasculature during conventional angiography and normalization with enhanced filling through intra-arterial administration of milrinone, nimodipine, or verapamil confirms the diagnosis.^{4,5,13,14} The major risk with intra-arterial vasodilator medications is in worsening, or creating a reperfusion injury, and therefore intervention might be best reserved to patients who show signs of repeated or worsening neurologic deficits.^{8,15} Vasodilators also decrease systemic blood pressure, which can exacerbate flow limitation, and should be given slowly. When treating the vasoconstriction with systemic medical therapy, the dosing and medical regimen typically follows that used in the treatment of subarachnoid hemorrhage with verapamil, nimodipine, and magnesium sulfate as potential options.⁸ The duration of treatment lasts from 4 to 12 weeks and although this therapy does not change the time course of vasoconstriction, might help in alleviating symptoms by minimizing new or repeated neurologic events.^{8,9,16}

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Submitted Aug 16, 2015; accepted Jan 10, 2016.