Received: 6 February 2023 | Revised: 1 March 2023 | Accepted: 15 April 2023

DOI: 10.1002/ccr3.7283

CASE REPORT

Clinical Case Reports Open Access WILEY

Acute fatty liver of pregnancy complicated by coagulopathy: A case report

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Key Clinical Message: We present the case of a rare obstetric emergency, which is usually fatal. Our case highlights suspicion of AFLP in patients presenting with jaundice in the third trimester with good maternal and fetal outcomes after a timely intervention.

Abstract: Acute fatty liver of pregnancy (AFLP) is a rare, obstetric emergency characterized by maternal liver dysfunction that can lead to maternal and fetal complications. We report a case of 28-year-old primigravida 39 weeks gestation diagnosed with AFLP complicated by coagulopathy with good maternal and fetal outcomes after a timely intervention.

KEYWORDS
acute fatty liver of pregnancy, acute liver failure, treatment outcome

1 | INTRODUCTION

The approximate incidence of AFLP, a disease of the third trimester unique to human pregnancy, is 1:7000–1:20,000.[1,2] AFLP is an uncommon cause of hepatic dysfunction during pregnancy compared to pre-eclampsia, obstetric cholestasis, and HELLP (hemolytic anemia, elevated liver enzymes, and low platelets) syndrome. We report a case of a 28-year patient in her first pregnancy at 39 weeks gestation who presented at term with jaundice and coagulopathy. She was delivered by caesarean section combating a series of anticipated complications such as hypoglycemia, transient diabetes insipidus, and coagulopathy necessitating massive transfusion of 6 U of fresh frozen plasma, 5 U of fresh whole blood, and 5 U of cryoprecipitate.

2 | CASE REPORT

A 28-year-old primigravid woman at 39 weeks +3 days of gestation was referred from a community hospital to a tertiary care center for evaluation and management of jaundice. Her primary complaints were yellowish discolouration of urine and sclera for 5 days. In addition, she also complained about polyuria and polydipsia for 2 days. She had regular antenatal follow-up; prior check-ups were uneventful. She had no history of medication use, gestational hypertension, flu-like symptoms, or travel to the malaria-endemic region. Human immunodeficiency virus and hepatitis panels were negative during her antenatal investigations.

On general examination, the patient was jaundiced with moderate pallor. Her blood pressure was 120/80 mm of Hg, pulse 100 b/min, and temperature was 98.4 F. Abdominal examination demonstrated term uterine size, longitudinal lie, breech presentation, four-fifths engaged fetal head, and fetal heart sound of 140 b/min. Per-speculum examination revealed no abnormalities. Per-vaginal examination revealed a posterior cervix that was soft in consistency, uneffaced, and closed. There was deranged liver function, hypoglycemia, and coagulation profile during admission (Table 1). Obstetric cholestasis

was ruled out because of normal bile acid level. HELLP syndrome was ruled out as the patient was normotensive with a normal platelet count. USG of the liver showed non-specific changes, including increased echogenicity and mild to moderate ascites. An obstetric scan showed a 3.4-kg fetus in breech presentation with the anterior upper uterine placenta and amniotic fluid index of 15.5 cm.

Acute fatty liver disease of pregnancy was diagnosed based on Swansea criteria (Table 2). Hypoglycemia was managed with 10% dextrose intravenously. Due to breech presentation in a primigravida lower segment cesarean section under spinal anesthesia was planned. Preoperatively, 2 unit of fresh frozen plasma (FFP) and 2 unit of fresh whole blood was transfused. In addition, injection of vitamin K 10 mg and tranexamic acid 1 gm was given. During the operation, 1 unit of fresh blood was further transfused. Intraoperatively around 200 mL of ascitic fluid was noted. A 3-kg male baby was delivered with an APGAR score of 7/10 and 8/10 in 1 and 5 min, respectively. The yellowish discolouration was noted over the uterus and placenta (Figures 1 and 2). Total blood loss during surgery was estimated to be 500 mL. Injection oxytocin (15 unit) and Inj methylergonovine 0.2 mg was given to prevent PPH. Postoperatively 1 unit of fresh blood, 4 unit of FFP, and 5 unit of cryoprecipitate was transfused to maintain normal coagulation. Postoperatively patient's clinical condition and laboratory markers improved (Table 3). The patient was discharged on the ninth postoperative day. The patient was counseled about follow-up in a nearby institution as she was unable to travel to our institution. In addition, patient was also counseled about the risk of recurrence in subsequent pregnancy and the need for close monitoring.

3 | DISCUSSION

This case highlights the importance of a high index of suspicion of acute fatty liver of pregnancy (AFLP) in a woman presenting with jaundice. Regarded as an obstetric emergency, data from the 1980s show mortality rates as high as

TABLE 1 Laboratory parameters on admission.

Laboratory parameter	Our patient	Reference range
Random blood sugar	2.6 mmoL/L	3.9–5.6 mmoL/L
Hemoglobin	8.6 gm/dL PBF: Microcytic hypochromic with target cell, spherocytes, and bite cell	10–14 gm/dL
Iron profile	Serum Iron: 53 µg/dL	60–170 µg/dL
	TIBC: 600 µg/dL	240–450 µg/dL
	Serum ferritin: 5 µg/L	11–307 µg/L
WBC	Total count: 14000	4000–11,000/µL
Platelets	163,000	150,000–400,000/µL
Bilirubin	Total: 14.8 mg/dL Direct: 9.2 mg/dL	Total: 0.1–1.2 mg/dL Direct: <0.3 mg/dL
Bile acid	6.7 µmoL/L	up to 11.0 µmoL/L
Coagulation and other	PT: 33 s	PT: 11–13.5 s
	INR: 2.75	0.8–1.1
	APTT: 60 s	21–35 s
	Fibrinogen: 76 mg	200–400 mg/dL
	D dimer: 2 mg/dL	<0.5 mg/dL
AST/ALT/ALP/LDH	158/169/591/641	AST (8–33 U/L), ALT (4–36 U/L), ALP (44–147 µkat/L), LDH (105–333 IU/L)
Serum creatinine	0.7 mg/dL	<0.87 mg/dL
Serum electrolyte	Sodium: 133	135–145 mEq/L
	Potassium: 4.2	3.5–5.5 mEq/L
Hepatitis panel (Hep A,B,C,E)	Negative	
Urine R/M/E	Trace albumin	

TABLE 2 Swansea criteria.

	Variable	Abnormal variable (our case)
Clinical features	1. Vomiting	−
	2. Abdominal pain	−
	3. Polyuria and polydipsia	+
	4. Encephalopathy	−
Laboratory	1. Hypoglycemia	+
	2. Leukocytosis	+
	3. Increase bilirubin	+
	4. Elevated ALT/AST	+
	5. Elevated ammonia	−
	6. Elevated urate	−
	7. Creatinine	−
	8. Elevated prothrombin time	+
Imaging	Bright liver/ascites	+
Histology	Microvesicular steatosis	Not done
Total variables	14	7

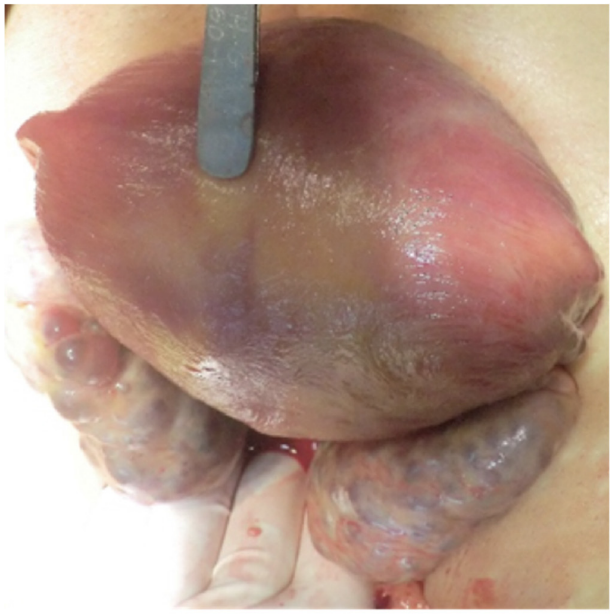

FIGURE 1 Yellow discoloration of uterus and ovaries.

70%, but more recent estimates are dramatically lower—around 2%, due to early intervention and delivery and the aggressive management of complications.[3] Our index case is also one, which highlights a favorable outcome due to prompt diagnosis and multidisciplinary management.

A number of risk factors are associated with the condition: first child, preeclampsia, male fetus, multiple pregnancies, low body mass index, and prior history of AFLP.[4] In our case, primigravida and male baby were the

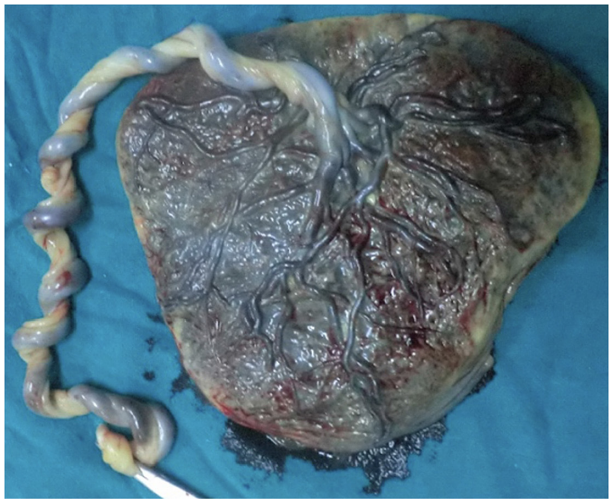

FIGURE 2 Yellowish discoloration of the placenta.

risk factors present. As far as the pathophysiology is concerned, problems with fatty acid metabolism seem to be a contributing factor to the development of the disease. Fetal long-chain 3-hydroxyacyl CoA dehydrogenase deficiency is linked to AFLP in about 20% of cases which is responsible for beta-oxidation of mitochondrial fatty acids.[4] This contributes build-up of harmful intermediate metabolites in maternal blood and liver cells, resulting in the disease. G1528C mutation, which has also been linked to HELLP syndrome and pre-eclampsia, was the most common mutation in patients with AFLP.[5] Although testing enzymes and mutation in infants can anticipate complications like hypoglycemia, we did not have testing available. Hence, frequent monitoring of newly born infant was done.

Although the diagnosis of AFLP has been made as early as 18 weeks and as late as 4 days after delivery, AFLP commonly manifests between the 30th and the 38th week of gestation.[6] This is because maternal body fat increases linearly until around 30 weeks of gestation and slightly decreases after the 30th week with exponential increases in fetal fat accretion. The decrease in the mother's fat stores is due to increased lipolysis and fatty acid transfer from the mother to the fetus through the placenta. This triggers increased lipid metabolism and mitochondrial fatty acid oxidation in the placenta (which has the same genetic makeup as the fetus) as well as in the fetus, hence triggering AFLP.[7] In our case, the patient presented at the 39th week of gestation.

One of the barriers to the diagnosis of AFLP is that it is very uncommon. More common diagnoses of jaundice occurring during pregnancy include viral hepatitis, HELLP syndrome, cholelithiasis, and intrahepatic cholestasis of pregnancy (ICP). In this case, negative viral markers ruled out hepatitis, and USG did not show any gallstones. Normal bile acid levels ruled out obstetric cholestasis. Moreover, patients with ICP commonly

TABLE 3 Postoperative coagulation profile follow-up.

Time (postoperative)	2 h	6 h	12 h	18 h	24 h	Day 2	Day 5
Hemoglobin (gm/dL)	10.2	10.3	10.9	11	11.3	11.2	12
PT/INR	24/2	20/2	18/1.5	22/1.73	22/1.73	20/1.57	16/1.3
APTT	60	55	48	39	40	42	30
Fibrinogen (mg/dL)	70	100	125	150	160	175	210
FDP (mg/L)	2	1	0.6	0.6	0.5	0.4	0.3
Platelet	159,000	155,400	154,700	155,000	154,000	153,000	154,600
Fresh blood	1 unit	–	–	–	–	–	–
Fresh frozen plasma	4 unit	–	–	–	–	–	–
Cryoprecipitate	5 unit	–	–	–	–	–	–

complain of pruritus, and their serum bilirubin levels do not usually exceed 6 mg/dL. AFLP can be indistinguishable from pre-eclampsia and HELLP syndrome as hypertension, hemolysis, elevated liver enzymes, and low platelet can be seen in both conditions, which may lead to an incorrect diagnosis.[8] However, severe comorbidities, such as profound hypoglycemia, renal failure, coagulopathy, disseminated intravascular coagulation, and encephalopathy, are more commonly associated with AFLP. In our case patient was normotensive, hypoglycemic and complicated by coagulopathy. Moreover, hypertension may also be absent in both cases of AFLP and HELLP syndrome.[9] Some patients with HELLP syndrome develop hypertension very late, even after liver enzymes are elevated or platelet count is decreased which is known as atypical HELLP syndrome. In our case, blood pressure was normal, but the diagnosis of AFLP as compared to atypical HELLP syndrome was made based on the Swansea criteria. 7/14 Swansea criteria were met, indicating AFLP (Table 2). In a study by Goel et al., the presence of six abnormal variables in Swansea criteria provided a positive predictive value for detecting microvesicular steatosis of 85% and a negative predictive value of 100%.[10] Liver biopsy is rarely done during pregnancy due to the danger it poses to the mother and fetus. It is also reserved for cases with diagnostic uncertainty and persistent liver dysfunction after delivery. Maternal stabilization and delivery should be prioritized over liver biopsy in patients with matching clinical features.[11]

Prompt delivery and supportive care are the mainstays of treatment and the delivery route depends on maternal/fetal status. Although vaginal deliveries are regarded as the safer option, in a study by Nelson et al., the rate of cesarean deliveries was almost 67%.[12] The treatment requires a multidisciplinary care team (hepatology, neonatology, anesthesia, blood bank) and frequent monitoring and treatment of complications. In our case, caesarean section was done as the woman was a primigravida with fetal breech presentation and the delivery was unlikely within 24 h. A continuous infusion of 10% glucose was done to prevent hypoglycemia. Blood dyscrasias incuding coagulopathy, thrombocytopenia, disseminated intravascular coagulation, and hemolysis, are frequently present and are the most deadly complication associated with AFLP.[13] In this condition, there is a decreased production of coagulation factors and procoagulant proteins, leading to coagulopathy in coexistence with hypercoagulability. A functional platelet defect can also occur due to coexisting uremia and endothelial abnormalities, decreased production of fibrinogen, reduced levels of antifibrinolytic pathway components, and upregulation of tissue plasminogen activator is observed, which leads to hyperfibrinolysis and disseminated intravascular coagulation.[14] Antifibrinolytic agents such as tranexamic acid that stabilize blood clots may have a role in high-risk patients with coagulopathy and an elevated risk for the development of disseminated intravascular coagulation, including patients with AFLP.[15] Hence, in our case, coagulopathy was managed with tranexamic acid, transfusion of blood products and vitamin K.

Hemorrhage, liver failure, and acute renal injury are the three main factors contributing to maternal morbidity and mortality.[12] Due to early detection, prompt delivery and development of critical care, the mortality rate has decreased over the past several decades.[8] Within a week following birth, most AFLP patients return to normal liver function.[12] Our patient also gradually returned to normal liver function and improvement in coagulopathy and was discharged on the ninth postoperative day, which point out the importance of early intervention and care to the patient. Patients followed postdelivery, all demonstrated a complete recovery of liver function with no evidence of cirrhosis or chronic hepatitis, and this further highlights the need for urgent management when AFLP is diagnosed and aggressive supportive care because the acute liver failure nearly always resolves with delivery of the fetus. Permanent fibrosis or long-term liver damage is uncommon.[16]

The baby born should also undergo screening and be monitored for signs and symptoms of fatty acid oxidation

disorders after delivery.[4] In addition, they should be screened and monitored for complications of hypoglycemia and metabolic derangements.[16] In our case, we did not have facilities to screen mutation and enzymes. Therefore, we monitored the baby closely who did not develop any complication.

4 | CONCLUSION

Early diagnosis and referral to a tertiary center with multidisciplinary facilities contributed to safe delivery and good materno-fetal outcome. However uncommon, AFLP should always be kept as a differential, which may be fatal if missed. Postdelivery follow-up of newborns and counseling regarding future risks should also be given adequate importance.

AUTHOR CONTRIBUTIONS

Swati Kumari: Conceptualization; resources; supervision; writing – original draft; writing – review and editing. **Ramesh Lamichhane:** Conceptualization; methodology; resources; writing – original draft; writing – review and editing. **Pawan karki:** Resources; writing – original draft; writing – review and editing. **Pritha Adhikari:** Resources; writing – original draft; writing – review and editing.

ACKNOWLEDGMENTS

We would like to acknowledge the patient herself and her relatives who allowed us to share their clinical report to the global platform so that others will be benefitted.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

The authors would like to declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

All the data generated or analysed during this study are included in the manuscript.

ETHICAL APPROVAL

As case reports are exempt from ethical approval in our institution, our article, which describes a case report, does not require additional permissions from the ethics committee.

CONSENT

Full written informed consent was obtained from the patient for publication of her case, and clinical images. A copy of written consent can be made available to the editor-in-chief of this journal upon request.

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How to cite this article: Kumari S, Lamichhane R, Karki P, Adhikari P. Acute fatty liver of pregnancy complicated by coagulopathy: A case report. *Clin Case Rep*. 2023;11:e07283. doi:10.1002/ccr3.7283