

A Fatal Case of Acute Fatty Liver of Pregnancy with Mods

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Abstract: Acute fatty liver of pregnancy (AFLP) is a potentially fatal liver disorder of pregnancy, whose clinical diagnosis is difficult. We present a 28 year old primigravida at 34 weeks with singleton pregnancy who was referred with altered liver function tests (LFT) and renal failure. Based on clinical features and investigations we diagnosed the case as AFLP. She had multi organ dysfunction (MODS) and despite of rigorous ICU management, she was deteriorating. She responded to induction of labour and a dead fetus was delivered vaginally; but she ultimately succumbed to her condition after 13 days.

Keywords – AFLP, altered LFT, renal failure, multiorgan dysfunction, induction of labour

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I. Introduction

Acute fatty liver of pregnancy (AFLP) is a rare and potentially life-threatening complication of pregnancy which tends to manifest in the third trimester of pregnancy/early postpartum period. It was first described by Stander and Cadden in 1934 as “acute yellow atrophy of liver”. AFLP affects 1 in 7000 to 1 in 16000 deliveries [1,2]. It is found to be more common in primigravida, multiple gestation, obesity and pregnancies with male fetus (ratio of 3:1) [3]. Though the fetomaternal mortality has come down in the last few years due to early suspicion and diagnosis and early termination, maternal mortality rate is still estimated to be 12.5-18% with neonatal mortality rate of 7-66% [3].

Diagnosis of AFLP is challenging and complicated and is often delayed because of significant overlap in clinical and biochemical features with HELLP syndrome. It is a diagnosis of exclusion. Aetiology is not known.

Some of the clinical and pathological features of AFLP are similar to those found in certain autosomal, recessive disorders of fatty acid oxidation and hence it's been suggested that AFLP may result from defects in β -oxidation of fatty acids (inherited deficiency of a mitochondrial enzyme – long chain 3-hydroxyacyl coenzyme-A dehydrogenase) in fetus and/or mother, resulting in accumulation of long chain fatty acids in maternal hepatocytes. [4,5]

At present, supportive care and expeditious delivery remain the best treatment. Fulminant hepatic failure and coagulopathy are the common complications. Acidosis and coagulopathy increases the risk of IUFD.

II. Case Report

A 28 year old primigravida at 34 weeks was referred to our emergency department from another secondary centre with shortness of breath, palpitation, decreased urine output, edema and raised liver enzymes. She had history of several episodes of loose stool and vomiting 3 days prior to admission for which she was treated in peripheral centre and later referred to the secondary centre. On examination she was afebrile, pulse rate was 120/min, respiratory rate 30/min, BP was 90/50mmHg. Pallor and edema were present. There was tenderness in whole abdomen, mostly in the epigastrium. Urine output was 25ml. She was admitted in ICU. Nephrology, Gastroenterology and Medicine opinion were taken.

On admission she had anemia, with high serum creatinine, prothrombin time (PT) and INR (details in table 1) and there was hyponatremia (121mmol/L). Total bilirubin was 5.5mg/dl with direct bilirubin of 5mg/dl and raised liver enzymes (table 10). Total leucocyte count (TLC) was 12290/mm³, CRP was 13.6mg/L and serum lipase was 2225U/L. Gradually after admission her creatinine levels were rising and pro-calcitonin was high. USG showed hepatomegaly with fatty changes with altered renal echotexture and left sided minimal pleural effusion. Also her LFT was deteriorating with falling platelet & hemoglobin and increasing PT, APTT. D-dimer was 5162 and FDP was positive, suggesting disseminated intravascular coagulation (DIC). All infectious (hepatitis A, B, C, E, leptospira) and autoimmune causes of hepatitis were ruled out by serology. Fresh frozen plasma (FFP) transfusion was given daily along with packed cell transfusion when necessary. Hemodialysis was done. Urine R/E showed increased pus cells, hematuria and albuminuria. All other supportive management was done. She was put on mechanical ventilation on 3rd day of admission. She was maintaining normal blood sugar and electrolytes levels.

A 1.7 kg female, IUD fetus was delivered on 4th day of admission, after misoprostol induction. 1st degree perineal tear was repaired. After delivery, hemoglobin and platelet count became very low. Blood and platelet transfusions were also given. From 6th day i.e. 2nd day puerperium, she had fever spikes. Urine culture showed *Candida tropicalis* and Endotracheal tube culture showed *acinetobacter*, and the sensitive broad spectrum antibiotics and antifungals were given. High vaginal swab was negative. TLC was also maintained throughout at around 10000-11000/mm³.

Her urine output, PT and creatinine levels were gradually improving. But LFT was deteriorating, with bilirubin rising to 30mg/dl; mostly direct bilirubin. Her sensorium was also declining along with serum ammonia of 240.7micromol/L, indicating hepatic encephalopathy. Tracheostomy was done on 12th day.

In total she had 5 hemodialysis, 6 units platelet, 6units packed cell and 22 units FFP transfusion. She started having hypotension and bradycardia from 12th day for which ionotropes were given. On 13th day, she had cardiac arrest.

Table no.1- Investigations of the patient

	Day 1	Day 2	Day 4	Day 8	Day 12
Hemoglobin(gm/dl)	8.5	9.4	5.6	7.4	8.2
Platelet(lacs/mm ³)	1.28	1.18	0.45	0.45	0.26
PT(secs)/ INR	32.6/ 2.55	42.9/ 3.42	24.5/ 1.9	18/ 1.4	15.6/ 1.2
Total bilirubin(mg/dl)	5.5	5.82		24.38	30.07
S.creatinine(mg/dl)	3.8	4.94	4.82	3.7	2.41
Blood urea(mg/dl)	74	106			
AST/ALT/ALKP/GGTP (U/L)	164/134/292/177			187/42/196/133	
Others	Serum Albumin- 2.1gm/dl Lipase- 2225 U/L Amylase- 120 U/L	CRP- 13.6mg/L Pro-cal- 3.6ng/ml	CRP- 45.4mg/L	CRP- 132.1mg/L	S.NH3- 240.7

III. Discussion

Liver disorders in pregnancy include infectious hepatitis, preeclampsia, HELLP syndrome, intrahepatic cholestasis of pregnancy and AFLP. Differentiating these entities is difficult [1,6,7].

Although the other causes are much more common than AFLP and many presentations of HELLP syndrome were present in this case; these were all ruled out on basis of clinical features and investigations. Ch'ng *et al.* first set the Swansea criteria for diagnosing AFLP that have been used by many institutions.[9,10] Six or more of the following features are used to diagnose AFLP in the absence of other explanation:

- i) Vomiting
- ii) abdominal pain
- iii) polydipsia/polyuria
- iv) encephalopathy
- v) elevated bilirubin >14 µmol/L
- vi) hypoglycaemia <4 mmol/L
- vii) elevated urate >340 µmol/L
- viii) leukocytosis >11x10⁹/L
- ix) ascites or bright liver on ultrasound
- x) elevated transaminases
- xi) elevated ammonia >47 µmol/L
- xii) renal impairment creatinine >150 µmol/L
- xiii) coagulopathy (PT >14 sec or APTT >34 sec)
- xiv) microvesicular steatosis on liver biopsy.

Using these criteria we anticipated the diagnosis of AFLP, as our patient had 10 of these. Pathologically in AFLP, there is accumulation of microvesicular fat in the liver, that literally disrupts normal hepatocyte function. Gross examination shows a small, soft, yellow and greasy liver. Prominent histological abnormalities are swollen hepatocytes with central nuclei and cytoplasm filled with microvesicular fat, periportal sparing, and minimal hepatocellular necrosis. Although the diagnosis of AFLP can be made by liver biopsy, today the diagnosis is usually made clinically. Ultrasound and computed tomography may be used to identify liver changes; however these imaging studies too have low sensitivity and specificity [11].

The majority of women who are diagnosed with AFLP are in the third trimester of pregnancy and the mean gestational age is 35 to 36 weeks, with a range of 28 to 40 weeks [12,13]. Isolated case reports [14,15,16] of AFLP have shown that it can occur as early as 26 weeks and as late as the immediate postpartum period.

Symptoms usually develop over days to weeks and include malaise, anorexia, nausea and vomiting, epigastric pain and progressive jaundice. There is usually severe liver dysfunction with hypofibrinogenemia, hypoalbuminemia and prolonged clotting time. Serum transaminase levels are moderately elevated. The

syndrome continues to progressively worsen. Marked hypoglycemia is common and obvious hepatic encephalopathy, severe coagulopathy and renal failure can occur[17]. Fetal death is common with severe disease. Delivery arrests rapid deterioration of liver function. When acute pancreatitis develops, the prognosis is more ominous.

Systemic complications of AFLP include fulminant hepatic failure, encephalopathy, renal insufficiency, coagulopathy, sepsis, hypoglycemia, gastrointestinal hemorrhage, pancreatitis, acute respiratory distress syndrome [18] and Mallory-Weiss syndrome [19] which cause maternal deaths[20]. Our patient had renal failure, acute pancreatitis, DIC, sepsis and ultimately developed fulminant hepatic failure and hepatic encephalopathy. Due to multi organ dysfunction, the outcome was poor.

Management of AFLP comprises of rapid delivery of the fetus and supportive care. There is no other definitive therapy. In most of the cases, liver dysfunction, and DIC improve after 2-3 days of delivery [11].

Initial treatment involves supportive management with intravenous fluids, intravenous glucose and blood products, including fresh frozen plasma and cryoprecipitate to correct DIC. Once the mother is stabilized, arrangements are made for delivery.

The most critical component of caring for a woman with AFLP is the delivery of her fetus. There is no clear benefit to immediate cesarean delivery versus induction of labor and vaginal delivery with meticulous supportive care. Delivery may increase the maternal risk of coma, hypoglycemia, renal failure, worsening acidosis and severe hemorrhage. It is preferable to begin a trial of labor induction with close fetal surveillance. Transfusions with variable amounts of FFP, cryoprecipitate, whole blood, packed red cells and platelets are usually necessary if surgery is performed or if lacerations complicate vaginal delivery. Hepatic dysfunction begins to resolve postpartum. Patients with severe hepatic injury remain at risk for respiratory failure, renal failure, GI bleeding, and nephrogenic diabetes insipidus and should be closely monitored during the immediate postpartum period. The rare patient who progresses to fulminant hepatic failure can be treated by liver transplantation. Surviving patients generally recover with no hepatic sequel. Further pregnancies are often uncomplicated but remain at risk for recurrent AFLP[21].

IV. Conclusion

AFLP is a maternal, and fetal emergency. Early diagnosis and delivery of baby is the only definitive treatment along with the supportive therapy for liver failure. Post-delivery intensive treatment is always required for correction of complications such as coagulopathy and encephalopathy.

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