Perioperative Care of a Patient with Acute Fatty Liver of Pregnancy — A & A

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Acute fatty liver of pregnancy (AFLP) is a late gestational complication with biochemical similarities to the inherited disorders of mitochondrial fatty acid oxidation and clinical similarities to fulminant hepatic failure. The following case illustrates our perioperative management of this rarely encountered disorder.

Report of Case

A previously healthy 38 kg, 31-yr-old C. P. female at 34 weeks' gestation complained of fatigue, nausea, and vomiting 8 days before admission. She was treated as an outpatient 5 days before admission for flu-like symptoms and dehydration with IV fluids and 2 days before admission with IV fluids, sodium citrate, ondansetron, and prochlorperazine until the nausea subsided and she returned home. Her physical examination was unremarkable and no diagnostic studies were performed. On the day of admission she had scleral icterus. Her heart rate was 115 bpm, her blood pressure was 122/57 mm Hg and her oxygen saturation by pulse oximetry (SpO2) was 92% on a 40% Yent mask. She was somnolent but aroused easily, was oriented to person, place, and time, and had no local neurological findings. The airway evaluation revealed full range of motion of the head and neck with a Class 1 airway. Her gag reflex was diminished and her deep tendon reflexes were brisk bilaterally with 2-3 beats of clonus; mild asterixis and pedal edema were noted. An abdominal sonographic examination demonstrated neither gallstones nor dilation of the biliary ducts. Her hepatitis B surface antigen was negative; other viral antigen levels were not obtained. Her hematocrit and platelet counts were 39.8% and 175,000/mm³ respectively. The prothrombin time (PT) was 18.5 s, the partial thromboplastin time was 42.7 s with an international normalized ratio of 2.2 and a fibrinogen level of 62 mg/dL. The thrombin time was 26.7 s and partially corrected to 17.2 s; the D-dimer level was >1 mg/mL. The blood urea nitrogen and creatinine were 26 and 3.2 mg/dL, respectively. The serum glucose was 84 mg/dL and the ammonia 25 μmol/L. The aspartate aminotransferase was 223 U/L, the lactate dehydrogenase 1,038 U/L, the alanine aminotransferase 314 U/L, the γ-glutamyl transferase 88 U/L, and the alkaline phosphatase 422 U/L. The cholesterol level was 52 mg/dL. The total bilirubin level was 9.7 mg/dL, the majority of which was direct. The fetal heart rate was 136-140 bpm with acceleration to 156 bpm. A clinical diagnosis of severe preeclampsia with hemolysis, increased liver enzymes and decreased platelets (HELLP) syndrome and/or AFLP was made; expedited operative delivery was the obstetrical treatment plan because of the patient's increasing somnolence since her initial evaluation.

Before surgery, 10 U of cryoprecipitate was administered IV; 4 U of fresh-frozen plasma (FFP) and 4 U of packed red blood cells were available in the operating room for the procedure. Magnesium sulfate (MgSO4) 4 g IV was also administered. Rapid sequence induction of general anesthesia was achieved with thiopental 250 mg IV and succinylcholine 100 mg IV, and the trachea was easily intubated. Maintenance of anesthesia was accomplished with 50% oxygen, 50% nitrous oxide and an end-tidal concentration of isoflurane no exceeding 0.5% until after delivery, when the isoflurane was discontinued. Fentanyl 200 μg IV and morphine 10 mg IV were administered after delivery of a live female infant 7 min after induction. The Apgar scores were 8 and 9 at 1 min and 2 min, respectively. Four units of FFP and 1,500 mL of lactated Ringer's solution were administered, and the urine output was 340 mL; the estimated blood loss was 500 mL. Although initially no clot was seen in the surgical field, adequate hemostasis was accomplished by the end of surgery. The patient was awakened and her trachea extubated after she followed commands. She was admitted to the intensive care unit and continued on oxytocin and MgSO4 (2 g/mun/hr) infusions. She remained stable during her immediate postoperative course with a Glasgow Coma Scale score of 15, a sinus tachycardia of 110-120 bpm with normotension and a nonlabored respiratory rate of 12-16 breaths/minute with normal breath sounds to auscultation and an SpO2 of 96-99%. Her hematocrit was 26% and her fibrinogen level 100.9 mg/dL with a thrombin time of 20 s, which partially corrected to 15.4 s. After an additional 10 U of cryoprecipitate and 2 U of packed red blood cells 4 h postoperatively she was transferred to a tertiary care center capable of liver transplantation.

The MgSO4 infusion was continued overnight because of a serum magnesium (MgSO4) level of 4.1 mg/dL before and 6.6 mg/dL just after transfer. Six hours later the patient had a respiratory acidosis (pH 7.24; PaCO2 63 mm Hg; PaO2 93% mm Hg) associated with depressed deep tendon reflexes, hypotension, stupor, and a (Mg2+) of 8.2 mg/dL. Her trachea was intubated and mechanical ventilation of the lungs was required for the next 34 h. The Mg2+ infusion was discontinued and her trachea extubated when her mental status was normal and the (Mg2+) of 4.8 mg/dL on postoperative day (POD) 2. She required a total of 24 U of FFP (8 U administered through POD3), 44 U of cryoprecipitate (34 U administered through POD3), and 6 U of packed red blood cells (4 U administered through POD3). No blood components were required after POD5. The blood urea nitrogen increased to its highest level of 58 mg/dL on POD4 and the creatinine increased to its highest level of 3.4 mg/dL on POD2; they decreased to 13 and 0.9 mg/dL respectively by POD7. The plasma cholesterol increased steadily to 152 mg/dL by POD8. The patient was eating on POD7 and was discharged on POD12, when the FT was 14.3 s, the partial thromboplastin time was 24.2 s, and the international normalized ratio was 1.3.

Discussion

The incidence of AFLP is estimated at 0.6-1.5 per 10,000 deliveries (1-3), much less than the incidence of HELLP syndrome, which occurs in 10-60 of 10,000 deliveries. Preeclampsia occurs in approximately 50% of AFLP cases. Half the AFLP cases occur in primigravidae and 10-15% occur in twin pregnancies. Though thought not to recur in subsequent pregnancies (4,5), at least six cases of recurrent AFLP have been reported since 1990 (3,6-9). The mortality of AFLP was 92% before 1976: currently it is <10% because of early diagnosis of less severe forms and aggressive treatment of more severe forms.

The biochemical lesion may be either an isolated deficiency of long-chain 3-hydroxy acyl-CoA dehydrogenase (LCHAD) or a complete deficiency of a trifunctional protein that catalyzes the last three steps of mitochondrial fatty acid oxidation. Deficiency of LCHAD has been found in children of women who had AFLP or HELLP syndrome during pregnancy; however, not all women carrying fetuses with LCHAD deficiency or trifunctional protein deficiency have liver disease. Liver disease in pregnant women occurs most often when the deficiency of enzymatic activity in the fetus is severe.
LCHAD metabolites produced by a fetus with this defect may accumulate and overwhelm the mitochondrial oxidation machinery in a heterozygous mother, already under metabolic stress from the increased demand for fatty acid oxidation in the latter stages of pregnancy. Severe preeclampsia appears to increase the risk of AFLP in such women (10).

Because the initial symptoms of AFLP are nonspecific, a high index of suspicion is necessary. AFLP is more likely to result in marked hypoglycemia, hyperammonemia, and an increased clotting time than is HELLP, although the liver enzyme abnormalities are usually more pronounced in HELLP syndrome than in AFLP. (Table 1X1.1-14; overlapping findings among the microangiopathies of pregnancy make the diagnosis challenging. In our patient, the coagulopathy and hypofibrinogenemia required aggressive support with blood component therapy. Our initial therapeutic goal was a fibrinogen level of 100 mg/dl and eventual correction of the PT and international normalized ratio by administering cryoprecipitate and FFP. Although it was unclear if the coagulopathy was strictly a primary fibrinolysis as a result of the hepatic failure or whether an additional secondary fibrinolysis was present, the coagulopathy was ultimately resolved through aggressive supportive therapy as well as gradual hepatic recovery.

Table 1. Clinical and Laboratory Characteristics of Liver Disease and the Microangiopathies of Pregnancy

| Mg²⁺ treatment was initiated because the patient had brisk deep tendon reflexes and an alteration in mental status. Although it is surprising that respiratory insufficiency occurred with a [Mg²⁺] of 6.2 mg/dl, the discontinuation of the Mg²⁺ infusion and increase in [Mg²⁺] to 4.8 mg/dl was the only intervention before extubation. As Mg²⁺ is excreted by the kidneys, it must be given with frequent clinical and biochemical monitoring and in reduced doses in the presence of impaired renal function. Nevertheless, perhaps the combined hepatic and renal dysfunction rendered this patient with AFLP more symptomatic at a lower threshold of hypermagnesemia.

Anesthetic care of the patient with severe hepatic dysfunction includes meticulous attention to procedures performed during their coagulopathic state. Gentle laryngoscopy with direct visualization of the airway during profound neuromuscular blockade is key in minimizing airway trauma and bleeding. In the midst of aggressive support with blood products, it may be difficult to judge functional hepatic recovery using PT and partial thromboplastin time. Hyperkalemia is neither a sensitive indicator of the severity of hepatic disease nor a negator of hepatic improvement, because confounding factors existed perioperatively for the increase of both the direct and indirect fractions. Moreover, changes in plasma albumin levels reflect neither acute liver dysfunction nor recovery. Although the liver is the sole source of albumin synthesis, the plasma half-life of albumin is approximately 15 days with a 5%-8% breakdown rate per day. Acute parenchymal liver disease is commonly associated with increased plasma triglycerides, decreased cholesterol esters, and abnormal lipoproteins, which may be very sensitive markers for hepatic injury and recovery. In pregnancy, this disparity may become more apparent because the serum level of free and esterified cholesterol is larger than in nonpregnancy. Although the transfusion of FFP (usual free cholesterol 30-100 mg/dl) will increase the plasma cholesterol, our transfusion of 8 U of FFP within the first 24 hours would likely have increased the cholesterol from the admission level of 52 mg/dl to 63-93 mg/dl. Indeed, the next cholesterol level obtained was 77 mg/dl. However, the cholesterol level continued to increase to 137 mg/dl by PODS despite the decreasing FFP requirement. We found the cholesterol level an acceptable marker of acute functional hepatic recovery.

AFLP never resolves before delivery, therefore expeditious delivery is the penultimate therapeutic intervention. We administered a general anesthetic rather than risking a protracted time to correct the coagulopathy to provide a regional block. Another important anesthetic consideration in these patients is increased intracranial pressure (ICP). This patient had evidence of mild neurologic dysfunction with a Glasgow Coma Scale score of 15, but careful neurologic monitoring is essential to AFLP management. Documentation of the mental status before and after a general anesthetic is crucial. Comprehensive perioperative planning after early intervention at the community hospital should include further consultation with and possible transfer to a center capable of liver transplantation (15). The indication for liver transplantation in these patients is neurologic deterioration in the presence of increased ICP. In most cases, however, with intensive support, patients recover within the first postpartum week.

Footnotes

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References


