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Case Report

ACUTE FATTY LIVER OF PREGNANCY: A CASE REPORT OF AN UNCOMMON DISEASE

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ABSTRACT

A 36 years old G5P2A2L1 presented with pain abdomen and impending scar rupture at 34 weeks of pregnancy. Emergency LUCS was done and post operatively diagnosed as acute fatty liver of pregnancy (AFLP). Post operative period was complicated by hepatic encephalopathy, dyselectrolytemia, coagulopathy. Although all the complications were corrected by 7 days, but sudden onset of severe thrombocytopenia due to unknown reason (?Sepsis) led to cerebro-vascular accident and finally a maternal mortality occurred. Some aspects of AFLP are still unknown that are to be investigated and managed respectively in future.

Key words: AFLP, coagulopathy, CVA, sepsis,

INTRODUCTION

Acute Fatty Liver in Pregnancy (AFLP) may be defined as acute liver failure with reduced hepatic metabolic capacity in the absence of other causes. The incidence of AFLP is reported to be 1 in 13000 pregnancies according to UKOSS (United Kingdom Obstetric Surveillance System). Fatty liver is more common in nulliparous with a male fetus and in 15% of cases there is a multifoetal gestation.[1] It usually occurs in late third trimester, rare cases have been reported as early as 23 and 26 weeks.[2] It is characterized by microvesicularsteatosis in the liver.

The precise etiology of AFLP is not known. It is thought to be due to a mitochondrial dysfunction in the oxidation of fatty acids leading to an accumulation in hepatocytes. The infiltration of fatty acids causes acute liver insufficiency. Some, if not all, cases of maternal fatty liver are due to recessively inherited mitochondrial abnormalities of fatty acid oxidation. Hallmarks of the disease include jaundice, coagulopathy and encephalopathy.

Women who develop AFLP are more likely to have a heterozygous long-chain 3-hydroxyacyl-coenzyme A dehydrogenase (LCHAD) deficiency.[1,2,3,4] LCHAD is found on the mitochondrial membrane and is involved in the beta oxidation of long-chain fatty acids. This gene mutation is recessive; therefore, outside of pregnancy under normal physiological conditions, women have normal fatty acid oxidation. However, if the fetus is homozygous for this mutation, it will be unable to oxidize fatty acids. These acids are passed to the mother, who, because of diminished enzyme function, cannot metabolize the additional fatty acids. Fatty liver is characterized by accumulation of microvesicular fat that literally 'crowds out' normal hepatocyte function. Symptoms and signs are vague and nonspecific such that making an early diagnosis is challenging. It usually develops over several days to weeks and includes malaise, anorexia, nausea and vomiting, epigastric pain and progressive jaundice. The presence of 5 among 14 **Swansea criteria** represents a validated method of supporting the diagnosis of AFLP. Though thrombocytopenia is not

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Table 1: Relevant Blood Reports done at the Hospital Central Laboratory Consecutively

DAY	HB	TC	PLATELET	Ur (mg/dl)	Cr (mg/dl)	BIL (mg/dl)	DIRECT BIL (mg/dl)	SGOT (U/L)	SGPT	ALP	Na+	K+	INR
DAY 1	11	15,000	2.1 LACS	56	2.3	10.68	9.52	120	45	644	152	3.5	2.6
DAY 2	11.2	19,400	1.98 LACS	79.7	1.6	13.12	10.8	70.4	36.8	663	137.62	3.29	3.1
DAY 3	12.7	25,000	2.0 LACS	92	1.2	15.5	8.5	51	RNA	203	182	2.8	2.8
DAY 4	12.9	25,000	1.5 LACS	110	0.7	14.4	7.7	ND	ND	204	High vaue	Low	2.0
DAY 5	ND	ND	ND	28	0.8	12.97	8.37	93	61	162	137	2.8	1.2
DAY 6	12.5	18,500	ND	107	0.8	8.1	6	89		184	143.36	2.94	ND
DAY 7	12.8	24,300	30,000	ND	ND	ND	ND	ND	ND	ND	ND	ND	1.2
DAY 8	ND	ND	60,000	23	0.8	4.8-M	3.67	49.7	37.4	396	133.0	3.31	1.3

• RNA- Reagent Not Available in lab, High and Low Value is reported in hospital if out of measuring range in available testing tools. ND – Not done

included in the Swansea criteria and is considered as a hallmark of HELLP syndrome, it is often found in AFLP, due to unknown reason.

Among various causes of pathological hepatic dysfunction, acute fatty liver of pregnancy (AFLP) is uncommon compared to pre-eclampsia and hemolytic anaemia, elevated liver enzymes and low platelets (HELLP) syndrome. Early diagnosis and prompt termination of pregnancy is necessary for better maternal and foetal outcomes.[1]

We present a case report of a 36-year-old woman with AFLP complicated by sepsis and multiple organ dysfunction syndrome (MODS) requiring intensive care in spite of prompt termination of pregnancy and the fatal outcome, in spite of all of our efforts due to the various complications of AFLP with surprising thrombocytopenia and DIC.

CASE REPORT

A 36 year old woman, G5P2A2L1 at 34 weeks of gestation was admitted to the hospital with a history of lower abdominal pain and bleeding per vagina from previous night. Her first abortion occurred at 5 months, delivered vaginally. Second pregnancy was a case of IUFD at 7 months, delivered a boy baby vaginally followed by check evacuation. Third pregnancy was successful by caesarean delivery of a girl baby who is living. The next pregnancy got aborted at 3-4 months.

This time she presented only with severe lower abdominal pain. She was oriented to person, place, and time. She had icterus, with no pedal oedema and non-hypertensive. No foetal heart sound on auscultation. Bedside USG proved it to be a case of IUFD and increased echogenicity of maternal liver. As she had severe scar tenderness at admission decision of immediate caesarean section was taken with the suspicion of impending rupture of previous caesarean scar. Bedside clotting test done and caesarean section was performed with delivery of a stillborn boy baby. It was found to be a case of impending rupture of previous scar during CS. She was transfused 4 units of FFP before operation and 2 units packed red cells transfused during operation. Her blood loss was 600 ml (approx.). Post operatively another 4 units of FFP was transfused. Patient was monitored at HDU and vitals were stable for 12 hours following delivery.

The blood reports on admission (Day 1) were Hb - 11g/ dl, TLC - 15,000/cm3, and platelet count – 210000/cu mm. Liver function tests showed aspartate aminotransferase 120 U/l, alanine aminotransferase 45 U/l, total bilirubin 10.68 mg/dl, direct bilirubin 9.52 mg/dl, alkaline phosphatase 644 U/l, total protein 6g/dl, and albumin 2.6 g/dl. Biochemical tests revealed blood urea 56 mg/dl, serum creatinine 2.3 mg/dl, serum glucose 80 mg/dl, Na^+ 152 mmol/L, K^+ 3.5 mmol/L, INR 2.6.

On 2nd postoperative day (Day 2) she suddenly developed restlessness and abnormal behaviour. Hepatic encephalopathy suspected and transferred to ICU though ventilator support was not needed. prothrombin time raised to 28 seconds with international normalized ratio (INR) of 3.1. Urine analysis showed mild proteinuria. All hepatitis profiles (hepatitis A, B, C, E) were negative. A presumptive diagnosis of AFLP with Hepatic Encephalopathy was made.

Twelve hours following admission to ICU, she became markedly tachycardic and tachypnoeic. USG whole abdomen showed increased echogenicity of liver, mild ascites and no gall bladder pathology. Arterial blood gas sample showed pH 7.520, PCO2 41.1mmHg, PO2 110 mm Hg, bicarbonate 35.0 mEq/L, and standard base deficit of 11.6 mEq/L. Her renal failure was corrected by volume replacement. It normalized in 2 days. Dialysis was not needed.

FFP of total 20 units over 6 days was transfused to correct coagulopathy. Although her renal failure improved, her serum bilirubin, sodium and potassium level was very much resistant to be corrected. Her bilirubin level started to decrease from day 6. During this period, she also received 5 units of packed red blood cells (PRBC) and was put on broad spectrum antibiotics. On 6thpostoperative day INR was 1.2. She was making a gradual recovery even she didn't need any oxygen support to maintain normal SpO2. Hepatic encephalopathy was corrected. She became well oriented with time, place and person. And we hoped her complete recovery in few days.

On 7th postoperative day suddenly she became drowsy again and on clinical examination she was found to have ?Cerebro Vascular Accident (CVA). Immediate CT scan was done and it was proved to be a case of left sided hemorrghagic CVA. Platelet count was surprisinglyfound to be 30,000 though INR was 1.2. Her leucocyte count also increased from 18500/cm3 to 24300/cm3. Platelet was transfused but it was too late to save the patient with a big size cerebral hematoma with ventricular extension. The patient died on 9th post-operative day due to CVA making all of us disappointed. (Table 1)

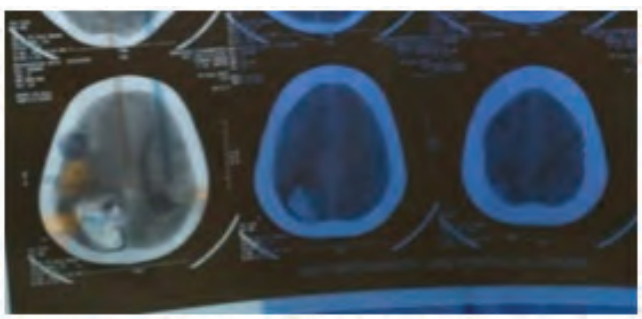

Photo 1 - Left sided hemorrghagic CVA

DISCUSSION

At presentation the bad obstetric history of our patient raised the suspicion of any genetic causes for liver dysfunction of the patient. She may be heterozygous carrier of LCHAD deficiency as she had history of one third trimester and one second trimester pregnancy losses of male fetuses. One living female child may be due to the genetic predisposition of AFLP. But this needs genetic testing which is not available in our hospital.

In our case, the clinical features of severe liver dysfunction appeared at the gestational age of 34 weeks. The symptoms initially mimicked those of acute viral hepatitis but clinical and laboratory evidence of severe coagulopathy, modest elevation of serum transaminase and bilirubin levels, hypoglycemia, an elevated ammonia value, and a low albumin level favoured the diagnosis of AFLP over HELLP syndrome. The liver biopsy is diagnostic but is not always feasible especially in patients with severe coagulopathy[8] and it seldom influences acute management.

The definitive management of AFLP is rapid delivery of the foetus and supportive care. Usually jaundice, liver dysfunction, and DIC may progress for one to two days after delivery but will then improve.[9] Before 1980, both the maternal and foetal mortality rates were about 85% and major causes were cerebral oedema, gastrointestinal haemorrhage, renal failure, coagulopathy, and sepsis. Mortality has been reduced to less than 10% at present because of better recognition and appropriate management.

In our case, the obstetric history of the patient is very much suggestive of AFLP as she had jaundice in pregnancy, in both the cases of 2nd trimester pregnancy loses with delivery of male fetuses, so the patient may have been heterogygous carrier of LCHAD deficiency. The patient went to the phase of encephalopathy even after termination of pregnancy. Surprisingly the bilirubin level was too high but transaminase levels were even lower than normal. Probably it may be due to extensive hepatocyte damage leading to underproduction of liver enzymes. Our patient presented rather late to us due to poor antenatal visit to hospital. Although we performed an early caesarean section, we were unable to interrupt the progression of the disease and her condition continued to deteriorate even after delivery.

In conclusion, AFLP is an uncommon, life-threatening complication of third trimester with variable presentation. While the natural history of the disease is improvement within 24–48 hours of delivery, it is recommended that patients who are critically ill at the time of presentation, who develop complications, or who continue to deteriorate despite emergency delivery, should be managed in the intensive care unit. Daily clinical assessment along with pathology and biochemistry reports are mandatory for detecting any abnormality as AFLP may turn not only to hepatic failure but associated coagulopathy even if corrected by FFP transfusion may not stop the underlying DIC. In present case sudden fall of platelet count from 2 lacs/cm^3 to 30,000/cm^3 may be due to underlying DIC that may have been provoked by sepsis. Though we suspected the case to have underlying DIC, it could not be substantiated by the relevant investigations like FDP, D-dimar and Fibrinogen levels (as FDP, D-dimar test facilities are not available in our hospital). Sudden fall of platelet count with increase in leucocyte count suggests that the new onset DIC may be provoked by

septicemia. Hepatorenal failure, Dyselectrolytemia, metabolic abnormality, DIC, CVA in a same patient proves that AFLP is very much challenging entity to deal with. It indicates that further case reports and researches are needed to gather more information regarding the spectrum of the disease and its all possible complications. In our case sudden fall of platelet count if would have been detected earlier, the CVA could have been avoided and the patient may have been saved.

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