Acute Fatty Liver of Pregnancy and Disseminated Intravascular Coagulation: A Case Report

Abstract
28-year-old G1P0 at 33 weeks gestation presented with abdominal pain, elevated blood pressures and worsening edema. Laboratory workup revealed abnormal transaminases and hypofibrinogenemia. Diagnoses of disseminated intravascular coagulation (DIC) and acute fatty liver of pregnancy (AFLP) were made and out of concern for placental abruption, an emergency cesarean section was planned. Preoperatively, cryoprecipitate and fresh frozen plasma (FFP) were administered. Cesarean delivery was performed under general anesthesia. Postoperatively, her course was complicated by ongoing metabolic derangements and acute liver failure. She was transferred to a liver transplant facility and remained hospitalized for several months with gradual clinical improvement.

Keywords: Acute fatty liver of pregnancy, disseminated intravascular coagulation, hepatorenal syndrome

Background
Peri-partum acute liver failure can be fatal. HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome and AFLP (acute fatty liver of pregnancy) are significant causes of maternal and perinatal morbidity and mortality. These conditions represent a disease spectrum with similar pathophysiology. The initial presentation of AFLP mimics that of HELLP syndrome and includes malaise, nausea, and abdominal pain. Key abnormalities include vasoconstriction, coagulopathy, and elevated transaminases. Disseminated intravascular coagulation (DIC) and hemorrhage are the most common complications of AFLP and make emergency surgery a serious challenge. The following report describes a case of DIC-complicated AFLP, the challenges faced in its management, and an atypical recovery course. Written authorization has been obtained from the patient granting permission for this report.

Case Description
28-year-old primigravida presented to an outside hospital at 33 weeks gestation with lower extremity edema and abdominal pain. Her pregnancy had been uncomplicated. Vital signs were stable with mildly increased blood pressures. Laboratory workup revealed an elevated serum creatinine of 1.5 µmol/L, platelet count of 95 × 109/L, aspartate aminotransferase (AST) of 78 IU/L, and alanine aminotransferase (ALT) of 78 IU/L. She was diagnosed with severe preeclampsia, given a 4 g bolus of magnesium sulfate and transferred to our institution. On arrival, she received betamethasone for fetal lung maturity and was maintained on 1 g/h infusion of magnesium sulfate. Hospital day 2 laboratory analysis indicated further derangements including hypofibrinogenemia (fibrinogen <50 IU/L), increased international normalized ratio (INR) of 1.9, and hemoglobin of 10.3 g/dl. Liver biochemical markers also increased with AST 88 IU/L, ALT 75 IU/L, total bilirubin 8 µmol/L, and direct bilirubin 6.9 µmol/L. Due to the concern for a concealed placental abruption, the decision was made to deliver expeditiously via cesarean section under general anesthesia. Maternal fetal medicine and hematology were consulted. Large bore intravenous (IV) access was established and immediately prior to being taken to the operating room, she received 15 units of cryoprecipitate and 1 unit of fresh frozen plasma (FFP).

Additionally, for hyperkalemia (potassium 5.7 mEq/L), she was given 10 units of regular insulin IV with an
ampule of 50% dextrose. Left radial arterial line was placed prior to the induction. Rapid sequence intubation with propofol and succinylcholine was performed and a sevoflurane/nitrous oxide combination was used for maintenance. No blood products were required intraoperatively. For uterine atony, she received 40 units IV of pitocin plus 250 mg intramuscular (IM) of hemabate. Immediate postoperative laboratory values included hemoglobin 7.8 g/dl, platelets 89 × 109/L, INR 1.5, fibrinogen 92 IU/L, serum potassium 5.0 mEq/L, and serum glucose 68 mg/dl. In recovery, she experienced heavy vaginal bleeding and a Bakri balloon was placed by the obstetrics team. She was admitted to the surgical intensive care unit (SICU) for postoperative care. On postoperative day (POD) 1, laboratory workup demonstrated hemoglobin 6.3 g/dl, fibrinogen 70 IU/L, total bilirubin of 8.4 µmol/L and increased serum creatinine of 1.8 µmol/L. Thromboelastography analysis confirmed hyperfibrinolysis, which prompted the use of an aminocaproic acid infusion. For hypoglycemia, she required a 5% dextrose infusion. She exhibited mental status changes and was unable to physically ambulate. While in the SICU, she continued to have metabolic derangements and developed worsening of liver and kidney function. On postoperative day 6, a foley catheter was placed, and she was transferred to the Medical Intensive Care Unit (MICU). In the MICU, she developed persistent nausea and vomiting, which improved with nasogastric tube decompression and yielded large volume (>500 ml) bilious output. Ongoing oliguria was treated with an albumin infusion. Further clinical deterioration prompted transfer on postoperative day 7 to a liver transplant facility. On admission to the liver transplant facility, model for end-stage liver disease (MELD) score was 31 (total bilirubin 10.6 µmol/L, INR 2.0, and serum creatinine 2.1 µmol/L). She was noted to have altered mental status, dyspnea, gross anasarca, and bilateral pleural effusions on chest X-ray. She was intubated for worsening dyspnea and somnolence and remained intubated for 3 days while receiving broad spectrum antibiotics and furosemide. The patient underwent magnetic resonance cholangiopancreatography to rule out biliary obstruction, which was unremarkable. Given her MELD score >30 with rapid decompensation, she was started on lactulose/rifaximin therapy. Renal lab tests indicated the development of hepatorenal syndrome (HRS) with serum creatinine of 2.9 µmol/L, urine sodium <10 mEq/L, fractional excretion of sodium 2.1%, and urine microscopy remarkable for granular casts. She was subsequently started on HRS protocol with albumin, midodrine, and octreotide and soon after displayed improvement in renal function. She was first given rectal lactulose and as her encephalopathy improved, she was transitioned to oral lactulose. The oral lactulose was titrated to 3-4 bowel movements per day. Lactulose/rifaximin therapy was discontinued after one week when she became fully alert and oriented. Daily MELD labs showed improving liver function. She was discharged home after a 54-day stay in the liver transplant facility on POD 61.

Discussion

In this report, we present a case of DIC-complicated AFLP requiring emergency delivery via cesarean section. AFLP has an incidence of 1 in 13,000 pregnancies. Prior to 1980, the mortality associated with AFLP was in excess of 80%. Mortality has since improved due to earlier recognition, prompt treatment and a multi-disciplinary approach to care. Maternal mortality rate is now estimated to be 7-18%, and the fetal mortality rate 9-23%. AFLP usually presents in the third trimester of the first pregnancy. The signs and symptoms at initial presentation vary, making the diagnosis difficult, or resulting in a delay. The differential diagnosis includes HELLP syndrome, viral hepatitis, and hormone-induced cholestasis. There is no specific non-invasive diagnostic modality. Liver biopsy is the gold standard test, but is invasive and requires a patient without coagulopathy. The clinical presentation of both HELLP syndrome and AFLP are very similar, but nausea, vomiting, epigastric/RUQ pain and jaundice are more commonly seen in AFLP patients. The pathogenesis is not completely understood, but may be related to an abnormality in fetal fatty acid metabolism. Normal liver tissue contains 5% fat; in AFLP, this is upwards of 13-19%. This fatty infiltration, in addition to ammonia production, leads to hypoglycemia and coagulopathy. Our patient’s initial presentation was more consistent with HELLP syndrome, as she had elevated blood pressure, edema, and elevated liver transaminases. Nausea, vomiting, and jaundice were absent. Initial labs indicated that she was coagulopathic (INR 1.9 and fibrinogen <50 IU/L). DIC is seen in only 27% of HELLP syndrome patients as opposed to 80-100% of AFLP patients. DIC is a severe and potentially fatal complication of AFLP secondary to severe hepatic dysfunction. Early identification and correction of the coagulopathy prior to any obstetrical procedure is important. For both, HELLP syndrome and AFLP, delivery is the definitive form of treatment with expected clinical improvement to follow. Prior to delivery, maternal stabilization should be achieved in regards to hypertension, electrolyte abnormalities, and coagulation parameters. Vaginal delivery is preferred. However, a cesarean section is common if rapid maternal deterioration is present. Parturients with liver disease can be considered for epidural anesthesia if the hepatic dysfunction is mild and stable. Careful risks should be considered, including ongoing coagulopathy, as well as potential toxicity from local anesthetics since they undergo hepatic degradation. Intraoperatively, careful management of hemodynamics, fluids, electrolytes, and acid-base status is paramount in addition to expedited delivery of the fetus. Postpartum management parallels the pre and post-operative course,
with a high risk of postpartum bleeding. Maternal deaths in AFLP are caused by sepsis, hemorrhage, aspiration, renal failure, pancreatitis, and gastrointestinal bleeding. Optimal management of potential complications is accomplished by closely monitoring vital signs, physical exam findings, laboratory studies and imaging studies as needed. \[6,7\]

The use of liver transplantation in AFLP is controversial. In majority of the cases, it is not required. Castro et al. suggested that patients often deteriorated in the postpartum period and then gradually improved. Furthermore, transplantation should be reserved for those with liver rupture complicated by hepatic necrosis (as indicated by computer tomographic findings), the presence of hepatic encephalopathy, severe metabolic acidosis together with worsening coagulopathy, and/or increasing FFP requirements. \[8\] In several larger series of patients with AFLP, they often demonstrate deteriorating liver function tests for up to one week and then recover. \[9\] There were 8 reported cases of liver transplantation for AFLP from 1987-2003. \[10\]

For this patient, spontaneous resolution did not follow delivery and her postoperative course was complicated. Our patient’s clinical course was atypical in that she had sustained deterioration along with the development of HRS. Luckily, she eventually had full clinical recovery without transplantation. Subsequent pregnancies in AFLP patients generally have a lesser risk of recurrence or at least a decreased intensity of the disease as compared to the first pregnancy. \[11\]

An uncommon but complex disease that shares signs and symptoms with HELLP, AFLP can be best managed with prompt recognition and expedited delivery of the fetus via a multidisciplinary approach. Pre-operative, intraoperative and postpartum care should focus on hemodynamic monitoring, fluid status, electrolyte balance, coagulopathy and multi-organ function to give the best chance for maternal and fetal outcomes.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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