

Asymmetric Posterior Reversible Encephalopathy Syndrome Complicating Hemodynamic Augmentation for Subarachnoid Hemorrhage-Associated Cerebral Vasospasm

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Abstract

Background Posterior reversible encephalopathy syndrome (PRES) is a rare complication of hemodynamic augmentation for subarachnoid hemorrhage (SAH)-associated vasospasm. The roles of hyperperfusion and hypoperfusion in the genesis of PRES remain uncertain.

Methods Case report.

Results We admitted a 35-year-old woman with Hunt & Hess grade II SAH secondary to rupture of a right middle cerebral artery (MCA) aneurysm. This was surgically clipped. Beginning on hospital day 3, she developed recurrent symptomatic vasospasm of the right MCA despite hemodynamic augmentation to a MAP as high as 130 mmHg and endovascular therapy. On hospital day 7, after 36 h of sustained MAP 120–130 mmHg, her level of arousal progressively declined, culminating in stupor and two generalized tonic–clonic seizures. MRI showed widespread, yet markedly asymmetric changes consistent with PRES largely sparing the right MCA territory. After the MAP was

decreased to 85–100 mmHg, she had no further seizures. 2 days later she was fully alert with mild left hemiparesis.

Conclusions PRES is a rare complication of hemodynamic augmentation that should be considered in the differential diagnosis of delayed neurological decline in patients with aneurysmal SAH-associated cerebral vasospasm. The markedly asymmetric distribution of PRES lesions with sparing of the territory affected by vasospasm supports the hypothesis that hyperperfusion underlies the pathophysiology of this disorder.

Keywords Posterior reversible encephalopathy syndrome · Subarachnoid hemorrhage · Aneurysm · Vasospasm · Hyperperfusion

Introduction

Cerebral vasospasm is a common complication and major cause of morbidity and mortality in patients with aneurysmal subarachnoid hemorrhage (SAH) [1, 2]. Despite its clinical relevance, the underlying pathophysiology is poorly understood [3]. As a result, treatment strategies remain suboptimal. Hemodynamic augmentation is the mainstay of medical therapy for this condition [2]. Along with suboptimal efficacy, hemodynamic augmentation is associated with a number of potentially severe complications, including myocardial ischemia, pulmonary edema, hemorrhagic infarction, and re-bleeding from an unsecured aneurysm [4].

Posterior reversible encephalopathy syndrome (PRES) is characterized by headache, altered mental status, seizures, visual abnormalities, or other focal neurological deficits [5], accompanied by a characteristic radiological pattern of bilateral subcortical white matter edema, typically of

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parieto-occipital predominance [6]. The most common underlying medical conditions include abrupt rise in blood pressure, eclampsia, immunosuppressive therapy, and myeloproliferative disorders. These conditions share with hemodynamic augmentation in the setting of SAH-associated vasospasm the common features of hypertension and endothelial dysfunction. Therefore, one would expect PRES to be a common complication of vasospasm treatment. There are, however, few reports in the literature of such an occurrence [7–11]. We describe a patient with asymmetric PRES, least prominent in the territory of vasospasm, as an unusual complication of this therapy that offers a unique perspective on the pathophysiology of this syndrome.

Report of Case

A 35-year-old woman presented to our emergency department with severe headache. Her blood pressure (BP) on admission was 121/78 mmHg [mean arterial pressure (MAP) 92]. She was mildly somnolent but fully oriented, without nuchal rigidity or focal abnormalities (Hunt and Hess grade II). Head computed tomography (CT) showed modified Fisher grade 3 SAH with thick clot in the right Sylvian fissure. Cerebral angiogram revealed a wide-necked 3 mm right middle cerebral artery (MCA) aneurysm. She was admitted to our intensive care unit and nimodipine 60 mg orally every 4 h was initiated.

On hospital day (HD) 2, the aneurysm was surgically clipped. Postoperatively, a phenylephrine infusion was started and titrated to a systolic BP goal of 120–160 mmHg. Prophylactic antiepileptic medications were not administered. On HD 3, she became somnolent and developed a subtle left hemiparesis. CT (Fig. 1a) and conventional angiography revealed vasospasm of the ICA terminus and MCA M1 and M2 branches on the right. This was treated with intra-arterial nicardipine, resulting in significant improvement in vessel caliber. After the angiogram, the goal systolic BP was changed to 140–180 mmHg. The following day both her mental status and leg weakness were significantly improved.

On HD 5, her level of arousal again declined and she developed left arm weakness. The systolic BP had ranged between 145/85 and 200/110 mmHg (MAP 104–118 mmHg) in the 12 h preceding the clinical symptoms. A conventional angiogram revealed recurrent moderate to severe vasospasm of the right M1 segment (Fig. 1b). Intra-arterial injection of nicardipine was attempted but led to systemic hypotension. Accordingly, balloon angioplasty of the M1 segment was performed, with good angiographic result (Fig. 1c). The systolic BP goal was increased to 160–200 mmHg. A standing dose of 250 ml of 5%

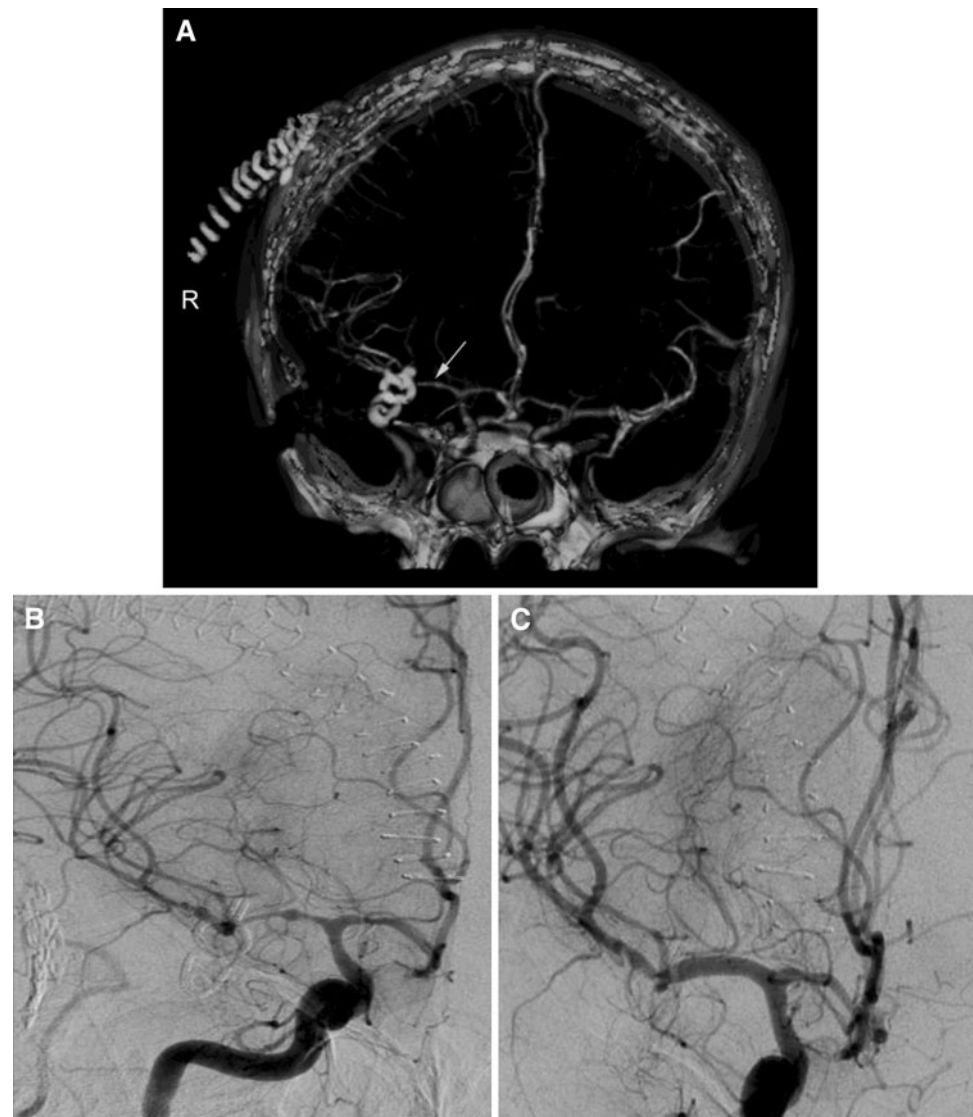
albumin every 6 h intravenously was added to potentiate the hemodynamic augmentation. Nimodipine was discontinued. On HD 6, she was oriented, attentive, and the left hemiparesis had again significantly improved.

Over the course of HD 7, she complained of worsening headache and her level of arousal slowly declined. This culminated in two generalized tonic–clonic seizures and stupor, requiring intravenous lorazepam and phenytoin and tracheal intubation. In the preceding 36 h, the systolic BP was between 160 and 190 mmHg, and the diastolic BP ranged between 80 and 115 mmHg [MAP 119–132 (Fig. 2)]. She had no evidence of infection or electrolyte abnormalities. An emergent head CT showed, in addition to a new area of hypodensity in the right frontal lobe surrounding the aneurysm clip, subtle areas of hypodensity at the cortical–subcortical junction in the occipital poles bilaterally. This raised concern for PRES, leading to discontinuation of phenylephrine and albumin. The MAP then rapidly decreased to below 100 mmHg (Fig. 2). An MRI of the head, performed about 12 h after the seizure, showed asymmetrically distributed FLAIR hyperintensities in the cerebellum and occipital lobes bilaterally, and the left cerebral hemisphere, supporting the diagnosis of PRES (Fig. 3). MR-perfusion imaging, also obtained at this time, showed no evidence of abnormal perfusion in any brain region and no difference in perfusion between the hemispheres. The patient had no further seizures. She recovered to her pre-ictal neurological status and remained stable with MAPs of 85–100 mmHg. She was extubated within 24 h. Her subsequent course was substantially complicated by lumbar drain-associated *Acinetobacter* meningoven-triculitis and worsening of the right MCA vasospasm with large infarction in that territory. On follow-up at 4 months after hospital discharge, she had no major cognitive deficits, had moderate left hemiparesis worst in the hand and ambulated independently.

Discussion

The main causes of secondary neurologic decline after aneurysmal SAH include re-bleeding, hydrocephalus, vasospasm, intracranial hypertension, and seizures [1]. Hemodynamic augmentation administered for the treatment of vasospasm may, in turn, further contribute to several of these conditions. This case description, in combination with a small number of other reports in the literature [7–11], illustrates this point and indicates that PRES is a potential complication of hemodynamic augmentation that should be considered in the differential diagnosis of delayed neurological decline in such patients. While the constellation of symptoms our patient developed (headache, deterioration in mental status, and seizures) is

Fig. 1 CTA coronal thick slab 3D volume rendered image (a), HD3, showing vasospasm of the right ICA terminus and MCA (arrow), with sparing of the left MCA. Conventional angiogram, HD 5, demonstrating severe vasospasm of the right MCA M1 and M2 segments before treatment (b) and significant improvement after infusion of nicardipine and balloon angioplasty (c)



characteristic for PRES, these findings are non-specific, and in this setting the diagnosis requires a high level of suspicion.

The basic pathologic abnormality underlying PRES is subcortical vasogenic edema [12, 13]. On CT and MR imaging, the brain typically demonstrates patchy, bilateral, and symmetric white matter changes with preferential involvement of the parietal and occipital lobes [14]. After these areas, the cerebellar hemispheres, posterior frontal lobes, and inferior temporal lobes are most commonly affected, and in severe cases, the brainstem, basal ganglia, and thalami can be involved. Asymmetric lesions have rarely been reported [15]. On MR, PRES lesions appear hyperintense on T2-weighted images and are most readily appreciated on fluid attenuated inversion recovery imaging. Contrast enhancement, mass effect, and hemorrhage are uncommon. Diffusion-weighted imaging is generally unremarkable and useful in differentiating vasogenic from

cytotoxic edema [16, 17]. However, focal areas of restricted diffusion have been described in up to one-fourth of patients, indicating areas of ischemia and possibly adverse outcomes [18].

Although the radiographic characteristics of PRES are well defined, the pathophysiology remains controversial. Two main conflicting hypotheses have been formulated, both based on disturbances of cerebral autoregulation. The hyperperfusion theory postulates that severe hypertension exceeding the upper limit of cerebral autoregulation leads to passive overdistension of cerebral arterioles, blood–brain barrier disruption, and extravasation of fluid and plasma proteins into the brain parenchyma [12]. This has been observed in animal models [19] and is paralleled in some human cases by the demonstration of regional hyperperfusion on MR perfusion and SPECT studies [20, 21]. The hypoperfusion theory emerged with the description that some patients with eclampsia or severe hypertension

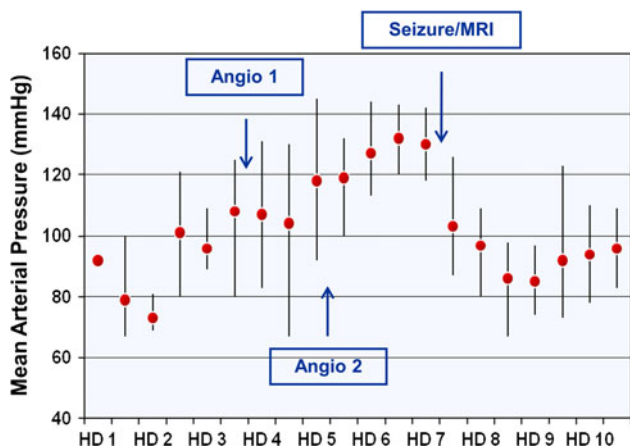
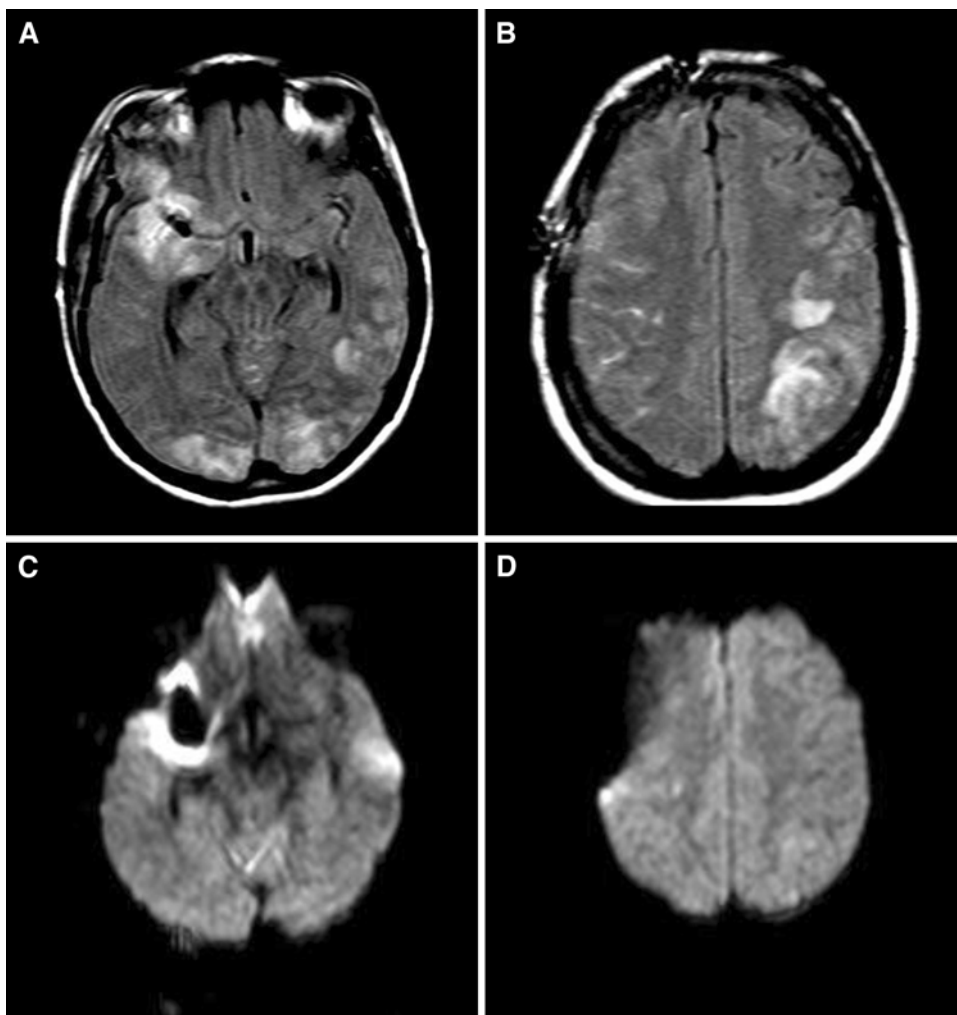


Fig. 2 Mean arterial pressures (mean and range) averaged over 12 h time periods from admission to HD 10. Timing of angiograms for vasospasm treatment is indicated. A dramatic and sustained increase in MAP over baseline values is temporally associated with the development of PRES

who developed PRES had posterior hypodensities on CT and simultaneous vasospasm on conventional cerebral angiography in corresponding vessels [22]. This was interpreted as autoregulatory overcompensation leading to vasoconstriction, decreased cerebral perfusion, and subsequent ischemic injury with edema. The observation that PRES lesions commonly follow a watershed distribution has been cited as support for this hypothesis [6].

Our patient developed PRES after several days of hemodynamic augmentation for recurrent vasospasm. Treatment with phenylephrine and intravenous albumin led to sustained and progressive elevation of MAP over the course of five days. While her systolic BP remained below 200 mmHg, she had a rapid increase in diastolic BP that mostly accounted for the change in MAP. Importantly, this was a young patient without previous history of hypertension who arrived normotensive in the acute phase of SAH. Thus, her pre-morbid blood pressure—and therefore

Fig. 3 Axial FLAIR (a and b) and diffusion-weighted (c and d) MRI, HD 7, demonstrating asymmetric distribution of PRES lesions. The bilateral PCA territories and the left MCA territory are affected, while the right MCA territory is largely spared



her upper limit of autoregulation—were likely low compared to the typical SAH patient. Our case suggests that in this setting hemodynamic augmentation should be used very cautiously.

This scenario suggests that PRES developed in our patient secondary to hyperperfusion due to a sustained MAP above the upper limit of autoregulation—rather than hypoperfusion. We do not interpret the normal MR-perfusion findings as evidence against this hypothesis, as this study was obtained many hours after the MAP was lowered and during a time in which the patient's clinical manifestations were improving. Although data regarding blood flow from detailed transcranial Doppler studies performed on the day of symptom onset would have provided a good test of our hypothesis, such data were not obtained in this patient. Further supporting a causative role of hyperperfusion in the development of PRES in our patient is the markedly asymmetric distribution of PRES lesions, with sparing of the territory of the vasospastic right MCA, in which flow was limited relative to other vascular territories. Contrary to what is proposed by the hypoperfusion theory, there were no PRES lesions in the area of vasospasm and, in fact, this region appeared protected against the development of vasogenic edema.

Conflict of interest The authors report no conflict of interest.

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