Coexisting Neurologic Disease in Pregnancy

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DISCLOSURE

I have no financial relationships with commercial support to disclose.
Outline

- Multiple sclerosis
- Landry-Guillain-Barré disease
- Syringomyelia
- Hydrocephalus and VP shunt
- Spinal cord injury
- Subarachnoid hemorrhage
- Intracranial neoplasm
Multiple sclerosis

• Chronic, T-cell mediated autoimmune disease primarily affecting young adults
• Female: male 3:2
• Plaques of inflammatory demyelination scattered throughout the white matter of the CNS, including the spinal cord
Multiple sclerosis

• Etiology?
  – Immunologic response to a viral infection
  – Genetic predisposition
    • Overall incidence 0.1% in general population
    • 15% of patients have a relative with MS
    • Risk 4% if one parent has MS
    • Risk 20% if both parents have MS
  – Geographic
    • Significantly increased incidence in northern latitudes compared to tropics-Vitamin D?
Multiple sclerosis

- Symptoms
  - Muscle weakness
  - Ataxia
  - Spasticity
  - Diplopia
  - Sphincter dysfunction
  - Paraplegia
Multiple sclerosis

• Diagnosis
  – Typical history of clinical deficits separated in time as well as location, with exacerbations and remissions
    • Often worsened by stress, hyperthermia
  – CSF abnormalities (elevated IgG and myelin basic protein)
  – MRI
Effect of pregnancy on multiple sclerosis

- 254 women, 269 pregnancies
- Followed throughout pregnancy and 12 months postpartum
- Rate of relapse determined
- Disability score (0-10) determined

• Relapse rate
  – 0.7 per woman per year in year prior to pregnancy
  – 0.5 during first trimester
  – 0.6 during second trimester
  – 0.2 during the third trimester
  – 1.2 during first three months postpartum
  – Subsequently returned to pre-pregnancy rate
• Risk factors for postpartum relapse:
  – Increased relapse rate in year prior to pregnancy
  – Increased relapse rate during pregnancy
  – Increased disability score prior to pregnancy
• Disability score worsened by 0.7 during 33 month follow-up, with no apparent postpartum acceleration
• Neither breast feeding nor epidural analgesia had any effect on relapse rate or progression of disability
• Protective effect of pregnancy?
  – Progression of disability greater in nulliparous women
  – Risk of disease onset, risk of conversion to progressive course disease greater during non-pregnant state
    Runmarker B. *Brain* **1995;** 118:253
Obstetric management

• No effect on fertility or incidence of spontaneous abortions
• No apparent effect on pregnancy outcome
• Increased incidence of UTI’s in patients with abnormalities of bladder function
• Route of delivery determined by usual obstetric indications
• Assisted delivery may be necessary if significant fatigue/muscle weakness is present
Treatment

- Intravenous steroids
  - Useful for relapses
  - Reserve for severe exacerbations due to placental transfer
    - Dexamethasone-neonatal leukocytosis
    - Methylprednisolone-neonatal immunosuppression
- Azathioprine
  - Category D
    - Positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
    - Fetal liver lacks enzyme that converts to active metabolite; considerable experience with little demonstrated fetal risk

*Expert Opin Drug Saf. 2014 Sep 5:1-9*
• Immunomodulators
  – Interferons $\beta$-1-b and $\beta$-1-a have no apparent teratogenic effect but are associated with significant pregnancy loss (40% vs 5% in controls)
  
  Houtchens MK. *Semin Neurol* **2007; 27**:434
Anesthetic management-NSVD

• Epidural analgesia appears to have no effect on progress of disease

• A single retrospective study demonstrated that those women in epidural group that did have relapses were exposed to higher concentrations of local anesthetic


• Local anesthetic-opioid mixtures will allow lower concentrations to be administered
Anesthetic management-C/S

- Epidural anesthesia is the most appropriate choice
- No evidence that spinal anesthesia causes relapses
- Regional anesthesia of any type should be used with care in patients with marginal respiratory function
Anesthetic management-C/S

- If general anesthesia is required, succinylcholine should be used with care in patients with severe musculoskeletal involvement due to the possibility of massive potassium release.
- Hyperthermia should be avoided due to its role in exacerbations of disease.
A 34 year old G₁P₀ at 36 weeks gestation presented with a two week history of progressive lower extremity weakness, which over the preceding 24 hours had left her unable to walk. She also reported a history of lower extremity tingling and numbness which began one week prior to the onset of weakness.
The patient denied any significant past medical history. She reported an episode of gastroenteritis approximately one month previous to this admission. Because of the progressive nature of her illness and concerns that she would be unable to tolerate labor, the decision was made to perform a cesarean section.
On physical examination, the patient was noted to have markedly diminished motor strength bilaterally in the lower extremities. Sensation to pinprick was diminished to the $T_{10}$ level bilaterally. The remainder of the physical examination was normal.
All laboratory values were within normal limits. Forced vital capacity was measured intermittently in the twelve hours preceding surgery. FVC remained greater than 2 liters.
Landry-Guillain-Barré disease

- Acute inflammatory polyradiculopathy
- Incidence of 1:250,000
- Incidence unchanged in pregnant women
- In two-thirds of patients, preceded by viral gastroenteritis, respiratory infection, vaccination, or surgery.
Landry-Guillain-Barré disease

- Presentation: flaccid paralysis, beginning in the lower extremities and progressing cephalad, occasionally involving the cranial nerves
- Ventilatory failure may occur, as can aspiration pneumonitis
- Progresses over four weeks, with recovery occurring over six months
Landry-Guillain-Barré disease

- Treatment: primarily supportive (nutritional, respiratory)
- May respond to plasmapheresis if begun while disease is progressing.
  - Less helpful if disease is stabilizing or resolving
- Steroids not helpful and may increase respiratory morbidity
Obstetric management

- Vaginal delivery is preferable if patient has adequate ventilatory parameters
- Assisted delivery may be necessary during the second stage
Anesthetic management

• Labor and delivery
  – Epidural analgesia appears safe and allows the avoidance of depressant systemic analgesics

• Cesarean section
  – Epidural anesthesia is appropriate in patients with adequate ventilation
  – Decreased local anesthetic doses may be necessary
  – In patients with bulbar involvement and marginal ventilation, general endotracheal anesthesia may be preferable
The patient was brought to the operating room where a successful epidural anesthetic was initiated. 20 ml of 2% lidocaine was administered and a $T_4$ sensory level was obtained. A healthy baby girl was delivered with Apgar scores of 9$^1$/9$^5$. 
Postoperatively, the patient was transferred to the ICU where a five day course of gamma globulin was initiated. EMG performed on the second postoperative day was consistent with a diffuse motor-sensory mixed type demyelinating neuropathy.
The patient was discharged home on the seventh postoperative day, ambulating with a walker. At a six week postpartum visit she was ambulating without assistance.
Syringomyelia

- An expanding, cystic cavity within the spinal cord
- Can be secondary to trauma or neoplasm
- Chiari type I malformation: herniation of the cerebellar tonsils below the foramen magnum
Pathophysiology

• Intermittent obstruction of CSF from fourth ventricle leads to increases in intracranial CSF pressure
• This is transmitted to the central canal of the spinal cord, which dilates and dissect into adjacent neural tissue
Pathophysiology

- Presentation: upper extremity weakness, loss of pain and temperature sensation
- Extension of syrinx into brainstem (syringobulbia) can lead to cranial nerve involvement and autonomic neuropathy
Evaluation

- MRI to evaluate extent of syrinx, particularly brainstem involvement
- Assessment of autonomic dysfunction
- Pulmonary function tests
Evaluation

• Even in patients without evidence of elevated intracranial pressure, vigorous coughing and straining can lead to clinical deterioration
  – Should vaginal delivery be planned, maternal expulsive efforts in the second stage should be minimized
Anesthetic management

• Due to reports of neurologic deterioration after dural puncture, most have advised against epidural or spinal anesthesia
  Haughton VM. *Am J Neuroradiol* 2003; 24:169

• Epidural anesthesia has been reported
  Nel MR. *Br J Anaesth* 1998; 80:512

• General anesthesia acceptable if efforts to decrease ICP are utilized
Hydrocephalus and VP shunt

- 77 pregnancies in patients with VP shunt
  - Epidural used in 38% of vaginal deliveries
  - Epidural used in 50% of cesarean sections
  - No complications directly related to anesthesia

  Bradley NK. *Neurosurgery* 1998; 43:448
Hydrocephalus and VP shunt

- There is no evidence of increased risk of shunt infection after regional anesthesia
- There is no support for the common practice of antibiotic administration to patients with VP shunts
- In patients with a functioning shunt and no evidence of increased ICP, there is no evidence that it is necessary to shorten the second stage of labor
Spinal cord injury

- Anesthetic and obstetric management will be influenced by the level of injury
  - Sacral injury
    - Alterations of bowel and bladder function
    - Relaxed perineal musculature
    - Normally painful contractions
Spinal cord injury

- Injury above $T_{10}$:
  - Painless contractions and increased risk of preterm delivery
  - May have inadequate expulsive efforts in second stage requiring assisted delivery
• Injury above $T_6$
  – Increased risk of autonomic hyperreflexia
  – Bladder distention, uterine contraction, or other noxious stimuli will initiate reflex arc causing vasoconstriction below level of injury
  – Central inhibition of sympathetic tone does not extend below the level of injury
  – The only compensatory mechanism is vasodilatation above the level of the injury
Spinal cord injury

– With high injury, the amount of vascular bed available to vasodilate is inadequate to compensate for vasoconstriction below the injury, yielding severe hypertension
– Epidural analgesia is the most effective method for blocking this reflex
– Other methods of controlling blood pressure must be available (vasodilators, $\alpha$-blockers)
Spinal cord injury

• Epidural anesthesia most suitable technique for cesarean section in patients with adequate respiratory function
• General anesthesia: avoid succinylcholine
Subarachnoid Hemorrhage in Pregnancy

- Coagulopathy
- Hypertensive intracerebral hemorrhage
- Vasculitis
- Mycotic aneurysm
- Congenital aneurysm
- Arteriovenous malformation
UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-2012

- 3.47 million births
- 26 deaths due to intracranial hemorrhage
  - 13 SAH
  - 13 intracerebral hemorrhage
    - 6 subarachnoid hemorrhage
    - 5 intracerebral hemorrhage

https://www.npeu.ox.ac.uk/mbrrace-uk
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<tr>
<td>% of SAH</td>
<td>23%</td>
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<td>26.7</td>
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<tr>
<td>EGA</td>
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<td>30.5 (ns)</td>
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Dias MS. Neurosurgery 1990; 27:855
Timing of craniotomy-aneurysm

- Hemorrhage prior to “viability” (<32 weeks)
  - Early surgery (improved maternal-fetal outcome)
  - Pregnancy allowed to proceed to term
- Hemorrhage after viability
  - Delivery by cesarean section
  - Immediate definitive surgery
Timing of craniotomy-AVM

- Unruptured-resection can be delayed until delivery
- Symptomatic (seizures, ischemia, mass effect)-resection regardless of gestational age
- Ruptured, neurologically stable-Early surgery appears to improve maternal outcome but not yet confirmed
- Delivery as in aneurysm resection
Interventional neuroradiology

- Coiling of both unruptured and ruptured aneurysms is increasingly common in pregnant patients
  
  Piotin M. *Am J Obstet Gynecol* 2001; 185:1261

- Decreased incidence of vasospasm
- Similar incidence of obstructive hydrocephalus
- Smaller rate of successful aneurysmal obliteration
Interventional neuroradiology

- Proper abdominal shielding decreases fetal radiation exposure to level of background radiation
- General anesthesia typically used
- Capability of rapid blood pressure manipulation is essential
- Blunt responses to endotracheal intubation
- FH monitoring
Obstetric management

- Clipped aneurysm, resected AVM
  - Routine; no special precautions
- Known aneurysm
  - No advantage to elective cesarean section
  - Provision of adequate pain relief
  - Avoidance of valsalva maneuver in second stage
Anesthetic management

• Labor
  – Can dural puncture lead to aneurysmal rupture due to increased transmural pressure gradient?
  – This complication has never been reported
    Leffert LR, Schwamm LH. Anesthesiology 2013; 119:703

• Cesarean section
  – Epidural analgesia
  – General anesthesia
    • Measures to decrease sympathetic response to surgical stimulation: narcotics, lidocaine, vasodilators
Intracranial neoplasm

- Incidence is unchanged compared to non-pregnant age matched women
- Symptomatology commonly increases
  - Increased blood volume
  - Increased sodium and water retention
  - Decreased colloid oncotic pressure
  - Hormonal influences on tumor growth
Hormonal influences on tumor growth

• 39% of meningiomas have progesterone receptors
  Cahill DW. J Neurosurg 1984; 60:985

• Relative risk of menigioma in postmenopausal women is 0.58

• When menopause was surgically induced, relative risk decreases to 0.12
  Schlehofer B. J Natl Cancer Inst 1992; 84:1346
Surgical management-neoplasms

- Expectant management of benign lesions in the absence of progressive symptomatology
- Urgent surgery for presumed malignant lesion
- Urgent surgery for progressive deterioration, e.g. pituitary adenoma with worsening visual field defect, elevated ICP
- Delivery by cesarean section after 32 weeks
Controlled Hypotension

- 8 near term ewes
- Nitroprusside infused to reduce mean BP by 20%
- 3 required less than 1 mcg/kg/min
  - All lambs survived
- 5 required mean dose of 25 mcg/kg/min
  - All fetuses were dead within 30 minutes

Controlled hypotension-case reports

  - COMMON FACTORS
    - FH monitoring
    - Acid-base status
    - Limited doses
Fetal effects of osmotic diuretics

- Mannitol 12.5 g/kg administered to rabbits
- Fetal sodium increased from 145 to 162 meq/L
- Fetal osmolality increased by 23%
  

- 200 gm mannitol administered to humans increased fetal osmolality significantly

  Battaglia F. *Pediatrics* 1960; 25:2

*However- there is no evidence that commonly used doses (0.5-1.0 gm/kg) have any adverse effect*
Hyperventilation and fetal $O_2$ delivery

• Shift of maternal oxyhemoglobin dissociation to the left
• Uterine vasoconstriction secondary to hypocarbia
  – Doubtful-administration of CO$_2$ to normalize $p_a$CO$_2$ does not improve UBF in hyperventilated sheep
• Decreased stroke volume and cardiac output secondary to increased intrathoracic pressure
• Appropriate $p_a$CO$_2$=28-30 mmHg
  – $p_a$CO$_2$-ETCO$_2$ gradient may be altered by pregnancy
Hypothermia

- Mild hypothermia (33-35 C) is well tolerated by the fetus and can be safely utilized when maternal indications are present.
- More profound hypothermia is unlikely to have any additional protective effect and may cause fetal arrhythmias.
Obstetric management

- Management will depend to a great extent on intracranial pressure.
- In patients with compensated ICP, vaginal delivery may be performed.
- In patients with markedly decreased intracranial compliance, abdominal delivery should be followed by immediate craniotomy.
Anesthetic management

- A pain-free delivery will help minimize increases in cerebral blood flow and thus ICP
- Accidental dural puncture may lead to herniation if ICP is elevated
- However-other analgesic techniques (systemic narcotics) have their own risks
- U/S guidance of LEA placement
Anesthetic management

• If epidural analgesia is administered, rapid injections of large volumes of local anesthetic should be avoided.
• For cesarean section, general anesthesia is indicated.
• Sympathetic responses to noxious stimulation should be blunted.
• These measures may lead to neonatal depression.