AFLP: Essentials for the MFM Consultant-Subspecialist
James N Martin Jr, MD for November 15, 2016 MFM Series

What is acute fatty liver of pregnancy (AFLP)? Is it “acute”?
Disorder unique to human pregnancy
1:10,000—1:20,000 pregs (2-4 cases in Mississippi annually)
Microvesicular fatty infiltration of maternal hepatocytes (and placenta, etc)

Average gestational age at diagnosis 36 wks (26-42) (Wang et al)
Average maternal age = 25.2 years; 85% G1
30-31% are multiple gestations
“Acute” is a misnomer because this develops over an extended time

What is the pathogenesis of AFLP?
Defective mitochondrial beta-oxidation of fatty acids by mother and/or fetus
Long-chain, medium-chain, short-chain acyl-CoA dehydrogenase deficiency
Likely that only specific genetic defects lead to increased risk for AFLP
Most common maternal mutation: G1528C (this alters amino acid 474; Glutamic acid becomes glutamine on the protein E474Q)
Testing for G1528C that is negative DOES NOT RULE OUT LCHAD deficiency

Is there danger to newborn?
When stressed, infants with LCHAD are at risk to develop fatal nonketotic hypo-Glycemia, imitating Reye’s syndrome or defects in fetal urea cycle
Some can develop neonatal dilated cardiomyopathy, progressive neuromyopathy
THEREFORE: all AFLP patients → test for G1528C, if negative → check for others
When should the OBGYN/MFM suspect AFLP, how to diagnose?

“Usually a clinical diagnosis”

Third trimester, antepartum
Sxs: GI-N,V,anorexia; CNS-malaise; Skin-Jaundice

50% have PE, many have HELLP-like presentation

SWANSEA Criteria proposed 2002 by Ch’ng from Southwest Wales

Sxs: abdominal complaints, vomiting, hypoglycemia, encephalopathy
Labs: INCR bilirubin, AST, Uric, AKI, Ammonia, WBCs; DECR glucose;
Pathological INR/commencing DIC

What is in the differential diagnosis with AFLP?

Hyperemesis gravidarum
Intrahepatic gestational cholestasis
Preeclampsia
HELLP syndrome

How does the MFM distinguish HELLP from AFLP?

See ref Steadman, Martin 1991 shown above

Thrombotic microangiopathy (HELLP) vs
Consumptive coagulopathy (AFLP)

Look at the order of change in labs
Early thrombocytopenia=HELLP, later thrombocytopenia=AFLP
AST disproportionately elevated relative to thrombocytopenia=AFLP
Fibrinogen decreases, PT prolongation>>>low platelets (AFLP)
Total bilirubin rises, serum ammonia, hypoglycemia (before IV started),
Antithrombin3 very decreased (AFLP)
CNS findings of malaise, change in mental status (AFLP)
AKI greater than expected for HELLP (AFLP)
What other complication commonly afflict the AFLP patient?
- Infection, hemorrhage/bleeding
- Transient Central Diabetes insipidus (reduced clearance of placentally derived Vasopressinase by damaged liver → decreased vasopressin → Transient polyuria, polydipsia
- Pancreatitis

When is imaging of liver indicated?
- If clinical and laboratory picture is unclear, diagnosis is uncertain
- To rule out hepatic infarct or hematoma

When is liver biopsy indicated?
- If diagnosis unclear and it is imperative to know
- If coagulopathy not advanced and dangerous for biopsy
  **Insist on oil red O staining**
  Assess placenta for same when patient delivered

Is the patient at risk of AFLP recurrence?
- Yes, even if testing is negative; exact risk number uncertain
- **MFM surveillance of subsequent pregnancy is appropriate**

What are appropriate components of AFLP patient management?
1-Evaluate the Mother
2-Evaluate the Fetal Status (risk of fetal acidosis, distress, stillbirth)
3-Stabilize the Mother
  a. **GLUCOSE THERAPY:** Glucose infusion
  b. **HEMOTHERAPY:** Reverse the coagulopathy
    a. FFP, cryo, pRBCs, platelets
    b. **PEX especially if advanced/emergent/AKI/pulmonary/CNS etc**
  c. Monitor for pulmonary edema (low colloid osmotic pressure)
    a. Judicious fluid therapy
    b. Judicious blood component replacement therapy
    c. If AKI, very judicious!
  d. **SUPPORTIVE THERAPY/meticulous medical management**
  e. Patience (recovery 7-10 days)
4-Deliver
  a. CS generally best to speed recovery onset
  b. Vaginal if delivery soon, labor advanced; clinical judgment
5-Support recovery
  a. Intensive care setting often advantageous
  b. Pulmonary support commonly needed
  c. Reasons for/Advantages of PEX
REFERENCES for AFLP:

UpToDate July 2016 Acute Fatty Liver of Pregnancy (Bacq, Lee, Travis)


Knight M, Nelson-Percy C, Kurinczuk JJ, Spark P, Brocklehurst P for UK Obstetric Surveillance System. A prospective national study of acute fatty liver of pregnancy in the UK. Gut 2008 Jul;57(7):951-6. (excellent summary of 57 women among 1.1M pregnancies 2005-2006, 5 cases per 100,000 maternities; 2% maternal death; perinatal mortality 104 per 1000 births)


Vigil-de Gracia P, Montufar-Rueda C. Acute fatty liver of pregnancy: diagnosis, treatment, and outcome based on 35 consecutive cases. J Matern Fetal Neo Med 2011 Sept;24(9):1143-6. (11% maternal deaths; AKI/ARF in 94%; abdominal pain in 51%)


Nelson DB, Yost NP, Cunningham FG. Acute fatty liver of pregnancy: clinical outcomes and expected duration of recovery. Am J Obstet Gynecol 2013 Nov;209(5):456.e1-7. (51 cases at Parkland 1975-2012; 7-10 days for labs to normalize; 4% maternal death; 53% had abdominal pain)

**Differential Diagnosis of AFLP:**


**Plasma Exchange for AFLP (107 patients):**
Fangli J et al, Discovery Med 13(72):369-373. (39 patients)
Majidi MRS and Vafaeimanesh J, Case Rep in OBGYN vol 2013, ID 615975. (3 pts)
Postpartum plasma exchange as adjunctive therapy for severe acute fatty liver of pregnancy.

Martin JN Jr, Briery CM, Rose CH, Owens MT, Bofill JA, Files JC.

Abstract
Acute fatty liver of pregnancy (AFLP) is a rare disease of progressive hepatic insufficiency and secondary systemic compromise that poses significant fetal-maternal risk. Plasma exchange (PEX) is an effective bridge therapy to sustain liver function and enable hepatocellular regeneration to occur in nonpregnant patients following acute decompensation of a chronic liver disease or while awaiting liver transplantation. The application of PEX for patients with AFLP is a novel concept; since 1988 we have utilized postpartum PEX (PPEX) as adjunctive medical therapy for six patients with severe AFLP. Before PPEX initiation, four patients had signs and symptoms of encephalopathy, three required ventilatory support, five had advanced liver insufficiency, and all six were developing renal failure. PPEX was initiated 2-8 days following delivery and repeated (two to four times, mean = 3) at 24-48-h intervals thereafter. All patients responded with composite clinical (symptoms/signs) and laboratory improvement; the average length of hospitalization following final PPEX for five of six patients was 7 days. No significant PPEX-related complications occurred. PPEX utilization in patients with severe AFLP may enhance maternal recovery by preventing secondary sequelae from hepatic insufficiency until spontaneous healing can occur. Further study appears to be indicated to validate a role for PPEX as supportive therapy for puerperal patients with AFLP suffering multiorgan failure.

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