

Case report: Aggressive blood pressure management for carotid endarterectomy hyperperfusion syndrome

[Présentation de cas : le traitement énergique de la tension artérielle pour le syndrome d'hyperperfusion après une endartérectomie carotidienne]

James Scozzafava MD, Muhammad S. Hussain MD, Tom Yeo MD, Thomas Jeerakathil MD FRCPC, Peter G. Brindley MD FRCPC

Purpose: Cerebral hyperperfusion syndrome (CHS) is a rare but potentially devastating complication following cerebral revascularization. Management of CHS requires aggressive blood pressure control to prevent stroke and intracerebral hemorrhage. This case report documents a severe case of CHS, and outlines a successful outcome associated with aggressive blood pressure control.

Clinical features: A 67-yr-old gentleman, nine days post left carotid endarterectomy, required tracheal intubation and intensive care unit admission following seizures and acute right-sided weakness. A computed tomography scan and magnetic resonance imaging revealed significant vasogenic edema in the left middle cerebral artery territory, without evidence of infarction. The history and radiographic findings suggested CHS. As such, a systolic blood pressure target was set at 90–140 mmHg. This blood pressure parameter was lower than typically targeted following acute ischemic or hemorrhagic stroke. Rapid clinical improvements were seen by day five, and tight blood pressure control was maintained throughout. Repeat computed tomography and magnetic resonance imaging revealed improved edema and no evidence of infarct or hemorrhage.

Conclusion: Cerebral hyperperfusion syndrome is believed to occur following restoration of blood flow to a brain with impaired autoregulation due to chronic hypoperfusion. Massive brain edema and hemorrhage can result from higher pressures. Clinicians should be aware of this potential complication following cerebral revascularization procedures, and the importance of establishing blood pressure targets which are considerably lower than for other patients with similar clinical presentations.

Objectif: Le syndrome d'hyperperfusion cérébrale (SHC) est une complication rare, mais potentiellement dévastatrice après la revascularisation cérébrale. Le traitement du SHC exige un contrôle serré de la tension artérielle pour prévenir l'accident vasculaire et l'hémorragie intracérébrale. Nous présentons un cas sévère de SHC et l'heureux résultat associé au contrôle étroit de la tension artérielle.

Éléments cliniques : Neuf jours après une endartérectomie de la carotide gauche, un homme de 67 ans a dû être intubé et admis à l'unité des soins intensifs pour convulsions et faiblesse au côté droit. La tomographie et l'imagerie par résonance magnétique ont révélé un important œdème vasogénique dans le territoire de l'artère cérébrale moyenne gauche, sans évidence d'infarctus. Les antécédents et les résultats radiographiques étaient en faveur d'un SHC. Une tension artérielle systolique cible a donc été fixée à 90–140 mmHg. C'est une tension plus basse que celle qui est généralement ciblée après un accident ischémique ou hémorragique aigu. De rapides améliorations cliniques ont été observées au cinquième jour. Le contrôle étroit de la tension artérielle avait été constamment maintenu. La reprise des examens d'imagerie a montré une diminution de l'œdème et aucune évidence d'infarctus ou d'hémorragie.

Conclusion : Le syndrome d'hyperperfusion cérébrale est connu pour survenir à la suite de la restauration du débit sanguin dans un cerveau où l'autorégulation est affectée par une hypoperfusion chronique. Un œdème cérébral massif et une hémorragie peuvent être causés par des pressions plus élevées. Les cliniciens doivent connaître cette complication possible suivant la revascularisation cérébrale et l'importance d'établir des tensions artérielles cibles qui soient considérablement plus basses que pour d'autres patients au tableau clinique similaire.

From the Divisions of Neurology and Critical Care Medicine, University of Alberta, Edmonton, Alberta, Canada.

Address correspondence to: Dr. Peter Brindley, Division of Critical Care Medicine, Unit 3C4, University of Alberta Hospital, Edmonton, Alberta T6G 2B7, Canada. Phone: 780-407-7381; Fax: 780-407-6018; E-mail: peterbrindley@cha.ab.ca

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CEREBRAL hyperperfusion syndrome (CHS) is a serious complication of cerebral vascular surgery. It typically occurs during the first week following carotid endarterectomy (CEA) or carotid angioplasty, but can occur as late as one month postvascularization.¹ While the incidence varies, recent evidence suggests that the incidence of CHS following CEA is as high as 3%.²⁻⁴ The rationale for intensive care unit (ICU) admission, urgent investigations, and lower blood pressure (BP) targets than targeted following acute stroke^{5,6} mean that operating room and critical care staff need to be familiar with CHS. We present a case of severe CHS and successful outcome associated with aggressive BP management. Patient consent was obtained prior to writing this case report, in accordance with our institutional guidelines.

Case presentation

A 67-year-old gentleman with a past history of coronary artery disease, hyperlipidemia and hypertension underwent an elective CEA for prevention of stroke. Carotid disease was suspected due to neck bruits during routine physical examination. Carotid ultrasonography and angiography confirmed 90% irregular ulcerative stenosis of the left internal carotid artery, and 99% stenosis of the right internal carotid artery. A left CEA was planned to preserve the dominant hemisphere, and because of collateral blood flow to the right hemisphere via the anterior communicating artery.

Carotid endarterectomy was performed uneventfully under general anesthesia, using a 3 × 5 Sundt shunt (Integra Neurosciences, Plainsboro, NJ, USA) between the left common carotid and distal internal carotid artery, and a Vascutek patch (Vascutek USA Inc., Ann Arbor, MI, USA) over the endarterectomy. Doppler ultrasound confirmed normal flow pattern in all vessels. Surgery was uneventful and the patient was discharged home two days later, neurologically intact. Medications at the time of discharge included clopidogrel 75 mg *po* daily, atorvastatin 80 mg *po* daily, and metoprolol 100 mg *po* bid.

Nine days later, the patient was rushed to hospital following two witnessed generalized seizures. After administration of lorazepam and phenytoin, his trachea was intubated, and he was transferred to the ICU. He was afebrile, in normal sinus rhythm with a heart rate between 60–100 beats·min⁻¹, and a BP which fluctuated between 100/50 to 190/100 mmHg. His cardiac examination was normal, but neurologically he had a right facial droop, 3/5 right-sided arm and leg weakness, and brisker right-sided deep tendon reflexes.

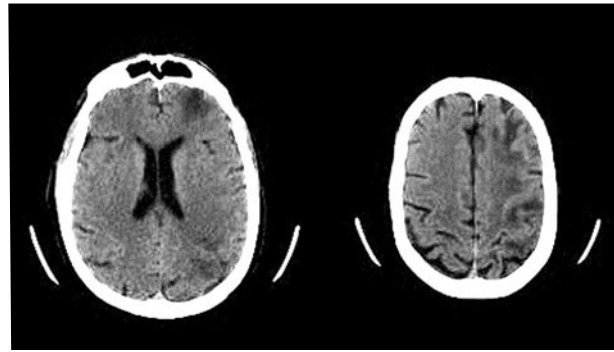


FIGURE 1 Multiple areas of white matter hypodensity in the left hemisphere.

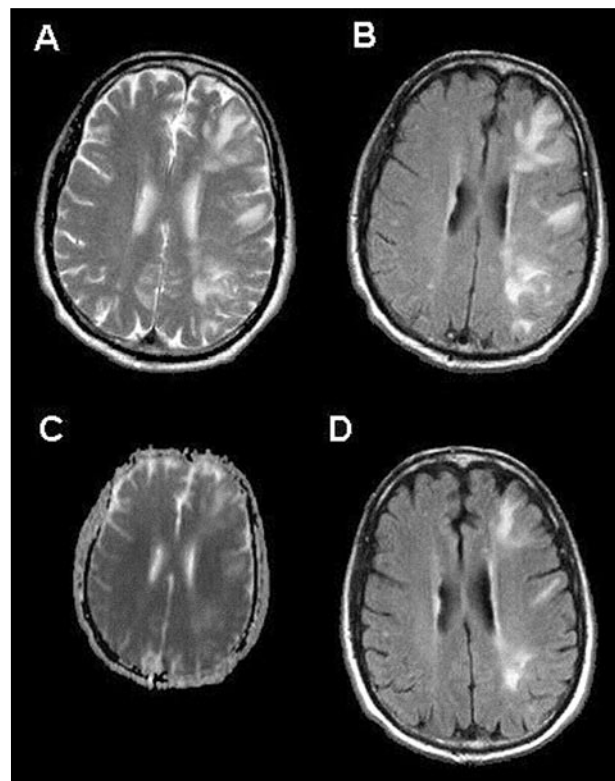


FIGURE 2 T2 weighted (panel A) and fluid-attenuated inversion recovery (FLAIR; panel B) magnetic resonance imaging showing multiple areas of white matter hyperintensity, corresponding to the areas of hypodensity seen on the initial computed tomography scan. Apparent diffusion coefficient (ADC) map (panel C) also shows areas of hyperintensity, indicating changes are related to vasogenic edema as opposed to infarction. After one week with aggressive antihypertensive therapy, the repeat FLAIR magnetic resonance imaging shows improvement (panel D).

TABLE Hemodynamic response during a continuous infusion of labetalol

	<i>Initial</i>	<i>Day 1</i>		<i>Day 2</i>		<i>Day 3</i>		<i>Day 4</i>		<i>Day 5</i>	
SBP (mmHg)	190	145	120	100	110	120	130	130	130	135	135
DBP (mmHg)	100	70	65	60	60	65	60	65	60	70	75
HR (beats·min ⁻¹)	70	70	70	110	90	70	60	60	70	60	60
Labetolol (mg·min ⁻¹)	----	4	3	0	2	1	0	----	----	----	----

SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate. Mean values of SBP, DBP and HR for each 12-hr period following admission. Blood pressure was monitored through a radial arterial line. Twelve-hour averages for each parameter are listed, as well as the average infusion rate of labetalol during the period of treatment.

Computerize axial tomography (CT) of the head (Figure 1) showed hypodensity throughout the left hemisphere, predominantly involving the subcortical white matter, with cortical involvement in the peripheral frontal, parietal and temporal lobes. Because CT findings were inconsistent with typical stroke, urgent magnetic resonance imaging and magnetic resonance angiogram/venogram of the head and neck were undertaken (Figure 2). The examinations showed extensive vasogenic edema in the territory supplied by the left middle cerebral artery. There was no acute hemorrhage, and diffusion studies showed no infarction. The magnetic resonance angiogram confirmed a widely patent left endarterectomy and intact collateral circulation, whereas the magnetic resonance venogram was unremarkable.

The patient was admitted to neuro-ICU with the diagnosis of acute CHS, and a plan to maintain strict BP control with a target systolic pressure between 90–140 mmHg, as determined via right radial arterial pressure monitoring. Blood pressure control was maintained using a labetalol infusion (2–8 mg·min⁻¹ initially), and later as bolus doses of 10–20 mg *iv* (hemodynamic response, Table). Concurrent oral antihypertensive medications were started, including metoprolol 100 mg bid, ramipril 2.5 mg bid, and hydrochlorothiazide 12.5 mg bid. The labetalol infusion was weaned gradually over three days, while avoiding antihypertensives with the potential for vasodilation, such as nitroprusside, nitroglycerin and hydralazine. On the second day following initiation of therapy, transcranial Doppler showed no evidence of microemboli, and the electroencephalogram was normal. Daily electrocardiograms and cardiac enzymes (CK, CKMB, troponin I) were negative for myocardial ischemia or infarction. Clopidogrel 75 mg·day⁻¹ was re-initiated after a repeat CT head scan revealed resolution of edema, and no hemorrhage.

In contrast to the typical course following ischemic or hemorrhagic stroke, the patient improved rapidly. He was fully awake within 48 hr of admission, at which

point his trachea was extubated. The fifth day following admission, the patient's seizures had resolved and he had no residual neurological deficits, at which point he was transferred to the ward. On day seven, a repeat magnetic resonance imaging with diffusion (Figure 2) showed evidence of significant improvement in the vasogenic edema, and no restricted diffusion to suggest infarction or hemorrhage. He was discharged on the following oral medications: clopidogel 75 mg daily, atorvastatin 80 mg daily, metoprolol 50 mg bid and ramipril 5 mg bid. He was educated regarding out-patient BP monitoring, with follow-up appointments to optimize vascular risk factors and BP.

Discussion

This case report describes a successful outcome following severe delayed CHS, and highlights the risk factors, and as well as the goals of BP management compared to patients with a typical stroke.

Carotid endarterectomy hyperperfusion syndrome was first described by Spetzler *et al.* in 1978 as a rare complication following surgical resection of arteriovenous malformations.⁷ Spetzler *et al.* theorized that chronic cerebral vascular disease leads to loss of cerebral autoregulation. Subsequent revascularization conferred higher intracerebral blood flow to a vasculature bed less capable of compensating. As such, surgical restoration of blood flow could result in postoperative cerebral edema, stroke and intracerebral hemorrhage. Spetzler's theory was expanded to carotid revascularization in the 1980's by Sundt *et al.*, who described a triad of headaches, focal seizures, and intracerebral hemorrhage post-CEA.⁸

Carotid endarterectomy hyperperfusion syndrome has been reported following cerebral revascularization by carotid angioplasty and stenting. However, due to the relative frequency of CEA, it remains the most commonly associated intervention.⁹ Estimates of incidence following CEA range from 0.4% to greater than 3%.^{2,10–12} As with arteriovenous malformation surgery, the etiology is believed to be supranormal

postoperative cerebral perfusion pressure in a previously hypoperfused brain. Preoperatively, chronic hypoperfusion distal to the high-grade stenosis results in chronic arterial dilatation and impaired autoregulation. Surgical correction elevates perfusion pressure, but impaired autoregulation prevents protective reflex vasoconstriction.

Early stroke following CEA has been reported in 0.9 to 7% of patients. Hingorani *et al.* reviewed 444 consecutive CEA patients and found the incidence of stroke within 30 days to be just over 1%.³ Two of these five strokes were believed to be the result of hyperperfusion syndromes. This led Hingorani to conclude that CHS may be under-recognized.

Seizures following CEA are uncommon, but cerebral edema in CHS increases the risk. Nielsen and Naylor reported the incidence of seizures after CEA to be from 0.8% to 3%, and associated with subsequent stroke and hemorrhage. The incidence was greater in patients with labile hypertension, bilateral carotid disease and poor collateral circulation.^{13,14} These authors concluded that postoperative seizures, in the absence of infarction or hemorrhage, should increase suspicion of CHS.

When suspected on clinical grounds, the diagnosis of CHS should be confirmed by urgent radiological investigation. Unfortunately, CT lacks the sensitivity and specificity to delineate CHS from arterial and venous infarcts. Therefore, urgent perfusion magnetic resonance imaging is recommended. In regards to carotid imaging, transcranial Doppler ultrasound detects early hemodynamic changes in arterial flow velocity, but may not be sufficiently sensitive in CHS.¹⁵ Prompt magnetic resonance angiography or four-vessel cerebral angiography may be required. Prompt cerebral angiography also remains the best means of detecting correctable lesions within the carotid artery. Findlay has shown that this invasive approach is not associated with increased morbidity or mortality.¹⁶

The most catastrophic event secondary to CHS is intracerebral hemorrhage, and the progression from hyperperfusion to hemorrhage significantly worsens prognosis. The Mayo Clinic reviewed 2,362 consecutive CEAs and found that intracerebral hemorrhage occurred in 14 (0.6%) of patients within two weeks of surgery.¹⁷ Other reports have listed the incidence of hemorrhage associated with CHS to be as high as 1.2%.^{18,19} Intracerebral hemorrhages were fatal in 60% of cases, and associated with severe morbidity in 25%. Risk factors were similar to those for postoperative seizure and stroke and included advanced age, labile hypertension, high-grade stenosis, and poor collateral flow.²⁰ Because of the concern of hemorrhage, many

neurologists and intensivists are cautious about reinstating anti-platelet therapy following CHS. However, given that thromboembolism remains the most common cause of stroke in patients with carotid disease, anti-platelet therapy is likely safe and warranted, following clinical and radiological improvement.

Following routine CEA many centres recommend short-term ICU admission because of potential complications including hemorrhage at the surgical site, and resultant cardiac instability. However, there is a lack of controlled studies to justify routine ICU admission. In fact, O'Brien and Ricotta concluded that only a few patients benefited, and recommended ICU admission be based on risk factors including advanced age, coronary artery disease, poorly controlled hypertension, and high-grade carotid stenosis.²¹ Because of the significant risk of stroke and hemorrhage, and the presumed need for tight BP control, there is a stronger argument to expedite ICU admission for those suspected of CHS.

Given the putative mechanism for CHS, experts have suggested maintaining systolic BP between 90–140 mmHg.^{5,15,16,18} Of note, however, this recommendation is based upon a physiologic rationale, rather than data from randomized controlled trials. Furthermore, uncertainty remains regarding optimal BP management in acute ischemic and hemorrhagic stroke. In acute stroke, lower BP may reduce edema and hemorrhagic complications. However, aggressive BP reduction could decrease perfusion which could expand the area of infarction.²² This has resulted in liberal BP parameters in acute stroke. However, narrower parameters may be necessary in CHS compared to stroke, because most stroke patients are assumed to have intact auto regulation. In contrast, CHS patients likely cannot tolerate high perfusion pressure. This key difference is essential to understand the aggressive lowering of BP in CHS. Furthermore, vasodilating antihypertensive medications are avoided because of the potential to aggravate pre-existing cerebral vasodilation.

Rigorous randomized controlled trials are required to determine the optimal hemodynamic treatment parameters and duration of therapy in patients with CHS. Case reports/case series offer a measure of current best evidence. Our experience highlights clinical risk factors and a diagnostic approach to CHS. Aggressive targeting, and maintenance of a relatively low systemic BP in a critical care setting were associated with a favourable outcome in a patient with CHS.

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