Successful Clinical Application of the Molecular Adsorbent Recirculating System in a Patient with Acute Fatty Liver of Pregnancy

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Acute fatty liver of pregnancy (AFLP) occurs in about 1 in 15,000 deliveries, most commonly in the third trimester, with hepatic failure or hepatic encephalopathy [1]. The underlying pathogenesis is not well understood. Recent molecular advances suggest that AFLP may result from mitochondrial oxidation of fatty acids or fetal long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency [2]. Early diagnosis, followed by prompt delivery and supportive care, provides significant improvement in outcome for both mother and baby. In most cases, liver function improves and returns to normal within 1 to 4 weeks after delivery if there is no chronic liver disease [3].

A 30-year-old Indian woman in her 31st week of gestation was admitted to our hospital on September 5, 2005. She had had an entirely normal antepartum course. She denied any use of medications. She complained of sudden onset right upper epigastric pain, anorexia, and headache, which had been present for 2 days. There was no other significant past medical history. General physical examination revealed an afebrile patient with blood pressure of 130/80 mmHg, proteinuria (1+), icteric sclera, and edema of the feet. The fetal heart rate was 140 beats/min.

Laboratory findings showed a normal platelet count of 130,000/μL, white blood cell count of 16,600/μL, and a hemoglobin level of 10.5 g/dL. The medical department was consulted regarding her jaundice, and the consulting hepatologist observed that her liver function test results were obviously abnormal, with elevation of serum total bilirubin (12.8 mg/dL), glutamic-pyruvic transaminase (GPT; 147 IU/L) and glutamic-oxaloacetic transaminase (GOT; 112 IU/L). The alkaline phosphate level was increased to 424 U/L. A coagulogram revealed a prolonged prothrombin time (>60 seconds) and a partial thromboplastin time of 62.3 seconds. The markers for hepatitis virus were negative.

An abdominal ultrasound showed the florid stage of acute hepatitis. Jaundice and the clinical situation worsened. Abdomen computed tomography (CT) showed a prominent fatty liver. Therefore, the clinical scenario strongly suggested AFLP. Supportive care was provided, including fluid resuscitation, nutrition, anti-hypertension treatments and correction of hypoglycemia with D10W infusion and 50% dextrose boluses, as needed before delivery.

At the same time, transfusions of 4 units of packed red blood cells, 18 units of fresh frozen plasma and 18 units of cryoprecipitate were given before delivery to correct the coagulation defect. The patient developed chest pain, dyspnea, regular lower abdominal pain, and disorientation of consciousness. The fetal monitor showed fetal distress. She was immediately sent to the operating room. Emergency cesarean section was carried out to deliver an asphyxic female baby with a birth weight of 1,350 g and Apgar scores of 5 and 7 at 1 and 5 minutes, respectively, after neonatal resuscitation. Estimated blood loss, including amniotic fluid, was 600 mL. The amniotic fluid was meconium-stained.

After delivery, the patient underwent a clinical course of exacerbation with respiratory failure, acute renal failure, acute hepatic failure, and hepatic encephalopathy. The patient presented comatose and had bloody sputum with bubbles and oliguria. On the second day after surgery, the physical signs included severe edema of the whole body, and little ascites was

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seen on sonography. Biochemistry showed serum creatinine of 2.1 g/dL and uric acid of 9.3 mg/dL. Liver function tests showed 21 mg/dL of blood urea nitrogen, 351 U/L lactic dehydrogenase, 78 IU/L GPT and 36 IU/L GOT.

Comprehensive medical treatments, including diuresis, drug hemostasis, blood component therapy and continuous venovenous hemofiltration (CVVH), were performed in order to remove the toxic metabolite and severe edema. The renal function was effectively improved, with an increase in urine volume and reduction of whole body edema. In spite of full medical support with CVVH to remove the ammonia, her hepatic function did not improve and the total bilirubin remained at 27.7 mg/dL. The patient was comatose with a Glasgow coma score of 5/15. At this point, the serum ammonia was measured and was found to be elevated to 345 μg/dL on the sixth day of hospitalization. Therefore, a diagnosis of hyperammonemic encephalopathy was made.

On postpartum days 8 and 9, the patient was treated with molecular adsorbent recirculating system (MARS) artificial liver support therapy because of her consciousness disturbance and hyperbilirubinemia with impending liver failure. After the first MARS treatment, the total bilirubin level decreased significantly from 20.1 to 14.3 mg/dL. This was associated with a dramatic improvement in her consciousness level, back to Glasgow coma score 13/15. The following day, she received the second MARS treatment and the total bilirubin level decreased to 13.8 mg/dL. By the end of the second session, the patient had full recovery of consciousness, allowing for early extubation. The patient's multiple organ failure condition and its serious complications continued to improve, i.e. neuromyopathy, pneumonia, pleural effusion and pancreatitis.

She was transferred to the general ward on the 26th day of hospitalization. She then developed a low-grade fever and progressive right-sided abdominal pain with localized tenderness in the pelvis at the site of her cesarean section wound. An abdominal CT scan showed multiple intra-abdominal abscesses. She received several abscess aspirations with purulent discharge. The purulent material was examined and the culture showed coagulase-negative staphylococci. This was effectively controlled by empirical antibiotics (intravenous cefepime). Throughout the 94 days of hospitalization, the patient and her baby received the best of care in our hospital. Both of them were discharged in good condition.

We report the first application of MARS therapy for treating a patient with AFLP associated with multiple organ failure. The clinical feature of the case was AFLP appearing in the early third trimester of pregnancy, with awareness of functional liver abnormalities, especially early stage recognition, in this primigravida Indian woman.

Hypoglycemia may have occurred in this patient who had an altered mental status, and such patients usually cannot tolerate labor. Dextrose infusion (10%) is typically adequate to prevent hypoglycemia [4]. Further examination showed that the liver function deteriorated quickly; bilirubin levels reached 27.7 mg/dL and serum ammonia levels during coma were elevated to 345 μg/dL. The latter mainly points to a diagnosis of hepatic encephalopathy.

The high morbidity and mortality of these recognized complications, as well as the relentless progression of the liver failure, prompted the use of MARS. The patient showed improvement in mental state after each session of MARS, and there were decreases in the levels of serum bilirubin, ammonia, urea nitrogen and transaminase.

MARS is an extracorporeal device that uses albumin as a dialysate to remove toxins from the patient's blood and activated charcoal to bind the toxins [5]. Our patient underwent two courses of albumin dialysis using MARS. Her poor liver function was immediately reversed and clinical symptoms improved. The most common adverse effect associated with MARS therapy is moderate hypokalemia [6]. Thrombocytopenia worsened during MARS sessions requiring transfusion support. MARS can be used to support patients through the most critical and fatal phase of the disease.

In general, AFLP is considered to be a reversible form of acute liver failure that does not require liver transplantation, except in a very few cases of liver failure persisting or progressing after delivery. Death occurs in many such cases while awaiting liver transplantation. Currently, maternal mortality has decreased to less than 10% because of early recognition of the disease resulting in prompt delivery and intensive care during the postpartum period. If the patient survives, this syndrome does not reappear in subsequent pregnancies [7].

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