

THE MASTER CLASS

Recognizing Stroke Is a Life or Death Issue



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In high-risk obstetrics, we are faced with a variety of critical presentations: threatened early pregnancy loss, pregnant patients with preexisting medical conditions, and the development of acute medical complications during pregnancy.

Fortunately, the most serious complications of pregnancy—seizures, myocardial infarctions, and cerebrovascular events—are rare.

Despite their infrequency, we must become sufficient-

ly familiar with the presenting symptoms of these life-threatening complications of pregnancy to be able to employ our clinical skills at a moment's notice.

Recent advances in stroke management make quick action vital. Medications or surgery not only may save the lives of the woman and fetus, but may preserve brain function in the woman as well.

Very often, but not always, clues to the possibility of a stroke may lie in the woman's medical history of hypertension, preeclampsia, seizures, or a bleeding disorder.

We need to be alert to these risk factors for stroke, and make sure that we include stroke in the differential diagnosis even when the patient's symptoms may be mas-

querading as less serious complications of pregnancy.

This month, my guest Master Class professor is Baha Sibai, M.D., a world expert on hypertensive disorders and complications in pregnancy who has authored or coauthored more than 350 peer-reviewed publications on the topics of preeclampsia and eclampsia.

Dr. Sibai is professor and director of the department of obstetrics and gynecology at the University of Cincinnati. He formerly directed the division of maternal/fetal medicine at the University of Tennessee, Memphis. ■

DR. REECE, who specializes in maternal-fetal medicine, is the vice chancellor and dean of the college of medicine at the University of Arkansas in Little Rock.

Stroke in Pregnancy and the Postpartum Period

Stroke is a rare but potentially devastating occurrence during pregnancy and the postpartum period. Maternal mortality is reported to be as high as 26%, and survivors may face long-term neurologic sequelae. Associated fetal mortality and morbidity also remain high. Although stroke is not preventable, early intervention can be key to saving lives and preserving brain function in some patients.

Therefore, even if the likelihood is that an obstetrician will never encounter a patient who suffers a stroke, it is critical that we all make the diagnosis promptly, obtain neurologic and other consultations appropriately, and direct state-of-the-art treatment of cerebrovascular disorders in this special population.

It is important to recognize that stroke occurs in young women of childbearing age at a rate of 10.7 per 100,000. Some have postulated that the risk is elevated during pregnancy for a number of reasons, including hypercoagulability, venous stasis, and blood pressure fluctuations. Indeed, some estimate that the risk of stroke is 13-fold higher in pregnant than in nonpregnant women, although the rarity of the condition makes the true prevalence a matter of debate.

Postpartum Risk Is Higher

The risk of stroke in the postpartum period is almost certainly higher still. Postpartum strokes generally occur from 5 days to 2 weeks after delivery—a vulnerable time when a headache from cerebral vasoconstriction syndrome may be mistaken for postepidural puncture syndrome.

The issue of stroke during pregnancy and the postpartum period is of increasing relevance to obstetricians. The incidence of stroke rises with age, and women are becoming pregnant at older ages than ever before; obstetric patients aged 45-50 years have become increasingly common. Obesity is also a risk factor for stroke, and pregnant women mirror American society at large, in which obesity has become epidemic. Longstanding hypertension and diabetes mellitus, both associated with

obesity, further increase the risk of stroke.

Stroke can happen at any time. The clinical presentation is similar to that seen in nonpregnant patients; however, these symptoms can mimic those seen in preeclampsia and eclampsia, and the possibility of stroke may be overlooked.

Another potential delay in diagnosis and treatment may arise in patients who, like many nonpregnant patients, hesitate to seek immediate medical care when experiencing symptoms of stroke. Headache, for example, is common in pregnancy. Some women do not take it seriously unless it is very severe.



BAHA SIBAI, M.D.

It is prudent to counsel all patients—and especially those with relevant risk factors—to seek care for any symptom that may be associated with stroke:

headache; visual changes; epigastric pain; seizures; nausea and vomiting; or neurologic defects (focal or global). Severe hypertension and widened pulse pressures are symptomatic of stroke as well.

Cerebrovascular events may be associated with drug ingestion, infection, neoplasms, or trauma, as well as with metabolic factors. Researchers have been unable to determine the etiology of stroke in 23%-32% of cases.

Many medical conditions increase the risk of stroke, including cardioembolic diseases such as rheumatic heart disease or atrial septal defects; atherosclerosis (which may account for 15%-25% of cerebral infarctions in pregnancy); and disorders such as sickle cell disease, thrombophilias, central venous thrombosis, arteriovenous malformations and aneurysms, and cerebral vasoconstrictive syndrome.

Risk factors believed to be associated with pregnancy and the postpartum period include cesarean delivery and pregnancy-related hypertension. The link to hypertensive disorders of pregnancy seems to be an association in numerous studies, yet it is important to recognize that hypertension may be the result of a stroke rather than its cause. Seizures and central neurologic insult can undermine cerebral autoregulation and cause blood pressure to rise. Eclampsia and stroke pro-

duce similar clinical laboratory and neuroimaging findings.

Review of Stroke Cases

In a review of our 20-year institutional experience with postpartum stroke, we identified 20 cases among 130,000 deliveries at the E.H. Crump Women's Hospital of the University of Tennessee in Memphis (Am. J. Obstet. Gynecol. 2000;183:83-8).

In all cases, patients were discharged and later readmitted with findings consistent with a diagnosis of stroke. The mean age of these patients was 26 years; the mean gestational age at delivery was 27.3 weeks; and the mean birthweight was 2,617 grams, representing a group of patients with earlier deliveries and lower birthweights who were somewhat older than our obstetric population in general.

Of these 20 patients, 6 had a history of chronic hypertension. Preeclampsia was present in four pregnancies, and eight patients (40%) underwent a cesarean delivery, a rate approximately threefold higher than that in our overall obstetric population.

C-sections were performed for various reasons: three for nonreassuring fetal status, three for failure to progress, one for malpresentation, and one as an elective repeat C-section. Importantly, no intrapartum or postpartum complications presaged stroke in any patient.

A review of antepartum, intrapartum, and in-hospital postpartum blood pressure values found normal measurements or well-controlled blood pressure in all women except one, whose blood pressure was elevated on postpartum day 3.

We found no correlation among trial of labor, mode of delivery, and the type of stroke suffered or outcome. We found no association with anesthesia type and stroke.

Presenting symptoms included headache in 16 patients, neurologic signs (motor weakness, blindness, aphasia, or coma) in 12, seizures in 11, and visual changes in 10.

Two deaths occurred, one associated with a cocaine-related hemorrhage and

the other with a ruptured anatomical malformation.

A review of the medical records suggested that no case could have been prevented by the recognition of risk factors or alternative medical care.

In the diagnosis of stroke, the history and physical examination are critically important, although imaging is often needed to further clarify the diagnosis and distinguish stroke type and features.

The two basic causes of stroke are ischemia and postpartum hemorrhage.

Ischemia (infarction) may be caused by vascular thrombosis, embolism, vasospasm, or marked reduction in systemic perfusion pressure (hypotensive ischemic injury).

Postpartum Hemorrhage

Postpartum hemorrhage is divided into intracerebral or subarachnoid hemorrhage. Intracerebral hemorrhage refers to bleeding directly into brain tissue from small intracerebral vessels, caused by severe hypertension and/or coagulopathy or vascular malformations. In subarachnoid hemorrhage, blood seeps onto the brain's surface and merges with ambient cerebrospinal fluid,

often as a result of a ruptured aneurysm or arteriovenous malformation.

Strokes of arterial origin most often occur during the second or third trimester, or within the first few weeks

post partum. Symptoms include acute decompensation of cortical function, aphasia, hemiplegia, and/or hemianopsia.

Strokes of venous origin, on the other hand, are most likely to occur from 3 days to 4 weeks after delivery. Common symptoms include a severe, progressive headache; papilledema; weakness; convulsions; and/or aphasia.

Our review of 20 postpartum cases involved cerebritis (12 women), venous infarction (7 women), arterial infarction (6), intracerebral hemorrhage (5), and atrophy (1).

Among the 18 patients who survived, 12 suffered no residual defects, whereas

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others suffered hemiparesis, aphasia, or weakness. Although not statistically significant, there appeared to be a trend toward more adverse outcomes in women who suffered intracerebral hemorrhage vs. cerebral infarction.

Neuroimaging studies should be performed in any patient with symptoms that may be consistent with stroke. CT is widely available and may be very useful in confirming the diagnosis; however, a negative CT should not rule out further testing in the face of suspicious symptoms and/or physical examination findings. In our series, the initial CT was negative in 3 of 20 patients, with subsequent MRI or MRI angiography required to accurately diagnose stroke and elucidate its features.

Four-vessel traditional angiography, echocardiography, and lumbar puncture are other diagnostic modalities.

How to Weigh Stroke History, Pregnancy

With enhanced diagnosis and management of stroke, more patients are recovering well. These patients will increasingly seek advice about the risks of subsequent pregnancy.

We recently conducted a review of 35 pregnancies in 23 women with a history of stroke, including 9 pregnancies in 4 women whose previous stroke had occurred during pregnancy or the postpartum period (*Am. J. Obstet. Gynecol.* 2004;190:1331-4).

Their risk factors for the prior stroke included thrombophilias, sickle cell disease, cardiac malformations, hypertension, oral contraceptive use, cerebral arteriovenous malformations, head trauma, meningitis, endocarditis, and idiopathic etiologies.

Anticoagulation was prescribed in two pregnancies in patients who had a reported history of pregnancy/postpartum stroke. Our findings were reassuring.

There were no recurrent thrombotic episodes during pregnancy or the postpartum period, although one patient required admission to the ICU for uncontrolled hypertension.

This result aligns with findings from another study (*Neurology* 2000;55:269-74), which found a 1% recurrence rate. The chance of recurrence in patients with thrombophilia is likely higher, perhaps 20%.

It makes sense to prescribe anticoagulation for women at risk of thromboembolic stroke, either low-dose aspirin plus prophylactic doses of unfractionated heparin, or low-molecular-weight heparin.

All women with a history of stroke deserve close monitoring during pregnancy, delivery, and the postpartum period.

Of course, appropriate consultation is an integral part of stroke management, and may include a maternal-fetal medicine specialist as well as neurologists, neurosurgeons, radiologists, anesthesiologists, and later, rehabilitation specialists, social workers, and physical and occupational therapists.

Treatment hinges on protecting salvageable brain tissue; stabilizing the patient and preventing further complications such as aspiration; controlling blood pressure and other physiologic factors; and initiating physical rehabilitation.

As evidenced in our series, young patients have a great capacity for recovery in many cases.

My overall recommendation for stroke management is to admit the patient to labor and delivery, perform a thorough maternal and fetal evaluation, and use a multidisciplinary approach to care throughout.

Order antihypertensive medication if the systolic blood pressure is 160 mm Hg or greater, the diastolic blood pressure is 110 mm Hg or greater, or if the mean arterial pressure is 125

mm Hg or greater.

Antiseizure, antiemetic, and anticoagulation medications should be administered as needed.

Neither medications nor surgery should be withheld because of pregnancy.

Deliver the patient in cases of maternal instability or nonreassuring fetal status; labor or rupture of membranes; or gestational age greater than 34 weeks.

When Intervention Is Necessary

At a gestational age of less than 24 weeks, intervention should be guided by the woman's diagnosis and condition.

Between 24 and 32 weeks' gestation, administer steroids for fetal lung maturity and conduct daily reassessments of the maternal and fetal condition with a planned delivery at 34 weeks, or term delivery if circumstances warrant.

Between 33 and 34 weeks, steroids should be administered and the baby delivered.

The nature of the stroke will determine the best course of medical and surgical management for the cerebrovascular event.

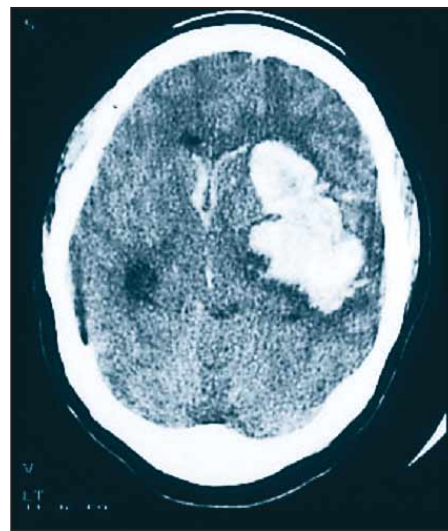
When anticoagulation is needed, keep in mind that warfarin crosses the placenta and has been linked to teratogenicity in the first trimester and bleeding complications in the third trimester. Heparin has been associated with thrombocytopenia, osteoporosis, and bleeding disorders, although it does not cross the placenta. After vaginal delivery, I recommend withholding anticoagulation for 6 hours. I recommend withholding anticoagulation for 12 hours following C-section.

When infection is implicated in stroke, antibiotics should be administered along with anticoagulation.

Low-dose aspirin may be sufficient to treat patients with a single episode of transient ischemic attack.

Hypertensive encephalopathy requires intensive management during labor and for 48 hours post partum. Response to antihy-

Even though occurrence is rare, it calls for prompt diagnosis and direct state-of-the-art treatment of cerebrovascular disorders in this special population.



This CT shows the brain of a pregnant woman who had a hemorrhagic stroke.



This MRI shows the brain of a pregnant woman who had an ischemic stroke.

pertensive therapy confirms the diagnosis. Volume contraction may be present, evidenced by a sharp drop in diastolic blood pressure and a rise in heart rate on standing from the supine position. Normal saline infusion for 24-48 hours may be considered to achieve volume expansion, decrease the

activity of the renin-angiotensin-aldosterone axis, and maintain better blood pressure control. Careful attention should be paid to volume status, blood pressure urinary output, electrocardiographic readings, and

mental status. Antepartum patients should have continuous fetal monitoring.

Eclampsia is treated with supportive care, including oxygenation; minimization of aspiration and future injuries; and lowering of blood pressure. Magnesium sulfate is used for the prevention of eclamptic seizures, although seizures may persist in 10% of patients. The medication should be maintained throughout labor and for 24 hours post partum.

Disturbances in the fetal heart rate are commonly seen after an eclamptic seizure, although resolution usually occurs within 5-10 minutes. Proceed to cesarean delivery only for obstetric indications, as vaginal delivery is preferred following a seizure.

Labor can be induced with oxytocin or prostaglandins.

Carefully monitor the patient's overall fluid status. These patients may have pro-

found hemoconcentration, which necessitates close hemodynamic monitoring when epidural anesthesia is used and after severe blood loss. Acute blood loss can be a serious complication in hypovolemic patients. Limit fluids to prevent pulmonary edema secondary to capillary leakage.

Thrombolytic therapy with intraarterial re-

combinant tissue plasminogen activator has been used to treat ischemic stroke in pregnancy. This treatment must be administered within a window of 6 hours or less to be effective.

Course of Treatment

Patients who receive a diagnosis of arteriovenous malformation or aneurysm before hemorrhage should be referred for surgical embolization or clipping, as it is believed that patients with AVM may be at increased risk of bleeding during pregnancy. Patients with AVMs are also prone to bleed during delivery.

Once an intracerebral hemorrhage has occurred, the extent of the bleeding will determine the course of treatment. If the brain stem is compromised, surgical decompression is necessary. Surgery may also be necessary if the bleed is subarachnoid in origin; however, surgery itself may damage overlying normal brain tissue, and surgical morbidity is high.

If the bleeding and the patient are stable, surgery can be avoided. Blood pressure should be well controlled and seizures prevented. Steroids have not proven beneficial.

In summary, I would encourage obstetricians to become well versed in the symptoms of stroke and to have a low threshold for clinical suspicion of such symptoms, which may mimic common complaints of pregnancy.

A rapid diagnosis and close consultation with an interdisciplinary team of colleagues may maximize outcome in patients suffering one of the most feared and serious complications of pregnancy. ■

DATA WATCH

Rising Cost of Hospital Stay for Acute Cerebrovascular Disease



Source: Agency for Healthcare Research and Quality