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Early identification of women with HELLP syndrome who need plasma exchange after delivery

O. Simetka [a,b,*], J. Klat [a,b], J. Gumulec [c], E. Dolezalkova [a], D. Salounova [d], M. Kacerovsky [e]

[a] Department of Obstetrics and Gynecology, University Hospital Ostrava, Ostrava, Czech Republic
[b] Faculty of Medicine, University of Ostrava, Ostrava, Czech Republic
[c] Department of Hematooncology, University Hospital Ostrava, Ostrava, Czech Republic
[d] Department of Mathematical Methods in Economy, VSB-Technical University of Ostrava, Ostrava, Czech Republic
[e] Department of Obstetrics and Gynecology, Charles University and University Hospital, Hradec Kralove, Czech Republic

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ABSTRACT

Objectives: To compare the laboratory course of HELLP syndrome between patients who recover and those who progress to postpartum thrombotic microangiopathic syndrome (PTMS) and require postpartum plasma exchange (PPEX) and to describe maternal characteristics and morbidity in women with PTMS.
Methods: In this retrospective analysis, 81 patients recovered and 5 progressed. Values for aspartate aminotransferase (AST), lactate dehydrogenase (LDH), bilirubin, platelets (Plt), urea, and creatinine at 0, 8, 16, 24, 48, and 72 hours postpartum in both groups were analyzed and compared. We also described maternal characteristics and morbidity of patients who progressed to PTMS.
Results: Patient groups differed significantly at 72 hours postpartum for Plt and LDH values and at 24 and 48 hours for bilirubin. Trends for AST and Plt differed significantly between the recovery and progression groups in the first 48 hours. Patients who progressed had acute kidney injury and other severe maternal morbidity, including one case of maternal death.
Conclusions: Women with HELLP syndrome without clear Plt and AST improvement in the first 48 hours and with acute kidney injury, neurological impairment, or respiratory distress syndrome are at risk of progressing to PTMS. They should be administered PPEX between 24 and 72 hours postpartum.

1. Introduction

HELLP syndrome is a rare and severe complication of pregnancy. If diagnosed early and managed properly, the condition of most patients usually starts to improve within the first 24–48 hours after delivery [1,2]. Extremely rarely though, the patient does not respond to the expedited termination of pregnancy (delivery of the fetus and placenta) and usual supportive treatment, and a progressively worsening clinical and laboratory picture develops with features of consumptive coagulopathy and multiorgan injury. The patients with this course of the disease have higher morbidity and mortality compared to patients with typical HELLP syndrome, but their condition usually improves after administration of postpartum plasma exchange (PPEX) [1,3,4].

Little has been reported about the characteristics of patients with this condition, called postpartum thrombotic microangiopathic syndrome (PTMS). The first review to attempt a classification was published only recently and

* Corresponding author. Department of Obstetrics and Gynecology, University Hospital Ostrava, 17. listopadu 1790, Ostrava 708 52, Czech Republic. Tel.: +420 59 737 1802; fax.: +420 597 374 812.
E-mail address: ondrej.simetka@fno.cz (O. Simetka).

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suggested the term PTMS [1,2]. According to that review, only 28 cases have been described in the English-language literature so far, either as case studies or small groups of patients. Furthermore, no consensus exists regarding indication criteria for PPEX and the number of exchanges that should be administered.

We searched our database of patients with HELLP syndrome who were treated in our institution in the last 10 years. In the time period, we managed 87 cases of HELLP syndrome, of which 5 had a complicated course of the disease that involved features of PTMS. The primary study aim with these data was to compare the laboratory course of the disease between patients with HELLP syndrome who responded to the usual therapy and those who progressed to PTMS and required PPEX. The second aim was to describe maternal characteristics and maternal morbidity of women with PTMS to identify features for early identification.

2. Materials and methods

This is a retrospective analysis of patients who were admitted to the Department of Obstetrics and Gynecology at University Hospital Ostrava, Czech Republic, between March 2004 and February 2014 with complete and incomplete HELLP syndrome. We included both patients who delivered in our institution and those who were transferred from other hospitals for postpartum care. The inclusion criteria were complete class I–III HELLP syndrome defined by Mississippi classification (platelets (Plt) $< 150 \times 10^9$/l, aspartate aminotransferase (AST) above 1.16 μkat/l (0.69 μkat/l in class III), and total lactic dehydrogenase (LDH) above 10 μkat/l). Patients were divided into the class I-III based on the platelet count (class I under 50×10^9/l, class II $50–100 \times 10^9$/l and class III $100–150 \times 10^9$/l). Additional criteria were used to confirm hemolysis in HELLP syndrome such as low haptoglobin and the presence of schistocytes. Incomplete HELLP was defined as absence of hemolysis, elevated liver enzymes or a low platelet count.

In cases of non-improving HELLP syndrome, an effort to differentiate it from thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), or immune thrombocytopenic purpura (ITP) has been made.

Pre-eclampsia was defined by the onset of hypertension (>140/90 mmHg) and proteinuria above 0.3 g/24 hours in the second half of the pregnancy and eclampsia was defined as presence of generalized convulsions in the presence of pre-eclampsia.

We divided the patients into two groups: those who responded to the usual treatment and had obvious clinical and laboratory recovery within 72 hours (group 1), and those who did not improve following delivery and the usual supportive treatment and had multiorgan injury and were therefore indicated for PPEX (group 2). The exclusion criterion was a chronic condition that indicated PPEX.

The research protocol was approved by the Institutional Review Board or Ethics Committee before the study began. Informed consent was not required for the study.

2.1. PPEX indication

The indication for PPEX was based on clinical (non-responsive HELLP syndrome with multiorgan failure) and laboratory findings that were either worsening or showed no clinically significant improvement after delivery and with the usual treatment. Consensus of an obstetrician, hematologist, and intensivist was required.

Bedside PPEX was performed with a COBE Spectra Cell Separator, Terumo BCT, Lakewood, USA to accomplish 3.5–4.0 l plasma exchange using fresh frozen plasma as the primary replacement fluid. PPEX was done every 24–48 hours until clinical and laboratory improvement of the patient; again, the consensus of the team of specialists was required.

2.2. Laboratory testing

Blood samples were taken every 8 hours (±2 hours) until 48 hours after delivery or until full or obvious recovery of the laboratory values; samples were taken less frequently later on, usually once daily. Values were recorded at 0, 8, 16, 24, 48, and 72 hours. The zero time value was the last value before delivery of the respective parameter. In the case of Plt, it was the last value before the pre-partum administration of platelets. The maternal and delivery characteristics were obtained from the hospital information system and patient records.

2.3. The standardized treatment of HELLP syndrome

The usual management of suspected or confirmed HELLP syndrome in our institution was as follows: administration of magnesium sulfate (4 g i.v. bolus followed by 1 g/hour for 24 hours after delivery or last eclamptic seizure); corticosteroids (betamethasone or dexamethasone) i.m. in patients under 35 gestational weeks, even in situations precluding completion of the fetal lung induction protocol; early expedited delivery of the fetus and placenta; and antihypertensive drugs. Since March 2012, corticosteroids have been administered to all patients according to the Mississippi protocol (dexamethasone 10 mg + 10 mg + 5 mg + 5 mg i.m. every 12 hours) [2,5,6].

Careful postpartum monitoring was conducted of fluid balance and prescription of intravenous fluids and intravenous diuretics to achieve sufficient diuresis with the aim of achieving negative fluid balance after delivery. Other treatment (blood, plasma, fibrinogen, antibiotics) was given as needed.

2.4. Statistics

Laboratory values of AST, LDH, bilirubin, Plt, urea, and creatinine at 0, 8, 16, 24, 48, and 72 hours in both groups were analyzed. Data were compared between the groups using the median test.

To describe development of laboratory values over time, we used natural logarithms of growth coefficients of each laboratory parameter, i.e., quotients of neighboring values for each parameter. We then compared development of all parameters in time between both groups (interactions). For