ACUTE RENAL FAILURE IN THE COURSE OF HELLP SYNDROME

Monika E. Dzwigala, Agnieszka Dobrowolska-Redo, Ewa Romejko-Wolniewicz

1. Students' Scientific Group next to 2nd Department of Obstetrics and Gynaecology, Medical University of Warsaw, Poland
2. 2nd Department of Obstetrics and Gynaecology, Medical University of Warsaw, Poland

#Corresponding author: Agnieszka Dobrowolska-Redo, e-mail: agnieszka.dobrowolskaredo@gmail.com, Warsaw Medical University, Karowa St 2, p.o. box 00-315 Warsaw, Poland, phone number: +48 22 5966 421, fax +48 22 5966 487

RUNNING TITLE HELLP syndrome complications
KEYWORDS HELLP syndrome, renal failure, diagnostic problems, preeclampsia, pregnancy, premature birth
WORD COUNT 1670
CONFLICT OF INTERESTS no conflicts of interest

ABSTRACT

HELLP syndrome is a severe pregnancy complication with high mortality among mothers and children. Incidence of HELLP syndrome according to literature is about 1% of all pregnancies. HELLP syndrome is associated with preeclampsia in one-quarter of patients. Current researches on HELLP syndrome address etiology, treatment and prediction of the syndrome. Currently there are no useful predictors and established treatment is the delivery. This study presents the case of HELLP syndrome in 37 year-old patient at 28th week in her first successful pregnancy after in-vitro fertilization technique.
BACKGROUND

HELLP is the abbreviation of three main features of the syndrome: haemolysis (H), elevated liver enzymes (EL), and low platelet count (LP). Thrombocytopenia, haemolysis and increased transaminase levels can also be observed in a patient with severe preeclampsia (PE). However, main features of preeclampsia are: hypertension ≥ 140/90 mmHg measured twice with 6 hours interval and proteinuria over 300 mg per day. It is still under discussion, if HELLP syndrome is a separate entity. It is known that HELLP syndrome can be observed without preeclampsia, after delivery and is not a manifestation of disseminated intravascular coagulation (DIC).

The first person who described HELLP syndrome was Louis Weinstein in 1982 [1]. This pregnancy complication affects 0.5 to 0.9% of all pregnancies and in 10% to 20% it occurs with preeclampsia [2]. Maternal mortality is estimated to be at about 1% [3]. This syndrome can develop during pregnancy or after childbirth in the postpartum period. This is a reason for strict observation for 48 hours after delivery, in certain cases even prolonged to 7 days. The mechanisms of HELLP syndrome are not well known. There are a few theories describing pathophysiology. One of them is similar to the PE’s onset: the cause is a disorder of microcirculation due to the imbalance between prostacyclin and thromboxane. As a result of immune factors, coupled with impaired synthesis of prostacyclin (PGI), vascular bed does not expand, resulting in abnormal morphological and functional adaptation of the vascular system, maternal and feto-placental, which leads to an increase in pressure and excessive permeability of capillary vessels of the organs. PGI deficiency causes damage to the endothelium in the placenta and in the organs, leading to increased permeability of the vessel walls, proteinuria and oedema. Endothelial damage may also occur as a result of microvascular complications by creating micro clots and fibrin concretion in the blood capillary. This in turn leads to hepatic congestion and damage to the liver cells, resulting in decreased flow and inhibition of the development of the foetus. It is known that improper function of placenta resulting in release of inflammatory factors cause endothelial dysfunction and leukocyte, complement- and clotting- activation leading to constriction of vessels [4]. Fibrin complexes with platelets lead to hypoxia and infarction of end organs such as the liver. Genetic basis of HELLP syndrome is very complicated, more than 178 genes have been found in relation to preeclampsia or HELLP syndrome [4]. However, one example of a genotype-phenotype correlation regarding HELLP syndrome has been described: in heterozygotic women having a Glu474Gln long-chain 3-hydroxyacyl-coenzyme A dehydrogenase (LCHAD) mutation, deficient foetuses have a 77% risk of severe pregnancy complications such as acute fatty liver of pregnancy (AFLP) or HELLP syndrome [4].

HELLP syndrome maternal complications are: pulmonary oedema, renal and liver failure, liver rupture or hematoma and haemorrhage. Preterm birth and growth restriction are complications observed among babies of mothers affected by HELLP syndrome [5].

CASE DESCRIPTION

A 37-year-old patient at 28 gestation weeks’ (gravida 1 - post assisted conception in-vitro fertilization technique, para 0) was admitted to the Department of Obstetrics of tertiary referral centre from the district hospital due to upper abdominal pain, aspartate transaminase and alanine transaminase significant growth over 1000 IU/l and drop of platelets to 31*10^9/l within 3 hours. The patient began to feel worse a week before admission. During physical examination at the emergency department patient presented: high blood pressure, elevation of heart rate and normal body temperature. The cervix of the uterus was closed, 1.5 cm long. Membranes were intact, no uterine contractions were observed. Patient was urgently transferred to labour ward with the diagnosis: HELLP syndrome and threatening intrauterine asphyxia. The patient’s condition at the labour ward was stable. At the admission to the ward dexamethasone was administered. Soon, after one hour and twenty minutes since admission to labour ward, decrease in foetal heart rate was observed down to 80 heart beats per minute. No alignment was observed and patient was urgently referred to Caesarean Section (CS). She delivered a girl weighing 1000g, 1-3-5 points in APGAR scale, intubated in the tenth minute of life. There were several complications during the CS. Blood was found in the abdominal cavity (about 400 ml), left appendage was bleeding resulting in resection of the left fallopian tube. Total estimated blood loss was one and a half litre. During surgery 4 units of packed red blood cells, 4 units of fresh frozen plasma and 10 units of cryoprecipitate were transfused. The diuresis decreased since operation. Respiratory failure developed within 16 hours leading to pulmonary oedema. During the first day after CS the patient was transferred to the intensive care unit (ICU) where she was intubated and mechanically ventilated for 4 days. Due to acute renal failure continuous renal replacement therapy technique (CRRT) was introduced throughout the duration of her stay in the ICU (8 days). Stabilization of cardiovascular system was successfully obtained with antihypertensive therapy. The patient was consulted times 4 by a gynaecologist and 2 times by a nephrologist. After eight days since labour, the patient was transferred to the Department of Transplantation Medicine and Nephrology with persisting improper renal parameters and hematoma in the abdominal wall. During 10 days stay at the Department of Transplantation Medicine and Nephrology patient undergone haemodialysis four times. She obtained improvement in inflammation parameters. After 12 days of the treatment, increasing diuresis with the tendency to polyuria was observed. A probable cause of kidney failure was acute tubular necrosis due to haemorrhage (large blood loss, initially during surgery, followed by extensive bleeding into the abdominal wall, resulting from severe thrombocytopenia accompanying the HELLP syndrome). Additional problems that occurred during the treatment at the ICU were: a large hematoma in the abdominal wall, high blood pressure during renal failure, a bacterial infection with Citrobacter freundii, Klebsiella pneumoniae ESBL (+) and Enterococcus faecalis.

The baby was discharged after a sixty-nine- day stay in the hospital without any severe complications and in
good condition. After delivery the baby presented: respiratory distress syndrome, apnoea of prematurity, intraventricular haemorrhage, perinatal asphyxia, hyperbilirubinemia and anaemia of prematurity. It spent the first eighteen days in neonatal ICU, then fifty-one days at the neonatal pathology ward. The weight gain was 1490 g and height gain was 7 cm.

After 1.5 years the patient spontaneously got pregnant and delivered a healthy baby at term without any complications.

COMMENTS

HELLP syndrome is a compilation of haemolysis, elevated liver enzymes and low platelets. This triad is describing complete HELLP (syndrome cHELLP). In some cases, partial HELLP syndrome (pHELLP) can be observed such as: H, EL, LP (6). Strict diagnostic criteria are important since there is different prognosis for pHELLP and cHELLP (7). Partial syndrome is less traumatic for the mother and the baby. More aggressive and proactive approach should be administered to women with cHELLP. There is no agreement about the etiology and also there are many studies searching for risk factors. Documented risk factors are: previous HELLP syndrome, PE, incidence of HELLP syndrome in family (mother, sister), Caucasian race, higher mean arterial blood pressure (MAP), but not as high as in patients with PE [8]. Preeclampsia risk factors are: African-American origin and higher level of MAP in first trimester [8], obesity, first pregnancy, age below 20 and above 40 years, diabetes mellitus, thrombophilia, foetus with trisomy. Most frequently noted complications of HELLP syndrome are: acute renal failure, DIC, eclampsia [9, 10, 11]. It is important to notice that some studies suggest the association between assisted conception, HELLP syndrome and preeclampsia [12, 13, 14]. HELLP syndrome is mainly diagnosed during pregnancy at a median gestation of 36 weeks (range between 25 and 41 weeks) [15]. Treatment of HELLP syndrome is delivery: natural (induced) or CS. It has been suggested in some studies that plasma exchange can reduce mortality by improving organ function such as liver, kidneys or brain [11]. Differential diagnosis of HELLP syndrome can be a challenge. Instead of HELLP syndrome, an obstetrician can diagnose: AFLP, antiphospholipid syndrome (AFS), viral hepatitis, haemolytic uremic syndrome (HUS), cholangitis, PE, thrombotic thrombocytopenic purpura (TTP). AFLP can be excluded, when there is no history of one or two weeks of malaise, headache, anorexia, nausea, vomiting. PE diagnostic criteria are: hypertension and proteinuria which are usually not observed in the course of HELLP syndrome. During TTP the intense thrombocytopenia, high level of specifically cleaves unusually-large von Willebrand factor (UL-VWF) and very low or undetectable von Willebrand factor-cleaving protease also known as a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS13) activity is observed [16]. HUS can be distinguished when the characteristic triad is present: renal failure, microangiopathic haemolytic anaemia and thrombocytopenia. Finally, AFS can be confirmed serologically. It was suggested in some studies, that the best manner to diagnose HELLP syndrome (unless it is urgent) should be magnetic resonance [16]. Simpler diagnostic factor was also recalled in studies: hypoglycaemia which accompanies HELLP syndrome. The most difficult aspect is to understand and distinguish PE and HELLP syndromes because one of the etiology theories is similar (damage of foetal trophoblast in first trimester) and some symptoms are identical. However, differences can be observed, for instance levels of messenger RNA in maternal blood are more often abnormal in the course of HELLP syndrome versus PE, which suggests that earlier and more severe lesion of trophoblast occurred, which is usually observed in the HELLP syndrome. It was reported that also inflammatory response (without any infection) is higher in patients with HELLP syndrome than in patients with PE [17].

In conclusion, unfortunately there is no useful predictor and prophylaxis of HELLP syndrome, which leaves room for further research and possible creation of clinically needed guidelines and diagnostic procedures. It should be remembered that patients demonstrating the characteristic triad: H, EL, LP and upper abdominal pain should not be observed in a district hospital or by attending physician but immediately transferred to the hospital with the highest level of referral. This is the best and only chance for a happy end for both the mother and the child.

CITE THIS AS

MEDtube Science Dec, 2016; Vol. IV (4), 12 – 15

ABBREVIATIONS

HELLP – haemolysis, elevated liver enzymes and low platelet count
H – haemolysis
EL – elevated liver enzymes
LP – low platelet count
PE – preeclampsia
DIC – disseminated intravascular coagulation
PGI – prostacyclin
LCHAD – Glu474Gln long-chain 3-hydroxacyl-coenzyme A dehydrogenase
AFLP – acute fatty liver of pregnancy
CS – Caesarean Section
ICU – intensive care unit
CRRT – continuous renal replacement therapy technique
ESBL – extended-spectrum beta-lactamases
cHELLP – complete HELLP syndrome
pHELLP – partial HELLP syndrome
MAP – mean arterial blood pressure
AFS – antiphospholipid syndrome
HUS – haemolytic uremic syndrome
TTP – thrombotic thrombocytopenic purpura
UL-VWF – unusually-large von Willebrand factor
ADAMTS13 – metalloproteinase with a thrombospondin type 1 motif, member 13

REFERENCES

1. Weinstein L., Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a sever


