

Postpartum Angiopathy with Cerebral Infarction, Subarachnoid Hemorrhage and Intraparenchymal Hemorrhage: A Case Discussion

Alexander J.P.W. Hartmann, M.D.*, Edward Livingstone II M.D.***, and Timothy Meadows M.D.**

Department of Neurology, University of Minnesota* and Hampton Roads Neurology**

Case:

A 25-year-old female two weeks postpartum presented to the emergency department with the chief complaint of a headache. She had been evaluated five days prior to admission at an outside hospital for sudden onset of severe right-sided headache with no history of headaches. A head computed tomographic (CT) scan at that location revealed subarachnoid hemorrhage, after which the patient was transferred for further evaluation. A cerebral angiogram was performed which was completely normal, including the venous phase. The patient's headache resolved and she was discharged home. Five days later, she returned to the emergency department with recurrence of her headache and new complaints of numbness and weakness in her left hand.

Her medical history was remarkable only for being two weeks postpartum from an uncomplicated pregnancy and vaginal delivery. She also reported a remote history of Bell's palsy, but had otherwise been healthy and denied any substance use. Her family history was remarkable for rheumatoid arthritis in her mother and scleroderma in her maternal grandmother. She denied taking any medications or having allergies. Her vital signs were stable upon admission. The exam showed shortened attention span and reduced concentration, and a left homonymous hemianopia. Strength was intact throughout with slowed alternate motion rate in her left upper extremity. Toes were downgoing bilaterally.

A new CT scan of head was performed which showed bi-hemispheric convexity subarachnoid hemorrhage, and well as a new area of right frontal intraparenchymal hemorrhage (figure 1). There was also a questionable area of low attenuation in the right temporoparietal region. Magnetic resonance imaging (MRI) with diffusion weighted, gradient echo and post contrast sequences showed areas of restricted diffusion consistent with infarction in the right lateral parietal lobe, posterior insula, and external capsule. Small caliber of basilar and posterior cerebral arteries was also noted on MRI (figures 2 and 3).



Figure 1: CT scan of head on hospital day 1 showing the presence of subarachnoid hemorrhage that is more prominent on the right side.

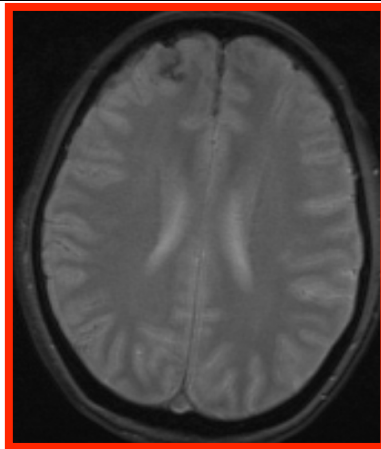


Figure 2: Gradient echo MRI showing right frontal intraparenchymal hemorrhage.

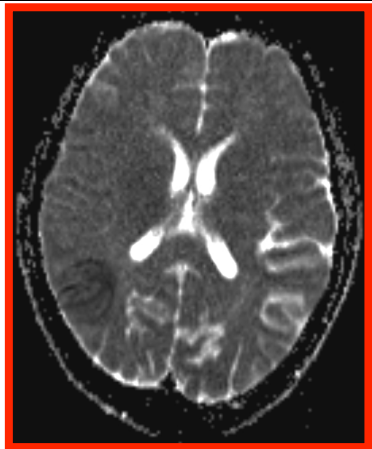


Figure 3: Diffusion weighted sequence image showing restricted diffusion in the right parietal lobe.

Laboratory workup included the following: White blood cells 12,700/mm³, hemoglobin 11.9 gm/dL, hematocrit 36.5%, platelets 341,000/ml, prothrombin time 10.6 seconds, international normalized ratio 0.99, fibrinogen 427 mg/dL, myeloperoxidase antibody- negative, proteinase 3 antibody- negative, antinuclear antibody -negative, anti-ds DNA antibody -negative, homocysteine- 7 µmol/L, erythrocyte sedimentation rate- 35 mm/hr, C-reactive protein- 38.3 mg/L, rapid plasma regain- negative, human immunodeficiency virus antibody- negative, urine drug screen - positive for opiates, which had been administered in the emergency department for the patient's headache.

Additional testing included electrocardiogram, which showed normal sinus rhythm, and transesophageal echocardiogram, which was unremarkable.

Repeat cerebral angiogram showed significant luminal narrowing most prominent in both the right middle cerebral artery and the right vertebral arterial distributions (Figure 4). Given these findings and the patient's history, a diagnosis of postpartum angiopathy (PPA) was made and the patient was treated with IV steroids as well as nimodipine. The patient's clinical presentation improved rapidly over the next several days, and she was discharged on a prednisone taper and nimodipine three days after her diagnostic angiogram. Her only remaining deficit upon discharge was a slight left visual field defect.

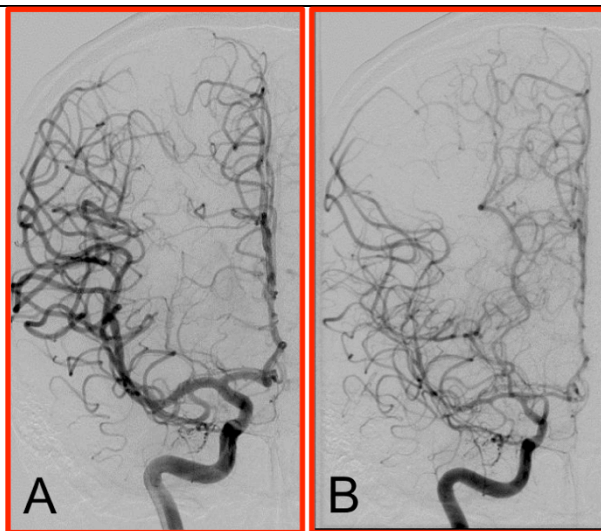


Figure 4: A) Normal initial cerebral angiogram, done six days prior to admission. B) Repeat angiogram on hospital day 3 showing diffuse vasoconstriction of the intracranial internal carotid artery, middle cerebral artery, and anterior cerebral artery.

Discussion:

PPA is a rare and poorly understood disease process, described above in an otherwise healthy patient. It is related to a larger family known as the Reversible

Cerebral Vasoconstriction Syndrome (RCVS).¹ Due to the rare incidence of PPA, there is no true standard of care, although case studies have reported successful treatments with steroids, cytotoxic agents, and vasodilators typically with favorable outcomes.^{2, 3}

A challenge with a new presentation of PPA is differentiating this disease process from Primary Angiitis of the Central Nervous System (PACNS). Although the clinical picture and radiographic findings on CT and MRI may overlap with PPA and PACNS, it is important to recognize the difference in pathophysiology and clinical course for these two entities. PPA more commonly affects young women.⁴ PACNS more commonly affects the middle aged with no gender predilection and a mean age of diagnosis of forty-seven years in a study of 101 patients.⁴ Additionally, as one may surmise from the differing pathophysiology of these syndromes - inflammation vs. vasoconstriction - the onset of symptoms tends to be much more sudden in PPA, and more insidious in cerebral vasculitis.⁵ Inflammatory markers, surprisingly, may not be of much value in distinguishing between these processes, as ESR is elevated in a minority of cases of either disease.^{3, 4}

Diagnostic procedures also differ between these entities. PACNS is a small vessel vasculitis, and angiography may produce unalarming results in the face of a serious clinical presentation. Sensitivity of angiogram in diagnosing PACNS varies from 50-90 percent depending on the study,⁵ hence requiring biopsy for definitive diagnosis. Angiographic findings in vasoconstriction syndromes tend to involve larger arteries stemming from the Circle of Willis,⁶ as was ultimately seen in the case discussed above. As to why the patient's initial angiogram was normal, even after her initial subarachnoid bleed, the vasoconstriction may be a phenomenon that fluctuates over time.⁴ Hence, it may be that the initial angiogram was performed at a time when the major blood vessels were of a comparatively normal luminal diameter.

With the pathophysiology of PPA still poorly understood, vasoconstrictive medications seem a likely scapegoat, and are not uncommonly elicited in the medical history. However, a case series of 45 patients with PPA revealed a history of vasoactive medication use in only 19 of the patients, while the other 27 were reported as spontaneous cases.⁷ Additionally, while a history of migraine is sometimes suggested as a risk factor for developing this syndrome, the same case series found migraine in only five of the patients, a prevalence not dissimilar from that in the general population.⁷ It does seem that patients with a history of migraine do however have worse clinical sequelae, such as intracranial hemorrhage, in a prospective study looking at cases of RCVS including several cases of PPA.⁸

In addition to PPA, there are two other important neurological entities to be considered in the postpartum period: eclampsia and Posterior Reversible

Encephalopathy Syndrome (PRES), which have been shown elsewhere to be closely related.⁹

Eclampsia is known to be associated at least with peripartum cerebrovascular events. In one study of women in the peripartum period, the rate of comorbid ischemic stroke was 27%, while that of intracerebral hemorrhage was 14%.¹⁰ However the relationship between eclampsia with PPA specifically is less clear. In a study comparing the radiographic findings in four patients with postpartum eclampsia and four patients PPA, one of the eclampsia patients was incidentally found to have angiopathy on angiogram, and one of the PPA patients was found to have preeclampsia, although she did not meet the clinical requirements to make the diagnosis of full eclampsia.² Another review of 4 cases of concomitant PPA and PRES, discussed more below, found 3 of the 4 to be having seizures suggestive of possible eclampsia. However none of these patients had the proteinuria encountered in eclampsia.¹¹ It is unclear if the cerebral vasoconstriction that has been described with eclampsia is a reaction to the hypertension associated with eclampsia, or if whether it represents an independent, primary process.¹²

Regarding PRES, there is a more firmly established relationship between this entity and PPA. In a prospective series of 67 RCVS patients, including several patients with PPA, two of the six cases that developed concomitant PRES syndrome were cases of PPA.¹³ A severe case of PPA with PRES was recently reported in Belgium. The patient progressed to coma and required intubation, although was ultimately discharged with a Modified Rankin Score of 0, suggesting that developing PRES in and of itself does not necessarily reflect negatively on prognosis.¹⁴

Conclusion:

PPA is an uncommon disease process, for which data remains limited. Its presentation may mimic other disorders, and a thorough workup including CT, MRI, and angiography is warranted. Although its presentation may be alarming, outcomes are generally quite favorable in the literature reviewed as was the case here. There is established comorbidity between PPA and PRES with a fairly low incidence. Although vasoconstriction has been demonstrated in eclampsia, the exact relationship between eclampsia and PPA as a distinct entity is not well known.

Teaching Points:

1) A postpartum woman with neurologic deficits should be taken seriously, with imaging performed if necessary.

- 2) PPA may present as intraparenchymal hemorrhage, subarachnoid hemorrhage, ischemic stroke, or more than one of these as was the case here.
- 2) If PPA is suspected, one negative angiogram does not rule it out.
- 4) Consider repeat angiogram before proceeding to brain biopsy.
- 5) Outcome is favorable with treatment of combination of steroids and calcium channel blockers.

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Corresponding Author:

Alexander J.P.W. Hartmann, M.D.
Department of Neurology, University of Minnesota
420 Delaware St SE MMC 295
Minneapolis, MN 55455
Tel 612-626-6519
Fax 612-625-7950
Email: hart0653@umn.edu