## Commentary

Delayed cerebral ischemia (DCI) is the major threat to neurological recovery in those surviving the ictus and early brain injury after aneurysmal subarachnoid hemorrhage (SAH). This frequent complication may result in cerebral infarction, as first demonstrated in autopsy studies and more recently with CT and best of all with MR imaging.[1,2] Development of infarction appears to be one of the strongest predictors of poor recovery after SAH.[3] DCI has been associated with cerebral vasospasm, a transient pathologic narrowing of the proximal intracranial arteries, first demonstrated on angiography over a half-century ago.[4,5] However, a causal and direct link between vasospasm and tissue ischemia is increasingly being challenged as divergent evidence emerges. Not only do many patients with angiographic vasospasm not develop ischemic neurological deficits, there are some patients with SAH who deteriorate and/or develop infarction in the absence of visible corresponding vasospasm.[6] DCI may instead be related to abnormalities with autoregulation and the microcirculation.[7] Furthermore, therapies that inhibit or reverse vasospasm have not consistently reduced infarction or improved patient outcomes.[8]

A case report in this journal presents a patient with aneurysmal SAH who developed delayed neurological deterioration in the absence of large-vessel vasospasm (as adjudicated by transcranial Doppler ultrasound; angiography was not performed).[9] Symptoms were refractory to hemodynamic therapy and bilateral deep cerebral infarcts developed in the territory of perforator arteries. The authors suggest that small vessel abnormalities (e.g. perforator vasospasm or microvascular thrombosis) would best explain the development of such "angio-negative" infarcts after SAH.

While it would have been useful to evaluate the intracranial circulation with angiography in such a case, the presence of normal TCD velocities is a fairly sensitive marker of vessel narrowing and thus useful in excluding hemodynamically significant large-vessel vasospasm. The apparent disparity between ischemic deficits (and infarction) and lack of TCD-findings highlights the limitations of only evaluating larger intracranial vessels in SAH patients. Previous studies have documented that deep infarctions are not uncommon after SAH, but these were often asymptomatic or associated with proximal vasospasm in other cases.[1,2] Here DCI led to cryptogenic (TCD-negative) infarction that clearly contributed to significant deterioration and neurological morbidity. Furthermore, the time course reminds us that ischemic deficits may emerge even a week or more after SAH.

Measurement of regional cerebral perfusion may better delineate the pattern and monitor the risk of ischemia than TCD or even angiography. Our recent PET-imaging study demonstrated that hypoperfusion was frequent even in the absence of angiographic vasospasm.[10] It may be that perfusion imaging (e.g. CT or MR perfusion) could have demonstrated reduced cerebral blood flow (CBF) in the deep brain territories of this patient, confirming ischemia as the underlying pathophysiology.

Finally, this case reminds us that ischemia after SAH (whether related to vasospasm or in its absence) does not always respond well to hemodynamic therapies. Induced hypertension, nonetheless, remains the mainstay of medical therapy for DCI; its rationale rests on the ability of raising systemic blood pressure to augment CBF, which itself is reliant on a breakdown in normal autoregulation. No controlled studies have demonstrated the clinical efficacy of such interventions, despite strong anecdotal evidence. Furthermore, studies measuring the effects of hemodynamic interventions on cerebral perfusion (e.g. CBF) have been conflicting and

at best marginal.[11] At least in the presence of large-vessel vasospasm, endovascular interventions, such as angioplasty, appear useful in reversing vasospasm and ischemic deficits. How best to manage microvascular ischemia is even less clear, but deserves serious future attention.

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## References

1. Shimoda M, Takeuchi M, Tominaga J, Oda S, Kumasaka A, Tsugane R. Asymptomatic versus symptomatic infarcts from vasospasm in patients with subarachnoid hemorrhage: Serial magnetic resonance imaging. Neurosurgery 2001;49:1341-8.
2. Rabinstein AA, Weigand S, Atkinson JLD, Wijdicks EF. Patterns of cerebral infarction in aneurysmal subarachnoid hemorrhage. Stroke 2005;36:992-7.
3. Rosengart AJ, Schultheiss KE, Tolentino J, Macdonald RL. Prognostic factors for outcome in patients with aneurysmal subarachnoid hemorrhage. Stroke 2007;38:2315-21.
4. Weir B, Grace M, Hansen J, Rothberg C. Time course of vasospasm in man. J Neurosurg 1978;48:173-8.
5. Fisher CM, Roberson GH, Ojemann RG. Cerebral vasospasm with ruptured saccular aneurysm--the clinical manifestations. Neurosurgery 1977;1:245-8.
6. Rabinstein AA, Friedman JA, Weigand SD, Robyn L, Fulgham JR, Manno EM, *et al.* Predictors of Cerebral Infarction in Aneurysmal Subarachnoid Hemorrhage. Stroke 2004;35:1862-6.
7. Pluta RM, Hansen-Schwartz J, Dreier J, Vajkoczy P, Macdonald RL, Nishizawa S, *et al.* Cerebral vasospasm following subarachnoid hemorrhage: Time for a new world of thought. Neurol Res 2009;31:151-8.
8. Macdonald RL, Higashida RT, Keller E, Mayer SA, Molyneux A, Raabe A, *et al.* Clazosentan, an endothelin receptor antagonist, in patients with aneurysmal subarachnoid haemorrhage undergoing surgical clipping: A randomised, double-blind, placebo-controlled phase 3 trial (CONSCIOUS-2). Lancet Neurol 2011;10:618-25.
9. Salunke P, Gupta SK. Symptomatic Bilateral Isolated Perforator vasospasm following aneurysmal subarachnoid Haemorrhage. J Neurosci Rural Pract 2013;1:45-47.
10. Dhar R, Scalfani MT, Blackburn S, Zazulia AR, Videen T, Diringer M. Relationship Between Angiographic Vasospasm and Regional Hypoperfusion in Aneurysmal Subarachnoid Hemorrhage. Stroke 2012;43:1788-94.
11. Dankbaar JW, Slooter AJ, Rinkel GJ, Schaaf IC. Effect of different components of triple-H therapy on cerebral perfusion in patients with aneurysmal subarachnoid haemorrhage: A systematic review. Crit Care 2010;14:R23.

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