The Clinical Course of Acute Fatty Liver of Pregnancy Compared to Other Diseases of Hepatic Fatty Infiltration: A Case Report

Abstract

Background: Acute fatty liver of pregnancy (AFLP) is a rare and potentially fatal disease affecting women in their third trimester of pregnancy. Its severe clinical presentation is drastically different from other more common diseases of hepatic fatty infiltration, such as nonalcoholic fatty liver disease (NAFLD).

Case Presentation: A 36-year-old woman developed AFLP causing acute liver failure postpartum and was transferred to our hospital for a potential status 1a liver transplant. The patient presented with markedly decreased hemoglobin, hematocrit, and platelet count. Her liver enzymes, creatinine, uric acid, and lactic acid levels were notably elevated. She was placed on supportive care with blood products as needed for coagulopathy. She progressed to respiratory failure requiring mechanical ventilation and kidney failure requiring hemodialysis. The patient responded well to supportive care and was discharged 6 weeks later.

Conclusion: Diseases of hepatic fatty infiltration can present with strikingly different clinical courses, so the less common variants should not be overlooked. We present a patient who possessed risk factors for NAFLD but instead developed the more serious AFLP, which progressed to multi-organ failure.

Keywords: Acute fatty liver; Pregnancy; Nonalcoholic fatty liver; Multi-organ system failure

Case Report

A 36-year-old Hispanic female was transferred to our hospital for a potential status 1a liver transplant due to acute liver failure 2 days postpartum. Her prenatal course included gestational diabetes, mild gestational hypertension, and suspected placenta abruption leading to emergent C-section. She delivered a healthy baby boy at 39 weeks and 4 days. The patient had no history of pre-eclampsia or eclampsia but 1 day prior to her C-section she had a blood pressure of 158/98 mmHg. Her husband recalls her experiencing mild right upper quadrant pain and some mild nausea during the days prior to her C-section, but otherwise, she was well. She has no prior history of liver disease. The day before her transfer to our hospital, the patient’s obstetrician noted very dark urine, decreased urine output, and abnormal vital signs including tachycardia and hypertension. Her lab work on that day was notable for a hemoglobin of 6 g/dL, hematocrit of 18%, and platelets of 18 x10^9/L, which are markedly changed from her lab work 2 days prior to transfer. Additionally, 2 days prior to her transfer, her INR and PT increased to 4.4 and 40, respectively. She was hypoglycemic and had notably increased liver enzymes, alkaline phosphatase, bilirubin, and creatinine levels (Table 1).

On the day of transfer, she had an elevated uric acid level of 9.1 mg/dL and lactic acid level of 8.1 mmol/L. Lab work was done to exclude other etiologies of liver disease. Hepatitis A antibody IgM,
hepatitis B surface antigen, hepatitis B surface antibody total, B core antibody total, B core IgM, hepatitis C antibody, and hepatitis E antibody were negative. The patient progressed to respiratory failure requiring intubation, and kidney failure requiring hemodialysis the day before her transfer as well.

Table 1: Pertinent lab changes following delivery.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day of C-Section</th>
<th>1 Day Postpartum</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>12.5</td>
<td>6</td>
<td>Oct-15</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>37.9</td>
<td>18</td>
<td>28-40</td>
</tr>
<tr>
<td>Platelets (x10^9/L)</td>
<td>184</td>
<td>18</td>
<td>146-429</td>
</tr>
<tr>
<td>INR</td>
<td>0.9</td>
<td>4.4</td>
<td>0.8-0.94</td>
</tr>
<tr>
<td>Prothrombin time (sec)</td>
<td>12.2</td>
<td>50</td>
<td>9.6-12.9</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>12</td>
<td>14</td>
<td>03-Nov</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.5</td>
<td>2.2</td>
<td>0.4-0.9</td>
</tr>
<tr>
<td>Glucose, fasting (mg/dL)</td>
<td>88</td>
<td>21</td>
<td>&lt;95</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>55</td>
<td>14,347</td>
<td>Feb-25</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>33</td>
<td>16,331</td>
<td>Apr-32</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>253</td>
<td>341</td>
<td>38-229</td>
</tr>
<tr>
<td>Bilirubin, total (mg/dL)</td>
<td>0.3</td>
<td>7.2</td>
<td>0.1-1.1</td>
</tr>
</tbody>
</table>


She was put on a mechanical ventilator and heavily sedated immediately upon arrival to our hospital’s intensive care unit. Physical exam findings were pertinent for icteric eyes and distended abdomen. Abdominal computed tomography (CT) revealed heterogeneous enhancement of the hepatic parenchyma suggestive of fatty liver infiltration and abnormal perfusion (Figure 1). There was no evidence of hemorrhage or subcapsular hematoma. Delayed phase imaging showed significantly decreased contrast excretion by the kidneys, suggesting renal failure. She was placed on supportive care with blood products as needed for coagulopathy and continuous veno-venous hemodialysis (CVVHD) with fluid removal for her renal failure. The patient had components of atypical hemolytic uremic syndrome (aHUS) due to her low platelet count, undetectable haptoglobin, elevated lactate dehydrogenase, and schistocytes on blood smear. While this diagnosis is being considered, it is imperative that postpartum women be treated immediately to prevent end stage renal disease. Therefore, our patient was given Eculizumab in response. The suspected presence of aHUS lent support to the differential diagnosis of HELLP syndrome. However, the patient’s presentation of hypoglycemia, elevated uric acid, disseminated intravascular coagulation, and multi-system organ failure strongly support the diagnosis of AFLP over HELLP syndrome. Additionally, patients with HELLP syndrome usually present with pre-eclampsia, which was absent in this particular case.

Her AST/ALT levels began decreasing and her DIC resolved. However, after being removed from ventilation, she developed tonic-clonic seizures. The patient was intubated again and given Ativan 2mg IV in response. Brain CT showed no acute abnormalities. The patient’s condition gradually improved, and she was extubated. On the day of discharge, she was hemodynamically stable. Her platelets increased to 256 x10^9/L. Her AST and ALT levels decreased to 116 U/L and 98 U/L, respectively, and continue to follow a downward trend.

Figure 1: Abdominal computed tomography showing heterogeneous enhancement of the hepatic parenchyma.

Discussion

Common symptoms of normal pregnancy include abdominal pain, nausea, and vomiting. These symptoms are not unique to pregnancy and may also be signals of other hepatobiliary diseases. Our patient initially experienced mild episodes of these symptoms along with elevated liver enzymes. The patient’s medical history of gestational diabetes, mild gestational hypertension, and Hispanic ethnicity made her a good candidate for traditional NAFLD. Although AFLP and NAFLD are both characterized by excessive lipid accumulation of hepatocytes, each displays drastically different clinical presentations and pathologies. AFLP is a rare and potentially life-threatening condition that typically occurs in the third trimester of pregnancy. Early diagnosis, prompt delivery, and supportive care are the hallmarks of treatment [1,2]. When the diagnosis is delayed, the condition can progress to multi-organ system failure requiring mechanical ventilation and intensive care unit support, as seen in our patient. NAFLD has a much higher prevalence in western countries [3-5] but follows a much more favorable clinical course. It is important to understand the difference between these fatty liver conditions because although classified similarly, they possess significant variations in pathology, presentation, and treatment.

The distinctive feature of AFLP is the presence of hepatocyte microvesicular fatty infiltration. The cytoplasm appears foamy on histology due to fat accumulating around centrally located nuclei.
The clinical presentation of AFLP is characterized by rapid onset and poor prognosis if not treated early. The most common initial symptoms are nausea/vomiting, abdominal pain, jaundice, malaise, and anorexia. In severe cases, the disease can progress to multi-organ system failure requiring critical management in an intensive care unit [1,2,12]. This rapid progression was seen in our patient who experienced mild right upper quadrant pain and nausea prior to her C-section, but immediately developed acute liver failure, renal failure, and acute respiratory distress syndrome postpartum. She was subsequently placed under supportive care with mechanical ventilation and hemodialysis. Laboratory tests include elevated liver enzymes, bilirubin, uric acid levels, and white blood cell count with a decrease in platelet count. The presence of coagulopathies and hypoglycemia is common [7,8,13]. Treatment is maternal stabilization and prompt fetal delivery. Infant death and stillbirths are possible outcomes for newborns, so fetal stabilization is imperative as well [14]. Symptoms of cardiomyopathy, liver failure, and hypoglycemic encephalopathy in infants are exacerbated by long-chain fatty acids so restrictive dietary therapy is recommended [15,16]. In contrast, patients with NAFLD are usually asymptomatic. A subset of NAFLD patients who have nonalcoholic steatohepatitis (NASH) may experience mild abdominal pain and malaise [17]. Because of the asymptomatic nature of the disease, NAFLD is frequently noticed when patients have laboratory work done for other reasons but the resulting labs show elevated liver aminotransferases. However, the increase in AST and ALT levels do not correspond to the severity of hepatic inflammation or fibrosis [18,19]. The disease progression is slow, but if left unmanaged, may develop into cirrhosis [20,21]. The most effective treatment of NAFLD is risk factor management. Risk factors include obesity, insulin resistance or diabetes, and dyslipidemia [22]. The most common cause of death in patients with NAFLD is cardiovascular disease so weight loss and healthy diet have shown effective in combating the disease [23].

There is an underlying genetic predisposition to AFLP Long-chain 3-hydroxyacyl CoA dehydrogenase (LCHAD) is involved in beta-oxidation of fatty acids in the mitochondria. During pregnancy, the levels of free fatty acids (FFA) in maternal blood increase because of the enhanced activity of hormone-sensitive lipases on triglycerides. A deficiency in LCHAD can lead to accumulation of long-chain 3-hydroxyacyl metabolites that are toxic to the liver. FFA accumulation promotes lipotoxicity in maternal hepatocytes facilitating reactive oxygen species formation. These changes activate inflammatory cascades that lend way to acute liver failure, which may underlie the pathogenesis of AFLP [24]. Multiple studies have shown a correlation between LCHAD deficiency and the development of AFLP in pregnant women [1,25-27]. Because this is an inherited defect, it is recommended that the mother and her children undergo molecular testing. Predisposing factors for NAFLD include obesity, metabolic syndrome, and Hispanic ethnicity. Genome-wide association studies have been conducted to find explanation for the increased prevalence of NAFLD among Hispanics. Studies have shown there is a higher prevalence of hepatic steatosis in Hispanic patients (45%) compared to white (33%) and black patients (24%) [28]. Genetic variation of the gene PNPLA3 has been associated with increased liver fat content and hepatic inflammation. The allele responsible for these changes is most prevalent in Hispanics, contributing to their susceptibility towards NAFLD [29].

Our patient possessed multiple risk factors that predisposed her to NAFLD, but developed AFLP instead. This case of AFLP demonstrates a severe and almost life-threatening disease course that is unique from traditional disorders of hepatic fatty infiltration. To our knowledge, this is the first report to directly compare the diagnostic approaches, clinical characteristics, treatment, and pathogenesis of AFLP and NAFLD. It is important to identify those at risk for AFLP because of its critical presentation. Having an awareness for this particular condition in clinical practice may help diagnose these patients sooner to provide prompt and adequate treatment.

Conflicts of Interest
None declared.

Authors’ Contribution
A.C. drafted and revised the manuscript. C.B. edited and finalized the manuscript.

Acknowledgement
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References
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