



HELLP Syndrome with Long-Lasting Severe Sepsis: A Case Report

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Abstract

Preeclampsia is a disease manifesting itself in the second half of pregnancy, and characterised by hypertension and proteinuria. It affects 5% to 7% of pregnant women all over the world making it the most common cause of maternal and fetal morbidity and mortality. HELLP syndrome (Hemolysis-Elevated Liver enzymes-Low Platelets) occurs in about 4%-20% of the preeclamptic pregnant women and it is often associated with high maternal and perinatal morbidity and mortality rates. HELLP syndrome may require monitoring in the intensive care unit because of the increased morbidity and mortality rates it brings about as a result of potential complications such as acute respiratory distress syndrome (ARDS), intracerebral hemorrhage, acute renal failure, hepatic rupture, disseminated intravascular coagulation, and septic shock. We aim to present the case story of a long-lasting but successful postoperative treatment for severe sepsis of a patient with HELLP syndrome who was monitored in our intensive care unit after a caesarean section.

Key Words: Pre-eclampsia; HELLP Syndrome; Maternal Morbidity And Mortality; Sepsis; Thrombocytopenia.

HELLP Sendromu Olan Hastada Uzun Süren Ciddi Sepsis: Bir Olgu Sunumu

Özet

Preeklampsi; hipertansiyon ve proteinuri ile karakterize, gebeliğin ikinci yarısından sonra görülen bir hastalıktır. Tüm dünyada gebelerin %5 ile %7'sini etkileyen, maternal ile fetal mortalite ve morbiditenin birinci nedenidir. HELLP sendromu (Hemolysis-Elevated Liver enzymes-Low Platelets) ise preeklamptik gebelerin yaklaşık %4-20'sinde görülen, yüksek maternal ve perinatal morbidite ve mortalite ile ilişkili bir tablodur. HELLP sendromlu hastalarda akut sıkıntılı solunum sendromu (ARDS), intraserebral kanama, akut böbrek yetersizliği (ABY), hepatik rüptür, yaygın damar içi pıhtılaşma bozukluğu (YDİPB) ve septik şok gibi komplikasyonlar maternal morbidite ve mortalite artması nedeniyle yoğun bakım ihtiyacı ortaya çıkabilmektedir. Sezeryan sonrası postoperatif dönemde yoğun bakım ünitesinde takip ettiğimiz ve uzun süren ciddi sepsis nedeniyle tedavi ettiğimiz HELLP sendromlu bir hastanın sunulması amaçlanmıştır.

Anahtar Kelimeler: Preeklampsi; HELLP Sendromu; Maternal Morbidite ve Mortalite; Sepsis; Trombositopeni.

INTRODUCTION

Characterised by hypertension, proteinuria, and manifesting itself in the second half of pregnancy, preeclampsia is the initial cause of fetal and maternal morbidity and mortality affecting 7%-5% of pregnant women in the world (1). Its pathophysiology still unknown, preeclampsia is thought to result from reduced organ perfusion and endothelial damage (2). As a serious complication of pregnancy, preeclampsia is also associated with maternal inflammatory response and increase in endothelial cell activation (3).

HELLP syndrome occurs in about 4-20% of preeclamptic pregnant women and it is associated with high maternal and perinatal morbidity and mortality. Due to complications such as ARDS, intracerebral haemorrhage, acute renal failure, hepatic rupture, and septic shock, patients with HELLP syndrome may suffer from increased maternal morbidity and mortality and, thus, may require intensive care (4).

In this paper, we aim to present the case of a patient with postoperative HELLP syndrome who was monitored in the intensive care unit due to prolonged severe sepsis.

CASE REPORT

The 33-year-old patient who was being followed due to preeclampsia had seizures in the 33rd week of her pregnancy and was brought to the emergency department. The emergency laboratory test values were as follows: Hg: 12.9g/dL; Htc: 36.3%; and leukocyte value: 16,650 uk/L. The other results, including the bilirubin values, were normal. The pregnancy was terminated with emergency caesarean section under general anesthesia. Developing postoperative metabolic acidosis, the patient was intubated and taken to the intensive care where we started mechanical ventilation. The vital signs on her admission to the postoperative intensive care unit were as follows: arterial blood pressure: 160/105mm Hg; heart rate: 125 beats/min; oxygen saturation: 99%; and body temperature: 36 degrees C. Her APACHE score was 29 while the SOFA

score was 10. The laboratory figures on her admission to the intensive care unit admission were listed as: Hg: 8.8 g/dL; Htc: 26.4%; number of leukocytes: 22.07 UK/L; platelets: 28000mm³; PT: 14 secs; PTT: 30,2 secs; INR: 1,2; BUN: 15mg/dL; creatinine: 0.39mg/dL; AST: 2319 u/L; ALT: 1035 U/L; LDH (lactate dehydrogenase): 1153 U/L; total bilirubin: 3.57mg/dL (N=0.3 to 1.2); direct bilirubin: 0.02mg/dL (N=0.01 to 0.02); indirect bilirubin: 3.55mg/dL (N=0 to 1.1), respectively. Because the patient had anaemia, we administered 3 units of red blood cells and 2 units of thrombocyte apheresis suspension. To control hypertension, we started 5 microg/kg/min of nitroglycerin infusion. Because of the high levels of arterial blood pressure on the second day, we started esmolol infusion. Considering that the patient had anaemia, leukocytosis, thrombocytopenia, and critically high LFT (liver function tests) results, we began to consider the possibility of HELLP syndrome and re-planned the treatment (Table 1).

Because the patient had leukocytosis, her PaCO₂ was 29.7 mm/Hg, and heart rate was 105-120 beats/min, we decided that the patient had "Systemic inflammatory response syndrome" (SIRS) and started the support treatment without delay. We started fluid resuscitation, oxygen support, nutritional support, and empiric antibiotics (ceftriaxone 2x1g/day). In order to find the underlying causes, we collected culture for infection but did not observe any multiplication in the samples. The LFTs began to decline on the second day of hospitalisation as platelets increased to normal values. The LFT enzymes eventually reached the normal values on the fourth day. On the second day of her admission, the patient's BUN figure was 37mg/dL, creatinine was 2.41mg/dl, WBC values were 30.89 UK/L, and lactate value was 3.4 mM/L. Considering a potential ARF, we started to provide fluid therapy and to follow urine output. As BUN/creatinine reached 143/7.3 IU/L on the sixth day, we applied renal replacement therapy (hemofiltration). All biochemical values of the patient during her hospitalisation are shown in Table 1. On the 8th day the patient's hospitalisation, leukocytosis and

procalcitonine were 4.1 ng/ml upon which we decided to take cultures to investigate the focus of infection. During her hospital stay, the patient developed three serious gram (-) sepsis and septic shocks. In the first episode of sepsis (on the 8th day), we detected *Klebsiella pneumonia* reproduction in her blood and urine cultures. The sensitivity profile was identified to have imipenem, meropenem, amikacin, colistin, and trimethoprim-sulfometoksozol so we started to give meropenem 3x500 mg. In the second episode of sepsis (on the 13th day), we detected *Pseudomonas Aeruginosa* reproduction. In accordance the patient's antibiotic susceptibility profile (sensitive to colistin only), we applied colistin. Despite adequate antibiotic treatment, we identified *Acinetobacter Baumannii* reproduction in her urine culture samples on the 18th day of her hospitalisation. This was probably due to hypotension (MAP <65 mmHg), tachycardia (132 beats/min), and leukocytosis (21,000 uk/L) the patient developed throughout. Parallel to the sensitivity profile of the patient, we added 2x50 mg of tigecycline to the already continuing colistin treatment. Due to the ongoing hypotension regardless of the appropriate fluid replacement, and keeping the possibility of a septic shock in mind, we applied vasopressor therapy that would keep MAP at around 65-90 mmHg (dopamine 5-20 ug/kg/min; norepinephrine 1-30 g/min), CVP 8-14 cmH₂O, and 250 to 1000 ml of crystalloid solution in every 15-30 minutes to keep urinary output at >0.5 ml/kg/min. We also started oxygenation maintaining SaO₂>92% value and blood transfusion keeping hematocrit >30% figure. Nutrition is very essential in patients with sepsis since they are in a catabolic process; to this end, we administered a daily amount of 25-30 kcal/kg (ideal body weight) of calorie support. On the 30th day of hospitalisation, the patient was discharged having entirely declined parameters infection and hemodynamic stability.

At the end, we explained the patient that the details of her case would be published in a scientific article and obtained her consent.

Table1. The biochemical parameters of the patient during hospital stay.

	Hg (gr dL ⁻¹)	Leucocyte (uK L ⁻¹)	Thrombocyte (mm ³)	AST (IU. L ⁻¹)	ALT (IU. L ⁻¹)	LDH (IU. L ⁻¹)	CRP (mg ml ⁻¹)	Procalcitonin (ng ml ⁻¹)
Day 1	8,8	22,07	28000	2319	1035	1153	140	25
Day 2	13,1	19,53	118000	1189	446	850	155	18
Day 5	9,8	21,00	76000	63	85	550	168	15
Day 8	9,2	20,46	172000	65	54	250	167	4,61
Day 13	8,8	17,20	585000	49	28		85	4,83
Day 18	10,7	21,00	212000	59	47		194	4,86
Day 30	9,2	14,68	172000	56	40		45	0,74

AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase; CRP: C-reactive proteins

Endothelial cell injury and inflammation are responsible for the pathophysiology of preeclampsia. HELLP syndrome, which is characterised by microangiopathic hemolytic anemia, hepatic dysfunction, and thrombocytopenia, is a serious complication of pregnancy that can lead to maternal and fetal mortality by affecting many systems.

Microangiopathic hemolysis, one of the major features of the HELLP syndrome, is related to hemolytic anemia (5). Hemolysis is followed by the destruction of red blood cells, which, in turn, leads to an increase of serum LDH levels and a decrease in the hemoglobin concentration. Therefore, hemolysis can be diagnosed by considering high LDH and indirect bilirubin values (6). In our case, hemolysis was present since the patient's

admission to the intensive care unit; the presence of anaemia, and high LDH and indirect bilirubin values support our argument.

DISCUSSION

Early diagnosis and effective treatment are required to achieve the best outcome for both mother and baby. In HELLP syndrome, the termination of birth should be the first step of definitive treatment (6). Some authors state that some time should be spared for supportive treatment but it is very risky to choose this option and requires the consent of both the practitioner and the family (7). As in the case presented here, the preferred method to terminate pregnancy should be cesarean section. After the removal of the placenta, symptoms tend to regress slowly. Generally, even after 48 hours after the birth, laboratory values may still show deterioration though results are expected to improve in the next 48 hours. In our case, the clinical picture did not improve within the first 96 hours. During this period, the patient had severe fever, leukocytosis, and high procalcitonin values though we did not observe reproduction in her culture results. However, after the eight day, having determined the foci of infection, we were able to concentrate on the long-lasting severe sepsis and sepsis-related organ failures.

There is controversy regarding the treatment of HELLP syndrome. Practitioners have tried several different approaches most of which were therapeutic solutions such as dexamethasone, several blood products, and magnesium sulfate (8).

Endothelial damage, vasospasm, platelet activation, and reduction of EDRF emissions (endothelium-derived relaxing factor) are among the pathogenesis of HELLP syndrome and acute renal failure. ARF is a serious clinical condition characterized by sudden decrease in renal function and azotemia. It rarely accompanies preeclampsia and eclampsia pathologies with an incidence and mortality rate of 7,3% and 13%, respectively (9). Our patient had ARF and we had to perform continuous renal replacement therapy (hemofiltration) in order to secure the kidneys and to eliminate the complications connected to renal failure.

While procalcitonin is a specific and sensitive marker of systemic bacterial infections in our today, it also shows the severity and presence of preeclampsia in patients without infections (10). In our case, the high levels of procalcitonin since her hospitalisation explain the long period of time our patient had to spend in the intensive care unit and, thus, the severity of the case. Despite the fact that the relationship mechanisms between preeclampsia and some types of infections, especially urinary tract infections, are not clearly defined, such relationships are now known to exist for sure. Infection is not usually regarded as the direct cause of preeclampsia but the presence of a strong relationship between preeclampsia in sepsis and inflammatory processes are distinctly defined (11). As the focus of infection, we have similarly detected repeated Klebsiella pneumonia and

Acinetobacter baumannii reproduction in the urine and blood cultures and Pseudomonas aeruginosa reproduction in sputum culture. Many studies show that E.coli and Klebsiella pneumonia are the most frequent factors for urinary tract infections in pregnant women (12).

Chronic hypertension and pre-eclampsia are high risk assets in maternal sepsis. Chronic hypertension has already been determined as risk factor for severe sepsis progression independent of preeclampsia. This is because, compared to normotensive pregnant women, patients with chronic hypertension are more likely to develop critical hypo-perfusion at high blood pressures, which can ultimately trigger severe sepsis (11).

CONCLUSION

The most common obstetric problems in intensive care units are eclampsia and HELLP syndrome and both has high maternal and fetal morbidity and mortality rates. Especially patients with HELLP syndrome with a history of convulsion should be closely monitored in intensive care units after cesarean section since clinical conditions may worsen in such patients; in this way, reducing rate of complications will also reduce morbidity and mortality in due course. To improve survival in sepsis during pregnancy and the postpartum period, early diagnosis, keeping the infection source under control, and targeted therapy are all very essential. To achieve this, practitioners should apply adequate fluid therapy, appropriate antibiotics, and central hemodynamic monitoring.

This case report was presented as a poster study at the TARK 2013-47 International Congress in 20-23 November 2013.

REFERENCES

1. Kvehaugen AS, Dechen R, Ramstad HB, et. al. Endothelial Function and Circulating Biomarkers are Disturbed in Women and Children After Preeclampsia. Hypertension.2011; 58:63-9.
2. Lain KY, Roberts JM. Contemporary concepts of the pathogenesis and management of preeclampsia. J Am Med Assoc 2002;287:3183-6.
3. Borzychowski AM, Sargent IL, Redman CW. Inflammation and pre-eclampsia. Semin Fetal Neonatal Med 2006;11: 309-16.
4. Yosunkaya A, Keçecioglu A, Erdem TB, Borazan H.Yoğun Bakım Ünitimizde Sık Rastlanan Obstetrik Sorun: Hellp Sendromu (15 Olgunun Analizi). Selçuk Tıp Üniv. Derg 2011; 27(1):18-23.
5. Baxter JK, Weinstein L. HELLP syndrome: the state of the art. Obstet Gynecol Surv 2004, 59:838-45.
6. Haram K, Svendsen E, Abildgaard U. The HELLP syndrome: Clinical issues and management. BMC Pregnancy and Childbirth 2009, 9:8-23.
7. Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynecol 2004, 103:981-91.
8. Eser B, Güven M, Ünal A, Coşkun R, Altuntaş F, et al. The role of plasma exchange in HELLP Syndrome. Clin Appl Thrombosis/Hemostasis. 2005; 11(2):211-7.
9. Sibai BM, Ramadan MK, Usta I, Salama M, Mercer BM, Friedman SA. Maternal morbidity and mortality in 442 pregnancies with hemolysis, elevated liver enzymes, and

- low platelets (HELLP syndrome). Am J Obstet Gynecol 1993; 169:1000-6.
10. Montagnana M, Lippi G, Albiero A, et al. Procalcitonin values in preeclamptic women are related to severity of disease. Clin Chem Lab Med 2008; 46(7): 1050-1.
 11. Acosta CD, Knight M, Lee HC, et. al. The Continuum of Maternal Sepsis Severity: Incidence and Risk Factors in a Population -Based Cohort Study. PLoS One. 2013; 8(7):e67175. www.plosone.org.
 12. John R, Barton MD, and Baha M. Sibai MD. Severe sepsis and septic shock in pregnancy: Clinical expert studies. 2012; 120 (3).

Received/Başvuru: 31.01.2014, Accepted/Kabul: 08.04.2014

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For citing/Atıf için

Doğu B, Arslan M, Gisi G, Guler S, Oksuz H, Yavuz C, Bahar S, Uygungelen A. HELLP syndrome with long-lasting severe sepsis: a case report. J Turgut Ozal Med Cent 2015;22:40-3 DOI: 10.7247/jtomc.2014.1725