POSTPARTUM HELLP SYNDROME WITH UNUSUALLY HIGH LEVELS OF LIVER ENZYMES

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Hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome, a severe variant of preeclampsia/eclampsia, characterized by intravascular hemolysis, elevated levels of liver enzymes and a low platelet count, may cause many maternal antepartum or postpartum problems. It is known that about 20% of women with severe preeclampsia or eclampsia may progress to HELLP syndrome, while mortality rates vary from 0% to 24% [1]. Herein, we present a case of a twin pregnancy complicated by severe preeclampsia and HELLP syndrome with unusually high serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels up to 3,894 U/L and 3,581 U/L, respectively. Neither hepatic rupture nor failure was induced by HELLP syndrome in a self-limiting clinical course post partum.

A 46-year-old woman, gravida 1, para 0, conceived twins subsequent to *in vitro* fertilization and embryo transfer, although she developed preterm labor as early as the 26th gestational week. Prior to her pregnancy, this woman revealed an otherwise normal blood pressure and liver enzymes. Tocolytic treatment with ritodrine and magnesium sulfate for preterm labor, and corticosteroids to facilitate fetal lung maturation were used. Intermittent bouts of hypertension with systolic blood pressure reaching levels as high as 150 mmHg and diastolic blood pressure levels up to 90 mmHg combined with a puffy face and general edema were noted from the 28th gestational week onward. Risk factors for preeclampsia, including advanced age, nulliparity and twins, were relevant to this patient, with imminent progression to preeclampsia. Not until the 33rd gestational week did the woman reveal significant proteinuria. Simultaneously, this woman complained of orthopnea and shortness of breath as the chest film showed pulmonary edema. This patient's blood pressure remained about 150/90 mmHg. Antepartum fetal surveillance was reassuring from the non-stress test and amniotic fluid index. Cesarean section was resisted until maternal compromise (day 9 in hospital) evidenced by preeclampsia and HELLP syndrome (hemoglobin, 10.4 g/dL; platelets, 148,000 per μL; serum AST and ALT levels, 101 and 139 U/L, respectively). Preterm twins were born with normal Apgar scores of 8 and 9 at 1 and 5 minutes, respectively, post delivery, with one infant weighing 2,058 g and the other 1,660 g. The patient recovered steadily after oxygen supplementation, diuretics, and fluid restriction over 24 hours.

Two days (day 11 in hospital) after delivery, the patient developed right upper abdominal pain, soon followed by development of a somewhat jaundiced face. Serum biochemistry investigations revealed highly increased AST and ALT levels of 3,894 and 3,581 U/L, respectively, along with total and direct serum bilirubin levels of 2.8 and 0.9 mg/dL, respectively, lactate dehydrogenase 3,627 U/L, and uric acid 8.3 mg/dL (day 11 in hospital). No evidence of the existence of any hepatitis virus was detected from the serum study, and the patient's postoperative hemoglobin declined from 7.7 g/dL to 6.8 g/dL in 24 hours (days 11 to 12 in hospital). The coagulation profile included a mildly low platelet count of 140,000 per μL and a fairly normal prothrombin time and partial thromboplastin time, a fibrin degradation protein level of greater than 40 μg/mL (normal, < 10 μg/mL), a D-dimer level of 5,522 ng/mL (normal, < 500 ng/mL), and a fibrinogen level of 397 mg/dL (normal, 200–400 mg/dL) 2 days after delivery (day 11 in hospital). Abdominal ultrasound in this patient revealed mild infiltration of fatty liver without evidence of hepatic rupture or hemoperitoneum.

A total of 30 mg dexamethasone was administered to this patient for her hepatic dysfunction, such therapy consisting of three separate doses at 12-hour intervals. Throughout the hospital course, the patient always

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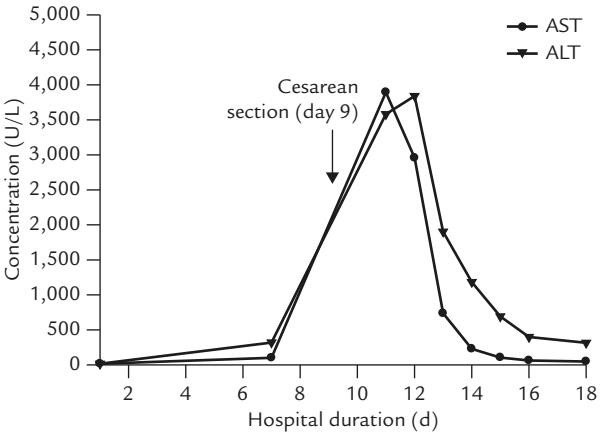

Figure. The change in liver enzyme levels and hospital course of the patient with HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome. AST = aspartate aminotransferase; ALT = alanine aminotransferase.

remained alert. The unusually high serum AST and ALT levels present at the 33rd gestational week declined drastically to 229 and 1,184 U/L, respectively, 5 days post partum (day 14 in hospital) and to 63 and 399 U/L, respectively, 9 days post partum (day 18 in hospital; Figure). The clinical symptoms and laboratory data revealed a dramatic improvement over the 2-week postpartum period, while her serum AST and ALT levels (23 and 28 U/L, respectively) indicated no liver disease.

Preeclampsia remains quite a common obstetric complication, and plays a role in maternal death. HELLP syndrome accounts for around 20% of women with severe preeclampsia in the USA [1]. The pathophysiology of preeclampsia may result from microangiopathy that leads to injury of the vascular endothelium with systemic involvement [1]. HELLP syndrome could be considered to be a type of "gastrointestinal preeclampsia" and a placenta-instigated, liver-targeted acute inflammatory condition [2,3]. Maternal death caused by HELLP syndrome featuring unusually high serum levels of AST and ALT is still a matter of concern for clinicians, because there appears to be a relative paucity of optimal treatment modalities for the condition to avoid possible fatal sequelae such as subcapsular hemorrhage, hepatic rupture, disseminated intravascular coagulopathy, and sepsis [4]. Recent studies of maternal morbidities associated with HELLP syndrome include eclampsia (6%), placental abruption (10%), acute renal failure (5%), pulmonary edema (10%), and subscapular liver hematoma (1.6%) [5].

Among the toxicities of beta-mimetic agents such as ritodrine, pulmonary edema is a well-known example of their activation of the renin-angiotensin system, and increased sodium and water resorption [6]. In addition, to be borne in mind is the possibility of a synergistic effect with combined magnesium sulfate treatment for poorly controlled preterm labor even at a safe therapeutic dosage. Elevation of liver enzymes is a rare complication of ritodrine which occurs more frequently in a twin than a singleton pregnancy (9.1% *vs.* 1.9%) [7]. It is difficult to exclude the possibility that this patient had ritodrine-induced liver function impairment alone, but preeclampsia complicated with HELLP syndrome is likely to be the reason for such high serum AST levels. Briefly, the changes in volume homeostasis and damage to the vascular endothelium could be the mitigating factors in all patients with preeclampsia and those subsequently progressing to HELLP syndrome.

Whether corticosteroid treatment actually improves HELLP syndrome remains controversial in the literature [8,9]. Following positive outcomes, steroids may play an effective role as regards reducing the mortality and morbidity rate in women suffering from HELLP syndrome [10]. However, sufficient evidence needs to be gained from large-scale studies [11]. According to our experience presented herein, corticosteroid therapy did not seem to be harmful in HELLP syndrome featuring unusually high serum AST and ALT levels.

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