ACUTE FATTY LIVER OF PREGNANCY MASQUERADING AS HELLP SYNDROME

Santhosh Narayanan[1], Divya Prakash[2], Gomathy Subramaniam[3], Lakshminarayanan[4]

[1]Senior Resident, Department of General Medicine, Government Medical College, Kozhikode.
[2]Senior Resident, Department of Pathology, Government Medical College, Kozhikode.
[3]Professor and HOD, Department of Radiodiagnosis, Government Medical College, Kozhikode.
[4]Professor and HOD, Department of General Surgery, Government Medical College, Kozhikode.

HOW TO CITE THIS ARTICLE: Narayanan S, Prakash D, Subramaniam G, et al. Acute fatty liver of pregnancy masquerading as hellp syndrome. J. Evid. Based Med. Healthc. 2018; 5(20), 1592-1595. DOI: 10.18410/jebmh/2018/335

PRESENTATION OF THE CASE

A 28-year-old woman, $G_2P_1L_1$ at 34-weeks gestation was admitted to our hospital with a history of generalized pruritus for 2 weeks. She also complained of malaise, nausea, vomiting, and yellow coloured urine since last ten days. There was no history of fever. She had no respiratory/urinary/neurological complaints. Antenatal history was uneventful. She had no documented evidence of systemic hypertension. Supportive treatment for acute viral hepatitis was given at a private clinic and she was referred to us for further care.

Physical examination revealed a well-nourished, somnolent, but easily arousable woman. Her temperature was 36.7°C, pulse rate was 104/min, respiratory rate 20/ min, and blood pressure 120/80 mmHg. She was oriented to person, place, and time, and her focal neurological findings were non-contributory. She was icteric, with mild edema of the legs. Abdomen was no tender.

Complete blood counts revealed a haemoglobin: 11g/ dl, total leucocyte count: 10, 400/cumm, and platelet count: 96, 000/cumm. Peripheral smear did not show haemolysis and serum lactate dehydrogenase (S.LDH) levels was high/ Liver function tests showed aspartate aminotransferase: 208 U/l, alanine aminotransferase: 304 U/l, total bilirubin: 18.3 mg/dl, direct bilirubin: 12.7 mg/dl, alkaline phosphatase: 532 U/l, total protein: 6g/dl, and albumin: 2.6 g/dl. Biochemical tests revealed blood urea: 40 mg/dl, serum creatinine: 2.5 mg/dl, serum glucose: 60 mg/dl, and serum ammonia: 106 µmol/L. Coagullogram revealed a prothrombin time of 60 seconds with international normalized ratio (INR) of 3.2, fibrinogen: 62 mg/dl, and fibrin degradation products (FDP): 360 µg/ml. Urine analysis showed mild proteinuria. Serology tests like HBsAg, HCV, and HIV were all negative.

Induction of labour was done with prostaglandin E1 considering worsening coagulopathy and hepatic dysfunction. Delivered male baby wt. 1.76 kg with IUGR but had atonic post-partum haemorrhage. She was treated with fresh frozen plasma, whole blood, oxytocin, ergots. She was transferred to medical ICU. She had intractable hypoglycaemia, worsening sensorium and decreasing urine output for next three days. There was also development of multiple petechial spots all over body with continuing coagulopathy. Suspecting adrenal haemorrhage, fasting serum cortisol done which was on the lower limit of normal-7.2(6-19). Thyroid function showed a sick euthyroid state with low TSH and normal T3, T4 levels. Her blood and urine cultures were negative and there was no clinical evidence of sepsis. She started improving after 5 days and made a good recovery at the end of 2 weeks. Genetic analysis for LCHAD deficiency mutations showed the patient was negative for the common variant.

CLINICAL DIAGNOSIS

Acute fatty liver of pregnancy.

DIFFERENTIAL DIAGNOSIS

Jaundice during pregnancy may be due to numerous causes like cholestasis, cholelithiasis, viral hepatitis, pre-eclampsia with or without HELLP syndrome, and AFLP. Intrahepatic cholestasis of pregnancy usually presents during the third trimester, but itching is the characteristic symptom and serum bilirubin concentration is rarely higher than 6mg/ dl. Cholelithiasis can occur at any time during pregnancy and is accompanied by pain in the right upper quadrant, and fever, and USG is usually diagnostic. Acute viral hepatitis in pregnancy presents as a systemic illness with fever, nausea, vomiting, fatigue, and jaundice, however, aminotransferase concentrations are markedly elevated (>500U/liter). All these causes were ruled out in our case on the basis of presentation, symptoms, and investigations.

PATHOLOGICAL DISCUSSION

The hallmark of the acute fatty liver of pregnancy is hepatic micro vesicular steatosis (Figure 1) accompanied by lactic acidosis along with clinical and laboratory features of hepatic failure, such as encephalopathy, hyperammonaemia, hypoglycaemia and coagulopathy.[1] Acute fatty liver of pregnancy is a rare condition that is unique to human pregnancy. It affects pregnant women usually in the third trimester of pregnancy. It is sometimes associated with a very high maternal and perinatal mortality. It is necessary to diagnose this condition quickly, as prompt delivery can ensue good outcome. Long chain 3-hydroxyacyl CoA dehydrogenase (LCHAD) is an enzyme

Financial or Other, Competing Interest: None.
Submission 22-04-2018, Peer Review 25-04-2018,
Acceptance 09-05-2018, Published 14-05-2018.
Corresponding Author:
Dr. Santhosh Narayanan,
#27/685, 'Santhosh',
Kuthiravattom Post,
Kozhikode – 673016.
E-mail: drsanthosh4@gmail.com
DOI: 10.18410/jebmh/2018/335

which is a part of the enzyme complex known as the mitochondrial trifunctional protein (MTP). It is believed that G1528C and E474Q mutations of MTP gene lead to LCHAD deficiency. When a woman heterozygous for these mutations has a foetus homozygous for this defect, it results in accumulation of foetal fatty acids which return to the mother's circulation. This extra load of long chain fatty acids and hence triglycerides lead to fat deposition in the hepatocytes and impaired liver functions resulting in acute fatty liver of pregnancy.[2]

Pre-eclampsia with liver involvement, HELLP syndrome, and AFLP manifest specific patterns, particularly in relationship with the timing of gestational age, however, they share many similarities in clinical features and laboratory abnormalities, and differentiation between them may be difficult. The manifestations of pre-eclampsia are usually observed in the second half of pregnancy, whereas the symptoms of HELLP syndrome and AFLP frequently appear in the third trimester. The incidence of HELLP syndrome is much higher (1:5, 000) than that of AFLP (1:13,000). Severe coagulopathy, jaundice, hepatic encephalopathy, ascites, hypoglycaemia, and a mild to moderate elevation of transaminase levels are the key features of AFLP.[3]

There are no specific diagnostic criteria to diagnose AFLP. UKOSS group has put forward the "Swansea" criteria.

6 or more of the following after excluding other causes	
Clinical	Vomiting
	Abdominal pain
	Polydypsia/Polyuria
	Encephalopathy
Biochemical Hepatic	Bilirubin >14 umol
	AST/ALT (100%) >42 IU/L
	Ammonia (50%) >47 umol/L
Renal	Urate (88%) >340 umol/l Creatinine (58%) >150 umol/l
Endocrine	Glucose (78%) < 4 mmol/l
Haematological	Leucocytosis (98%) >11 x109/l Coagulopathy- PT >14 secs OR APTT > 34 secs (often with Plt count >100 x1012) (>50%)
Radiological	Abdominal USG Bright Liver echo texture/Ascites (25%)
Histological	Liver Biopsy Microvesicular steatosis

Table 1. Swansea Criteria

The differences between AFLP and HELLP are depicted in Table 2 below.

	AFLP	HELLP
Prevalence	0.005% to 0.01%	0.2% to 0.6%
Onset	Third trimester, rarely in second trimester	Third trimester or postpartum
Family history	May or may not be present	Usually not present
Co-existence of pre-eclampsia	50%	100%
Striking feature	Liver failure	Hemolysis, thrombocytopenia
Liver enzymes	Raised (100-200 fold)	Raised (10-20 fold)
Bilirubin	<5 mg/dl	<5 mg/dl unless severe necrosis occurs
Platelets	Normal or low normal	Always decreased
Prothrombin time	Prolonged	Normal
Hypoglycaemia	Present	Absent
Pathology	Micro vesicular steatosis	Patchy necrosis and haemorrhages

Table 2. AFLP vs. HELLP

DISCUSSION OF MANAGEMENT

In pregnancy, pathological conditions causing abnormality of liver function tests need to be differentiated from normal physiologic changes. Among various causes of pathological hepatic dysfunction, acute fatty liver of pregnancy (AFLP) is uncommon compared to pre-eclampsia and haemolytic anaemia, elevated liver enzymes and low platelets (HELLP) syndrome. Early diagnosis and prompt termination of pregnancy is necessary for better maternal and foetal outcomes.[4]

Management of jaundice during pregnancy especially in third trimester remains a dilemma for the obstetrician because of its varied aetiology, unpredictable prognosis and guarded perinatal outcome. Diagnosing the aetiology of jaundice is extremely important in pregnant patients as certain conditions like acute fatty liver of pregnancy (AFLP), HELLP syndrome and intra-hepatic cholestasis of pregnancy (ICP) may require early termination of pregnancy even in the presence of jaundice and or coagulation failure.[5] On the other hand, in conditions like acute viral hepatitis one must try to prolong pregnancy till the liver has recovered. Thus, the maternal and foetal outcomes of pregnancy can significantly be improved by appropriate management. Acute fatty liver of pregnancy is a rare but life-threatening cause of jaundice in the third trimester of pregnancy and early postpartum period. It is associated a high maternal and neonatal mortality. Once diagnosed, prompt delivery is associated with a significantly improved outcome but peripartum management becomes difficult if the pregnancy is complicated by coagulation failure also.

Maternal stabilization needs dextrose infusion and treatment of coagulopathy (administration of FFP, cryoprecipitate, packed red blood cells and platelets), as needed.[6] Fluid status should be vigilantly monitored because low plasmatic oncotic pressure leads to pulmonary congestion. Hypoglycaemia should be treated with a continuous infusion of 10 percent dextrose solution. Some patients with severe hypoglycaemia may require multiple supplementary 50 percent dextrose solutions.[7]

The route of delivery depends on a combination of factors: status of mother and foetus, and the probability of successful labour induction. The foetus should be continuously monitored to assess for the presence of any concerning foetal heart rate patterns, especially bradycardia. Induction of labour is a fair option if the mother and foetus could be stabilized and vaginal delivery is likely to be accomplished within 24 hours.[8] Caesarean delivery is indicated if accomplishing a successful vaginal birth within 24 hours is unlikely or if there is concern for rapidly progressing maternal/foetal decompensation. In the setting of coagulopathy, delivery should be undertaken with concomitant administration of appropriate blood products.[9]

Patients with acute fatty liver of pregnancy are extremely susceptible to developing coagulopathies due to decreased hepatic production of coagulation factors and/or disseminated intravascular coagulation (DIC). As a result, these patients are at high risk for bleeding complications.[10] Frequent serial monitoring (i. e., every several hours) of the patient's platelet count, international normalized ratio (INR), partial thromboplastin time, and fibrinogen levels should be undertaken to assess for overt or evolving coagulopathy.[11]

The liver tests and coagulopathy usually start to normalize shortly after delivery. A transient worsening of liver and renal functions and coagulopathy may occur during the first few days after delivery followed by a definitive improvement.[12] In most severe cases, mostly when diagnosis has been delayed, there may be many more days of illness requiring maximal supportive management in an intensive care unit, including mechanical ventilation because of coma, dialysis for acute renal failure, parenteral nutrition because of associated pancreatitis, or even surgery to treat bleeding from a preceding caesarean section. Most severely ill patients recover and have no sequelae of the liver disease itself However, substantial morbidity and mortality can occur.[13,14]

To conclude, acute fatty liver of pregnancy is a rare life-threatening emergency that usually occurs in third trimester. Usual clinical course is improvement within 24-48 hours of delivery, but requires close monitoring. Intractable hypoglycaemia and coagulopathy may be a horrendous task to manage at times. Acute fatty liver can recur in subsequent pregnancies, even if the search of LCHAD mutation is negative and hence requires maternal counselling.[15]

FINAL DIAGNOSIS

Acute fatty liver of pregnancy complicated by sepsis, coagulopathy in the postpartum period.

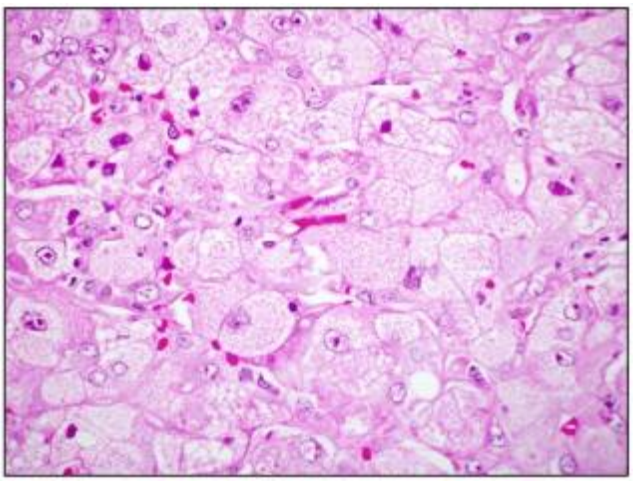

Figure 1. Microvesicular Steatosis in Acute Fatty Liver of Pregnancy

REFERENCES

[1] Bacq Y. The liver in pregnancy. In: Schiff ER, Sorrell MF, Schiff L, et al, eds. Schiff's diseases of the liver. 10th edn. Lippincott: Williams and Wilkins 2006:1281-1304.

[2] Riely CA. Liver disease in the pregnant patient. Am J Gastroenterol 1999;94(7):1728-1732.

[3] Pereira SP, O'Donohue J, Wendon J, et al. Maternal and perinatal outcome in severe pregnancy-related liver disease. Hepatology 1997;26(5):1258-1262.

[4] Reyes H. Acute fatty liver of pregnancy: a cryptic disease threatening mother and child. Clin Liver Dis 1999;3:69-81.

[5] Castro MA, Fassett MJ, Reynolds TB, et al. Reversible peripartum liver failure: a new perspective on the diagnosis, treatment, and cause of acute fatty liver of pregnancy, based on 28 consecutive cases. Am J Obstet Gynecol 1999;181(2):389-395.

[6] Tan LK. Obstetric cholestasis: current opinions and management. Ann Acad Med Singapore 2003;32(3):294-298.

[7] Airede LR, Nnadi DC. The use of the condom-catheter for the treatment of postpartum haemorrhage - the Sokoto experience. Trop Doct 2008;38(2):84-86.

[8] Ko HH, Yoshida EM. Acute fatty liver of pregnancy. Can J Gastroenterol 2006;20(1):25-30.

[9] Lee NM, Brady CW. Liver disease in pregnancy. World J Gastroenterol 2009;15(8):897-906.

[10] Knox TA, Olans LB. Liver disease in pregnancy. N Engl J Med 1996;335(8):569-576.

[11] Jackson S, Kler RS, Bartlett K, et al. Combined enzyme defect of mitochondrial fatty acid oxidation. J Clin Invest 1992;90(4):1219-1225.

[12] Isaacs JD, Sims HF, Powell CK, et al. Maternal acute fatty liver of pregnancy associated with fetal trifunctional protein deficiency: molecular characterization of a novel maternal mutant allele. Pediatr Res 1996;40(3):393-398.
[13] Matern D, Hart P, Murtha AP, et al. Acute fatty liver of pregnancy associated with short-chain acyl-coenzyme A dehydrogenase deficiency. J Pediatr 2001;138(4):585-588.
[14] Yang Z, Yamada J, Zhao Y, et al. Prospective screening for pediatric mitochondrial trifunctional protein defects in pregnancies complicated by liver disease. JAMA 2002;288(17):2163-2166.
[15] Bellig LL. Maternal acute fatty liver of pregnancy and the associated risk for long-chain 3-hydroxyacyl-coenzyme a dehydrogenase (LCHAD) deficiency in infants. Adv Neonatal Care 2004;4(1):26-32.