

Peripartum care of the parturient with acute fatty liver of pregnancy

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Abstract : Acute fatty liver of pregnancy (AFLP) is a rare, but serious life-threatening clinical entity, the etiology of which is unknown. The clinical presentation of this disease is varied and timely diagnosis often difficult. Since multiorgan involvement (and dysfunction) complicates diagnosis, no uniform peripartum obstetric and anesthetic recommendations can be made. Still, once the diagnosis of AFLP is established, prompt delivery is indicated. We herein present a case of acute fatty liver and hepatic failure that developed during the third trimester of pregnancy. Favorable maternal and fetal outcome was accomplished.

Key words : Pregnancy ; liver failure ; acute fatty ; liver disease ; obstetric anesthesia.

INTRODUCTION

Acute fatty liver of pregnancy (AFLP), which was first described in 1934 (1) is a rare and serious clinical entity associated with significant maternal and fetal mortality and morbidity (2, 3). The clinical presentation of this disease is varied and timely diagnosis often difficult. Delayed diagnosis of AFLP can lead to severe form of hepatic failure and life-threatening multiorgan system dysfunction (MOSD) (4). Since multiorgan involvement and dysfunction complicate diagnosis, no uniform peripartum obstetric and anesthetic recommendations can be made. Still, once the diagnosis of AFLP is established, prompt delivery is indicated. We herein present a case of parturient who developed AFLP and MOSD at 27 weeks gestation (favorable maternal and fetal outcome was accomplished) and review the peripartum management of this rarely encountered clinical entity.

REPORT OF CASE

A 41 year old 98 kg, 160 cm gravida 4, para 1-0-2-1 at 27 weeks gestation was admitted to Labor and Delivery (L&D) suite with the working diagnosis of acute hepatic encephalopathy secondary to suspected acetaminophen overdose (positive N-acetyl-p-aminophenol toxicology screen). The

patient had no significant history of liver and/or gallbladder disease, or alcohol abuse ; however, she was taking acetaminophen for migraine headaches. Magnetic resonance imaging (MRI), computed tomography (CT) studies, and lumbar puncture performed at an outside institution were all negative.

Initial symptoms at admission included nausea, vomiting, and malaise. Laboratory blood tests demonstrated an aminotransferase level of 1500 IU/L (10-45), serum ammonium of 157 micrograms/dL (11-55), blood glucose of 56 mg/dL (65-110), and platelet count of 296,000/mm³ (130-400). Serum creatinine level was 1.3 mg/dL (0.5-1.5), blood urea nitrogen was 26 mg/dL (8-18), serum sodium was 148 mEq/L (135-145), serum chloride was 119 mEq/L (97-107), and serum bicarbonate level was 16 mEq/L (24-31). Coagulation profiles revealed an elevated international normalized ratio (INR) of 1.7, prothrombin time (PT) of 11.7 seconds, and partial thromboplastin time (PTT) of 26.7 seconds (25-33).

Upon her admission to the L&D suite the patient was obtunded and in acute respiratory distress. Her blood oxygen saturation was 92%, her blood pressure was 105/60 mmHg, her heart rate was 122 beats per minute, and her respiratory rate was 40 breaths per minute. Fetal distress was promptly diagnosed triggering an emergency Cesarean section. After a brief period of preoxygenation rapid sequence induction of general anesthesia with cricoid pressure was conducted. Meanwhile, arterial line placement was successful

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and a first measurement showed a respiratory alkalosis (pH 7.52 ; PaCO₂ 20 mm Hg ; PaO₂ 69 mm Hg, Base Excess -4.2). Laryngoscopy revealed a grade 2 view (Cormack and Lehane classification) with successful intubation of the trachea. Maternal hemodynamic parameters were closely monitored and remained stable. The premature neonate was delivered 4 minutes after induction of anesthesia with APGAR scores of 1, 4, and 4 after 1, 5, and 10 minutes, respectively. Endotracheal intubation of the neonate was required, who was taken to the neonatal intensive care unit (NICU) for further supportive care. The patient's surgery concluded uneventfully with an estimated blood loss of 800 ml.

The patient was transferred to the intensive care unit (ICU) for further supportive care and treatment of AFLP and MOSD. Initial work up for liver failure (quantitative acetaminophen level) was negative. Hepatic serology demonstrated vaccination to hepatitis type B ; however, viral hepatitis was excluded by serology and quantitative assessment. However, ultrasonographic examination demonstrated acute fatty liver disease of uncertain origin without evidence of biliary obstruction. Fresh frozen plasma was administered daily to maintain INR < 1.5 and fibrinogen > 100 mg/dL. By post-operative day 4, coagulopathy resolved as synthetic liver function returned to normal. She was extubated approximately two weeks later after resolution of hepatic encephalopathy. The treatment of respiratory, cardiovascular, and renal failure responded well to goal-directed fluid management guided by the pulmonary artery catheter. Upon discharge 3 weeks later, her liver function was normalized, and the MOSD had resolved.

DISCUSSION

Fatty liver of pregnancy is a rare condition with an estimated incidence of 0.6-1.5 per 10,000 deliveries (5). AFLP is a life-threatening condition with maternal mortality reaching 18%, and fetal mortality approaching 23% (6). The pathophysiology of AFLP is not known. However, some cases of AFLP are due to enzymatic deficiency in long-chain 3-hydroxyacyl-coenzyme-A dehydrogenase (LCHAD) or a complete deficiency of a trifunctional protein involved in catalysis of mitochondrial fatty acid oxidation (5, 7). As a result the LCHAD metabolites accumulate in the body and exhaust the already stressed mitochondrial oxidation systems, damaging the maternal liver. Early delivery is thought to curtail further passage of

abnormal fatty acids from the fetus to the mother, rescuing the patient from further insult (6-8).

Unlike AFLP, there is no evidence to suggest that non-gestational forms of liver failure, including viral hepatitis, improve by early delivery (9, 10). A comprehensive history, liver tests panel, an ultrasound, and viral serologies should be performed to rule out non-gestational forms of progressive liver failure (2, 6).

The differential diagnosis of AFLP includes other forms of gestational liver diseases, such as severe preeclampsia associated with hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome) (4, 5, 11-16). The incidence of HELLP syndrome in pregnancy is estimated to be 1 to 6 in 1000 deliveries (4). It is believed that preeclampsia coexists with AFLP approximately 50% of the time (5). It has also been speculated that an overlap between AFLP and pregnancy induced hypertension (PIH) might suggest that AFLP is a manifestation of PIH as is the HELLP syndrome. Acute fatty liver of pregnancy typically presents with severe hyperammonemia, increased plasma transaminase levels, hypoglycemia, fatty liver infiltration, and is more likely to lead to hepatic encephalopathy than its preeclampsia (4, 15, 16), which aids the differential diagnosis. Additionally HELLP syndrome is almost always associated with severe thrombocytopenia and hypertension (4, 15, 16).

Considering the diagnosis of intrahepatic cholestasis of pregnancy (ICP) is reasonable, however, profuse vomiting and severe coagulopathy helps exclude this entity (17). Still, two cases of AFLP coexisting with ICP have been documented. Pruritis associated with cholestasis helped aid in the diagnosis in one case (17).

The peripartum anesthetic management of AFLP depends on the severity of liver dysfunction and on the urgency of delivery (3, 8, 15). In cases of severe liver dysfunction with coagulopathy and encephalopathy, general anesthesia is indicated. Avoidance of hepatotoxic drugs and maintenance of hepatic blood flow are crucial to prevent further deterioration of hepatic function during induction and maintenance phases of anesthesia (8). Arterial blood pressure monitoring is important to avoid substantial increases in intracranial pressure during laryngoscopy (15). Careful neurological maternal monitoring is vital (5, 15). Finally, hypoglycemia should be closely monitored and treated with glucose infusions until resolution of hepatic dysfunction (3).

In summary our case report provides one more piece of evidence that appropriate diagnosis

and early intervention (delivery of the fetus) can substantially reduce the morbidity and mortality associated with AFLP.

References

1. Standler H. J., Cadden J. F., *Acute Yellow Atrophy of the Liver in Pregnancy*, AM. J. OBSTET. GYNECOL., **28**, 61-69, 1934.
2. Ebert E. C., Sun E. A., Wright S. H., *et al.*, *Does early diagnosis and delivery in acute fatty liver of pregnancy lead to improvement in maternal and infant survival ?*, DIG. DIS. SCI., **29**, 453-455, 1984.
3. Antognini J. F., Andrews S., *Anaesthesia for caesarean section in a patient with acute fatty liver of pregnancy*, CAN. J. ANAESTH., **38**, 904-907, 1991.
4. Steingrub J. S., *Pregnancy-associated severe liver dysfunction*, CRIT. CARE CLIN., **20**, 763-776, 2004.
5. Mjahed K., Charra B., Hamoudi D., *et al.*, *Acute fatty liver of pregnancy*, ARCH. GYNECOL. OBSTET., **274**, 349-353, 2006.
6. Santana Cabrera L., Hernandez Medina E., O'Shanahan Navarro G., Sanchez-Palacios M., *Multi-organ failure secondary to acute fatty liver of pregnancy*, MED. INTENSIVA, **30**, 81, 2006.
7. Toro Ortiz J. C., Cerqueira Dapena MJ., Porta Pampalona I., *et al.*, *Acute fatty liver of pregnancy*, J. MATERN. FETAL. NEONATAL. MED., **12**, 277-278, 2002.
8. Holzman R. S., Riley L. E., Aron E., Fetherston J., *Perioperative care of a patient with acute fatty liver of pregnancy*, ANESTH. ANALG., **92**, 1268-1270, 2001.
9. Fesenmeier M. F., Coppage K. H., Lambers D. S., *et al.*, *Acute fatty liver of pregnancy in 3 tertiary care centers*, AM. J. OBSTET. GYNECOL., **192**, 1416-1419, 2005.
10. Browning M. F., Levy H. L., Wilkins-Haug L. E., *et al.*, *Fetal fatty acid oxidation defects and maternal liver disease in pregnancy*, OBSTET. GYNECOL., **107** (1), 115-20, 2006 Jan.
11. Bahloul M., Dammak H., Khlaf-Bouaziz N., *et al.*, *Acute fatty liver of pregnancy. About 22 cases*, GYNECOL. OBSTET. FERTIL., **3** [Epub ahead of print], 2006.
12. Sinha A., Olah K. S., *Acute fatty liver of pregnancy : an unusual presentation*, J. OBSTET. GYNAECOL., **25**, 60-61, 2005.
13. Krishna R., Valavan R. T., Sathyanarayanan V., Rajendiran C., *Acute fatty liver of pregnancy : a case report and a review of the literature*, TROP. GASTROENTEROL., **24**, 135-136, 2003.
14. Corke P. J., *Anaesthesia for caesarean section in a patient with acute fatty liver of pregnancy*, ANAESTH. INTENSIVE CARE, **23**, 215-218, 1995.
15. Thomas S. D., Boyd A. H., *Prolonged neuromuscular block associated with acute fatty liver of pregnancy and reduced plasma cholinesterase*, EUR. J. ANAESTHESIOL., **11**, 245-249, 1994.
16. Ko H., Yoshida E. M., *Acute fatty liver of pregnancy*, CAN. J. GASTROENTEROL., **20**, 25-30, 2006.
17. Davidson K. M., *Intrahepatic Cholestasis of Pregnancy. Liver Disease in Pregnancy*, SEM. PERINATOL., **22**, 104-111, 1998.