



Stroke in Pregnancy

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- **9,000 Deliveries per year**
- **NICU-one of the largest in the country**
- **1500 serious and critically ill newborns per year**

Incidence of Stroke in Pregnancy

- Stroke is a rare but serious complication of pregnancy.
- It is the most common cause of serious long term disability after pregnancy
- It occurs in 30 per 100,000 deliveries.
- Risk of stroke is 3 fold higher in women during pregnancy and the postpartum period than age matched non-pregnant women.

Incidence of Stroke in Pregnancy

- The highest risk occurs within the peripartum period, 2 days prior to and one day after delivery but persists up to 6 weeks postpartum
- Ischemic strokes are more common prior to delivery
- Hemorrhagic strokes are more common in the postpartum period

Risk Factors for Stroke in Pregnancy

- Hypertension
- Diabetes
- African American Race
- Cardiac Valve Disease
- Hypercoagulable Disorders
- Sickle Cell Anemia
- Systemic Lupus Erythema
- Chronic Kidney Disease
- Tobacco Use
- Substance Abuse
- Migraine

Risk Factors for Stroke in Pregnancy

Pregnancy Induced Risk Factors

- Gestational Hypertension
- Preeclampsia/Eclampsia
- Hyperemesis Gravidarum
- Pregnancy Induced Cardiomyopathy



Risk Factors for Stroke in Pregnancy

Physiologic changes in pregnancy

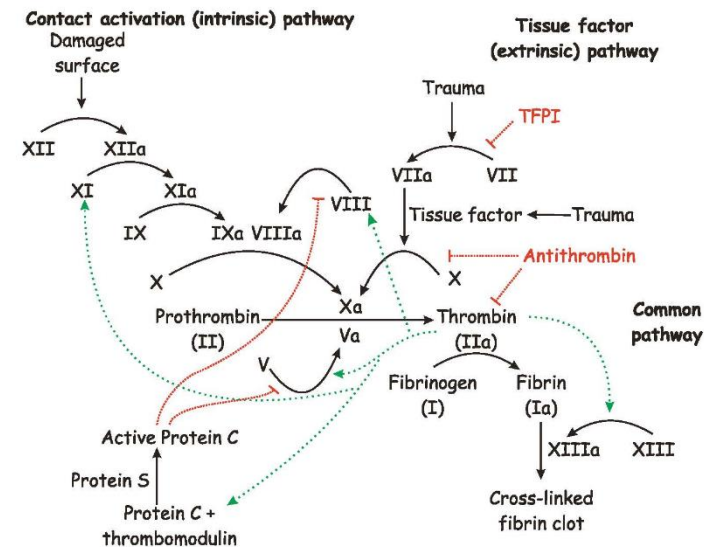
- Increased plasma volume
- Increased cardiac output
- All 4 cardiac chambers and valves enlarge
- Hypercoagulable state in 3rd trimester and postpartum



Risk Factors Stroke in Pregnancy

Pro-thrombotic state with an increase in procoagulant factors as pregnancy progresses

- Fibrinogen increases
- Fibrinolytic activity decreases
- Increase in Factors VIII, IX, X
- Protein S decreases
- Functional protein C resistance
- Prothrombin fragments increase



https://en.wikipedia.org/wiki/File:Coagulation_full.svg

Mechanism of Stroke in Pregnancy

Ischemic Stroke

- Cardiac Embolism
 - Amniotic Fluid Embolism
 - Cervical Artery Dissection
 - Cerebral Venous Thrombosis
 - Reversible Cerebral Vasoconstrictive Syndrome
 - Posterior Reversible Encephalopathy Syndrome
- Chamber enlargement
Right to left shunt
Neck strain during labor
Hypercoagulable state
Venous infarcts
Endothelial dysfunction
Preeclampsia/Eclampsia

Mechanism of Stroke in Pregnancy

Hemorrhagic Stroke

- Preeclampsia/Eclampsia
- Cerebral Venous Thrombosis
- Ruptured Cerebral Aneurysm
- Arteriovenous Malformation



Preeclampsia and Eclampsia

- Preeclampsia affects 4.6 % of pregnancies
- Linked to intracerebral hemorrhage
- Most common cause of stroke in pregnancy

Preeclampsia and Eclampsia

- May occur after gestational week 20 until 8 weeks post-partum.
- Preeclampsia: HTN, proteinuria and edema.
- Eclampsia: HTN, proteinuria, and edema + seizures.

Preeclampsia and Eclampsia

- Eclampsia causes 60,000 maternal deaths per year worldwide.
- 1-2% of patients with severe preeclampsia will go on to develop eclampsia.
- Mortality rate of up to 14%



Preeclampsia and Eclampsia

Hypertension: Diastolic blood pressure of at least 90 mm Hg or a rise of at least 15 mm Hg; systolic blood pressure of at least 140 mm Hg or a rise of at least 30 mm HG (measured on 2 occasions, 6 hours or more apart)

Proteinuria: Greater than 300 mg in 24-hour urine collection or 30 mg/dl in 2 random urine specimens collected 6 hours apart.

Edema: Weight gain of 5 pounds over a week, 2+ pitting edema

Oliguria: Less than 400 ml urine in 24 hours*

Neurologic Symptoms: Stupor, headache, scotoma, blurred vision*

Pulmonary: Edema, cyanosis*

Gastrointestinal: Hepatic dysfunction, right upper quadrant or epigastric pain*

Hematologic: Thrombocytopenia, hemolytic anemia*

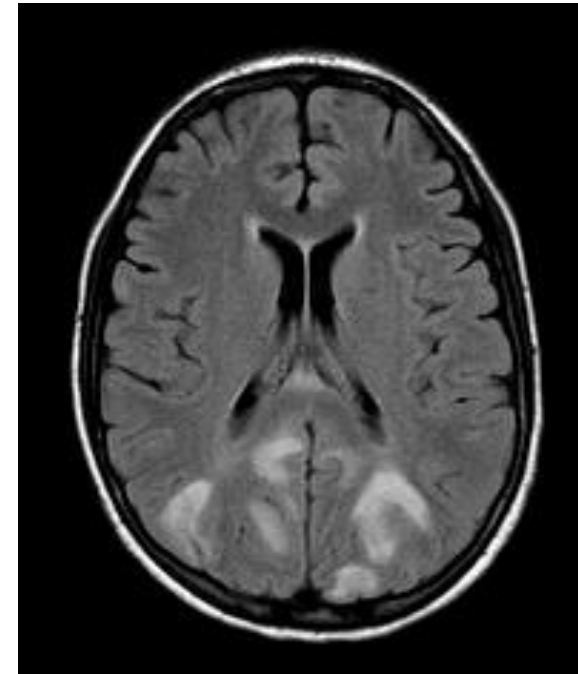
*Diagnostic criteria for severe preeclampsia

Preeclampsia and Eclampsia

Posterior Reversible Encephelopathy Syndrome PRES

Distinctive clinikoradiologic syndrome

- Acute Hypertension
- Headache (may be thunderclap)
- Visual auras and field cuts
- Altered mental status
- Seizures



Posterior Reversible Encephalopathy Syndrome *PRES*

May or may not be associated with preeclampsia/eclampsia

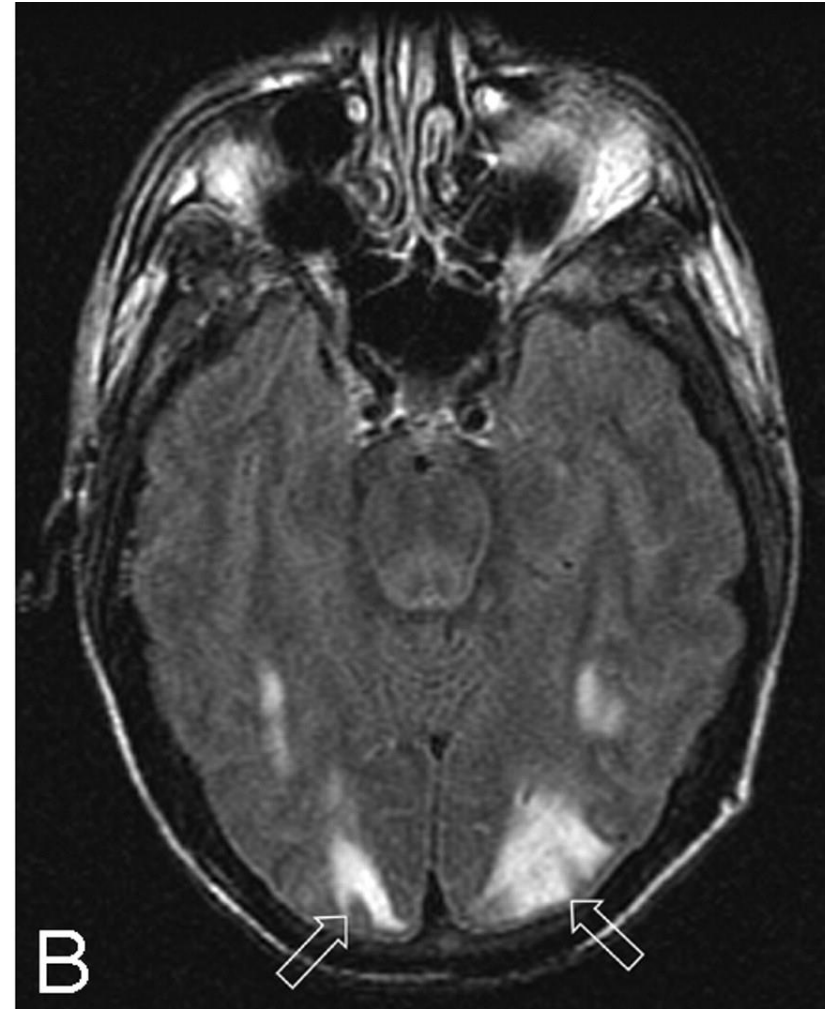
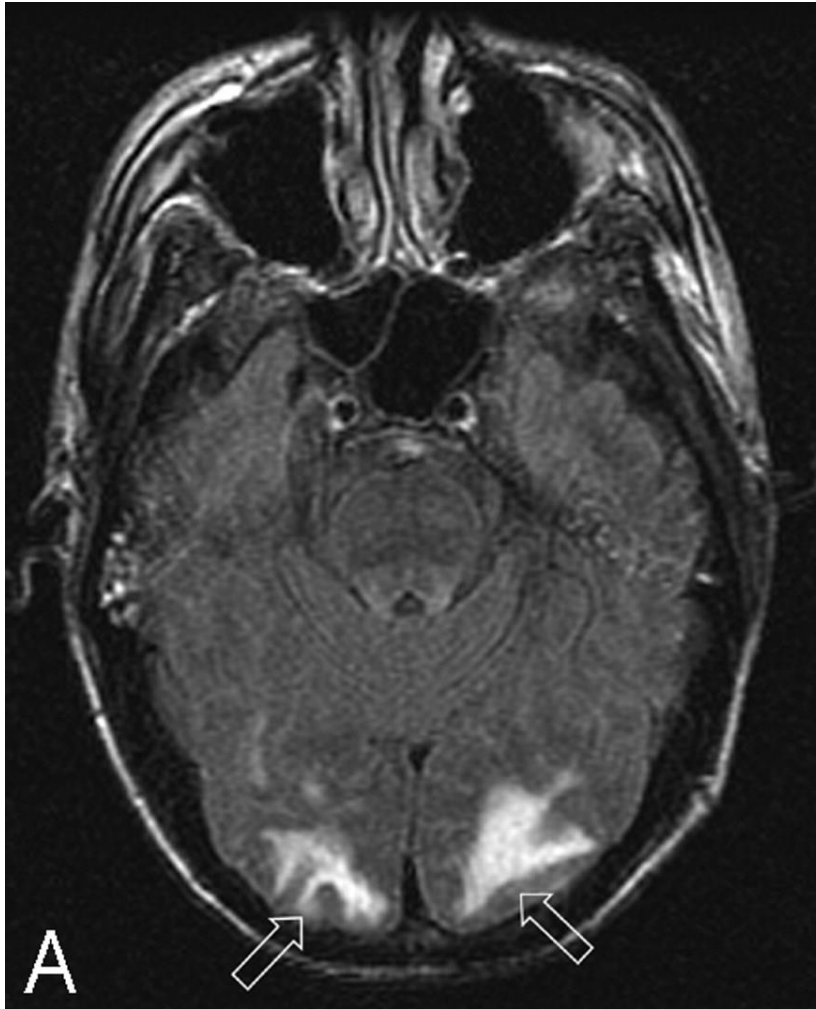
Patients develop vasogenic cerebral edema due to impaired cerebral autoregulation and endothelial dysfunction.

Often triggered by arterial hypertension.

Classic brain MRI findings: T2/fluid attenuated inversion

Recovery hyperintensities with parieto-occipital predominance.

Preeclampsia and Eclampsia



Neurology in Pregnancy Neuroimaging Considerations

- MRI is the diagnostic modality of choice during pregnancy.
- Gadolinium contrast is FDA class C and should be avoided during pregnancy when possible. In animal studies, it has been associated with spontaneous abortion and developmental anomalies.
- Imaging of the arterial and venous circulation can be performed using time-of-flight sequences.
- During breast-feeding, gadolinium administration is not contraindicated.
- In an emergency setting, CT scan may be the best choice

Case 1

A 36 year old female who was pregnant with her first child was at 37 weeks gestation when she developed visual loss in the left side of both eyes. She was brought to her local emergency room where she was noted to have a blood pressure of 180/100 and heart rate was 92. Neurologic exam revealed a right homonymous hemianopsia. She complained of headache and then became lethargic. CT scan of the head revealed no hemorrhage. A stroke alert was initiated and she was lifeflighted to Presbyterian Hospital. On arrival, she began to have a generalized tonic clonic seizure.

Case 1

The patient was seen by the neurology resident on the stroke service. General exam revealed 3 plus pitting edema. Neurologic exam revealed a lethargic, postictal patient with hyperreflexia. Recognizing the signs of eclampsia, the resident loaded her with Magnesium and sent her by ambulance to Magee Women's Hospital where the OB staff awaited her arrival. She was delivered by emergency cesarean section. When examined the following day, the patient was awake, alert, smiling while holding her newborn. Her visual loss had resolved.

Cerebral Venous Thrombosis

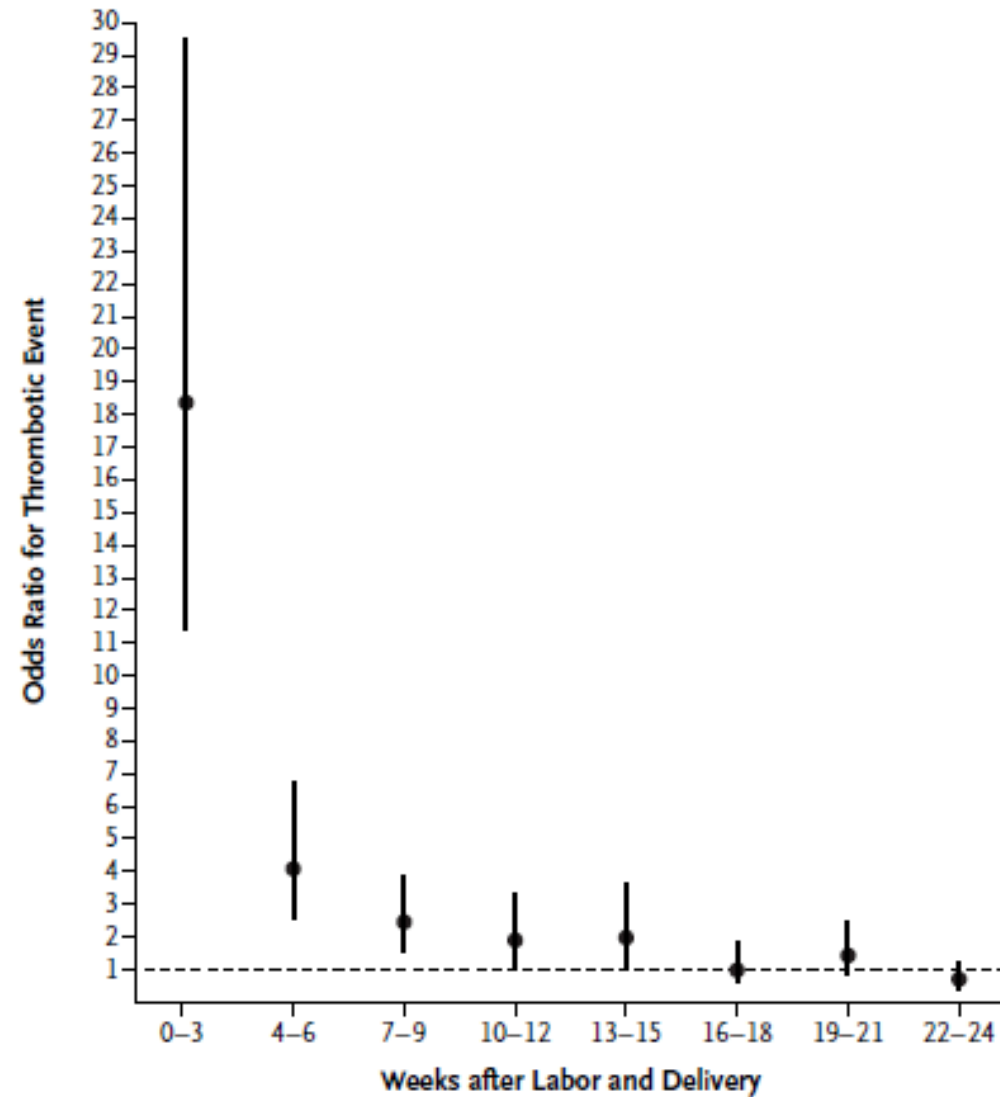
In the third trimester of pregnancy and postpartum period, women are in a hypercoaguable state.

Blood clot may form in the cerebral veins causing cerebral venous obstruction.

Venous infarcts may form producing focal deficits, hemorrhages and seizures.

Coma and death can follow.

Risk of thrombosis after delivery



Kamel et al. NEJM 2014

Cerebral Venous Thrombosis

Postpartum women are particularly susceptible.

Study of 113 cases of aseptic CVT

5 occurred during pregnancy

67 occurred during puerperium

Increased risk in women with hereditary hypercoagulability.

Damaged endothelium from pushing in labor, intracranial hypotension after epidural and postpartum diuresis may also contribute to risk.

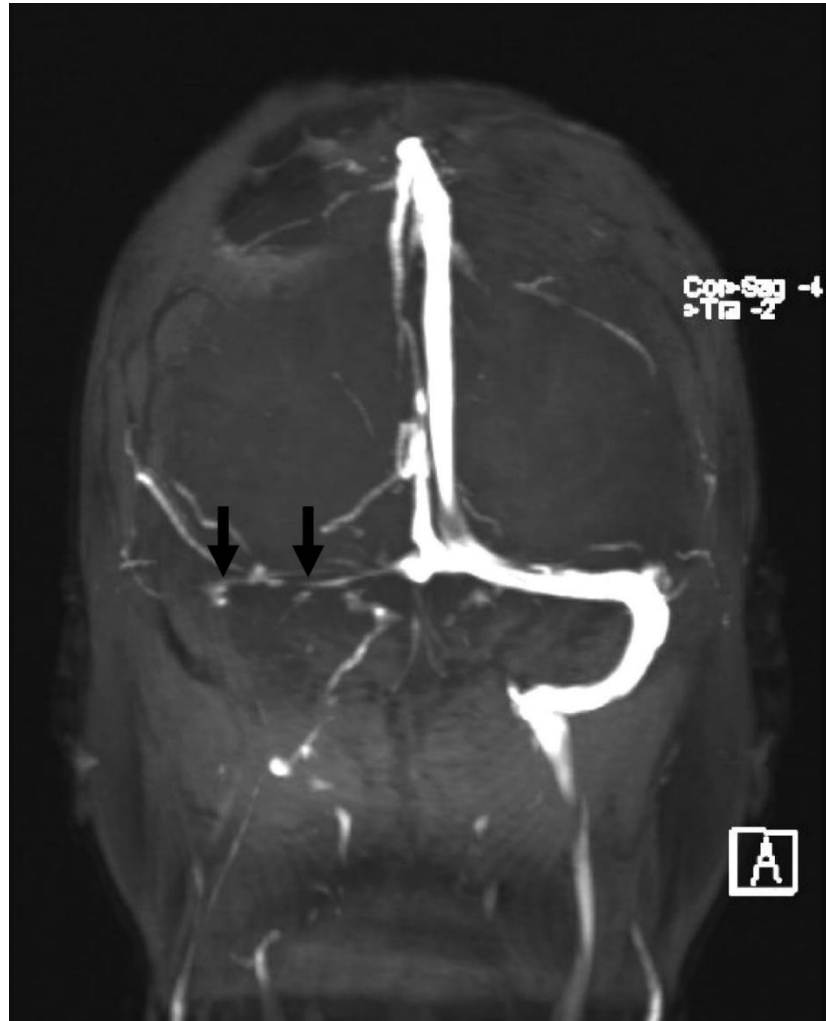
Case 2

The patient is a 32 year old female who underwent epidural anesthesia prior to vaginal delivery. Epidural placement was challenging due to body habitus. Inadvertent dural puncture occurred. The following day the patient developed a postural headache. It was bilateral, severe and was associated with “echoing” hearing change. The patient was treated with hydration and Tylenol without improvement. She underwent a blood patch and symptoms improved. She was discharged to home but returned to the ER the following day with complaints of persisting headache.

Case 2

She received a second blood patch, noted partial improvement and was discharged to home. She contacted the Chief of Anesthesia 2 days later complaining of persisting headache symptoms. Arrangements were made for her to be seen in the OB Neurology clinic the following day.

The patient complained of severe diffuse headache. She also reported echoing sound quality and blurred vision. She had no history of migraines. She did not report photophobia or phonophobia. Neurologic exam was non-focal. The patient underwent MRI and MRA which were normal. MRV revealed cerebral venous thrombosis.



**Cerebral Venous
Thrombosis**

Cerebral Venous Thrombosis Treatment

- Heparin may be started 24 hours after delivery.
- Begin warfarin 48-72 hours later
- Continue Coumadin for 3-6 months, then stop and obtain hypercoagulation panel one month later to rule out other factors contributing
- Use of heparin and warfarin are safe in breastfeeding mothers.

Ruptured Cerebral Aneurysm

- Risk of aneurysmal rupture during pregnancy rises with gestational age and peaks at 30-34 weeks.
- If a ruptured aneurysm is left untreated, maternal mortality is 63% with fetal mortality of 27%.
- Early surgical intervention lowers risk to 11% and 5% respectively.
- Unruptured aneurysms often found as incidental finding in pregnant women with headaches. Studies show that the risk of bleeding during delivery is the same for those delivered by cesarean and vaginal delivery.

Arteriovenous Malformations

- Risk of Hemorrhage of unruptured AVM in pregnant and non-pregnant women is roughly equal.
- When an AVM bleeds during pregnancy, risk of rebleeding during pregnancy exceeds risk of rebleeding in the non-pregnant population.
- Several fold risk of bleeding on the day of delivery.
- Risk of bleed on day of delivery is the same regardless of mode of delivery

Reversible Cerebral Vasoconstrictive Syndromes

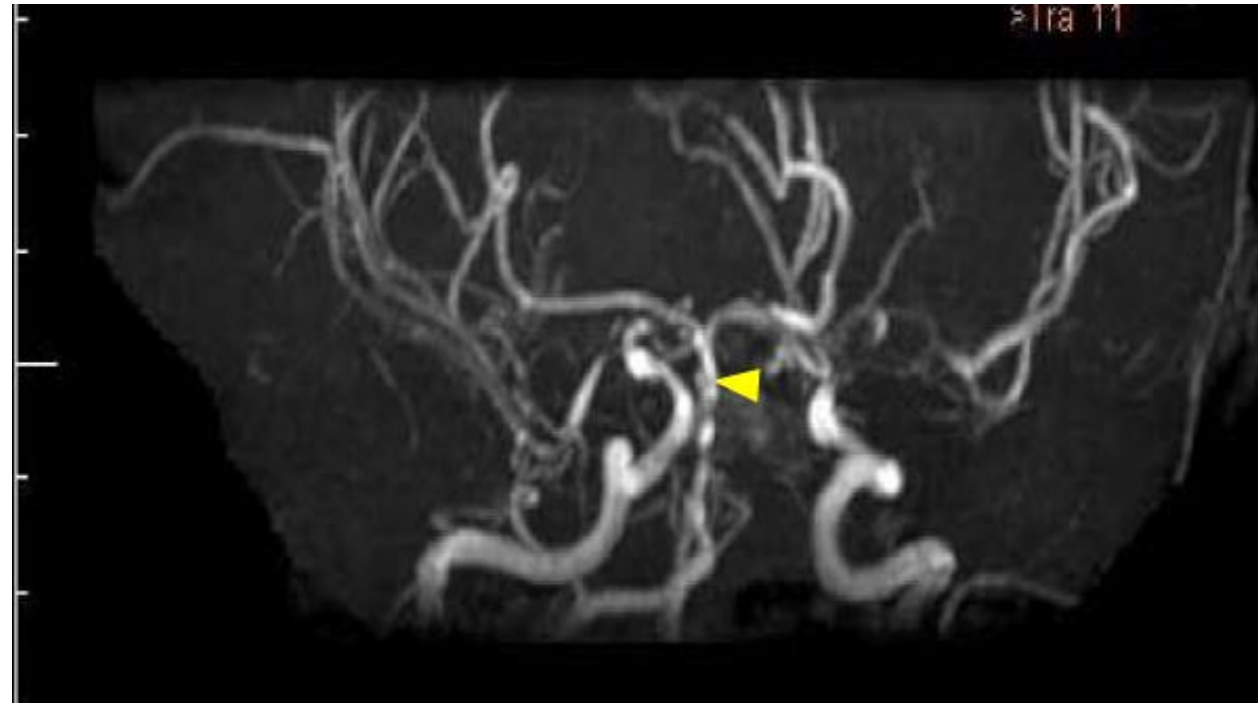
- Previously known as Postpartum Angiopathy
- Patients develop multifocal intracranial arterial vasoconstriction
- Symptoms
 - Recurrent severe thunderclap headaches
 - Can be associated with focal deficits, confusion, and seizures
- 2/3 occur within 7 days postpartum, usually following an uncomplicated delivery.
- Angiogram reveals narrowing and dilatation of one or more cerebral arteries in a segmented multifocal pattern. “String of beads”

Reversible Cerebral Vasoconstrictive Syndromes

- Subarachnoid Hemorrhages occur in 22% of patients
- Ischemic or hemorrhagic parenchymal stroke occurs in 7%
- 10% co-occur with PRES
- Exposure to some medications appear to be a trigger:
 - » SSRI's
 - » Ergot alkaloids
 - » Epinephrine in epidural anesthetic agent

Reversible Cerebral Vasoconstrictive Syndromes

- CTA or formal angiogram to evaluate for classic “string of beads” appearance



Carotid Dissection

Rare cause of postpartum stroke

Occurs when the arterial wall integrity is disrupted allowing blood to penetrate and collect between its layers

If collection becomes large enough, arterial occlusion can occur producing a stroke.

Patients present with headache and neck pain

Can be associated with Horner's Syndrome

- Ptosis

- Miosis

- Anhydrosis

Case 3

A 28 year old female at 39 weeks gestation began to experience regular contractions at home. She presented to the triage unit at Magee Women's Hospital. While attempting to check in at the registration desk, she suddenly developed difficulty with word finding. She misused words and speech was not intelligible. When she attempted to write, her right arm became flaccid. She was brought promptly into the emergency room where a stroke alert was called.

Case 3

On exam, blood pressure was 122/72. Pulse was 80. General exam revealed a pregnant female with normal heart sounds, normal respirations and no carotid bruits. No edema was present in the lower extremities. Neurologic examination revealed an awake, alert female with aphasia. She was unable to name simple body parts. She used neologisms in her speech. She was able to follow demonstrated commands better than verbal commands. Cranial nerve exam revealed a slight decrease in her right nasolabial fold. She was unable to lift her right arm against gravity. Power in other extremities was normal. Sensory exam was difficult to assess due to her aphasia. Reflexes were intact. Stat non-contrast MRI of the brain, MR angiogram of the head and neck, and MR venogram were ordered. Administration of TPA was considered.

Case 3

After returning from MRI, the patient's symptoms were noted to be significantly improved. She was able to communicate to some degree and complained of a throbbing right sided retro-orbital headache. At that point her husband arrived and provided further history. The patient had similar presentation on 3 occasions and had undergone extensive evaluations at other facilities. She was diagnosed with migraine with aura. She was monitored in the ICU and treated with IV Tylenol and hydration. Fetal monitoring was reassuring. Headache improved, labor progressed, and the patient delivered a health baby girl.

Case 4

34 year old obese female G1P0 at 31 weeks gestation who acutely developed left-sided weakness and neglect at 10:40 PM. She arrived and was seen in the ED at 1 hour from symptom onset.

No medications

BP 149/76. NIHSS 12

Glucose 102

Labs notable for Hb 10.7 and platelets 110,000

CTH within normal limits

Case 4 - Differential diagnosis

- Ischemic stroke (vs hemorrhagic stroke)
- Preeclampsia +/- posterior reversible encephalopathy syndrome
- Venous infarct due to cerebral venous thrombosis
- Migraine with aura

Treatment considerations during pregnancy

- Stat CT scan of the head was normal
- Should we give tPA?
 - Large molecule that does not cross the placenta
 - Pregnancy category C
 - Same risk of intracranial hemorrhage as in the general population.
 - One case report of intrauterine hemorrhage
- 2018 AHA/ASA Guidelines
 - IV TPA administration may be considered in pregnancy when the anticipated benefits of treating moderate or severe stroke outweighs the anticipated increased risks of uterine bleeding

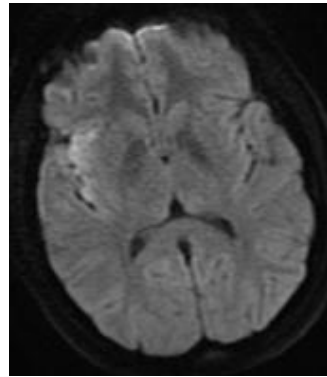
Treatment considerations during pregnancy

- Is endovascular therapy an option?
 - Case reports with good outcomes

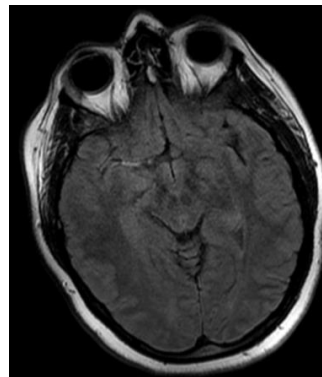


Case 4

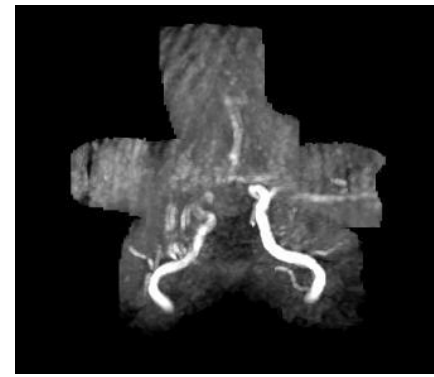
- tPA was not given and MRI/MRA was obtained



DWI



T2 FLAIR



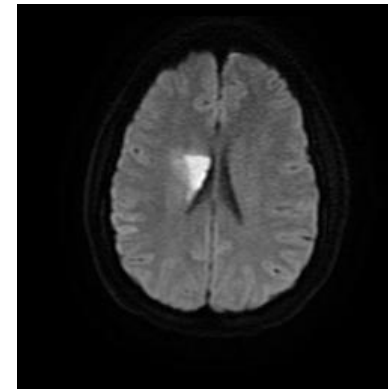
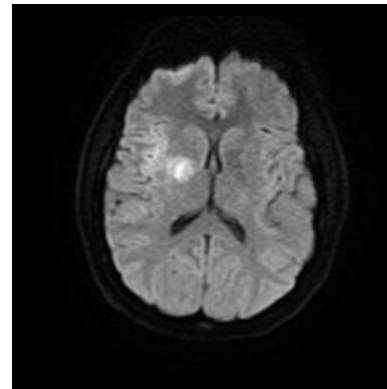
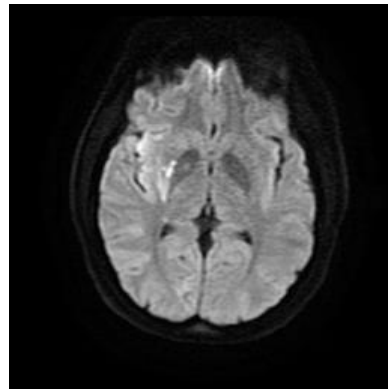
MRA-TOF

Case 4

A cerebral angiogram demonstrated a right ICA terminus occlusion requiring 3 passes of manual aspiration, 2 passes of stent retriever device, and finally angioplasty with 2 balloon mounted coronary. Recanalization was achieved with door to reperfusion time of 3 hours and 19 minutes. The platelet inhibitor Eptifibatide was given during the procedure and the patient was loaded with clopidogrel and aspirin, with a recommendation to continue clopidogrel 75 mg and aspirin 81 mg daily. NIHSS post-procedure was 1. NIHSS was 0 the following day.

Case 4

- Cerebral angiography demonstrated R ICA terminus occlusion requiring extensive thrombectomy and intracranial stenting
- NIHSS 12 → 1



Case 4

Planning delivery in a patient on Plavix and Aspirin.

Multidisciplinary team

- Obstetrics
- Neurology
- Stroke Team
- Obstetrical anesthesia
- Pharmacist

Case 4

Stroke team: patient at high risk of reocclusion if take off of Plavix

Anesthesiology: Epidural or spinal anesthesia contraindicated

Obstetrician: Patient at risk for hemorrhage if delivery done while on Plavix

Solution: Transition to IV antiplatelet agent Cangrelor.

Case 4

The patient did not feel she would be able to undergo a prolonged labor without access to neuraxial anesthesia and elective cesarean section under general anesthesia was planned.



Case 3

Five days prior to the scheduled cesarean section, clopidogrel was discontinued and the Cangrelor IV continuous infusion was initiated at a rate of 0.75 mcg/kg/min. ICU status was maintained to ensure rapid response to loss of IV or tubing occlusion given the extremely short offset of effect of the medication. Aspirin was continued. The patient was type and cross matched for blood products and the blood bank made aware of the high-risk nature of the surgery so that if necessary, a massive transfusion protocol could be initiated.



Case 4

The patient was monitored during delivery by EEG and somatosensory evoke potential. The stroke team was on alert to be ready for intervention should the patient occlude her stents during delivery. The patient was prepped and draped, and underwent general anesthesia induction. The cangrelor infusion was paused at the time of skin incision. The cesarean section was uncomplicated. After hemostasis of the uterine incision was achieved (25 minutes from incision to closure), the cangrelor infusion was restarted. Estimated blood loss was 400 cc.

The mother recovered uneventfully and the baby did well.

