Case Report

Recurrent Intracranial Hemorrhage Due to Postpartum Cerebral Angiopathy
Implications for Management

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Background—Postpartum cerebral angiopathy as a cause of hemorrhagic stroke in young women is not well recognized. It is unknown whether this disorder represents a true inflammatory vasculitis or transient vasoconstriction related to the hormonal events of pregnancy and the postpartum period.

Case Description—A 39-year-old woman presented with postpartum intracranial hemorrhage and, 32 months later, with subarachnoid hemorrhage, following normal pregnancies. Cerebral angiography obtained after each stroke demonstrated diffuse irregularity of branches of the middle cerebral arteries consistent with a diffuse vasospastic process or classic vasculitis. Neurological deficits resolved and results of a transcranial Doppler study normalized after a short course of high-dose corticosteroids following the second stroke.

Conclusions—Postpartum cerebral angiopathy should be considered in the differential diagnosis of recurrent intracranial hemorrhagic stroke in young women. Recognition of this condition may preclude treatment with potentially toxic therapies for vasculitis and will have important implications for counseling women on subsequent pregnancies. (Stroke. 1998;29:1995-1998.)

Key Words: cerebral hemorrhage □ vasoconstriction □ pregnancy □ vasculitis

Pregnancy is an important risk factor for stroke in young patients; the incidence of stroke is 13 times that found in nonpregnant women of similar age. The relationship between pregnancy and stroke remains controversial; a recent large, population-based study found the postpartum state rather than pregnancy itself to be associated with an increased risk of cerebral infarction and hemorrhage. Intracranial hemorrhage during the peripartum period is responsible for 10% of all maternal deaths; most are associated with pregnancy-induced hypertension, sinus thrombosis, or subarachnoid hemorrhage due to rupture of saccular aneurysms or arteriovenous malformations, but in some patients the cause is unknown. We describe a patient who presented on 2 separate occasions with postpartum intracranial hemorrhage and neuroimaging consistent with postpartum cerebral angiopathy.

Case Report

A 39-year-old woman presented with a right frontal intraparenchymal hemorrhage 9 days after spontaneous vaginal delivery of her third child (Figure 1A). She had a mild left hemiparesis and decreased level of consciousness on admission, both of which resolved in the hospital after 2 weeks. She was well throughout her pregnancy and in particular was normotensive, without edema, proteinuria, seizures, or headaches. A 4-vessel cerebral angiogram demonstrated irregularity of a temporal branch of the right middle cerebral artery (MCA) (Figure 1B); this was attributed to vasospasm, although the possibility of vasculitis was considered. The angiogram was otherwise normal, with no evidence of vascular malformation or aneurysm. While in the hospital she was treated with dexamethasone (4 mg IV every 6 hours for 10 days) for control of intracranial pressure.

Four months later a repeat cerebral angiogram demonstrated somewhat decreased but persistent irregularity in the MCA branch. The patient was doing well with no neurological deficits.

Elective cesarean section was recommended for her next delivery 32 months later because of the intracerebral bleed. Five days after giving birth, she experienced sudden headache with nausea and vomiting. CT scan of the brain demonstrated no new changes. She refused a lumbar puncture. Four days later she returned with sudden confusion, drowsiness, headache, and vomiting. On admission, she was not following commands and had a mild fluent aphasia and right hemiparesis. A brain CT demonstrated a small left frontal subarachnoid hemorrhage (Figure 2). Cerebral angiography demonstrated that the inferior temporal branch of the right MCA was

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unchanged from 1994, but many branches of the left MCA showed marked beading, and other distal right MCA branches remote from the area of subarachnoid hemorrhage were now irregular (Figure 3). A brain MRI 1 week after the event demonstrated new areas of high signal intensity bilaterally within the centrum semiovale that had not been present on the MRI performed 1 week after the first hemorrhage and were thought to represent areas of ischemic damage (Figure 4).

As before, there had been no medical problems during the pregnancy, and the patient remained normotensive, without proteinuria or edema. The personal and family histories were negative for coagulopathy and collagen-vascular or autoimmune disease. Laboratory examination revealed a mild postpartum anemia but was otherwise unremarkable, including normal results for renal function, urinalysis, international normalized ratio, partial thromboplastin time, thrombin time, antithrombin III, functional protein C, protein S, D-dimers, fibrin monomers, and negative protein C resistance. Tests were negative for antinuclear and anticardiolipin antibodies, and complement indices were normal.

The patient was treated with methylprednisolone (1 g IV daily for 3 days), followed by prednisone tapering from 60 mg daily over 2 weeks. On discharge 6 days after admission, the patient’s only complaint was of right arm and perioral numbness. Transcranial Doppler performed just before dis-
Postpartum cerebral angiopathy (PCA) as a cause of ischemic and hemorrhagic stroke in young women is not well recognized. Although usually a benign and nonrelapsing disease, fatalities have been reported, and our patient has demonstrated that it may recur.

There are 22 reports of women presenting shortly after a normal pregnancy with the sudden onset of headache, vomiting, seizures, and focal neurological deficits in the absence of intracranial hemorrhage. Some of these cases were associated with the use of vasospastic drugs, with preeclampsia, or with labile hypertension, suggesting an alternative etiology for the presentation. In the remaining cases, no etiology for the neurological deficits was found despite extensive workups for stroke risk factors. Cerebral angiography in each case revealed areas of stenosis and ectasia in multiple intracranial vessels, suggesting vasculitis or a diffuse vasospastic process.

There are at least 4 additional reports of women presenting shortly after a normal pregnancy with intracranial hemorrhage secondary to postpartum cerebral angiopathy. One of these women had an intraparenchymal bleed; 3 suffered subarachnoid hemorrhage revealed by CT and lumbar puncture. No etiology for the bleeds could be found, and none of the patients had evidence of hypertension or toxemia during pregnancy or the postpartum period. In each case, angiography revealed a classic vasculitic picture involving several intracranial vessels, often bilaterally, and not confined to the area of hemorrhage. Two of the patients underwent repeat cerebral angiography that showed complete normalization of vessels. Three of the patients had rapid resolution of neurological deficits, while the fate of the fourth patient was not reported.

The pathogenesis of postpartum cerebral angiopathy is unknown, and the term “angiopathy” has been chosen intentionally to reflect the uncertain underlying pathophysiology of this condition. The rapid improvement in symptoms and resolution of angiographic findings within weeks of presentation suggests transient vasoconstriction rather than a true inflammatory vasculitis. Cerebrospinal fluid analyses in cases of postpartum cerebral angiopathy have been normal or have shown a modest pleocytosis or elevated protein. Post-mortem examination in 1 fatal case showed no inflammatory changes in the vessels involved. These features, along with the early improvement observed in flow velocities on transcranial Doppler, strongly support a vasospastic process.

Calabrese et al have suggested that postpartum cerebral angiopathy may represent a continuum of vascular pathology, with an initial vasospastic lesion ending in a true arteritis. Such a pathophysiology could explain the persistence of irregularity in the right MCA branch observed in our patient after the first intraparenchymal bleed. Experimental data have shown that acute hypertension can produce areas of vasospasm and dilatation, and some reported cases of postpartum cerebral angiopathy have been associated with acute and transient attacks of hypertension in the absence of toxemia. In this way, postpartum cerebral angiopathy may represent a hormonally mediated effect on the vessel intima precipitated by acute elevations in blood pressure; mild intimal hyperplasia was observed in a fatal case. Because hypertension was not demonstrated in our patient and in other cases of postpartum angiopathy, a direct vasospastic effect secondary to insults other than hypertension must be considered.

There are now several reports of a benign form of isolated central nervous system angiitis occurring in the absence of pregnancy or the postpartum. Patients are usually healthy young women with relatively benign disease characterized by acute headache, seizures, neurological deficits, and angiographic findings consistent with vasospasm or vasculitis. This nearly identical clinical picture suggests that postpartum cerebral angiopathy may be an important clinical subset of benign angiitis of the central nervous system.

Postpartum cerebral angiopathy is a significant pathological entity that should be considered in the differential diagnosis of postpartum hemorrhage. Our case emphasizes the association of intracranial hemorrhage with this disorder and its potential for recurrence in subsequent pregnancies, which introduces important questions regarding recommendations made to patients considering future pregnancies.

Our patient and others have had good outcomes with short courses of high-dose corticosteroids. Recognition of this condition may preclude unnecessarily aggressive and potentially toxic treatment with long courses of immunosuppressive therapy for vasculitis. In at least 1 other case, there was full recovery without steroid treatment; thus, the role of corticosteroid treatment in this condition requires further investigation. Elucidation of the pathophysiology of this
condition will be important in the future counseling and management of these patients.

References

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