ACUTE FATTY LIVER OF PREGNANCY AND PREECLAMPSIA
IN A TRIPLET GESTATION

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Abstract- Acute fatty liver of pregnancy (AFLP) is a rare entity and a potentially fatal disorder. It is reported to be more common in multiple than singleton pregnancies. Sometimes it coincides with preeclampsia but the exact etiology is not yet understood. A 31-year-old G2 P1 patient admitted at 33 weeks of pregnancy with signs and symptoms of jaundice, gastroenteritis, hypertension, malaise, urinary incontinence and preterm contractions. She had history of idiopathic hypothalamic amenorrhea and by a recent trial with gonadotropins, she had got triplet gestation. After admission her general condition deteriorated. She underwent Cesarean section at once and all fetuses survived. She had severe postpartum hemorrhage. The results of laboratory tests indicated coagulopathy and liver function abnormalities. The AFLP was diagnosed on the third day of hospital stay. She was discharged one week later. Again she returned with complaint of severe sustained headache. Computed tomography showed subdural hemorrhage and drainage of hematoma was performed immediately. Finally the patient recovered from all of these critical conditions. This is the first report of AFLP in a patient with history of idiopathic hypothalamic amenorrhea. AFLP should be suspected in every pregnant patient with preeclampsia and gastroenteritis symptoms in the third trimester of pregnancy.

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Key words: Acute fatty liver of pregnancy, preeclampsia, idiopathic hypothalamic amenorrhea

INTRODUCTION

Acute fatty liver of pregnancy (AFLP) is an uncommon, potentially fatal disorder. It is a well documented medical condition and is important due to implications on maternal and fetal morbidity and mortality. It occurs in the third trimester of pregnancy. Sheehan defined the histologic appearances of fatty infiltration in this disorder in 1961 (1, 2). The incidence of AFLP has been reported from one in a million pregnancies in 1966 to one in 6692 pregnancies in 1996 (3).

The AFLP is reported to be more common in multiple than singleton pregnancies. The etiology has not been yet understood. About 50% of these patients have concomitant signs of preeclampsia with or without HELLP syndrome (hemolysis, elevated liver enzymes, low platelets count) (4).

AFLP is characterized by a prodrome of nonspecific symptoms, including nausea, vomiting and epigastric pain, followed by jaundice, profound hepatic failure, coagulopathy, encephalopathy, or coma, acute renal failure and frequently hypoglycemia (5). Pancreatitis is a potentially lethal complication of AFLP. It typically appears after hepatic and renal failure (6).

This is the first report of AFLP and preeclampsia in a patient with history of idiopathic hypothalamic amenorrhea who after a recent trial of gonadotropins had got triplet gestation.
CASE REPORT

A 31 year-old woman with known idiopathic hypothalamic amenorrhea was referred to our infertility clinic for second trial of induction of ovulation. In this trial of pregnancy with gonadotropins she got triplet gestation.

At 32 weeks of gestation she developed gastrointestinal symptoms, including nausea, vomiting and malaise, and in spite of conventional treatments her general condition deteriorated. She was hospitalized at 33 weeks of pregnancy because of jaundice, epigastric pain, malaise, urinary incontinence and preterm labor.

In immediate evaluation, her blood pressure was 150/90 mmHg and urinalysis showed 1+ proteinuria and 2+ bile and a diagnosis of preeclampsia was made. Other laboratory findings on the first day of admission included leukocytosis, prolonged prothrombin time (PT) and partial thromboplastin time (PTT), hyperbilirubinemia, elevated liver transaminases, elevated alkaline phosphatase, normal hemoglobin, hematocrit, sodium, potassium, glucose, and decreased albumin to globulin ratio. The metabolic profile of the patient is shown in Table 1.

Because of ill condition and preterm labor, she underwent prompt Cesarean section that resulted in delivery of two female and one male fetuses (1900, 1850, 1950 grams); two of them were meconium stained but all had good Apgar scores and did well in the newborn period (Fig. 1). She had severe postpartum hemorrhage that stopped with transfusion of 7 unit of fresh frozen plasma (FFP), 5 units of packed red cells and bimanual massages.

She underwent further investigation. Sonography of the liver was normal. The serologic tests for hepatitis A and B were negative. ANA was weakly positive; G6PD was sufficient. She was discharged on the 7th post operative day. Nearly 2 weeks after delivery all laboratory findings returned to normal. The diagnosis of AFLP was made retrospectively by attention to clinical symptoms and signs, biochemical findings and exclusion of the other differential diagnosis.

One month later, she returned with complaint of severe sustained headache. Computed tomography (CT) scan showed subdural hemorrhage. Immediate drainage of hematoma carried out and finally the patient recovered from all of these critical conditions. We obtained informed consent from our patient to publish details of her history.

Table 1. Laboratory data of the patient

<table>
<thead>
<tr>
<th>Data</th>
<th>Normal value</th>
<th>Days after delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT (s)</td>
<td>11</td>
<td>1  2  3  4  5  14  35 42</td>
</tr>
<tr>
<td>PTT (s)</td>
<td>30-45</td>
<td>62 19 20 17 11</td>
</tr>
<tr>
<td>Bilirubin T/D (mg/dl)</td>
<td>0.1-1.2 (T)</td>
<td>6.2-1.5 15.5-14.5 12.7-1.2 10.5-1.7 3.6/1.2 1/0.5</td>
</tr>
<tr>
<td>Plts (×10^3/mm³)</td>
<td>196-451</td>
<td>78 125 188</td>
</tr>
<tr>
<td>AST/ALT (U/L)</td>
<td>5-45/5-45</td>
<td>122/104 32/22 31/30 35/50 27/19</td>
</tr>
<tr>
<td>Alph (U/L)</td>
<td>80-360</td>
<td>494 254 161 147</td>
</tr>
<tr>
<td>WBC (×10^3/mm³)</td>
<td>4.5-11</td>
<td>15 19.3 9.2</td>
</tr>
<tr>
<td>Hb (mg/dl)</td>
<td>136-145</td>
<td>128 130 113 149</td>
</tr>
<tr>
<td>Na (mg/dl)</td>
<td>3.5-5</td>
<td>4.1 3.7 4.3 5.5</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.4–1.3</td>
<td>1 0.9</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>10-20</td>
<td>22</td>
</tr>
<tr>
<td>Uric Acid (mg/dl)</td>
<td>3.0-7.5</td>
<td>5.3 3.8</td>
</tr>
<tr>
<td>Albumin/Globulin</td>
<td>1.4-2</td>
<td>0.8 1 1.1</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>62-110</td>
<td>88 98</td>
</tr>
</tbody>
</table>

Abbreviations: PT, prothrombin time; PTT, partial thromboplastin time; Bili T/D, bilirubin total and direct; PLTS, platelet count; AST, aspartate aminotransferase; ALT, alanine aminotransferase; Alph, alkaline phosphatase; WBC, white blood cell; Hb, Hemoglobin; Na, sodium; K, Potassium; BUN, blood urea nitrogen;
DISCUSSION

AFLP is a rare, potentially fatal disorder, affecting women in the third trimester of pregnancy. The reported incidence of AFLP has been increasing and the maternal and the fetal mortality has been decreasing (1, 5). It is characterized by a nonspecific prodrome of symptoms followed by jaundice, profound hepatic failure with encephalopathy or coma, coagulopathy and frequently hypoglycemia (5). These patients typically present with a 1 to 2 week history of anorexia, nausea, vomiting, malaise and right upper quadrant pain. Symptoms of preterm labor or lack of fetal movement may be the presenting complaint. Physical examination reveals an ill-appearing, jaundiced patient. Hypertension, edema, and ascites may be present. Intrauterine fetal demise may occur, secondary to uteroplacental insufficiency (3).

Laboratory studies may reveal elevated white blood cells (WBC), normal or low platelet count. Prolonged PT and PTT, findings of marked depression of antithrombin-3 and disseminated intravascular coagulation (DIC) are possible with the disease (3, 5, 7). Urinalysis may reveal ketones, proteins or bilirubin; serum electrolytes may show a low bicarbonate level. Blood urea nitrogen (BUN) and creatinine may be elevated and uric acid is frequently high; plasma glucose is often below 60 mg/dl. Serum aminotransferase (SGPT, SGOT) elevation commonly ranges between 100 and 1000 U/L (3). Bilirubin is variable, usually exceeding 5 mg/dl. Alkaline phosphatase is 3 to 4 times normal. Serum albumin is usually low. Ammonia level may be elevated. Amylase and lipase may be elevated because of concomitant pancreatitis. The hepatitis profile helps to rule out hepatitis A and B. Today serologic markers for diagnosis of viral hepatitis are available thus making the distinction by biopsy unnecessary in most cases. Biopsy may be indicated, when the diagnosis is unclear or when liver function does not return to normal in the expected time after delivery (1, 5). Various diagnostic imaging techniques do not help to the management of AFLP (5). Some of these patients have concomitant signs of preeclampsia with or without HELLP syndrome (4). The HELLP syndrome is more common than AFLP in late pregnancy. The clinical and biochemical features of these two disorders overlap, suggesting that their underlying pathophysiologic mechanisms may be similar (1). The differential diagnosis of AFLP includes viral hepatitis, cholecystitis, the HELLP syndrome and cholestasis of pregnancy. The only known treatment of AFLP is termination which has the potential for hemorrhage. The etiology of AFLP has not yet been understood. Recent publications reveal that a dysfunction in the beta-oxidation of mitochondrial fatty acids may contribute to the etiology (8, 9).

Knowing that all patients have complete resolution of the liver failure confirms the diagnosis. The AFLP is a reversible peripartum liver failure, may be diagnosed and managed on the basis of clinical and laboratory criteria, with early recognition, early delivery and supportive care improved maternal and perinatal outcome is achieved. The patient had clinical picture consistent with the prodromal phase of AFLP and physical examination with findings of jaundice, preterm labor and urinary incontinence. Laboratory studies showed leukocytosis, prolonged PT and PTT, elevated serum aminotransferase (AST, ALT), elevated creatinine and elevated alkaline phosphatase. The tests for viral hepatitis were negative; the sonography of hepatobiliary system was normal, and she had concomitant preeclampsia. The patient also had thrombocytopenia, but this occurred with bleeding complication after emergency cesarean section. The diagnosis was consistent with AFLP not the HELLP.
Acute fatty liver of pregnancy

syndrome. Fundamental to the diagnosis was the finding of a prolonged PT and retrospectively the fact that the patient had complete resolution of the liver failure postpartum assisted in confirming the diagnosis. Cholestasis of pregnancy was excluded. The prompt decision for delivery saved the patient and her fetuses. Severe headache of the patient recovered one month after discharge after drainage of subdural hemorrhage.

It is recommended that patients with persistent nausea, vomiting, or epigastric pain in the third trimester, receive evaluation of liver enzymes, renal function tests, and complete blood count to rule out the diagnosis of AFLP (10). This case indicates that in AFLP, in addition to early diagnosis and prompt delivery, careful follow up during postpartum period is also mandatory.

REFERENCES