HELLP! Caring for the Critically Ill Pregnant Patient

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Disclosures

I have no relevant conflicts of interest

I will discuss “off-label” use of medications, as many are not approved in for use in pregnancy
Objectives

“Acute Care Hematology & More…”

- HELLP
- ↓PLT
- TMA
- ?
Case presentation

• 21 year old G3P2, presents at 36 weeks gestation
• Nausea, RUQ pain and tenderness
• BP 145/88, HR 108, afebrile, neuro intact
• Labs: Hgb 105 g/L, WBC 8.8, PLT 120,000, Creat 88 umol/L (1.0 mg/dL)
• AST 220  ALT  410  Bili  68 umol/L  LDH 880

?
Normal physiological changes in pregnancy
Hematological changes in pregnancy

- **Hemoglobin:** - RBC mass increases
  - plasma volume increases more
  - Hgb drop
  - 10 – 20 g/L

- **White blood cells:** - neutrophils increased by physiological stress
  - sometimes further increase related to delivery

- **Platelets:** - gestational thrombocytopenia (incr clearance & dilution)
  - generally > 70 x10⁹/L

- **Coagulation:** - procoagulant state
  - INR no change, PTT may be shortened (4 sec)
  - fibrinogen levels increased

ECOG 2016; 206:259
Biochemical changes in pregnancy

• **Renal:** decreased creatinine & urea by 25% (incr GFR)

• **Electrolytes:** complex water balance (dilution, decr osmotic threshold for ADH release, placental vasopressinase)
  - slight decr Na, more with preeclampsia, oxytocin infusion

• **Liver:** slight fall in AST, ALT, bilrubin, albumin
  - increase in Alk Phos and sometimes LDH

*Teasdale and Morton, Obstet Med 2018, online May 24th*
Case presentation

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Gestational thrombocytopenia

- Thrombocytopenia in the absence of other abnormalities
- During 2nd and 3rd trimester
- Usually > 70,000
- Resolution within days to 2 months postpartum
- No fetal thrombocytopenia
- May recur in subsequent pregnancies
- May be difficult to differentiate from ITP

Preeclampsia

• hypertension
• proteinuria
• after 20 weeks gestation
Preeclampsia - Etiology

- placental ischemia
- impaired trophoblastic invasiveness
- genetics
- abnormal implantation
- endothelial abnormality
- diffuse vasospasm

sFlt1 (from fetal side of placenta) blocks VEGF and PI GF

↓

maternal endothelial effects

Cerdeira et al, BJOG. 2018 Oct;125(11):1389-1395
<table>
<thead>
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<th>Reason</th>
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<td>intracranial hemorrhage</td>
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<td>acute renal failure</td>
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<tr>
<td>cerebral edema</td>
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<tr>
<td>hypertensive crisis</td>
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<td>eclampsia (seizure)</td>
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<td>hepatic (HELLP syndrome)</td>
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Preeclampsia

- Affects about 6% of all pregnancies
- In addition to hypertension:
  - renal
  - neurological
  - hepatic
  - hematological
- 50% will have PLT < 150 x10⁹/L
- Associated with HELLP syndrome
- Treatment:
  - blood pressure control
  - seizure prophylaxis with MgSO₄
  - manage organ dysfunction
  - appropriately timed delivery
HELLP syndrome

Symptoms and Signs of HELLP syndrome

- Fatigue
- Severe headache
- Excess weight gain
- Nausea
- Nose bleed
- Pain in the abdomen
HELLP syndrome

- Hemolytic anemia
- Elevated Liver enzymes
- Low Platelets

4 to 12% of preeclampsia
Occasionally presents post-partum

HELLP syndrome

- **Hepatic:**
  - Abdominal pain, nausea, vomiting
  - Elevated AST, ALT
  - Intrahepatic hemorrhage

- **Coagulopathy:**
  - Thrombocytopenia
  - DIC: 38%
  - Hemorrhage

- **Hemolysis:**
  - Microangiopathic anemia

- **Other:**
  - Renal failure
  - ARDS
HELLP - Management

- Treat Preeclampsia
- Blood products
- Monitor liver
- Delivery!
- Plasmapheresis if > 72 hr postpartum TTP?
- Steroids?

References:
Acute Fatty Liver of Pregnancy
Acute Fatty Liver of Pregnancy

uncommon 1 in 15,000 pregnancies

Clinical Features

• onset usually late third trimester
• anorexia, vomiting, jaundice
• abdominal pain
• coagulopathy, encephalopathy, renal failure
Acute Fatty Liver of Pregnancy

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Clinical Features

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Early reports: fulminant hepatic failure, high mortality

More recently: early recognition, improved outcome
Acute Fatty Liver of Pregnancy
Diagnosis: Swansea criteria

The patient should demonstrate at least six of the following:

- Nausea
- Abdominal pain
- Polydipsia/polyuria
- Encephalopathy
- Hypoglycemia
- Leukocytosis
- Ascites
- Increased aminotransferases and bilirubin
- Increased blood ammonia
- Renal failure
- Coagulopathy
- Metabolic acidosis
- Pancreatitis
- Microvesicular steatosis on liver biopsy

Ch’ng et al, Gut 2002; 51:876
Acute Fatty Liver of Pregnancy

Differential Diagnosis

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- intrahepatic cholestasis of pregnancy
- viral hepatitis
- acetaminophen overdose
## Acute Fatty Liver of Pregnancy

### Management

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Acute Fatty Liver of Pregnancy

Management

DELIVERY

- no reversal without delivery
- improvement occurs within 2 to 3 days
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- high incidence of placental damage

supportive
as for hepatic failure

specific
none effective plasmapheresis?

transplant
if deteriorate after delivery
Acute Fatty Liver of Pregnancy

- limited case-reports and a case series
- no good evidence to support use


Liver disease in pregnancy - Etiology

[Diagram showing metabolic pathways involving CoA, NADH, and enzyme deficiencies]
Liver disease in pregnancy - Etiology

- Association with infants with defect in fatty acid oxidation

- 79% of mothers carrying a fetus homozygous for a specific mutation of long chain 3-hydroxyacyl-CoA dehydrogenase had AFLP
  

- Mutations in LCHAD detected in 19% of women with previous AFLP
  
  *JAMA* 2002; 288:2163

- Some association with HELLP syndrome, placental infarcts

- Infants are at risk of hyperketotic hypoglycemia and fatty liver
Liver disease in pregnancy - Etiology

- LCHAD-deficient fetus (G1528C)
- Metabolic stress "third trimester"
- Environmental stress high fat diet

Thrombotic Microangiopathy in Pregnancy
Thrombotic Microangiopathy in Pregnancy

HELLP

TTP

aHUS

Pregnancy
# Thrombotic Microangiopathy in Pregnancy

- Differentiating these conditions

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<td>Incidence</td>
<td>1-4%</td>
<td>0.001%</td>
<td>0.001%?</td>
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<td>Timing</td>
<td>after 20 weeks</td>
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<td>Blood pressure</td>
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<td>Neurological</td>
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<td>MAHA, PLT↓</td>
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<td>Kidney injury</td>
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<td>Liver injury</td>
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<tr>
<td>Effect of delivery</td>
<td>improves (36hr)</td>
<td>none</td>
<td>progression</td>
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Thrombotic Microangiopathy in Pregnancy

• Pregnancy associated atypical HUS (p-aHUS)
  – OB complications & delivery may precipitate aHUS
  – may initially be diagnosed as preeclampsia/HELLP
  – Consider if:
    <20 weeks, no resolution at 72 hr, history of HUS
  – Complement gene abnormalities not always identified

Thrombotic Microangiopathy in Pregnancy

- **Treatment**

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<td>Plasmapheresis</td>
<td>eculizumab: limited data in pregnancy (case reports)</td>
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<td>Supportive Rx</td>
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<td>Mechanism</td>
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<td>type 1 angiotensinII receptor Ab?</td>
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<td>Rx</td>
<td>Delivery</td>
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Management of the Pregnant ICU patient
Management of the Pregnant ICU patient

• **Do necessary radiological procedures**
  - CT abdo/pelvis needs some consideration

• **Do not restrict drug therapy**
  - norepinephrine if needed (hypotension is bad)
  - some chemo/biologics safe, others not (no thalidomide!)

• **No changes to ventilation strategy**
  - mild/mod hypercapnia probably OK, maintain reasonable $\mathrm{O}_2$

• Left lateral positioning

• Blood for cross-match q 3 days

• Provide adequate nutrition (+ Fe, folate)

• Know resuscitation status of neonate

• **Multidisciplinary management:** OB, neonatology, OB Medicine
Prepare the ICU for Emergencies in Pregnancy
Pregnant patient in the ICU

Labour & Delivery Equipment (Checklist #1)

On Trolley:
1. Charting -
   i. this will require paper documentation
   ii. post c/s order sets (in the event that a c/s is done post procedure)
2. Cesarean Section Tray/Vaginal Delivery Tray
3. Sterile C-section pack
4. Package of sterile gowns
5. Sterile gloves - 2 of each size
6. Single examining sterile glove
7. Vaginal delivery basin set
8. Medication Tray - take an extra 10 vials of Oxytocin
9. Sponges - 4 packs of 5 sponges
10. Sutures
11. Scalpel blades
12. Kiwi Vacuum
13. Baby blankets 2 sterile, 3 non-sterile

In Fridge: (take from L&D fridge, check dates and put in med fridge on off service unit, with patient’s identification on it)
1. Hemabate
2. Ergot
3. Misoprostol

Infant Support Required Equipment (Checklist #2)

- 1x amp of Epinephrine 1:10,000
- 1x amp of Naloxone 0.4mg
- Omnibed/ Overhead warmer/ Isolette
- Temperature Probe
- 3x Silver Dots
- Intubation Kit, including 2x #2.5 ETT, 2x #3.0 ETT, 2x #3.5 ETT, stylet, magills, blades, oral airways (size 5 and 6), ETCO2 detector, scissors, 1 roll pink tape
- Flow-inflating Bag w/ size 00 and 0 masks
- Pressure Manometer for Flow-inflating Bag
- Oxygen tank (Grab and Go)
- SpO2 monitor (for SpO2 and HR)
- Sterile gown and gloves, hat and surgical mask
- Multi-purpose tray
- Umbilical catheters (2x 3.5Fr, 2x5Fr)
- #15 Scalpel blade
- 3x Chlorhexidine prep sticks
- 3x 10cc syringes
- 2x Bluell Filling Needles
- 2x amp of Normal Saline
- 1x amp of Sterile Water
- 3x 4x4 Sterile Gauze
- 1x amp of Vitamin K
- 1x Tuberculin Syringe w/ needle
- 2x IV Pumps
- 1x 500cc bag of D5W