Case Report

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Acute Fatty Liver of Pregnancy: A Case Series

Neha Agarwal[1], Suchita Dabhadkar[2]

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Abstract

Introduction: Acute fatty liver of pregnancy (AFLP), a rare but recognized obstetric and medical emergency, is a catastrophic illness for both the mother and unborn offspring. It develops rapidly in the last trimester of pregnancy and contributes to significant maternal and perinatal mortality. Its demands early diagnosis, immediate delivery of fetus, systematic approach for anticipating complications and dealing with them.

Aim and Objective: To enlighten the varied presentations of this rare entity which help in early diagnosis, prompt delivery and highlighting the importance of supportive care to reduce maternal morbidity and mortality.

Materials and Methods: The authors report an observational case series of patients who developed AFLP and were managed in critical care in a period of 3 months.

Results: A total of three cases of AFLP were diagnosed in a period of 3 months. Nausea, vomiting and anorexia were the most common symptoms. Jaundice was seen in all. Anticipation of the complications like postpartum haemorrhage, DIC, hepatorenal syndrome and sepsis and providing prophylactic treatment in that view can reduce the morbidity and in-hospital days for the patient.

Conclusions: AFLP has significant perioperative mortality and morbidity secondary to renal dysfunction, coagulopathy and massive transfusion related complications. Clinical outcome can be improved by early diagnosis, urgent delivery of fetus and supportive care from multidisciplinary team.

Keywords: Acute Fatty Liver of Pregnancy; Postpartum haemorrhage; DIC; Hepatorenal syndrome; Sepsis.

Author's Affiliation: [1]Fellow in High Risk Obstetrics and Critical Care, [2]Professor, Department of Obstetrics and Gynecology, Bharati Vidyapeeth, Pune 411030, Maharashtra, India.

Corresponding Author: Suchita Dabhadkar, Professor, Department of Obstetrics and Gynecology, Bharati Vidyapeeth, Pune 411030, Maharashtra, India.

E-mail: sdabhadkar9@gmail.com

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INTRODUCTION

AFLP also known as Acute fatty metamorphosis or acute yellow atrophy, is a rare yet potentially fatal complication of third trimester. Its incidence ranges from 1 in 3333 to 1 in 6691 pregnancies at tertiary care hospitals in India.[1,2,3] Its more commonly seen in nulliparous, multiple gestation, underweight women and women carrying a male fetus.[4,5,6]

Maternal and fetal demise are 10% and 45% respectively.[1]

Its etiopathogenesis is attributed to recessively inherited fetal homozygous mutation of HADHA gene at exon (1528 G>C) encoding mitochondrial LCHAD (Long Chain Hydroxy Acyl coA Dehydrogenase) enzyme. The mutation in LCHAD results in accumulation of 3hydroxy fatty acids, like 3 hydroxy myristic acid, 3 hydroxy palmitic acid and 3 hydroxy dicarboxylic acid in the placenta, which are then shunted to maternal circulation leading to development of acute liver injury (lipotoxicity and lipoapoptosis) observed in patients with AFLP. The increased free fatty acids also accumulate in neurons, myocytes, cardiomyocytes and placental trophoblasts hence explaining all the complications of disease. As long chain 3 hydroxy fatty acid accumulates in these cells, lipotoxicity occurs, uncouples mitochondrial oxidative phosphorylation and diminishes mitochondrial respiration.

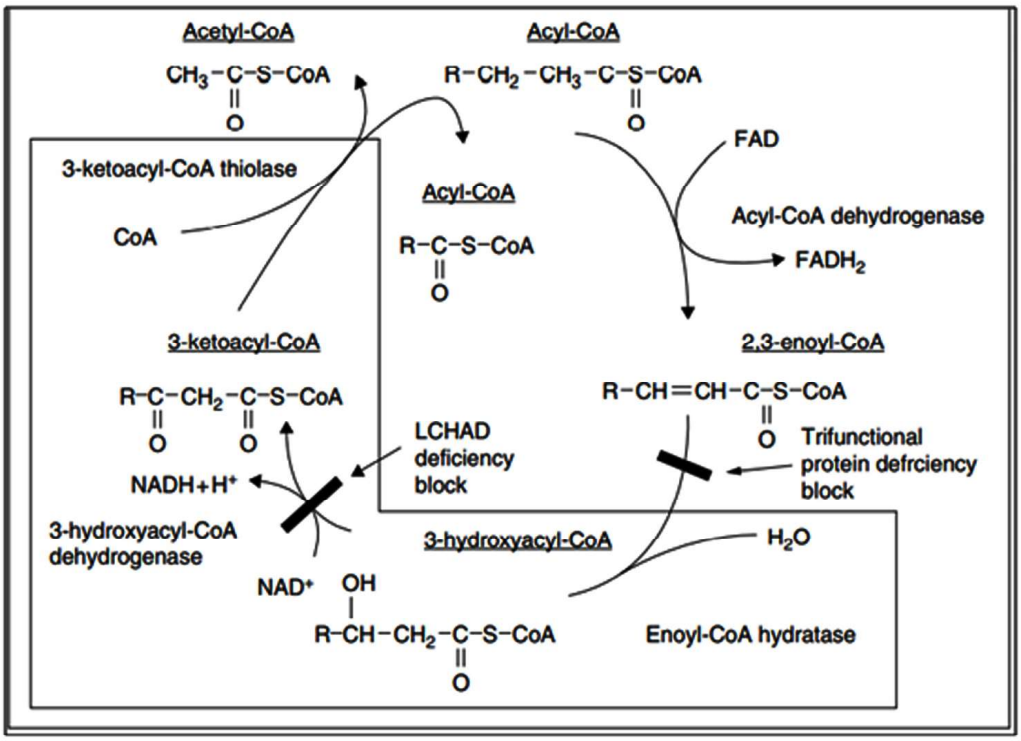

Fig. 1: The biochemistry of mitochondrial trifunctional protein (MTP) deficiencies.

Mitochondrial fatty acid β oxidation spiral where the MTP catalyzes long chain fatty acids substrates (see box). In isolated LCHAD deficiency, the pathway is blocked after the enoyl CoA hydratase reaction and before the 3 hydroxyacyl CoA dehydrogenase reaction, causing the accumulation of medium and long chain 3 hydroxy fatty acids and their metabolites. In complete MTP deficiency, the pathway is blocked after the acyl CoA dehydrogenase reaction and before the enoyl CoA dehydrogenase reaction, causing the accumulation of straight chain fatty acids and their metabolites.[7]

The diagnosis is made when 6 out of the following are present.

Swansea criteria[8]

Clinical	Vomiting, Abdominal pain, Polydipsia/ Polyuria, Encephalopathy
Biochemical	bilirubin >14 µmol/l
	AST/ALT >42 IU/l
	Ammonia >47 µmol/l
	Urea >340 µmol/l
	Creatinine >150 µmol/l
	Glucose < 4 µmol/l
	Leucocytosis >11x109/l
Coagulopathy	PT >14 sec or APTT>34 sec
Radiological	abdominal USG bright echotexture /ascites.
Histological	Gold Standard - micro vesicular steatosis.

Early diagnosis, multi-disciplinary team approach and termination of pregnancy are crucial for the management.

Mother should always be the priority in such cases. Coagulation abnormalities, hypertension, electrolyte imbalance and hypoglycemia need correction before termination of pregnancy. Ready availability of blood and blood products, ICU support and keen close observation of her vitals is the stepping stone.

Though vaginal delivery is best, caesarean birth is often performed due to rapidly deteriorating maternal condition and good NICU facility gives a fair chance of fetal survival.

CASE DISCUSSION

Case 1

Our first case was 24 years old primigravida at 34 weeks of gestation presented with complaints of generalized pruritis, anorexia and epigastric pain. She had 1 fever spike 3 days back. On examination was found to have jaundice, normal blood pressure and no bleeding manifestations. Per abdomen she had 34 weeks corresponding uterus with good fetal heart sounds. Her blood reports were completely deranged. Her haemoglobin was 14.3 g/dl, TLC count-19700, platelets-1.47 lakhs/mm3, glucose-62mg/dl, PT-18.9, APTT-48.6, INR-1.56, total bilirubin-10.3mg/dl (direct-7.5mg/dl and indirect-2.8mg/dl), AST-257 IU/l, SGPT-311IU/l, ALP-531U/l, Bile salts- 177µmol/l, urea-18mg/dl, creatinine-2.03, LDH-462 U/l, viral markers(HBsAg, HCV, HEV, HAV) were all negative. She was vitally stable and was prepared for emergency LSCS. She was given multiple blood products like Fresh Frozen Plasma and Cryoprecipitate before the incision. She was given general anaesthesia and isoflurane was used in induction, baby boy was delivered of 1.2 kg and shifted to neonatal ICU. Intraoperatively she developed atonic postpartum haemorrhage which was tackled by uterotonics and giving PRBC. Postoperatively was managed in the ICU-higher antibiotics-meropenem, hepatoprotective drugs-ursodeoxycholic acid and glutathione and Injection Vitamin K was used. She received multiple PRBC and FFP and her complete blood counts, Liver function tests along with coagulation profile were monitored daily. She recovered well after 6th postoperative day and was shifted out of ICU.

Case 2

Our second case was multigravida at 36 weeks gestation presented with vomiting, anorexia and epigastric pain. She had uneventful deliveries before. On examination had jaundice, normal blood pressure and no bleeding manifestations. Per abdomen her uterus was corresponding to 36 weeks pregnancy with good fetal heart sounds. Her haemoglobin was 15.9 g/dl, TLC count -23600, platelets -1.85 lakhs/mm3, glucose- 68mg/dl, PT-18.8, APTT-35.4, INR-1.5, total bilirubin-6.5mg/dl (direct-4.2mg/dl and indirect-2.3mg/dl), AST-909 IU/l, SGPT-776 IU/l, ALP-540U/l, urea-17mg/dl, creatinine-1.62, LDH-387 U/l and all viral markers (HBsAg, HCV, HEV, HAV) were negative. She was taken up for emergency LSCS in view of non-reactive NST and AFLP. She was transfused with Fresh Frozen Plasma and under general anaesthesia delivered baby boy of 2.275 kg. On 2nd postoperative day she was shifted out of ICU, however she had hyperkalaemia (K-6.5meq/l) which neededcorrection. On 7th postoperative day she was found to have partial wound gape which was treated with higher antibiotics and daily dressings.

Case 3

Our third case was a 19 years old, primigravida at 34 weeks gestation with headache and blurring of vision since 2 hours. On examination was found to have jaundice, pedal edema, blood pressure-150/100mm Hg and deep tendon reflexes were brisk. Per abdomen revealed a uterus of 32 weeks and good fetal heart sounds. Her haemoglobin was 13.2 g/dl, TLC count-23000, platelets-90,000 lakhs/mm3, glucose-55mg/dl, PT-20.8, APTT-39.4, INR-1.7, total bilirubin-7.5mg/dl (direct-5.2mg/dl and indirect-2.3mg/dl), AST-750 IU/l, SGPT-476 IU/l, ALP-440U/l, urea-17mg/dl, creatinine-1.92, LDH-780 U/l and all viral markers (HBsAg, HCV, HEV, HAV) were negative. She was posted for emergency LSCS in view of AFLP with severe preeclampsia. Her coagulation abnormalities were corrected by transfusing her Fresh Frozen Plasma. She delivered a male child of 1.2 kg and was managed further in NICU. She was managed postoperatively in ICU and given multiple transfusions as her coagulation studies kept deranging till 2nd postoperative day. However, she recovered uneventfully and was moved out of ICU on 5th postoperative day.

DISCUSSION

In our hospital, 3 cases of AFLP were treated during July 2021 to September 2021 of which 2 were primigravida's and 1 was multigravida. All presented in 3rd trimester and had jaundice. 1 of them had severe preeclampsia as well. All 3

delivered by caesarean, male children and all were managed in the critical care postoperatively. All 3 needed blood and blood product transfusion. The mean recovery period was 6th postoperative day.

AFLP is often a diagnosis of exclusion. Rare but potentially fatal complication encountered in the third trimester of pregnancy. Nearly 50% of these patients have preeclampsia as well. It needs to be differentiated from acute hepatitis, cholestasis of pregnancy and HELLP syndrome. Swansea criteria serves the purpose for easy and timely diagnosis. Systemic complications include fulminant hepatic failure, encephalopathy, acute renal failure, infection, pancreatitis, gastrointestinal haemorrhage, coagulopathy and hypoglycaemia. Maternal mortality of 100% in the past has now been reduced to 10%, due to early diagnosis and intervention.

Multidisciplinary approach and prompt delivery is the key to save the mother and her baby. Ready availability of blood and blood products, higher antibiotics, hepatoprotective drugs (Ursodeoxycholic acid and glutathione) are the most helpful in time of crisis.

AFLP is not an indication for caesarean, even though expeditious delivery is recommended. Attempts at induction of labour and vaginal delivery are appropriate as long as adequate maternal supportive care and fetal surveillance are possible. Even so, fetal compromise during labour is common and caesarean delivery is often necessary.

Recurrence risk in subsequent pregnancies is 25% with another carrying a homozygous mutant or compound heterozygous fetuses, it is uncommon and only a few cases have been documented. However, this may be false, as many women may refrain from having further pregnancies after such first occurrence. Thus affected women should be counselled and tested along with the baby for LCHAD and VLCHAD deficiency. Both genetic and metabolic tests (Tandem Mass Spectrometry) are available in India.

In future pregnancy, she can be offered amniocentesis or chorionic villus sampling for detection of fetus LCHAD status and hence her chances of developing AFLP.

CONCLUSION

Through this case series, I would like to re-emphasize the rare yet fatal nature of this disease. Not all cases, will present the same way and hence a high index of suspicion is important to quench the diagnosis. Prompt delivery and anticipation of complications, help to prevent mortality in these patients.

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