CASE REPORT

DOI: 10.5336/gynobstet.2015-46783

Postpartum Plasmapheresis Treatment in a Severe Liver Enzyme Disorder

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Received: 28.06.2015
Received in revised form: 06.11.2015
Accepted: 11.11.2015
Available online: 31.08.2018

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This case report was presented as a poster in "Turkey Maternal-Fetal Medicine and Perinatology, Perinatal Medicine 2015" Congress (23-26 April 2015, Istanbul).

ABSTRACT HELLP syndrome is a severe form of preeclampsia that was first described by Weinstein in 1982. It is characterized by hemolysis, elevated liver enzymes, and low platelet count. HELLP develops in approximately 0.5-0.9% of all pregnancies and in 10-20% of pregnancies complicated with preeclampsia. HELLP syndrome is a severe complication that increases the risk of both fetal and maternal mortality. The treatment for HELLP syndrome is primarily based on the gestational age, and though the most effective treatment is delivery, other options are also available. Plasmapheresis is the preferred option for the complication of progressive liver function disorder. We present a case report of a 34-year-old pregnant woman suffering from HELLP syndrome, who showed dramatic improvement after plasmapheresis.

Keywords: HELLP syndrome; plasmapheresis

The HELLP syndrome, characterized by microangiopathic hemolytic anemia, hemolysis, elevated liver function tests and low platelet count was first described by Weinstein in 1982.[1] The HELLP syndrome occurs in about 0.1 to 0.8% of all pregnancies and in 10 to 20% of pregnancies complicated with severe preeclampsia/eclampsia.[2] Disorders like preeclampsia and HELLP syndrome can cause complications like liver infarction, liver rupture and hemorrhage in the mother.[3] The definitive treatment is delivery, but depending on the maternal situation, other treatment options can also be considered.[3]

CASE REPORT

A 34-years-old, G3 P2 woman was admitted to our hospital at 38 weeks of gestation with right upper quadrant pain and high blood pressure (200/110-190/100 mmHg). Her condition was stable and she had tenderness in the upper right quadrant. The ultrasound examination showed fetal biometry in accordance with 34 weeks of gestation and severe oligohydroamniosis. Non-stress test was reactive. Laboratory tests revealed Hb 14.5 g/dL, platelet count 143,000/mm^3, ALT 77 IU, AST 108 IU, LDH 350 IU and urinary spot protein +3 positive. An intravenous bolus of 4 g $MgSO_4$ was ordered at 1 g/h. The patient underwent emergency cesarean section due to high BP and progressive elevation of liver function indicators. A healthy, 2250 gram baby was delivered by low transverse incision, with APGAR score 7/8. The $MgSO_4$ dose was increased to 1.5 g/hour since the BP could not be normal-

ized. In addition, 5 mg amlodipine and nitroprusside infusion was also ordered. Her postoperative laboratory tests showed Hb 9.1 g/dL, platelet count 22,000/mm^3, ALT 2515 IU, AST 4099 IU, LDH 6443 IU, total bilirubin 2.7 g/dL, direct bilirubin 1.39 g/dL, INR 0.94, D-dimer 6198 mg/L, and fibrinogen 2.39 mg/dL (Table 1), and peripheral blood smears showed schistocytes. The patient was referred to the departments of hematology, gastroenterology, nephrology and cardiology and her laboratory tests were repeated every six hours.

Due to the elevation of liver function indicators, an abdominal ultrasound scan was performed which revealed hypo-hyperechogenic areas in the right liver lobe consistent with necrosis. The ultrasound scan of the liver also showed normal left and lateral sides, free fluid in the perihepatic area and right pleural effusion. The patient was then referred to hematology and plasmapheresis was planned. Plasmapheresis was done once daily for three days with Fresenius-AS-TEC 204 (Fresenius Hemocare, Redmon, WA, USA) and fresh frozen plasma was used as replacement fluid. Three erythrocyte suspensions were used in total. Hemoglobin level was increased to 8 g/dL before plasmapheresis, and 4 mg doxazosin and 10 mg alfametildopa were given daily to manage hypertension. In addition, oral 500 mg ursodeoxycholic acid thrice daily and intramuscular 40 mg enoxaparin were prescribed. During follow-up, the elevated liver markers were dropped, the platelet count was elevated, and blood pressure was normalized. The patient was discharged on the 9th day of follow-up and given appointment for control examination. She did not need any antihypertensive drugs, and the signs of hemolysis were regressed. The baby was also healthy and did not have any complications.

TABLE 1: Laboratory result comparison before and after plasmapheresis.

	Before plasmapheresis	After plasmapheresis
Hemoglobin	9.1 g/dL	7.9 g/dL
Platelet	22 mm^3	69 mm^3
Prothrombin time	28.3 sn	35.5 sn
INR	0.94	1.01
AST	4099 IU	1332 IU
ALT	2515 IU	717 IU
LDH	6443 IU	2288 IU
BUN	15 mg/dL	8 mg/dL
Creatinine	0.68 mg/dL	0.64 mg/dL
Total bilirubin	2.71 mg/dL	3.0 mg/dL
Direct bilirubin	1.39 mg/dL	1.25 mg/dL

DISCUSSION

The diagnostic criteria for HELLP syndrome are hemolysis in peripheral blood smears with schistocytes, platelets below 100,000/mm^3 and increased total bilirubin (>1.2 mg/dL) and AST (>70 IU). Although the exact pathophysiology of HELLP syndrome has not been established, it is hypothesized that abnormal placental development and function that lead to preeclampsia can also contribute to the HELLP syndrome. Unlike preeclampsia, severe hepatic inflammation and intravascular coagulation frequently occur in HELLP syndrome.[4] Differential diagnosis includes viral hepatitis, cholangitis and other acute forms of liver diseases. Occasionally, ITP (immune thrombocytopenic purpura), acute fatty liver of pregnancy, hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, systemic lupus erythematosus and antiphospholipid syndrome can also mimic HELLP syndrome. The maternal mortality rate is approximately 1.1%, and the perinatal mortality rate is about 34% during the first 34 weeks of pregnancy and 7.4% after 34 weeks.[5] HELLP syndrome results in placenta ablatio, disseminated intravascular coagulation, acute renal failure, and cerebral and pulmonary edema. Perinatal morbidities noted in HELLP syndrome include intrauterine growth retardation, preterm birth, neonatal thrombocytopenia and respiratory distress syndrome. Perinatal morbidity depends more on the gestational stage rather than the pathological effect of HELLP syndrome.[6] The most effective treatment for HELLP syndrome is delivery. If fetal distress and/or maternal end-organ damage (DIC, renal failure, and placenta ablatio) are seen after 34 weeks, immediate delivery should be planned. Labetalol, hydralazine, and nifedipine should be administered as antihypertensive drugs, diuretics should be avoided due to the risk of uteroplacental hypoperfusion, and corticosteroid ther-

apy should also be considered.[7] Plasmapheresis is not a routine treatment option in HELLP syndrome yet, but some guidelines recommend it for managing HELPP.[8] However, further investigations are required regarding the indications, stage, and frequency of plasmapheresis treatment, as it is an invasive procedure and can result in complications like perforation, hemorrhagia, infection, sepsis, and anaphylaxis.[9] Simetka et al. suggested that plasmapheresis should be considered as an option if a patient does not respond to conventional therapies within 24-72 h and her condition continuously deteriorates.[9] Although plasmapheresis is recommended every 24-48 h, there are no set guidelines regarding the duration.[10] Some clinicians suggest that plasmapheresis can be stopped when the platelet count reaches 100.000 cells/mm^3 and the patient is stable.[2] If a patient does not respond to plasmapheresis within 24 h, the risk of multiorgan dysfunction and death increases, thus increasing the need for intensive care. In addition, even if a patient is responsive, the risk of hypertension, renal diseases, and neurological symptoms increases after recovery. Early diagnosis is important to prevent complications and to determine at-risk patients. Plasmapheresis can be a life-saving option for high-risk patients, especially when started within 24 h of HELLP diagnosis.[2] Erkurt et al. demonstrated that mortality rate is significantly reduced after plasmapheresis as long as it is started within the first 24 h.[8] One of the major causes of mortality in HELLP is renal failure. Eser et al. showed that plasmapheresis reduced the need for dialysis and risk of chronic renal failure.[10] Steroids and plasmapheresis do not target the etiology of the condition but affect the symptoms by suppressing the inflammatory process and clear out the cytokines from blood.[8] Nevertheless, the exact role of plasmapheresis in HELLP syndrome treatment needs to be elucidated, along with the etiology of HELLP syndrome to develop targeted therapies.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Özgür Kan;* ***Design:*** *Salih Taşkın, Feride Söylemez;* ***Data Collection and/or Processing:*** *Kazibe Koyuncu, Özgür Kan;* ***Analysis and/or Interpretation:*** *Feride Söylemez;* ***Literature Review:*** *Tuncay Yüce, Salih Taşkın;* ***Writing the Article:*** *Kazibe Koyuncu.*

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