Neuroimaging of Headaches in Pregnancy

Dara G. Jamieson, M.D.
Associate Professor of Clinical Neurology

Disclosures:
Speaker, Consultant: Boehringer – Ingelheim
Consultant: Bayer

Pregnancy Changes
Increased: blood volume, cardiac output, stroke volume
- Mild increase in coagulopathy
  - increased fibrinogen, vWF, FVIII, plasminogen activator inhibitors, platelet aggregation, protein C resistance;
  - decreased: protein S, ATIII
- Venous stasis
  - IVC, iliac v. compression

Headaches & Imaging
Many/most primary headaches are not need to be imaged.
- Avoid CT scans for patients with chronic headaches.
- Use MRI to image most chronic headache patients.
- Unnecessary imaging is increasing.

Prevalence of Incidentalomas: a function of excessive headache imaging

Migraine Patients
Subcortical white matter lesions: 6 - 40%
General Population
Developmental venous anomaly: 5 - 10%
Cerebral aneurysm: 1 - 5%
Cavernous malformation: 0.1 - 0.5%
Chiari I malformation: 0.1 - 0.5%

Imaging in Pregnancy
CT of head (no contrast)
- Ionizing radiation; less information than MRI; generally avoid
CTA of head/neck
- Contrast dye – prescribed; MRI - alternative
MRI/MRA (no contrast)
- Consents: EM fields causing teratogenicity; acoustic noise
  - Results: No evidence of fetal effects from EM fields
  - 1.5T in 1st trimester: no neonatal hearing loss
  - Suggestions: Maternal diagnosis trumps fetal risk
  - Imaging appears safe even in early pregnancy
  - 1.5T MRI if possible, as late as possible
- Gad should rarely be used

Headache in Pregnancy
1st trimester
- Primary headaches
  - Tumor – increased vascularity, inflammation
- Post-partum
  - Post-dural puncture headache - immediate
  - Cerebrovascular disease – first 6 weeks

Headache in Pregnancy
- Primary headaches
  - Migraines
    - Most common cause of headaches in pregnancy, including “thunderclap headache”
    - Period/worsen during 2nd & 3rd trimesters
    - Improved/resolved during 2nd & 3rd trimesters
    - New onset migraines may occur pregnancy
    - Imaging is rarely needed: measure, monitor
Headache in Pregnancy

1st trimester
• Primary headaches
2nd/3rd trimesters
• Tumor – increased vascularity, inflammation

Post-partum
• Post-dural puncture headache - immediate
• Cerebrovascular disease – first 6 weeks

Positional headache while pregnant

A 34 year old pregnant woman developed positional headaches whenever she bent over, lowered her head, sneezed or coughed starting a couple weeks prior to imaging. She denied nausea, vomiting, sensitivity to light or sound, or visual changes.

Headache in a 34 year old pregnant woman

• CC (7-28-10): Headache, vision loss
• HPI: 34 year old woman noted 3 weeks of headaches, different from her usual migraines. Headaches were holocephalic with photo/phonophobia and nausea/vomiting.
• For 2 weeks she noted L, then R, peripheral visual loss
• 32 weeks pregnant, G4P1012
• PMH: Migraines: (L temporal throbbing)
  MRI brain obtained 9-18-08

Positional headache while pregnant

Pituitary Hemorrhage

Sxs: headache, VF deficit, ophthalmoplegia, decreased consciousness, pituitary dysfunction
Causes: pregnancy, tumor, XRT, head trauma, blood pressure alterations, cardiac surgery, anticoagulation, dopamine agonists

Headache and vision loss in a 34 year old pregnant woman

MRI 9-18-08

• General medical examination was normal
• Mental status intact
• On CN testing:
  – VA: 20/40 to 20/20 ph OD, 20/200 in nasal field OS
  – Color: 10/10 OD, 1/10 OS
  – Pupils: APD OS
  – VF: supertemporal defect OD, full temporal defect OS
  – Rest of CN testing normal
• Motor, sensory, reflex, coordination, gait - normal

Headache and vision loss in a pregnant woman

How would you manage this woman?
A Instruct the neurosurgeon to resect the lesion.
B Instruct the neurosurgeon to get a small biopsy of the lesion.
C Give steroids and follow the lesion.
D Deliver the baby and perform an angiogram.
Headache and vision loss in a 34 year old pregnant woman

- CBC: hemoglobin 9.6
- Prolactin 93 (3.3-26.7 ng/mL)
- TSH, serum cortisol, ACTH: normal
- LH, FSH low c/w pregnancy
- ESR 62, CRP<0.5

A diagnostic procedure was performed.

Headache and vision loss in a 34 year old pregnant woman

- Underwent an endoscopic transphenoidal biopsy on 8-2-10
- The pituitary gland was enlarged with a posterior-superior hemorrhagic necrotic cyst.
- No evidence of adenoma was noted on the frozen specimens.
- The hypertrophic, normal gland was left intact.
- The dura was repaired; a fat autograft was placed in the pituitary cavity defect.

Classification of hypophysitis

- Primary
  - Lymphocytic hypophysitis
  - Granulomatous hypophysitis
  - Xanthomatous hypophysitis
- Secondary
  - Systemic Disease
    - Takayasu's disease
    - Crohn's disease
    - Langerhans cell histiocytosis
    - Sarcoidosis
    - Inflammatory pseudotumor
  - Infective
    - Bacterial
    - Fungal

Lymphocytic hypophysitis

- Autoimmune disease of the anterior > posterior pituitary
- Most common in peri-partum women
- Can occur in non-pregnant women, men
- Presents with headache, loss of vision, endocrine dysfunction
- Dxs to consider: pituitary adenoma, pituitary apoplexy, meningo, infectious or inflammatory processes
- Antipituitary antibodies (APAs) not a diagnostic tool for LYH.

MRI features of lymphocytic hypophysitis and pituitary macroadenoma

<table>
<thead>
<tr>
<th>MRI characteristics</th>
<th>Hypophysitis</th>
<th>Macroadenoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal on T1</td>
<td>Relatively low</td>
<td>Isointense</td>
</tr>
<tr>
<td>Signal on T2</td>
<td>High</td>
<td>Usually isointense</td>
</tr>
<tr>
<td>Contrast Enhancement</td>
<td>Marked</td>
<td>Moderate</td>
</tr>
<tr>
<td>Pattern of</td>
<td>Homogeneous</td>
<td>Focal</td>
</tr>
<tr>
<td>Dural Enhancement</td>
<td>Common (“dural tail”)</td>
<td>Rare</td>
</tr>
<tr>
<td>Shape</td>
<td>Symmetric</td>
<td>Dumbbell</td>
</tr>
</tbody>
</table>

Headache in Pregnancy

1st trimester
- Primary headaches
  - 2nd/3rd trimesters
- Tumor – increased vascularity, inflammation

Peri-partum/Post-partum
- Post-dural puncture headache – immediate
- Cerebrovascular disease – first 6 weeks postpartum
A 34 year old healthy woman noted a headache after childbirth. The headache was severe when standing, was worse on sitting. An MRI was obtained 5 days later.

**Post-partum Positional Headache**

- Postural headache (standing-worse or better)
- MRI
  - Pachymeningeal enhancement (venous congestion)
  - Sagging of the linea
  - Sagittal fluid collections
  - Spinal meningeal diverticula
- Low OP on LP
- CT myelography, MR imaging
- MR myelography (MRM) more sensitive than radioisotope cisternography (RIC)
- Improvement with time or epidural patching

**PPD2**

**PPD7** 15 months later

**Post Dural Puncture Headache on Spontaneous Intracranial Hypotension**

- Positional headache (standing-worse or better)
- MRI
- Low OP on LP
- CT myelography, MR imaging
- MR myelography (MRM) more sensitive than radioisotope cisternography (RIC)
- Improvement with time or epidural patching

**PDPH causing CVT**

A week later she presented again with several days of increasing headache. MRI/MRV showed thrombotic superior sagittal sinus, transverse sinuses, sigmoid sinuses, R IJ vein and superficial cortical vein.

**Pregnancy, Cerebrovascular Disease & Headache**

- PRES/Reversible Cerebral Vasoconstriction Syndrome Spectrum
  - Pre-eclampsia, Eclampsia, HELLP, Postpartum cerebral angiopathy
- Intracranial Hemorrhage – ICH, SAH
- Cerebral Venous Thrombosis
- Arterial Ischemic Stroke
  - Thrombotic
  - Embolic (30% cardioembolic)
  - Venous thrombus (paradoxical embolization)
  - Fat
  - Arterial fluid
  - Air (perigastal seal)
  - Choriocarcinoma
  - Arterial dissection
  - Arterial pathology (psamm, arteritis)

**Pregnancy, Cerebrovascular Disease & Headache**

- PRES/Reversible Cerebral Vasoconstriction Syndrome Spectrum
  - Pre-eclampsia, Eclampsia, HELLP, Postpartum cerebral angiopathy
- Intracranial Hemorrhage – ICH, SAH
- Cerebral Venous Thrombosis
- Arterial Ischemic Stroke
  - Thrombotic
  - Embolic (30% cardioembolic)
  - Venous thrombus (paradoxical embolization)
  - Fat
  - Arterial fluid
  - Air (perigastal seal)
  - Choriocarcinoma
  - Arterial dissection
  - Arterial pathology (psamm, arteritis)

**PDPH causing CVT**

The woman continued on warfarin (with intermittent compliance), neurologically intact. Repeat MRV 15 months later showed recanalization of the superior sagittal sinus, distal right transverse sinus and the right internal jugular vein. New lesions noted on MRI, 15 months later, were suspicious for demyelination.

**Post-partum ischemic stroke due to arterial dissections**

- Single or multiple vessels
- Days to 1 month after vaginal or sectioned delivery
- Not associated with underlying connective tissue disorder
- Can occur in cardiac, renal arteries
- Resembling preeclampsia cardiopathy unknown
Post-Partum Headache

• 40 year old woman G2P1
• Normal past medical history; prior pregnancy with post-partum bleeding
• Conceived with Clomid and artificial insemination
• Pregnancy BPs 120-130/60-80
• Delivered normal infant at term by C-section
• Day 3: d/c’d with BP 127/73 and a headache

Post-Partum Headache

• Day 8: vaginal bleeding; headache; BP 160/84; admitted to hospital; LE edema
• Day 9: headache; BP 174/81; methergine; d/c’d to home
• Day 17: admitted to hospital with back pain & headache; BP 198/95; trace LE edema & 1+ proteinuria; IV MgS; IV hydralazine [for >180/105]
• Day 18: CT; MRI, MRA, MRV

CT: Post-partum Day 18

MRI: Post-partum Day 18
FLAIR/DWI

MRA/MRV: Post-partum Day 18

Post-Partum Headache

• Day 19: headache better; BP 148/78
• Day 20: right arm/hand weakness; BP 172/90-191/97; MRI, MRV; left leg weakness; steroids; IV nicardipine
• Day 21: weakness bilaterally; dysphasia; BP 115/52 to 133/49; “tremors”
• Day 22: unresponsive; BP 96/48-143/73; +7.5 lbs in 48 hrs; MRI, MRA, MRV; yawning, “tremors”; IV levetiracetam

MRI: Post-partum Day 20
FLAIR/DWI

MRV: Post-partum Day 20

MRA: Post-partum Day 20
MRA: Post-partum Day 20

Post-Partum Headache
- Day 19: headache better; BP 148/78
- Day 20: right arm/hand weakness; BP 172/90-191/97; MRI, MRA: left leg weakness; steroids; IV nicardipine
- Day 21: weakness bilaterally; dysphasia; BP 96/48-143/73; +7.5 lbs in 48 hrs; MRI, MRA, MRV: yawn, “tremors”; IV levetiracetam

MRI: Post-partum Day 22

FLAIR/DWI

MRA/MRV: Post-partum Day 22

Post-Partum Headache
- Day 23: obtunded; bilateral flexor toes; BP 150/88 - 109/59
- Day 24: fixed gaze, irregular respirations; reactive pupils; “tremors”; BP 155/90-142/77; EEG “encephalopathy”; respiratory arrest on way to CT scan; intubated; CT done
- Day 25: brain dead; organ donor

CT: Post-partum Day 24

Posterior Reversible Encephalopathy Syndrome (PRES)
- Nomenclature
  - Not exclusively posterior; not always reversible
  - Hypertensive encephalopathy
  - Pre-eclamptic/eclampsia; HELLP
- Vasogenic cerebral edema (cortical, subcortical, spinal cord)
  - Vasoconstriction
  - Hyperperfusion
- Diverse clinical & radiographic presentations
  - Headache, seizures, visual symptoms, mental status changes
  - Parietal-occipital white matter, holohemispheric pattern; superior frontal region, cortex, subcortical nuclei, brainstem; spinal cord
  - Untreated: Reversible vasoconstriction syndrome (RCVS); intracerebral hemorrhage, ischemic stroke, coma, death

PRES
- Theory 1:
  - Hypertension/Hyperperfusion
    - Severe HTN exceeds autoregulatory capacity of brain, failed auto-regulation; hyperperfusion, endothelial injury, “leaky capillaries,” vasogenic edema
- Theory 2:
  - Vasoconstriction/Hypoperfusion
    - Evolving HTN leads to vasoconstriction, decreased perfusion, ischemia, edema
Hypertension in Pregnancy
- Complicates 10-20% of pregnancies with increasing incidence
- ~ 20% of maternal deaths in the US
- Presents very frequently with headaches prior to diagnosis
- More common in women with migraine
- Categories for Hypertensive Disorders
  - Chronic Hypertension
    - >140/90 to >20 weeks post partum
  - Gestational Hypertension
    - >140/90 to >20 weeks without proteinuria
  - Preeclampsia/Eclampsia/Hypertensive
    - >20% of pregnancies (20% develop eclampsia with seizure)
      - > 20% cases 4-6 weeks after delivery (increased stroke risk)
    - Multigravida: >140/90 to >20 weeks with proteinuria: >500 mg/deciliter
    - Preeclampsia superimposed on Chronic Hypertension
  - Preeclampsia

Eclampsia - ↑BP, Seizure
A 46-year-old female, 36 weeks pregnant, presented in active labor. Her BP was elevated (182/88 at presentation) continuing after an epidural decreased her pain. She complained of headache, and blurred vision, then had a generalized tonic-clonic seizure. A healthy baby was delivered by emergent sectioning. A nicardipine drip was used to treat continuing elevated BP. A CT scan of the brain was obtained. She was discharged to home, neurologically intact, taking two oral anti-hypertensive agents.

Eclampsia - ↑BP, Seizure
19 year old pregnant woman with elevated blood pressure and seizures
19 yr old, undomiciled woman, 31 wks pregnant, with known mild proteinuria, had 3 GTCs over 4 hours. Her BP was 190/140. Sonography showed placental abruption and no fetal heartbeat. She was given Versed, Dilantin, Hydralazine, Mg and she underwent emergency sectioning with delivery of a dead fetus. HCT showed bilateral parietal medial hypodensities and bilateral internal capsule hypodensities. An MRI was obtained.

19 year old pregnant woman with HELLP syndrome
She was intubated on propofol but no focality was noted on a limited neurological examination. Blood work was remarkable for elevated LFTs (AST 315, ALT 145), elevated LDH (1697), and decreased platelets (58K). Urinary protein was elevated.

HELLP Syndrome
- Occurs in up to 20% of women with severe preeclampsia, more commonly in white women and multigravid women
- H-Hemolysis
- EL-Elevated liver function tests
  - AST> 72 IU; LDH > 600 IU
- LP-Low platelets

19 year old pregnant woman with HELLP syndrome
The woman gradually improved neurologically. The MRI was repeated 9 days later, when she was neurologically normal.
A 43-year-old G4P2Ab1 delivered a healthy infant by repeat sectioning at 36 weeks, after SROM. BP and laboratory testing were normal. Urine showed trace protein. She was discharged on PPD4 with a BP of 129/78. She was seen in the ED on PPD7 with a 10/10 headache with n/v for a day. Her BPs were consistently elevated at 150's/100's, and was brought to the ED. She was admitted for an elective induction.

Her baseline platelet count was 4100, and was brought to the ED. She was intubated. Liver function tests were markedly elevated from a normal baseline on admission. Her platelet count decreased to 40,000 from a normal baseline on admission.

A 42-year-old G4P2Ab1 delivered a healthy infant by repeat sectioning at 36 weeks, after SROM. BP and laboratory testing were normal. Urine showed trace protein. She was discharged on PPD4 with a BP of 129/78. She was seen in the ED on PPD7 with a 10/10 headache with n/v for a day. Her BPs were consistently elevated at 150's/100's, and was brought to the ED. She was admitted for an elective induction.

Her baseline platelet count was 4100, and was brought to the ED. She was intubated. Liver function tests were markedly elevated from a normal baseline on admission. Her platelet count decreased to 40,000 from a normal baseline on admission.

A 35-year-old, healthy, G1P0 woman was admitted at 40 weeks for an elective induction. Her BP on admission was 150/100, staying at 150'-160'/100', for 24 hours until vaginal delivery. She complained of a headache and severe abdominal pain after delivery, with persistent BP elevation. At 5 hours after delivery, her headache worsened and left sided weakness developed suddenly. CTs were obtained at onset of weakness and 4 hours later after she was intubated. Liver function tests were markedly elevated from a normal baseline on admission. Her platelet count decreased to 40,000 from a normal baseline on admission.

A 40-year-old woman without significant PMH, G4P1122 had a persistent post partum, 10/10, frontal headache. Her sudden onset headache began prior to delivery and persisted through L&D to post-partum day 87. Her headache was associated with nausea and dizziness. She had bilateral LE edema since delivery, with proteinuria prior to delivery. Her BP was 136/61. Her neurological examination was normal. Her CBC and metabolic panel were normal. Spinal fluid showed 4100 to 2500 RBCs with xanthochromia. HCT was interpreted as negative.
Post-partum headache with normal BP

A healthy 43 year old woman delivered her 3rd child vaginally, after an uneventful pregnancy. Her blood pressures were consistently under 140/90 after delivery. She complained of an intermittent mild headache the day after delivery. On the second day after delivery her headache suddenly worsened and her blood pressure increased markedly. She became unresponsive.

Reversible Cerebral Vasconstriction Syndrome

- Case reports of reversible narrowing of cerebral vessels by Marie Fleming (1987)
- Followed by case series by Call and colleagues (1988) describing characteristic clinical and imaging findings—reversible cerebral segmental vasocostriction
- Call-Fleming syndrome

RCVS

- Sudden, severe headache, evidence of vasocostriction in cerebral vessels, and documented resolution of vasocostriction
- Can cause ischemic strokes especially in border-zone territories
- Associated with a variety of clinical states:
  - Pregnancy (postpartum cerebral angiopathy)
  - Migraine (migrainous vasospasm)
  - Drug use (SSRIs, nicotine, cocaine)
  - Benign angiopathy of the CNS

RCVS

- Clinical:
  - Sudden onset severe, “thunderclap” headache
  - Nausea
  - Vision changes
  - Photophobia
  - Encephalopathy
  - Focal deficits (ischemic, hemorrhagic)
  - Generalized seizures (up to 30%)
  - 1/3 with moderate-severe HTN

Variable Presentations of Postpartum Angiopathy

Fugate et al. Stroke. 2012; 43: 670-676

18 patients (mean age, 31 years; range, 15–41)
- Median gestation: 38 weeks.
- 12 (67%) - prior uneventful pregnancy
- Complications: (n=2, 11%) cerebral angiopathy associated with eclampsia, pre-eclampsia,HELLP syndrome, abruptio placentae, anaphylactoid purpura,HELLP syndrome, abruptio placentae, anaphylactoid purpura,HELLP syndrome, abruptio placentae, anaphylactoid purpura
- Migraine headaches (n=5, 25%)
- Gestational hypertension (n=2, 11%)
- Vasocostrictive medications (n=7, 38%)
- Neurological symptoms (began on median day 5 postpartum)
  - Headache (n=16, 89%)
  - Focal deficit (n=4, 14%)
  - Visual disturbance (n=4, 14%)
  - Encephalopathy (n=3, 17%)
  - Seizure (n=1, 28%)

Variable Presentations of Postpartum Angiopathy

Abnormal brain (MRI/CT) imaging (n=13, 72%) intracranial hemorrhage (n=7, 38%)
vasogenic edema (n=8, 44%)
infarction (n=6, 33%)
Clinical outcomes
full recovery seen in 9 (50%),
dead after a fulminant course in 4 (22%)
residual deficits in 5 (28%)

Headache 3 weeks after delivery

35 year-old woman had a post-partum headache for 8 days. Thirty days prior, pre-eclampsia, HELLP syndrome and intrauterine fetal demise were detected on routine screening of her first pregnancy. The fetus was delivered at 30 weeks. Blood pressures at home after delivery were 110-130/70-90, not on medication. She saw her obstetrician for the persistent headache, when her BP was 150/100. An MRI scan was ordered.

Post-partum headache
Post-partum headache

Post-partum headache CVT

Cerebral Venous Thrombosis

- Generally present with headache, less frequently seizures, focal deficits
- Thrombophilias (Factor V Leiden gene mutation, prothrombin 20210A gene mutation, methylenetetrahydrofolate reductase (MTHFR) 677TT polymorphism)
- Exogenous hormones
- Most common in post-partum period
- Treatment with IV heparin to SQ LMWH during pregnancy, to warfarin post-partum
- Possible increase in future risk of pregnancy related to prior CVT
- Avoid further pregnancies for two years.
- Consider use of anticoagulation (LMWH) with further pregnancies.

Pregnancy, Headache & Stroke

- Headache is an important premonitory symptom for cerebrovascular disease in pregnancy.
- The stroke risk is increasing with older pregnant women and women with migraines.
- The majority of strokes occur in the peri & post-partum periods.
- ICH & CVT are more common than ischemic stroke.
- Pre-eclampsia, eclampsia, HELLP, post-partum cerebral angiopathy may be on a continuum, presenting with headache.
- Monitoring blood pressure after delivery is crucial.
- Hypertensive disorder of pregnancy increases the risk of future ischemic stroke.

Post-partum sudden headache, then loss of brainstem reflexes

A 23 year old woman, 39 weeks pregnant, underwent emergent sectioning under epidural anesthesia, for fetal bradycardia. At about 10 minutes after the infant was delivered she suddenly complained of a headache, vomited and immediately became unresponsive. She was intubated immediately and a stroke code was called. She had dilated, unreactive pupils; no brainstem reflexes; and no motor response to pain. Her NIHSS was 31. A CT scan, then an MRI scan, were obtained.

Post-partum sudden onset of unresponsiveness: perimesencephalic air and anesthesia

In about an hour she was awake with a normal neurological examination, denying a headache.