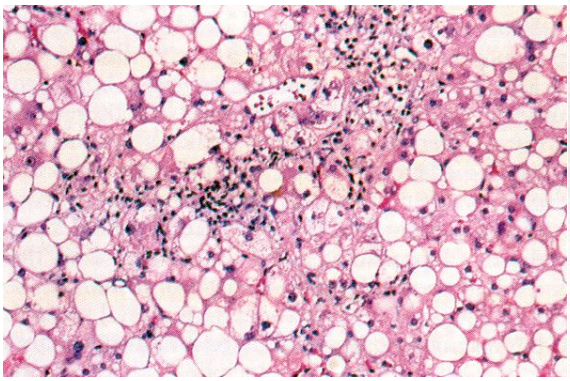
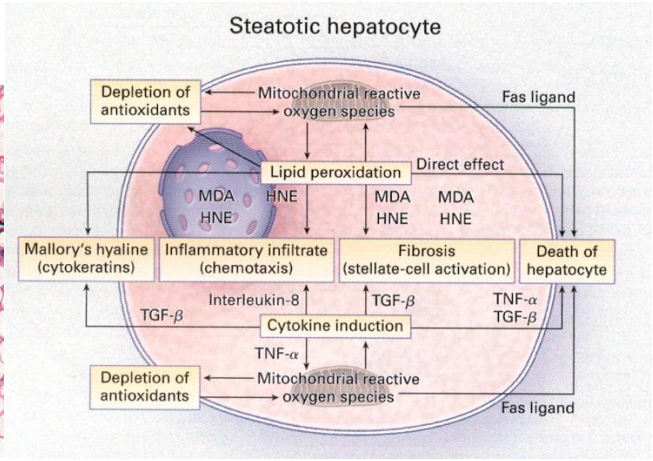
AFLP: Essentials for the MFM Consultant-Subspecialist
James N Martin Jr, MD *for* November 15, 2016 MFM Series

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

Obstet Gynecol Clin North Am. 1991 Jun;18(2):181-98.

Imitators of preeclampsia and HELLP syndrome.

Martin JN Jr[1], Stedman CM.

Author information

Abstract

The key to the differential diagnosis of these related conditions is knowledge of the natural history of each disease process; an awareness of how this usually translates in each instance into clinical and laboratory parameters; an appreciation for the wide spectrum of findings for each of these conditions, which are more aptly considered disease syndromes rather than single diseases; and the good fortune to encounter the patient early enough or midway in the course of her disease, prior to terminal stages when all subtle differences among disease syndromes almost disappear in a blur of grossly abnormal physiology and multiple organ failures.

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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)

Wang H-Y, Jiang Q, Shi H, Xu Y-Q, Shi A-C, Sun Y-L et al. Effect of caesarean section on maternal and foetal outcomes in acute fatty liver of pregnancy: a systematic review and meta-analysis. Sci. Rep. 6, 28826;doi: 10.1038/srep28826. *(best summary of totality of published data for 1350 subjects)*

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)*

Lau H-H, Chen Y-Y, Huang J-P, Chen C-Y, Su T-H, Chen C-P. Acute fatty liver of pregnancy in a Taiwanese Tertiary Care Center: a retrospective review. Taiwan J Obstet Gynecol 2010;49(2):156-9. *(11% maternal deaths; AKI/ARF in 83%, hypoglycemia in 61%, DIC in 61%; 18 cases over 22 years)*

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%)*

Zhang Y-P et al. Acute fatty liver of pregnancy: a retrospective analysis of 56 cases. Chin Med J; 2016 May 20; 129(10):1208-1214. *(review of 56 patients)*

Ibdah JA. Acute fatty liver of pregnancy: an update on pathogenesis and clinical implications. World J Gastroenterology 2006;12(46):7397-7404. *(very good review of oxidation problems/defects)*

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)*

Minakami H, Morikawa M, Yamada T, Yamada T, Akaishi R, Nishida R. Differentiation of AFLP from HELLP syndrome. J Obstet Gynaecol Res 2014 Mar; 40(3):641-9. *(advocates measuring AT3 and <65% suggests AFLP; 50% of AFLP patients did not have thrombocytopenia at presentation).*

Differential Diagnosis of AFLP:

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Marques P, Gunawardana K, Grossman A. Transient diabetes insipidus in pregnancy. Endocrin Diab Metab Case Reports, October 2015 ID: 15-0078.

Plasma Exchange for AFLP (107 patients):

Lamontagne R et al, Union Med Can 1970 June;99(6):1083-93.
Sohn U et al, Z Arzti Fortbild 1990;84(4):147-50.
Farine D et al. Am J Perinatol 1990 Oct; 7(4):316-8
Glaser V and Newman M. Z Geburtshilfe Perinatol 1991 Nov-Dec;195(6):272-4.
Castanon-Gonzalez JA et al, Gac Med Mex 1997 May-Jun;133(3):253-8.
**Martin JN Jr et al, J Clin Apher 2008;23(4):138-43. (6 patients)
Tang W et al, Artif Organs 2012 Mar;36(3):E39-47. (13 patients)
Fangli J et al, Discovery Med 13(72):369-373. (39 patients)
Chu YF et al, Artif Organs 2012 June;36(6):530-4. (11 patients)
Tang WX et al, Artif Organs 2012 June; 15(2):176-84. (17 patients)
Majidi MRS and Vafaeimanesh J, Case Rep in OBGYN vol 2013, ID 615975. (3 pts)
Yu C-B et al. Hepatobiliary Pancreat Dis Int 2014;13:179-183. (5 patients)
Hartwell L and Ma T, Dig Dis Sci 2014 Sept;59(9):2076-80.
Ding J et al. Gynecol Obstet Invest 2015;79(2):97-100. (6 patients)
Kobayashi T et al. J Obstet Gynaecol Res 2015 May;41(5):799-802.

J Clin Apher. 2008;23(4):138-43. doi: 10.1002/jca.20168.

Postpartum plasma exchange as adjunctive therapy for severe acute fatty liver of pregnancy.

Martin JN Jr[1], Briery CM, Rose CH, Owens MT, Bofill JA, Files JC.

Author information

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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