neurocritical care society Neurocrit Care (2010) 12:261–264
DOI 10.1007/s12028-009-9297-6

PRACTICAL PEARL

CT Perfusion Evidence of Early Global Cerebral Hypoperfusion After Aneurysmal Subarachnoid Hemorrhage with Cardiac Arrest

Joseph D. Burns · Jeffrey T. Jacob · Patrick H. Luetmer · Eelco F. M. Wijdicks

Published online: 4 December 2009

Abstract
Background Cardiac arrest and aneurysmal subarachnoid hemorrhage both cause sudden, severe cerebral hypoperfusion at ictus. Animal studies indicate that the resultant microvascular dysfunction and cerebral perfusion abnormalities are important determinants of the associated cerebral injury in both conditions. Although this suggests that perfusion imaging might be a useful tool for prognostication in patients with these conditions, this hypothesis has not been thoroughly investigated in humans.
Methods Case report.
Results A 49-year-old man developed cardiac arrest upon rupture of an intracranial aneurysm. When he arrived at our institution 10 h later, he was comatose, had neurogenic hyperventilation, absent corneal reflexes, and continuous multifocal myoclonus. Despite normal intracranial pressure, normal cerebral perfusion pressure, normal flow in the proximal cerebral arteries on CT angiography, and a lack of diffuse cerebral edema, CT perfusion imaging performed 12 h after ictus showed severe, diffuse hypoperfusion. After the development of refractory intracranial hypertension, physiologic support was withdrawn and the patient died.
Conclusions Early global cerebral hypoperfusion can be demonstrated by CT perfusion imaging after cardiac arrest associated with high-grade aneurysmal subarachnoid hemorrhage and may be indicative of poor neurologic outcome. CT perfusion should be investigated as a prognostic tool in these conditions.

Keywords CT perfusion · Cardiac arrest · Neurologic prognosis · Subarachnoid hemorrhage · Global cerebral hypoperfusion

J. D. Burns (✉)
Department of Neurology, Boston University School of Medicine, Collamore Building, C-3, 72 East Concord St., Boston, MA 02118, USA
e-mail: joseph.burns@bmc.org

J. T. Jacob
Department of Neurosurgery, Mayo Clinic College of Medicine, Rochester, MN, USA

P. H. Luetmer
Department of Radiology, Mayo Clinic College of Medicine, Rochester, MN, USA

E. F. M. Wijdicks
Department of Neurology, Mayo Clinic College of Medicine, Rochester, MN, USA

Introduction

Providing a rapid and accurate neurologic prognosis for patients who have suffered cardiac arrest or high-grade subarachnoid hemorrhage (SAH) represents a major challenge for the neurointensivist. Existing methods of prognostication after cardiac arrest are unable to indicate an accurate prognosis in a significant number of patients and often require days of clinical observation [1]. Similar problems exist in prognostication after high-grade SAH [2]. The ideal tool for neurologic prognostication in these situations would use objective data available immediately after the clinical event to provide an accurate and precise picture of the patient's ultimate neurologic function.

Animal models of cardiac arrest and SAH indicate that cerebral hypoperfusion that persists well after the return of a normal cerebral perfusion pressure and is responsible for a significant proportion of the cerebral injury caused by these conditions [3, 4]. This suggests that perfusion imaging might be a useful tool for neurologic prognostication in these

conditions. Nonetheless, early cerebral perfusion imaging has not been extensively studied in humans with these conditions. Here we present a clinical–radiological correlation of severe early global cerebral hypoperfusion demonstrated by CT perfusion imaging after aneurysmal SAH with cardiac arrest.

Case Summary

A 49-year-old man suddenly lost consciousness after engaging in strenuous physical activity. He was found by bystanders to be pulseless, and CPR was begun within minutes. When paramedics arrived approximately 20 min later, his cardiac rhythm revealed pulseless electrical activity. Spontaneous circulation eventually returned after an unknown period of resuscitation. He was then transported to a local emergency department where a head CT revealed diffuse SAH (Fig. 1a, c). At this point he was noted to have vigorous, continuous multifocal myoclonus, which was successfully treated with propofol. Therapeutic hypothermia was not instituted.

The patient was transferred to our neuroscience intensive care unit approximately 10 h after ictus. Upon arrival, his blood pressure was 149/112 mmHg and he had been hemodynamically stable prior to and during transport. On initial examination in the absence of pharmacologic sedation or paralysis, his eyes were closed and he was not responsive to any stimuli. He was markedly tachypneic, with a respiratory rate of 40 breaths per minute. The pupils were 4 mm and reactive to light. Corneal reflexes were absent. The oculocephalic and cough reflexes were present. Continuous multifocal myoclonus was present.

CT, CT angiography (CTA), and CT perfusion (CTP) of the brain were performed approximately 12 h after ictus. The CT showed extensive SAH and multiple areas of low attenuation in both cerebral hemispheres consistent with evolving ischemia. Notably, there was no evidence of diffuse cerebral edema. CTA demonstrated a 9 × 10 × 7 mm aneurysm of the supraclinoid left internal carotid artery and normal flow in the circle of Willis and its major branches. There was marked cerebral hypoperfusion on CTP, most prominently in areas with the most profound cortical hypoattenuation noted on the precontrast images (Fig. 1b, d).

An external ventricular drain was placed immediately after the CT studies and revealed a normal opening pressure of 15 mmHg. Three hours later, the patient developed hypotension requiring treatment with vasopressor agents, as well as intracranial hypertension refractory to osmotherapy. Although he did not fulfill criteria for brain death,

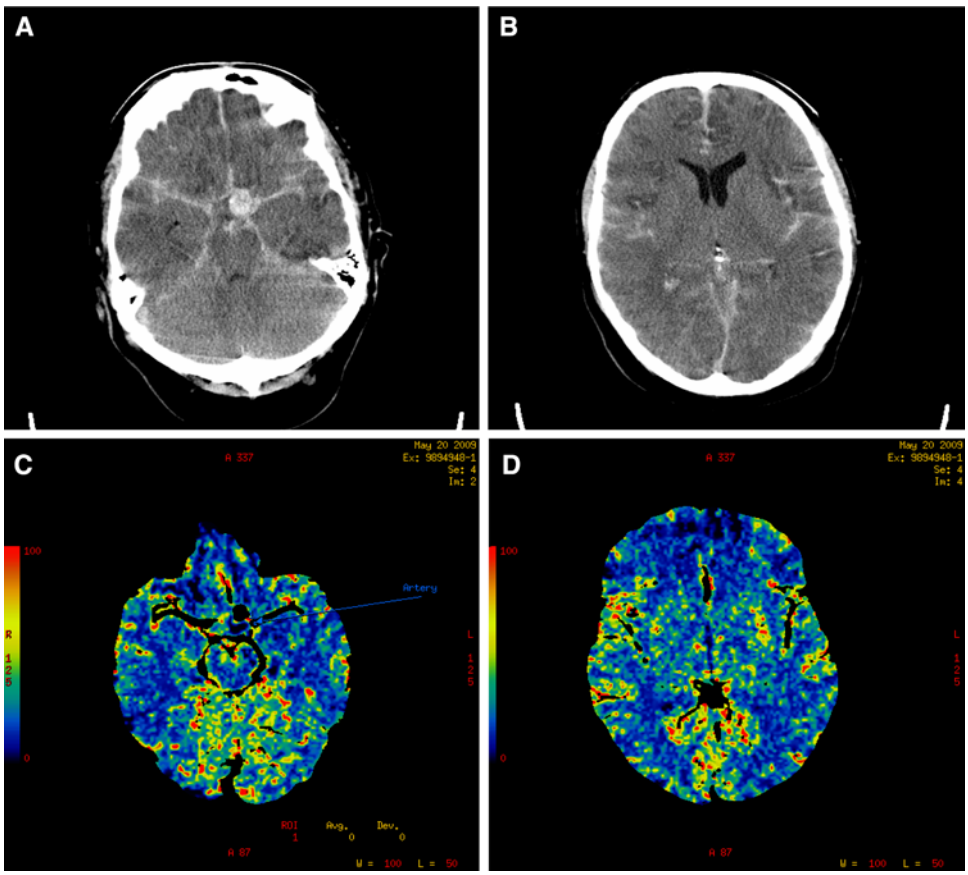

Fig. 1 **a**, **b** Pre-contrast CT demonstrates extensive diffuse subarachnoid hemorrhage and the presence of a partially thrombosed aneurysm on the supraclinoid portion of the left internal carotid artery (CTA not shown). Extensive low attenuation changes can be seen within the cortex of both cerebral hemispheres, consistent with evolving cortical ischemia. These changes are most marked in the frontal and insular cortex, but also involve portions of the parietal and occipital cortex. **c**, **d** CT perfusion demonstrates markedly reduced cerebral blood flow within the visualized portion of the cerebral hemispheres. These changes are most marked in the areas with the most profound cortical low-attenuation changes noted on pre-contrast images

he did not improve. Given the grave prognosis, his family decided to withdraw physiologic support and he died approximately 48 h after the onset of symptoms. No postmortem examination was performed.

Discussion

Disordered cerebral perfusion after cardiac arrest has been studied in detail in animal models and is thought to be responsible for a significant proportion of the cerebral injury that occurs after cardiac arrest [3]. It was originally described in a rabbit model by Ames and colleagues as the "no-reflow phenomenon," referring to a lack of filling of the cerebral microcirculation on reperfusion after arrested cerebral circulation [5]. In animal models, no-reflow is seen in increasingly greater proportions of the brain as the duration of circulatory arrest increased and is improved with hemodilution and increased post-arrest perfusion pressures [6]. Various mechanisms have been proposed as causes of no-reflow, including increased blood viscosity due to stasis, endothelial damage with the formation of capillary-obstructing endothelial blebs, and capillary compression by swollen glial cells [3]. A separate disorder of cerebral blood flow termed delayed global cerebral hypoperfusion has also been described in animal models of diffuse cerebral ischemia. This refers to diffuse hypoperfusion to below 50% of normal that begins approximately 30 min after resumption of normal circulation and persists for about 20 h [7, 8]. In a dog model, this was associated with a severe mismatch between cerebral oxygen uptake and delivery [8]. The mechanisms underlying this process are not known, but may be similar to those thought to be responsible for no-reflow [7].

Global cerebral hypoperfusion and resultant acute ischemic damage also occur after aneurysmal SAH in animal models. This is initially caused by a fall in cerebral perfusion pressure as intracranial pressure spikes due to aneurysm rupture [4, 9]. A significant and diffuse reduction of cerebral perfusion, however, has been shown to persist long after cerebral perfusion pressure returns to normal [4]. Indirect human evidence for this phenomenon exists in the form of "ictal infarctions" described on admission CT scans largely in poor-grade patients by Schmidt et al. [10]. The mechanisms underlying early global cerebral hypoperfusion after SAH are not well understood, but are thought to primarily involve endothelial dysfunction brought on by both the initial hypoperfusion insult as well as the pro-inflammatory, pro-thrombotic, and pro-vasoconstriction properties of extravasated subarachnoid blood [11].

Data regarding the natural history of cerebral perfusion after cardiac arrest in humans are sparse, difficult to compare, and yield inconsistent results. Although xenon-enhanced CT, PET, and SPECT have all been investigated for this purpose, thus far no clinically useful information has been learned [8, 12–15]. Similarly, meaningful human data from direct investigations of cerebral perfusion in the acute phase after subarachnoid hemorrhage are lacking. The CTP images from our patient, therefore, represent unique human evidence of early global cerebral hypoperfusion after aneurysmal SAH with cardiac arrest. It is notable that severe, diffuse hypoperfusion occurred despite normal filling of the proximal major cerebral arteries, a lack of diffuse cerebral edema, and in the presence of a normal cerebral perfusion pressure. These facts eliminate early vasospasm and elevated intracranial pressure as causes of the hypoperfusion and suggest that it is due to a global defect in the microcirculation. This is consistent with what is known from animal models of cerebral perfusion after cardiac arrest and subarachnoid hemorrhage, as described above. It is probable that in this patient, the effects of the two conditions were additive or synergistic.

This example of delayed global cerebral hypoperfusion as evidenced by CTP, coupled with clinical signs of poor prognosis (i.e., continuous multifocal myoclonus and absent corneal reflexes in our patient) and a poor outcome, suggests that CTP should be investigated as tool for early neurologic prognostication after cardiac arrest was well as after high-grade subarachnoid hemorrhage.

References

1. Wijdicks EFM, Hijdra A, Young GB, Bassetti CL, Wiebe S, Quality Standards Subcommittee of the American Academy of N. Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review). Neurology. 2006;67:203–10.
2. Komotar RJ, Schmidt JM, Starke RM, Claassen J, Wartenberg KE, Lee K, et al. Resuscitation and critical care of poor-grade subarachnoid hemorrhage. Neurosurgery. 2009;64:397–411.
3. Hossmann KA. Ischemia-mediated neuronal injury. Resuscitation. 1993;26:225–35.
4. Bedersen JB, Germano IM, Guarino L. Cortical blood flow and cerebral perfusion pressure in a new noncraniotomy model of subarachnoid hemorrhage in the rat. Stroke. 1995;26:1086–92.
5. Ames A 3rd, Wright RL, Kowada M, Thurston JM, Majno G. Cerebral ischemia. II. The no-reflow phenomenon. Am J Pathol. 1968;52:437–53.
6. Fischer EG. Impaired perfusion following cerebrovascular stasis. A review. Arch Neurol. 1973;29:361–6.
7. Nemoto EM, Snyder JV, Carroll RG, Morita H. Global ischemia in dogs: cerebrovascular CO2 reactivity and autoregulation. Stroke. 1975;6:425–31.
8. Sterz F, Leonov Y, Safar P, et al. Multifocal cerebral blood flow by Xe-CT and global cerebral metabolism after prolonged cardiac arrest in dogs. Reperfusion with open-chest CPR or cardiopulmonary bypass. Resuscitation. 1992;24:27–47.
9. Nornes H. The role of intracranial pressure in the arrest of hemorrhage in patients with ruptured intracranial aneurysm. J Neurosurg. 1973;39:226–34.

10. Schmidt JM, Rincon F, Fernandez A, Resor C, Kowalski RG, Claassen J, et al. Cerebral infarction associated with acute subarachnoid hemorrhage. Neurocrit Care. 2007;7:10–7.
11. Kozniewska E, Michalik R, Rafalowska J, Gadamski R, Walski M, Frontczak-Baniewicz M, et al. Mechanisms of vascular dysfunction after subarachnoid hemorrhage. J Physiol Pharmacol. 2006;57(Suppl 11):145–60.
12. Beckstead JE, Tweed WA, Lee J, MacKeen WL. Cerebral blood flow and metabolism in man following cardiac arrest. Stroke. 1978;9:569–73.
13. Edgren E, Enblad P, Grenvik A, et al. Cerebral blood flow and metabolism after cardiopulmonary resuscitation. A pathophysiologic and prognostic positron emission tomography pilot study. Resuscitation. 2003;57:161–70.
14. Roine RO, Launes J, Nikkinen P, Lindroth L, Kaste M. Regional cerebral blood flow after human cardiac arrest. A hexamethylpropyleneamine oxime single photon emission computed tomographic study. Arch Neurol. 1991;48:625–9.
15. Schaafsma A, de Jong BM, Bams JL, Haaxma-Reiche H, Pruim J, Zijlstra JG. Cerebral perfusion and metabolism in resuscitated patients with severe post-hypoxic encephalopathy. J Neurol Sci. 2003;210:23–30.