Acute Fatty Liver of Pregnancy: A Case Report and Literature Review
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Abstract
Acute Fatty Liver of Pregnancy (AFLP) is a rare, catastrophic disease affecting women in pregnancy. It usually occurs in the third trimester or post-partum period. It is usually a diagnosis of exclusion and a strong index of suspicion can lead to timely diagnosis. Delay in diagnosis is associated with morbid complications with high mortality. We report a case of 22 years old lady with 36 weeks pregnancy presented with malaise, nausea, vomiting and jaundice. A clinical diagnosis of acute fatty liver of pregnancy was made. Although early Cesarean section was performed, postoperative course was complicated by acute hepatic encephalopathy with hepato-renal shutdown and coagulopathy. Despite intensive management in critical care, the patient expired.

Introduction
Acute fatty liver of pregnancy (AFLP) affects 1 in 7000 to 1 in 16000 deliveries [1,2]. There is predilection for nulliparous women, women with multiple gestation and pregnancies with male fetus [3]. Maternal mortality rate is estimated to be 12.5-18% with neonatal mortality rate of 7-66% [3].

Diagnosing the etiology of jaundice is extremely important in pregnant patients as certain conditions like AFLP, HELLP syndrome and intra-hepatic cholestasis of pregnancy (ICP) may require early termination of pregnancy even in the presence of jaundice and or coagulation failure [1]. On the contrary, in conditions like acute viral hepatitis one must try to prolong pregnancy till the liver has recovered. Thus, the maternal and fetal outcomes of pregnancy can significantly be improved by appropriate management. However, differentiating these conditions is difficult due to unpredictable and similar presentation and laboratory investigations. Acute fatty liver of pregnancy is a rare but life threatening cause of jaundice in the third trimester of pregnancy and early postpartum period. It has very high maternal and fetal morbidity and mortality, especially if it is complicated by coagulation failure.

Case Report
A 22 years old primigravida with 36 weeks period of gestation was referred from a peripheral hospital to our tertiary care center with complaints of yellow discoloration of urine and eyes, malaise, anorexia and vomiting since 3-4 days. She had no complaints of pain abdomen, leaking or bleeding per vagina or decreased fetal movement. There was no significant past history. On examination she was conscious, oriented to time, place and person, cooperative and responding appropriately to verbal commands. The patient was well hydrated and afebrile. Her blood pressure was 120/84 mm Hg and pulse rate was 84 per min. She had icterus and mild pedal edema. Her cardiovascular and respiratory systems were normal on examination. Abdominal examination revealed relaxed uterus of 36 weeks size, with fetus in cephalic presentation and normal fetal heart rate. On ultrasound course was complicated by acute hepatic encephalopathy with hepatorenal shutdown and coagulopathy. Despite ultrasound abdomen showed normal liver and other organs.

A differential diagnosis of AFLP, acute hepatitis, HELLP syndrome was made. Viral markers (HBsAg, Anti-HCV, and Anti HAV) were negative ruling out viral hepatitis. Her blood pressure was normal throughout the hospital stay, ruling out gestational hypertension. There was no evidence of hemolysis or thrombocytopenia (to rule out HELLP syndrome). Persistent hypoglycemia despite correction aided towards diagnosis of AFLP. The patient was started on conservative management with syrup lactulose, high carbohydrate diet and anti-coma regime.

Patient started deteriorating with rising liver enzymes and deteriorating coagulation profile despite correction with fresh frozen plasma. She developed grade 1 hepatic encephalopathy. A decision for induction of labor was taken with informed written high risk consent. She was induced with vaginal misoprostol (25 µgm 4 hourly). Amniotomy was done at 4 cm dilatation of cervix and the liquor was blood stained and fetal heart rate showing bradycardia (90-100 bpm). Decision of emergency LSCS was taken after 18 hours of induction in view of antepartum hemorrhage and fetal bradycardia. She was transfused with four units fresh frozen plasma and two units red cell concentrate preoperatively. Emergency LSCS was done with informed high risk consent. A live male child of 2 kg birth weight was delivered. Intraoperative findings were normal and intraoperative period was uneventful. No significant retro-placental clot was noted and liquor was blood stained. Prophylactic Hayman’s suture with bilateral uterine artery ligation was done to prevent postpartum hemorrhage. An intra-peritoneal drain was put in. Transfusion with blood components was given intra-operatively and postoperatively (4 unit FFP+ 4 unit platelet) to correct coagulopathy. Patient was shifted to Intensive Care Unit in view of hepatic encephalopathy with coagulopathy with hepato-renal shut-down. Patient progressively deteriorated in post-operative period. She became tachypneic and tachycardic with increased abdominal distension and decreased urine output. She landed in Disseminated Acute Fatty Liver of Pregnancy: A Case Report and Literature Review

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Intravascular Coagulation. The drain output increased within first 24 hour of LSCS (2500 ml). She had to be dialyzed in view of acute renal failure and blood component therapy was given to correct coagulation profile. Patient was intubated and put on inotropes later on. Despite this management, she deteriorated progressively and expired on fourth day. The baby expired on fifth day due to birth asphyxia.

Discussion

It is well known that AFLP is neither inherited nor infectious [1]. 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. Fatty acid accumulation leads to hepatocyte dysfunction. The cause may be underlying fatty acid assimilation defects, which may be inherited. Women having AFLP may have a heterozygous long-chain 3-hydroxyacyl-coenzyme-A-dehydrogenase (LCHAD) deficiency, which is found on mitochondrial membrane and is involved in the beta oxidation of long-chain fatty acids [4-9].

Pregnancy with jaundice has many differential diagnoses like cholestasis, viral hepatitis, pre- eclampsia with or without HELLP syndrome, and AFLP. Intrahepatic cholestasis of pregnancy (ICHP) usually occurs in the third trimester, is characterized by itching in palms and soles mainly and serum bilirubin is mostly less than 6 mg/dl. Acute viral hepatitis in pregnancy presents as a systemic illness with fever, nausea, vomiting, fatigue, and jaundice, however, aminotransferase concentrations are markedly elevated (>500 U/liter). All these causes were ruled out in our case on the basis of presentation, symptoms, and investigations.

As discussed earlier, pre-eclampsia with deranged liver enzymes, HELLP syndrome, and AFLP have some distinct characteristics, particularly with regard to time of presentation. However, they also have some similarities in terms of clinical presentation and investigations. This makes differentiating these entities difficult [1,10,11]. The incidence of HELLP syndrome is much higher (1:5,000) as compared to AFLP (1:13,000) [12]. The distinct features of AFLP include severe coagulopathy, jaundice, hepatic encephalopathy, ascitis, hypoglycemia, and an elevation of transaminase levels. Some of these features are common to HELLP syndrome. In our case, the clinical features of severe liver dysfunction appeared at the gestational age of 36 weeks. The symptoms initially mimicked those of acute 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 favored the diagnosis of AFLP over HELLP syndrome.

"Acute yellow atrophy of the liver," a rare and fatal complication of pregnancy, was first described by Stander and Cadden in 1934 [4,6,13]. The liver biopsy is diagnostic but is not feasible in pregnant women especially with severe coagulopathy. Moreover, the management remains same, hence, an unnecessary intervention. Ultrasound and computed tomography may be used to identify liver changes however; these imaging studies too have low sensitivity and specificity [14]. In our case, presence of coagulopathy did not allow us to perform liver biopsy.

AFLP should be suspected in following conditions: (i) severe gastrointestinal symptoms, i.e., nausea, vomiting, abdominal pain, polydipsia/polyuria, and persistent jaundice appearing in late pregnancy (ii) abnormal liver function tests, leukocytosis and thrombocytopenia in third trimester of pregnancy, (iii) other associated organ derangements, i.e., renal insufficiency, coagulopathy, hypoglycemia, and hepatic encephalopathy, along with multiple organ dysfunction. Along with these, other causes of jaundice need exclusion.

Diagnosis

The diagnosis of AFLP is challenging and complicated. It is a diagnosis of exclusion. Specific investigations are lacking. The characteristic diagnostic investigations reveal deranged liver functions, coagulopathy, hypoglycemia, deranged renal function tests, thrombocytopenia and ultrasound imaging showing fatty liver. A specific criterion was devised to diagnose this rare condition. Patients with at least six or more of the Swansea criteria [15] confirm the diagnosis of AFLP; vomiting, abdominal pain, polydipsia/polyuria, encephalopathy, elevated serum bilirubin level, elevated uric acid, hypoglycemia, leukocytosis, elevated transaminases, ascites or bright liver on ultrasound scan, elevated ammonia, renal impairment, coagulopathy, and microvesicular steatosis on liver biopsy in addition to metabolic acidosis and occasionally biochemical pancreatitis.

Management

Management of AFLP comprises of rapid delivery of the fetus and supportive care. There is no other definitive therapy. In most of the cases, jaundice, liver dysfunction, and DIC improve after two to three days of delivery [14]. Maternal and fetal mortality rates were reported to be as high as 85% [16] earlier mostly due to cerebral edema, gastrointestinal hemorrhage, renal failure, coagulopathy, and sepsis. However, mortality has been lowered now, to less than 10% due to improvements in intensive care. Our patient presented rather late to us after the development of hepatic encephalopathy, acute renal failure, DIC, and fetal demise. Although we performed an early caesarean section, we were unable to interrupt the progression of the disease and her condition continued to deteriorate with serious complications like ARDS, sepsis, and worsening coagulopathy [1]. It is not clear whether ARDS occurred as a complication of acute liver failure (ALF), septicemia, or transfusion of multiple blood products, but it responded to supportive therapy.

Conclusion

AFLP is a rare, life-threatening complication of pregnancy with variable presentation, mostly in late pregnancy and post-partum occasionally. The progression is rapid and unpredictable. Prompt diagnosis and management in the form of early delivery and intensive care support may be life-saving. It is crucial to identify patients with nausea, vomiting or epigastric pain and persistent jaundice in the third trimester, to be suspected for the diagnosis of AFLP. The patients, who are critically ill at the time of clinical presentation, develop complications, or continue to deteriorate despite emergency delivery, and require collaborative management in the intensive care unit (ICU). Early diagnosis, prompt delivery, adequate supportive care, and a multidisciplinary approach are the key to a good outcome.

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