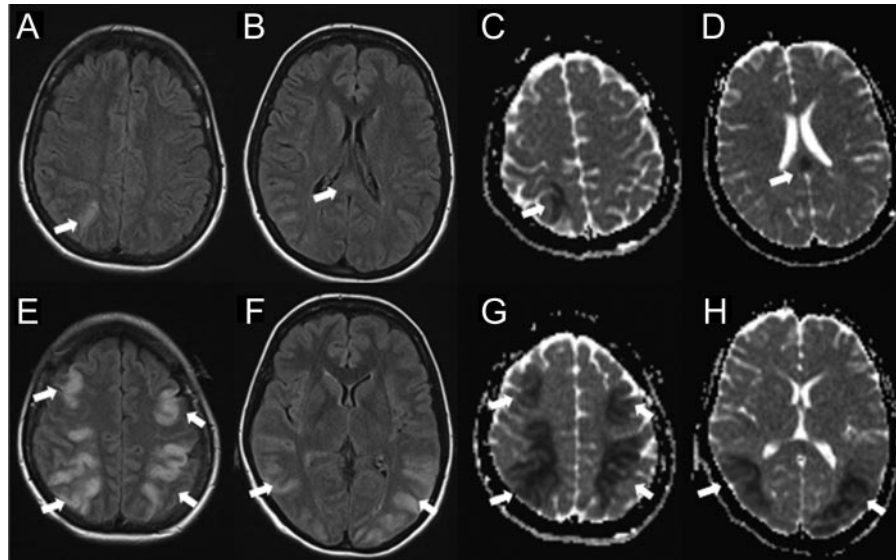


Clinical Reasoning: A 33-year-old woman with severe postpartum occipital headaches

Nancy Maalouf, MD
Sami I. Harik, MD

Correspondence & reprint
requests to Dr. Maalouf:
maaloufnancy@yahoo.com

Figure 1 Head MRI axial cuts: Fluid-attenuated inversion recovery (FLAIR) (A, B, E, F) and apparent diffusion coefficient map (C, D, G, H) sequences



Upper panel MRI, performed on admission, showed FLAIR hyperintensities and diffusion restriction in the right parietal lobe and in the splenium of the corpus callosum (arrows). Lower panel, done on hospital day 3 when the patient deteriorated, showed worsening lesions involving the cortex and subcortical white matter of the parietal, posterior frontal, and occipital lobes, bilaterally (arrows).

SECTION 1

A 33-year-old woman with history of occasional “migraines” complained of severe occipital headache, following an uncomplicated full-term vaginal delivery under epidural anesthesia. This headache was qualitatively and quantitatively different from her usual headaches. The diagnosis of low intracranial pressure headache related to inadvertent dural puncture was considered and 2 epidural autologous blood patches were performed with no relief. One week postpartum she presented to an outside hospital with complaints of poor concentration, difficulty in finding words,

getting dressed, and feeding herself, and left arm numbness. Examination showed a blood pressure of 179/119 mm Hg, poor attention span, apraxia, and decreased sensation in the left hand. General physical examination was unrevealing.

Head MRI (day 0) showed fluid-attenuated inversion recovery (FLAIR) hyperintensities (figure 1, A and B) and diffusion restriction with positive apparent diffusion coefficient (ADC) map (figure 1, C and D) in the right parietal lobe and in the splenium of the corpus callosum. The diagnosis of posterior reversible encephalopathy syndrome

From the University of Arkansas for Medical Sciences, Little Rock, AR.

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(PRES) was entertained and the patient was treated for that condition with the antihypertensive agents nifedipine and lisinopril. The patient's condition deteriorated. On the third hospital day, she became cortically blind and mute, and had motor perseverations and left-sided weakness. Repeat head MRI showed marked worsening

with lesions involving the cortex and subcortical white matter of the parietal, posterior frontal, and occipital lobes, bilaterally (figure 1, bottom panel).

Question for consideration:

1. What is the differential diagnosis?

SECTION 2

The differential diagnosis of multifocal infarcts in the distribution of many vascular territories is wide. It includes emboli from heart and aorta, disseminated intravascular coagulopathy, thrombotic thrombocytopenic purpura, moyamoya disease, vasculitis secondary to connective tissue and autoimmune systemic diseases, or viral/bacterial/fungal infections. Another possible rare entity is primary CNS angiitis. The presentation of this patient with postpartum headache, elevated blood pressure, and focal neurologic deficits suggested the diagnosis of PRES to the treating neurologist.

The sudden occurrence of severe headache in a young woman postpartum should also raise concern for sentinel headaches and subarachnoid hemorrhage because of their considerable morbidity and mortality and because they are eminently treatable if diag-

nosed early. These headaches are usually explosive, reach maximum intensity within minutes, and can last for hours to days. Subarachnoid hemorrhage is usually associated with symptoms and signs of meningeal irritation, altered consciousness, and focal neurologic signs. The presence of these signs in a peripartum woman should also raise the possibility of cerebral venous sinus thrombosis. Although these headaches commonly have a subacute onset, they might have a more acute presentation during puerperium. Pituitary apoplexy occurs as well in association with late pregnancy, presenting with acute headache, nausea, decreased visual acuity, ophthalmoplegia, and visual field defects.

Question for consideration:

1. What studies/tests should be performed?

SECTION 3

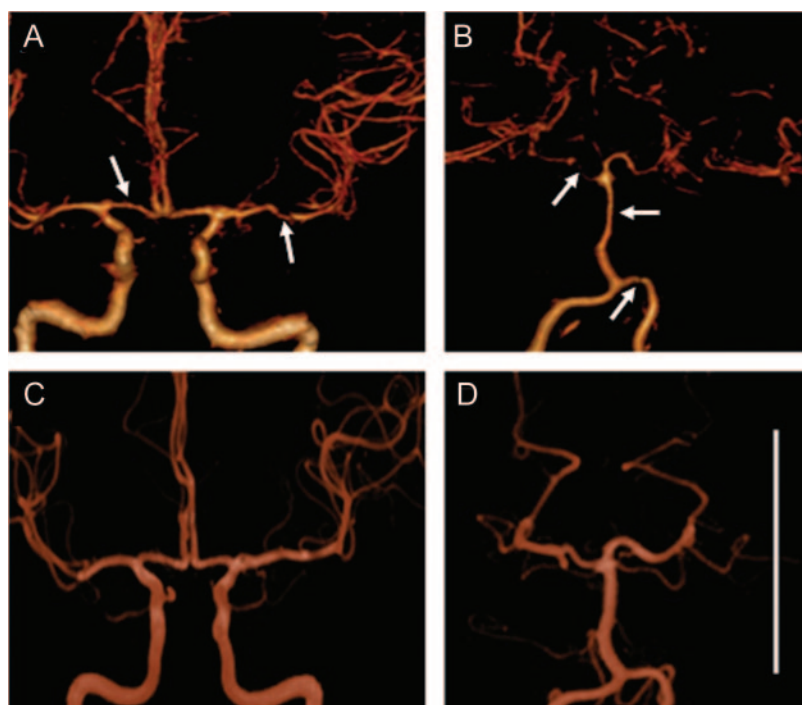
In the outside hospital, head magnetic resonance (MR) venography was unrevealing. EEG showed mild diffuse slowing. Lumbar puncture yielded clear CSF that was acellular with normal glucose and protein content. Bacterial and fungal cultures, cryptococcal antigen, herpes simplex virus PCR, VDRL, and cytology were all negative.

Because of clinical deterioration, the patient was transferred to our university hospital where a head CT angiography (CTA) revealed segmental narrowing of many intracranial vessels but primarily involving the vertebral, basilar, posterior, and middle cerebral arteries (figure 2, A and B). Transcranial sonography measured increased flow velocities in right middle (170 cm/s), right posterior (230 cm/s), left middle (130 cm/s), and left posterior (140 cm/s) cerebral arteries. Vasculitis workup including erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, antinuclear antibody, anti-neutrophil cytoplasmic antibody, double-stranded DNA, anti-SSA/Ro, anti-SSB/La antibodies, cryoglobulin, and angiotensin-converting enzyme was negative.

Based on the above, reversible cerebral vasoconstriction syndrome (RCVS) was suspected. The patient was treated with oral nimodipine, 60 mg every 4 hours; aspirin, 81 mg daily; and methylprednisolone, 125 mg IV every 6 hours for 6 days before the results of the vasculitis workup became available. The patient gradually improved: she became more alert but remained apathetic with partial expressive aphasia, apraxia, and perseveration. She perceived light and shades but her visual acuity remained below 20/200. She also had residual mild left hemiparesis with diffuse hyperreflexia and bilateral ankle clonus. Nimodipine was gradually tapered after 10 days and she was transferred to a rehabilitation facility.

Follow-up at 2 months after discharge showed her to be alert, with near-normal visual acuity (20/25) and intact color vision. She had residual right inferior quadrantanopia, apraxia, mild left hand weakness, and diffuse hyperreflexia. Head MRI showed evidence of encephalomalacia in the frontoparietal lobes, left occipital lobe, and splenium of the corpus callosum. Head MR angiography revealed complete

Figure 2 Head CT angiography (CTA) (A, B) and magnetic resonance angiography (MRA) (C, D)



Head CTA at day 6 reveals segmental narrowing of the left middle cerebral artery and the A1 segment of the right anterior cerebral artery (A, arrows); segmental narrowing of the posterior cerebral and left distal vertebral arteries with broad narrowing of the basilar artery (B, arrows). Head MRA 2 months after discharge shows complete reversal of arterial pathology (C and D). The magnification is similar in all parts of the figure; the white vertical band denotes 5 cm.

resolution of the previously noted vasoconstriction (figure 2, C and D).

DISCUSSION The most important information regarding the diagnosis and treatment of this patient was obtained before transfer to our hospital. The findings of positive diffusion-weighted imaging and ADC map in the right parietal lobe and splenium of the corpus callosum was indicative of ischemic stroke which is rarely seen in PRES.¹ The clinical and MRI worsening after antihypertensive treatment makes the diagnosis of ischemic strokes more convincing. What is the cause of cerebral ischemia? She had no clinical evidence of heart disease. CTA ruled out moyamoya and premature atherosclerosis, and clearly revealed segmental narrowing of large and medium-sized arteries at the base of the brain, highly suggestive of RCVS.

RCVS refers to a group of disorders sharing angiographic and clinical features including reversible segmental and multifocal vasoconstriction of cerebral arteries, and sudden severe headaches with or without focal neurologic deficits or seizures. These disorders were previously reported as Call-Fleming syndrome, benign angiopathy of the nervous system,

and postpartum angiopathy.² The pathophysiology of RCVS remains unknown, though transient disturbance in the control of cerebral vascular tone was hypothesized.³

There is gender preponderance of RCVS in women. Half of the patients give history of migraine.² The condition is idiopathic or related to a number of factors, including late pregnancy/postpartum and use of vasoactive substances such as triptans, selective serotonin reuptake inhibitors, pseudoephedrine, cannabinoids, cocaine, amphetamines, methylenedioxymethamphetamine (ecstasy), bromocriptine, and nasal decongestants.⁴ Postpartum angiopathy is an extremely rare complication that usually occurs in a normal pregnancy, as was the case in our patient. Two-thirds of those patients present in the first postpartum week.⁵ In 50%–70% of cases, it is associated with the use of vasoconstrictors, mostly ergots,³ to treat postpartum hemorrhage or to inhibit lactation. Intracranial hypotension, whether spontaneous⁶ or secondary to dural puncture,⁷ was also reported as a possible etiology of RCVS.

The diagnosis of RCVS is usually made on cerebral arterial imaging which shows diffuse and multifocal segmental narrowing of large and medium-sized arteries. The anterior and posterior brain circulations are involved. Occasional dilated segments, like strings and beads or sausage strings, were described. The diagnosis is confirmed only by documenting reversal of the vasoconstriction within few months.²

Vasoactive medications should be stopped. Clinical and angiographic resolution occurs spontaneously; however, calcium channel blockers like nimodipine are used with variable success. Long-term measures include secondary stroke prevention and treatment of complications.^{6–8} A short course of steroids may be justified to cover for cerebral vasculitis while awaiting results of workup, although a recent retrospective case-series study found worse outcome in patients who received steroids. However, this matter is confounded by the possibility that steroids were administered to sicker patients.⁹

The clinical outcome is usually good, with most patients recovering completely within days to weeks. The major complications of RCVS are localized cortical subarachnoid hemorrhages (20%–25% of cases) and ischemic strokes (5%–10%).⁵ Hemorrhagic complications and seizures occur earlier (within the first 10 days) compared to ischemic events (around 12 days from headache onset).² Association with PRES⁷ and recurrence¹⁰ were reported.

Patients with severe new-onset headache and focal neurologic deficits must be assessed urgently and several diagnoses must be considered. Initial diagnostic

studies should include an unenhanced head CT and lumbar puncture. If both studies are normal, head MRI, MR angiography of the head and neck, and MR venography are necessary. When this workup reveals segmental vasoconstriction, normal or near normal CSF studies, and a lack of any other underlying pathology, RCVS should be considered. In the case we presented, PRES was initially suspected, so blood pressure was aggressively controlled, which worsened brain ischemia. Thus, antihypertensive agents should be used with caution in RCVS, just like any other condition causing ischemic strokes.

AUTHOR CONTRIBUTIONS

Dr. Maalouf: drafting/ revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Harik: drafting/ revising the manuscript, study concept or design, analysis or interpretation of data.

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