

CASE REPORT

Posterior reversible encephalopathy syndrome with thalamic involvement during vasopressor treatment of vertebrobasilar vasospasm after subarachnoid hemorrhage

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Republished with permission from *BMJ Case Reports*
Published 11 December 2015;
doi:10.1136/bcr-2015-012103

Accepted 2 November 2015



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To cite: Madaelil TP, Dhar R. *J NeurolIntervent Surg* 2016;8:e45.

ABSTRACT

Hemodynamic augmentation is the primary medical intervention employed to reverse neurological deficits associated with vasospasm and delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. Failure to improve despite induced hypertension (IH) may raise concern for persistent hypoperfusion and prompt even more aggressive blood pressure augmentation. However, posterior reversible encephalopathy syndrome (PRES) is a hyperperfusion syndrome reported as a rare complication of IH that may confound this picture. We report a case of PRES with prominent thalamic involvement and impaired level of consciousness secondary to blood pressure augmentation for the treatment of symptomatic vertebrobasilar vasospasm. Recognition of this syndrome in distinction to worsening ischemia is particularly critical, as normalization of blood pressure should lead to rapid clinical improvement.

BACKGROUND

Hemodynamic augmentation, primarily consisting of induced hypertension (IH), forms the cornerstone of medical therapies to improve cerebral perfusion and reverse delayed cerebral ischemia (DCI). A number of complications of IH are well recognized, primarily cardiopulmonary decompensation and hemorrhagic transformation of stroke. Hypertensive encephalopathy attributable to breakthrough of cerebral hyperperfusion and development of cerebral edema (including the characteristic posterior reversible encephalopathy syndrome (PRES) pattern of white matter change) has also been reported in a few cases. Recognition of PRES is critical in this setting, as worsening mental status in the setting of DCI may be misattributed to worsening vasospasm and ischemia. In response, blood pressure may be further raised, placing the patient at risk of irreversible complications like intracranial hemorrhage. Instead, blood pressure needs to be cautiously lowered to reverse edema while avoiding recurrence of ischemia. Thalamic involvement is rare in PRES and may lead to further diagnostic confusion, especially in the setting of vertebrobasilar (VB) vasospasm and altered level of consciousness.

CASE PRESENTATION

A 55-year-old man presented with Hunt and Hess grade 4 diffuse (modified Fisher 4) subarachnoid

hemorrhage and was found to have a distal superior cerebellar artery aneurysm which was subsequently coil occluded. His neurologic examination improved after ventriculostomy placement for hydrocephalus; he was extubated on post-bleed day 2 and was able to follow commands at that time. His seizure prophylaxis was discontinued on post-bleed day 3. On day 7 he was more lethargic and underwent conventional cerebral angiography that revealed moderate bilateral vasospasm of M1 and A1 branches, and he was treated with intra-arterial verapamil. Phenylephrine infusion was started concurrently for reversal of DCI, with the goal of raising mean arterial pressure (MAP) from a baseline level of 80–100 mm Hg to 110–120 mm Hg and subsequently to 120–130 mm Hg, at which point his examination improved; he was more alert and able to respond and follow commands. He was subsequently weaned off pressors but a few days later his mental status again worsened. Repeat angiography on day 12 revealed worsened vasospasm in the VB system, which was treated with intra-arterial verapamil. Vasopressors were restarted and MAPs raised to 130–140 mm Hg. This time his neurologic deficits did not improve and he underwent EEG monitoring to exclude non-convulsive seizures. No seizures were detected and pressors were continued. The next day he underwent repeat angiography to reassess vasospasm; this showed persistent posterior circulation narrowing, again treated with verapamil. On returning to the ICU after angiography, he had a generalized tonic-clonic seizure with further worsening of mental status requiring intubation and reinitiation of anticonvulsants.

INVESTIGATIONS

Head CT (figure 1) on the day prior to his seizure showed hypodensity in the posterior white matter with subtle left thalamic hypodensity. MRI (figure 2) performed after the seizure confirmed severe bilateral posterior-predominant FLAIR-positive diffusion-weighted imaging-negative signal abnormality with prominent bilateral thalamic involvement.

DIFFERENTIAL DIAGNOSIS

At the time that his mental status continued to worsen despite attempts to reverse deficits with IH, the primary concern was for refractory DCI and worsening vasospasm. Hypodensity on CT could



Figure 1 Non-contrast head CT performed to investigate the cause of decreased mentation showing ill-defined posterior occipital hypodensity (originally interpreted as ischemic change secondary to vasospasm) (black arrows) and subtle left thalamic hypodensity secondary to vasospasm. However, clinical suspicion for posterior reversible encephalopathy syndrome (PRES) existed.

represent early changes of cerebral ischemia, although the pattern was atypical. Involvement of the thalamus could represent ischemia relating to his known VB vasospasm. However, given the symmetric posterior white matter abnormalities, PRES was raised as an alternative diagnosis. This was confirmed by MRI which ruled out primary cytotoxic ischemia causing bilateral thalamic signal abnormalities. Instead, the combination of radiographic findings and lack of improvement at higher MAP was highly suggestive of PRES.

TREATMENT

The patient was cautiously weaned off vasopressors, initially to lower MAP to 110–120 mm Hg. Once MRI was performed to exclude ischemia and confirm PRES, MAP targets were then

lowered further and more aggressively. He was weaned off phenylephrine and MAP returned to baseline levels (80–90 mm Hg) over 6–12 h.

OUTCOME AND FOLLOW-UP

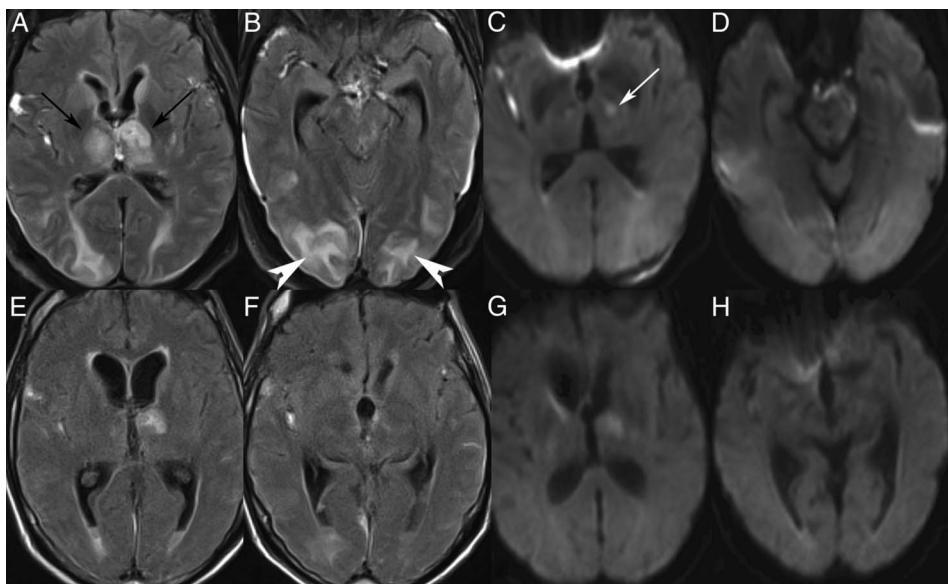
By the next day the patient was waking up easily, regarding, and starting to respond to commands. He was extubated and able to converse, swallow, and ambulate within 24 h. He had no further seizures and follow-up imaging 1 week later showed resolution of signal changes, confirming the presumptive diagnosis of PRES. The patient was discharged to an acute rehabilitation facility 2 weeks later.

DISCUSSION

Blood pressure augmentation is commonly used to treat DCI. However, awareness of treatment-related side effects should guide titration of vasopressors. PRES is especially critical since it is not often considered at first, but is a readily reversible cause of altered mental status during IH treatment that may mimic worsening DCI. Nine cases of PRES caused by hemodynamic augmentation for treatment of vasospasm have been reported.^{1–6}

To our knowledge, this is the first case to prominently involve the thalamus in this setting. Although many theories have been suggested in the pathogenesis of PRES, autoregulatory failure with hyperperfusion is felt to be the most likely cause with hypertension.⁷ PRES most commonly involves the posterior white matter of the cerebral hemispheres, most apparent as FLAIR hyperintensity in the parietal and occipital lobes.⁸ Thalamic involvement, although not common, may be seen in up to 30% of cases.⁹ Additionally, a central PRES variant that lacks typical parietal-occipital changes but almost always involves the thalamus with basal ganglia and/or the brainstem FLAIR hyperintensity has been described.¹⁰ Interestingly, lack of sympathetic innervation of the posterior circulation may explain the failure of autoregulation and increased risk of the syndrome in VB territories.¹¹ This pathophysiologic mechanism may have tipped the scales in favor of hyperperfusion and PRES, with the vasodilatory effect of intra-arterial verapamil superimposed upon hemodynamic augmentation in an effort to maintain vessel patency and perfusion in our patient with DCI. His presentation with a seizure may be another clinical clue, as seizures are rare in

Figure 2 FLAIR and diffusion-weighted images (A–D) from brain MRI obtained immediately after seizure post-angiography for treatment of vertebrobasilar vasospasm showing severe bilateral parieto-occipital (white arrowheads) and left greater than right thalamic (black arrows) FLAIR positive signal abnormality. A small left thalamic stroke (C) is present on the diffusion-weighted image (white arrow). Follow-up MRI performed 8 days later after cessation of hemodynamic augmentation and improved clinical mentation (E–H) shows resolving FLAIR posterior white matter changes and small residual left thalamic infarct consistent with posterior reversible encephalopathy syndrome (PRES) with central thalamic involvement.



DCI but common with PRES. Including our case, seizures may account for 20% of the initial presenting clinical signs for hemodynamic augmentation-induced PRES.^{1–7} Another contributing factor could be the possible seizure-provoking effects of intra-arterial verapamil. Only two cases of intra-arterial verapamil-induced seizures for the treatment of symptomatic vasospasm have been reported.^{12,13} Immediate reperfusion to ischemic brain (with VB vasospasm) and/or acute hyperperfusion are possible culprit mechanisms for seizure in this setting. This phenomenon has also been reported in thrombolysis for acute ischemic stroke where successful vessel recanalization and clinical recovery is heralded by a seizure.^{14,15} The third clue was based on imaging, as posterior cerebral hypodensity on head CT in the setting of acute decompensation and hypertension fit the clinical picture of PRES rather than ischemia/infarction.

Key messages

- ▶ Posterior reversible encephalopathy syndrome (PRES) should be considered with hypertensive treatment of vasospasm, especially if seizure or worsened mentation occurs with greater hemodynamic augmentation and hypodensity is not in the typical vascular territory or in a bilateral posterior distribution.
- ▶ Thalamic and basal ganglia involvement in PRES may lead to prominent disturbances in consciousness.
- ▶ Rapid reversal of deficits (and normalization of MRI) with removal of the offending agent confirms a diagnosis of PRES.
- ▶ Although rare, intra-arterial verapamil can induce seizures probably through an ischemic-reperfusion mechanism.

Contributors Both authors contributed equally to the preparation of this article.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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J NeuroIntervent Surg 2016 8: e45 originally published online December 18, 2015
doi: 10.1136/neurintsurg-2015-012103.rep

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