Early-Onset Preeclampsia with Pulmonary Edema and Massive Ascites: A Rare Presentation of Severe Preeclampsia or Concomitant Diagnoses?

Elizabeth St. Laurent, MS, OMS-IV
Rebecca Fryer, MPH, OMS-IV

With the mentorship of Tom McNeillis, DO
Obstetrics and Gynecology
A.T. Still University School of Osteopathic Medicine in Arizona
5850 E Still Circle, Mesa, AZ 85206
Introduction

Hypertensive Disorders of Pregnancy

- Preeclampsia along with eclampsia and HELLP syndrome, although three separate diagnoses, are on the continuum for hypertensive disorders of pregnancy.

- Hypertensive disorders of pregnancy occur in 3-8% of all pregnancies and are among the leading causes of maternal morbidity and mortality
  - Stroke, seizure, end-organ damage, death, etc.

- Preeclampsia, an endothelial disorder of the placenta, can progress to eclampsia, HELLP syndrome or both.
  - Contributes to 12-25% of fetal growth restriction cases and preterm births.
Hypertensive Disorders of Pregnancy

Preeclampsia
- New onset hypertension
- New onset proteinuria
- Symptoms indicating maternal end organ damage:
  - Pulmonary edema
  - Oliguria
  - Persistent headaches
  - Impaired liver function

Typically diagnosed after 34 weeks
Early-onset if diagnosed at 20w-33w6d

Eclampsia
- Preeclampsia diagnosis
  +
  - New onset seizure activity

HELLP
- Hemolysis
- Elevated liver enzymes
- Low Platelets

3 Classes:
I-platelet count below 50
II-platelet count 50-100
III-platelet count 100-150

This case presentation demonstrates a rare and severe presentation of early-onset preeclampsia with severe features, pulmonary edema, and massive ascites that ultimately resulted in class III HELLP syndrome and severe prematurity of the infant.

The patient required an emergency cesarean section with a T-shaped uterus incision.

The rapid onset of severe symptoms and presentation without concomitant rapid changes in labs makes this a unique case.
HPI: 28 year old caucasian, G1P0 female at 26w4d presented to OB triage on the recommendation of her physician due to extremely elevated uric acid levels (>1000) and a recorded blood pressure of 180/110. Patient reported rapid onset weight gain, diminished fetal movements, and frequent headaches in the past week. Patient denied labor symptoms but complained of back pain and was admitted to hospital at 26w4d for observation. Pregnancy was without complication up until this point. Negative testing for gestational diabetes. GERD symptoms since 8 weeks gestation, but manageable with calcium carbonate chews and diet modification.

Review of Systems
Gen: daily headache, malaise, myalgia, weight gain, night sweats; denies fever or chills.
CV: worsening facial and periorbital edema
Pulm: worsening orthopnea requiring wedge pillow; dyspnea w/ talking and at rest, exercise intolerance d/t dyspnea; dry cough
GI: constipation, nausea, denies hematochezia, melena
GU: increased urinary frequency, oliguria, right sided flank pain; denies dysuria, hematuria
Skin: pruritus, especially on face and hands; denies petechiae, palmar erythema, and spider angiomas

PMH: Anxiety and depression, controlled without medication; up to date on influenza vaccination, requested Tdap; provided consent for blood transfusion if necessary
PSH: None
All: None
Meds: prenatal vitamin daily; calcium carbonate chews prn
FH: Mother—Factor V deficiency
SH: High stress occupation; married, sexually active with one male partner; never smoked; never used illicit drugs; recent travel to Tucson by car; no social determinants of health impacting care

Physical Exam Findings

General: appears mildly uncomfortable, lying on right side with fetal heart and contraction monitors on abdomen

Face: extensive periorbital edema involving eyelids; Mouth and nares—dry and irritated

Neck: No thyromegaly or lymphadenopathy was noted; trachea midline

Heart: regular rate and rhythm, with no audible murmur noted

Pulmonary: Lungs clear to auscultation bilaterally

Abdomen: tight abdomen, difficult to accurately measure fundal height

Neuro: alert and oriented x 3; Deep tendon reflexes 2/4 bilaterally for upper and lower extremities.

Lower extremities: +1 pitting peripheral edema was noted along with 2+ dorsalis pedis pulses bilaterally

Msk: tight, ropey thoracic paraspinal musculature bilaterally; tight suboccipital muscles, especially prominent on right side
Assessment and Plan

1. **Preeclampsia with severe features**
   a. Labetalol 200 mg BID for blood pressure management
   b. Nifedipine 30 mg BID for blood pressure management
   c. Blood pressure monitoring q6h
   d. Check labs (CBC, LDH, BMP, AST/ALT, uric acid) twice weekly
   e. 24 hr urine collection to check protein and creatinine levels
   f. Monitor for worsening of preeclampsia symptoms
   g. Discuss potential necessity of early delivery, otherwise will plan for 34 weeks

1. **Fetal Well-Being Assessment**
   a. Non-stress test
      i. If non reactive, order biophysical profile
   b. Fetal umbilical artery doppler scan
   c. NICU consult due to severely premature gestational age
   d. Medication:
      i. Antenatal betamethasone 12 mg 2mL IM over 24 hr interval for lung maturation in case of early delivery
      ii. Magnesium sulfate for neuroprotection prior to 32 weeks and at time of delivery
      iii. Prenatal multivitamin oral qday

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Clinical Course
Fetal Testing: Non-Stress test (NST)

Measures fetal heart rate reactivity:

- Reactive if:
  - Baseline fetal HR: 110-160 bpm with moderate variability (5-25 interbeat variability)
  - 2 accelerations in 20 mins with no decelerations

Fetus had a non-reactive NST due to insufficient number of accelerations. Therefore, a biophysical profile (BPP) was ordered to assess fetal status.

Fetal Testing: Biophysical Profile

4 Components scored over 30 min period:
*Each component is worth either 0 (absent) or 2 (present) points, with an overall total of 8 points.

1. Fetal tone
   a. 1 episode of flexion-extension-flexion

2. Fetal movement
   a. 3 gross body movements

3. Fetal breathing
   a. 1 episode of rhythmic breathing

4. Amniotic fluid volume
   a. 2 x 2cm pocket (i.e. measured in 2 perpendicular planes)

Scores at or below 4/8 are considered concerning and may prompt immediate delivery.

Fetus’ BPP score: 8/8
Fetus’ Amniotic Fluid Index: 5.55 cm
- Oligohydramnios: < 5 cm
- Polyhydramnios: > 25 cm
Fetal Testing: Umbilical Artery Doppler

Measures the blood flow and its velocity through the umbilical cord to determine if there are any abnormalities either in the placenta, umbilical cord anatomy, or fetal circulatory system.

Patient’s UAD showing intermittent absent end diastolic velocity and increased resistance in the utero-placental circuit
- Shows placental insufficiency
- Often found in preeclampsia and IUGR

Normal UAD showing presence of end diastolic velocity and normal resistance in the utero-placental circuit

Additional Assessment and Plan

1. Intrauterine growth restriction (IUGR) with absent end-diastolic flow and low normal amniotic fluid index (AFI)
   a. Fetal non-stress test twice daily
   b. Umbilical artery doppler twice weekly
   c. Repeat growth ultrasound in 3 weeks
New Physical Exam Findings

CC: "I feel like I'm drowning."

**General:** appeared very uncomfortable and unwell, sitting up in bed leaning forward and could not complete sentences without dyspnea. On 4L of O2 via nasal cannula. Patient smelled "musky"

**Pulmonary:** diminished breath sounds especially on the right, with occasional crackle; wet sounding cough (lacking sputum production) leading to dyspneic episode

**Abdomen:** tight gravid abdomen, enlarged since admission, with fluid wave present. Painful palpation for upper right quadrant, negative Murphy's sign. Dullness to percussion near the umbilicus.

**Neuro:** alert and oriented x 3; Deep tendon reflexes 2/4 bilaterally for upper and lower extremities. No neurologic signs of magnesium toxicity noted.

**Lower extremities:** +3 pitting and weeping peripheral edema was noted along with 1+ weak bilateral dorsalis pedis pulses; feet cold to the touch

**Upper extremities:** PICC line in right arm and IV line in right hand caused bruising on upper extremities and discomfort

**Skin:** dry, especially on the arms and face, with excoriating marks

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Osteopathic Structural Findings

On osteopathic physical exam, the patient was noted to have:

- **OA:** rotated right, sidebent left with hypertonicity of the suboccipital muscles, especially on the right
- **C2-5:** rotated right, sidebent right.
- **Thoracics:** The musculature around the right scapula was especially tight. There was also somatic dysfunction at the C7/T1 junction in which the T1 was flexed forward. Red reflex was noted from T4-10 as well as a firm, but "wet" feeling to the tissues. Extremely tight paraspinal musculature in the upper thoracic region especially between T4-10
- Decreased thoracic kyphosis and slight increase in lumbar lordosis.
- **Viscerosomatics:** present bilaterally, but especially on right side for T6-10 levels.
- Significant bilateral **diaphragmatic tightness** was noted but it was difficult to diagnose due to abdominal distension and the patient's intense right upper quadrant pain.
- **Abdomen:** felt both turgid and boggy at the same time.
Osteopathic Treatment

Throughout the pregnancy, this patient was treated by osteopathic physicians, which provided substantial non-pharmacological pain relief and was well tolerated by the patient.

- Techniques utilized:
  - Balanced ligamentous treatment of cervical, thoracic, rib cage, and lumbar regions
    - to reduce the diffuse back pain and aid in respiratory efforts
  - Myofascial release
  - Diaphragm release
  - Thoracic-lumbar junction inhibition
  - Occipital-Atlantal release
    - Reduced systolic BP by 20mmHg
  - Effleurage of lower extremities
    - to reduce swelling in the extremities
    - provided in small increments to ensure that the patient's heart was not overloaded by the increase in venous return
  - Back pain in the viscerosomatic region of the lungs and liver became increasingly hypertonic throughout the pregnancy and required multiple repeat treatments.
    - A fascial tether was felt between the region of the liver to the right shoulder where the patient was experiencing the most severe pain

Additional Assessment and Plan

1. Right upper quadrant pain
   a. Liver ultrasound
   b. Liver function labs, CBC, LDH, BMP, AST/ALT, uric acid

2. Dyspnea
   a. Chest X-ray
      i. If pleural effusion noted, repeat chest x-ray in 24 hrs.
   b. Nasal cannula oxygen 4 L/min

3. Severe bilateral thoracic back pain
   a. Acetaminophen 650 mg 2 tab oral q4 hrs prn
   b. Cyclobenzaprine 5 mg oral q6h prn
   c. Ketorolac 30 mg IV q6h
   d. Osteopathic manipulation as tolerated
**Patient’s Imaging**

- RUQ U/S showing incidental steatosis of liver
- CXR showing new-onset bilateral pleural effusions

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**Fetal Health Deterioration: BPP Results**

<table>
<thead>
<tr>
<th>Day of Hospital Stay</th>
<th>AFI</th>
<th>BPP Score</th>
<th>Other findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 2</td>
<td>5.55</td>
<td>8/8</td>
<td>No evidence of placenta previa</td>
</tr>
<tr>
<td>Day 3</td>
<td>5.14</td>
<td>8/8</td>
<td>Lesion again noted in the placenta</td>
</tr>
<tr>
<td>Day 4</td>
<td>5.64</td>
<td>8/8</td>
<td>Free fluid seen in left lower quadrant. Bilateral pleural effusion noted.</td>
</tr>
<tr>
<td>Day 6</td>
<td>5.12</td>
<td>8/8</td>
<td>Free fluid seen in right lower quadrant.</td>
</tr>
<tr>
<td>Day 8 (AM)</td>
<td>1.27</td>
<td>6/8</td>
<td></td>
</tr>
<tr>
<td>Day 8 (PM)</td>
<td>1.5</td>
<td>4/8</td>
<td>Ascites seen in all 4 quadrants-Increased since prior scan. Bilateral pleural effusion.</td>
</tr>
</tbody>
</table>
## Mother’s Health Deterioration: Indication for C/S

<table>
<thead>
<tr>
<th></th>
<th>Comparison to Normal Lab Values</th>
<th>Change in Lab Values from Admission to Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets</td>
<td><img src="image" alt="Down Arrow" /></td>
<td>267k down to 111k</td>
</tr>
<tr>
<td>AST</td>
<td><img src="image" alt="Up Arrow" /></td>
<td>15 up to 75</td>
</tr>
<tr>
<td>ALT</td>
<td><img src="image" alt="Up Arrow" /></td>
<td>14 up to 62</td>
</tr>
<tr>
<td>Uric Acid</td>
<td><img src="image" alt="Up Arrow" /></td>
<td>7.7 up to 8.2</td>
</tr>
<tr>
<td>LDH</td>
<td><img src="image" alt="Up Arrow" /> <img src="image" alt="Up Arrow" /> <img src="image" alt="Up Arrow" /> <img src="image" alt="Up Arrow" /> <img src="image" alt="Up Arrow" /> <img src="image" alt="Up Arrow" /> <img src="image" alt="Up Arrow" /></td>
<td>547</td>
</tr>
</tbody>
</table>

### Snapshot of Patient’s Lab Values

![Graph of Patient’s Lab Values](image)
Delivery

- An estimated 1000cc’s of abdominal fluid was drained before delivery fetus
  - No analysis of the fluid was done
  - However, when ascitic fluid is analyzed in this type of case, it is often transudative

- Fetus was found in cephalic presentation and was delivered successfully
  - Immediately placed in care of neonatology
  - APGAR score of 1 at 5 mins
  - APGAR score of 6 at 10 mins

- Delivery of the placenta was uneventful and sent to pathology for analysis
  - 2 bulges on the fetal side
  - Ragged cotyledons on the maternal side

Placental Pathology

Placenta ultrasound showing complex structure visualized in the superior/anterior portion of the placenta measuring 2.1 x 2.3 x 2.2cm
Discussion

Unique Features

This case study demonstrates a unique presentation of preeclampsia for several reasons:

1) early onset before 34 weeks 
2) oliguria 
3) pulmonary edema 
4) decreased fetal growth 
5) oligohydramnios 
6) impaired liver function 
7) over 6g of protein in urine in 24 hour time period 
8) massive ascites (over 1000cc of fluid) with marked abdominal distention.

It is rare for all of these symptoms of preeclampsia to present in the same patient. In fact, this case actually shows the progression from preeclampsia to class III HELLP syndrome with ascites and pulmonary edema, ultimately resulting in impending adult respiratory distress syndrome.
Disposition of Mother and Follow-Up

- After delivery, mother's symptoms began improving and after receiving several doses of furosemide postpartum, her breathing and dyspnea began to improve.
  - Her platelets increased to 167k at time of discharge from 111k at time of delivery
  - 2 months after delivery her platelets normalized to 333k
  - Her RUQ pain dissipated
  - Discomfort at cesarean incision site persisted for 2 weeks
  - Upper thoracic pain remained for 2 weeks, likely due to irritated viscerosomatic reflexes.
- 2 months after delivery, she has returned to her pre-pregnancy weight with no problems breastfeeding.
- Additional postpartum lab work was ordered and showed indeterminate levels of anticardiolipin antibodies which will require further testing to rule out antiphospholipid syndrome and/or lupus.

Disposition of the Infant and Follow-Up

- Infant was born severely premature at 27 weeks 5 days, weighing 0.82kg
  - APGAR scores of 1 at 5 minutes, and 6 at 10 minutes were noted
  - Required invasive mechanical ventilation for 4 days and then transitioned to nasal CPAP
- Low birth weight confirms the IUGR diagnosis
  - Prior to delivery, it was noted on BPP's that the AFI was decreasing
  - It's possible the AFI was on the low end of normal prior to hospital admission
  - At the time of delivery there was oligohydramnios bordering on anhydramnios
- IUGR was an expected potential clinical outcome because of decrease in adequate blood to the fetus due to:
  - Mother's severe preeclampsia
  - Intermittent absent end-diastolic velocity on umbilical artery doppler
- The infant stayed in the NICU for 83 days and was discharged home with mild retinopathy of prematurity but no other long-term sequelae.
Lessons Learned

Liver Dysfunction During Pregnancy

Liver dysfunction during pregnancy can be multifactorial in its cause.

- Preeclampsia, HELLP syndrome, and acute fatty liver of pregnancy (AFLP) are pregnancy induced conditions in which liver function is impaired.
- HELLP and AFLP can both lead to preeclampsia despite their differences in cause.
  - Fifty percent of patients with AFLP have preeclampsia, and in patients with severe preeclampsia, twenty percent of those patients will go on to develop HELLP syndrome.
  - For patients presenting with preeclampsia symptoms, consider AFLP as part of the differential.

If a patient presents with preeclampsia symptoms, it is imperative to check:
- 1. Platelets
- 2. Coagulation studies
- 3. Urine protein
- 4. Liver function tests
- 5. Glucose levels
- 6. Blood pressure
Acute Fatty Liver Disease of Pregnancy

- Acute fatty liver of pregnancy is linked to a deficiency in mitochondrial long chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) leading to a build up of long chain fatty acyl metabolites
  - These metabolites are toxic to the liver of the fetus and mother
    - Deadly to both fetus and mother if not diagnosed and treated in a timely manner
  - Recessive
    - Carriers can have homozygous offspring with AFLP

- The Arizona newborn screening exam checks for LCHAD
  - Can help determine if a woman's symptoms were due to AFLP
  - Identifies the deficiency to prevent failure to thrive in newborns

Preeclampsia

Acute Fatty Liver Disease of Pregnancy (AFLP)

HELPP Syndrome
<table>
<thead>
<tr>
<th></th>
<th><strong>AFLP</strong></th>
<th><strong>HELLP</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LFT's</strong></td>
<td>Substantially High</td>
<td>Moderately High</td>
</tr>
<tr>
<td><strong>Platelet Count</strong></td>
<td>Normal</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Glucose</strong></td>
<td>Hypoglycemic</td>
<td>Euglycemic</td>
</tr>
<tr>
<td><strong>Hepatic Imaging</strong></td>
<td>Fatty infiltration</td>
<td>Hepatic infarcts, hematomas, rupture</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patchy, extensive necrosis</td>
</tr>
<tr>
<td><strong>Liver Biopsy</strong></td>
<td>Fat accumulation in pericentral hepatocytes</td>
<td>Fat accumulation in periportal hepatocytes</td>
</tr>
<tr>
<td><strong>Clinical Features</strong></td>
<td>Liver failure with coagulopathy, encephalopathy, DIC</td>
<td>Hemolysis (anemia) Thrombocytopenia (below 50k)</td>
</tr>
</tbody>
</table>

**Improved Differentiation between HELLP and AFLP**

1. **Improved differentiation between HELLP and AFLP**
   a. Consider a liver biopsy in cases where patients have symptoms that are difficult to differentiate between preeclampsia, HELLP, and AFLP.
      i. Liver biopsy at time of cesarean would have confirmed whether patient had HELLP syndrome from preeclampsia with severe features progression or due to AFLP.
      ii. While treatment for both conditions is delivery, it would prove useful in subsequent pregnancies and as a tool for fetal health in that beta oxidation of fatty acids is strongly correlated in acute fatty liver of pregnancy.
   b. Consider ordering coagulation studies in preeclamptic patients.
Relationship Between Blood Pressure Control and Fetal Status

Further research is needed in regard to blood pressure control in preeclampsia. There was a negative correlation between lowered blood pressure and reassuring fetal status in this case. As the mother’s blood pressure was more tightly controlled, the fetus performed more poorly. It would be worth considering how keeping blood pressures marginally elevated may benefit the fetus while posing only minimal risk to mother. This treatment would be with the purpose to keep placental perfusion up and baby in utero for longer to decrease neonatal morbidities. The fetus in this case had difficulty continuing to pass her biophysical ultrasounds as maternal blood pressure became controlled.

This case demonstrates the importance of:
1. Careful fluid management in preeclampsia
2. Early intervention of neuroprotective medications
3. Thrombosis prophylaxis
4. Close fetal monitoring
5. Frequent lab monitoring including coagulation panels in preeclampsia cases
6. Delivery prior to downtrending platelets.
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References


