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Maternal Death Following Misdiagnosis of Emolysis, Elevated Liver Enzymes, and Low Platelet Count (HELLP) Syndrome: A Case Report and Review of Literature

Sedigheh Ayati[1], Leila Pourali[1*], Atiyeh Vatanchi[1], Lida Jedi[1], Zahra Mohades Ardebili[2]

1. *Department of Obstetrics and Gynecology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*
2. *General Practitioner, Tehran University of Medical Sciences, Tehran, Iran*

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Corresponding Information:
Leila Pourali, Department of Obstetrics and Gynecology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
Email: pouralil@mums.ac.ir
Tel: 051-38012477

ABSTRACT

Background & Objective: HELLP syndrome is characterized by hemolysis, elevated liver enzymes, and low platelet count; it probably shows a severe form of preeclampsia. This syndrome usually occurs in third trimester of pregnancy and may be associated with severe complications, including subcapsular liver hematoma, eclampsia, pulmonary edema, liver or renal dysfunction, and even maternal death. This study aimed to report a case of maternal death misdiagnosis of HELLP syndrome.

Case Report: A 28-year-old pregnant woman with gestational age of 28 weeks referred to an emergency ward because of epigastric pain, nausea, and vomiting. She was discharged after receiving outpatient treatment. The next day, she was referred to the hospital because of seizure, decreased level of consciousness, and hypertension. A cesarean section was performed immediately. Unfortunately, some hours after the surgery, cardiac arrest occurred and she died in intensive care unit (ICU).

Conclusion: Nausea, vomiting, and epigastric pain in the late second or third trimester of pregnancy are among the significant symptoms which should be seriously taken into consideration. Therefore, it is recommended that a patient be hospitalized and precise evaluation be performed to rule out the life-threatening differential diagnoses, like HELLP syndrome, and to prevent dangerous complications which can lead to maternal death.

Keywords: HELLP syndrome, Pregnancy, Maternal death, Diagnosis

Introduction

Hemolysis, elevated liver enzyme levels, and low platelet counts (HELLP) syndrome is a rare life-threatening condition which usually occurs in third trimester of pregnancy and represents a severe form of preeclampsia **(1)**.

HELLP syndrome may be complete or partial/incomplete. The complete form includes all three major components; however, in the partial/incomplete form, one or two parts of the triad can be found **(2)**. The frequency of this syndrome is nearly 0.6% of pregnancies. HELLP syndrome occurs in 10% to 20% of patients with severe preeclampsia, 30% of which occur in the postpartum period **(3)**.

Pathophysiology of HELLP syndrome is not clear yet. Some researchers believe that HELLP syndrome is a subgroup of severe preeclampsia and their pathophysiologies are the same **(2)**. Clinical symptoms of this disorder are an epigastric pain, an upper and right quadrant of abdomen pain, nausea, and vomiting. Right upper quadrant abdominal pain can be colic or persistent. Many patients report a history of fatigue from the previous few days. 30% to 60% of patients suffer from a headache and 20% of them experience vision symptoms **(4)**. An increased weight gain during pregnancy and generalized edema can be seen in more than 50% of cases before the onset of HELLP syndrome **(5)**. Patients with this syndrome may present with nonspecific signs and symptoms of preeclampsia or symptoms of viral syndromes **(6)**.

Risk factors of this syndrome include age>35 years old, multiparity, history of hypertension in the previous pregnancy, Caucasian, multiple pregnancies, and history of antiphospholipid antibody syndrome (APS). 5% to 10% of people with HELLP syndrome suffer from APS **(7)**.

This syndrome occurs in 0.5% to 0.9% of pregnancies and in 10% to 20% of severe preeclampsia. About 70% of cases are diagnosed before delivery. Most of these cases are between 27 to 37 weeks of gestation and the remaining 30% are mainly diagnosed after delivery and, most often, in the first 48 hours after the delivery. In 15% to 20% of

cases, patients do not have proteinuria or hypertension before developing HELLP syndrome. Therefore, it is believed that the syndrome is a disorder except preeclampsia **(5)**. Diagnosis of HELLP syndrome is difficult when it is not accompanied by hypertension and proteinuria and its symptoms are sometimes mistaken for gastritis, influenza, acute hepatitis, and gallbladder diseases **(6)**. The mortality rate of the HELLP syndrome is quite high (approximately: 25%). This syndrome is considered as an emergent obstetrics event **(8)**. Differential diagnosis of this syndrome is APS, thrombotic thrombocytopenic purpura (TTP), hemolytic-uremic syndrome (HUS), and systemic lupus erythematosus (SLE), which are less prevalent but are associated with a high mortality rate and long-term complications. Failure to diagnose and treat this disorder may lead to maternal death **(6)**. There are some options for managing this syndrome: immediate delivery, expectant management, and delivery within 48 hours **(9,10)**. Maternal morbidities include disseminated intravascular coagulation, acute renal failure, pulmonary edema, subcapsular liver hematoma, eclampsia, sepsis, acute and severe respiratory failure, and retinal detachment, some of which may lead to maternal mortality **(10)**. The risk of eclampsia in patients with HELLP syndrome is greater in cases with higher LDH levels and headache **(10)**.

HELLP syndrome can be accompanied with eclampsia **(11,12)**. In almost all cases of eclampsia, preeclampsia is already present but it is not diagnosed **(13)**. More than 50% of eclampsia cases occur before delivery **(14)**. There are some ways to manage this syndrome: immediate delivery, expectant management, and delivery within 48 hours **(10)**.

Maternal mortality rate followed by eclampsia is about 1% in developed countries **(15)**; however, this rate is reported to be between 0% and 16% in different regions **(16,17)**. The aim of this report is to introduce a case of maternal death following the misdiagnosis of HELLP syndrome.

Case Report

A 28-year-old woman with gestational age of 28 weeks referred to the emergency ward of a hospital and complained of nausea, vomiting, and epigastric pain after eating fatty foods. Her previous delivery was 8 years ago with cesarean section due to meconium amniotic fluid. In the previous pregnancy, a history of hypertension was mentioned in the last 2 weeks of pregnancy. But in the current pregnancy, the blood pressure was normal. Her body mass index (BMI) was 33 kg/m^2. The patient was visited by a midwife at the maternity ward at 4 AM. At the time of examination, she had no uterine contractions and the cervix was closed. Blood pressure was 110/80 mmHg. The patient mentioned the history of eating fatty foods in the previous night, and she had been referred to a general practitioner at an emergency ward of the hospital by the midwife without consulting a gynecologist. She had been admitted to the emergency ward and received dextrose water 5% and hyoscine and ondansetron. No laboratory tests were performed and she had been discharged without being revisited by the physician. About 30 hours after her first visit at 11 AM, the patient was referred to the maternity ward by emergency ambulance with unconsciousness followed by seizure, and she was urgently visited by gynecologists. The patient was at a postictal phase with a GCS: 8 and had a blood pressure of 210/110 mmHg. The fetal heart rate was normal and fundal height was 28 weeks. Necessary tests were immediately done and hypertension was controlled by hydralazine and sulfate magnesium. The patient was transferred to an operating room for cesarean section. Finally, a 700-gr preterm male infant with Apgar score of 6-7 was born, and then died after several days in the neonatal intensive care unit (NICU).

After cesarean section, her blood pressure was 180/110 mm Hg, pulse rate: 110/min and respiratory rate: 16/min in the operating room. Her tongue and lips were bruised and her mouth was bloody. Due to the low platelet counts and severe intubation, she had epistaxis. Owing to the continuation of bleeding after the cesarean section, anterior and posterior tampons were placed. The other clinical features of the coagulation disorder, including purpura and ecchymosis, were also visible.

Laboratory tests at admission before cesarean section were as follows: a peripheral blood smear showed less than 1% of schistocytes, hemoglobin 11.6 mg/dl, platelet count: 34000/µL, proteinuria 4+, LDH=3543, AST=82, and ALT=41; other coagulation and creatinine tests were normal.

In the operating room, the patient received 20 platelet units, 5 units of fresh frozen plasma (FFP), and 6 units of cryo. She was transferred to ICU with an intubation. Some rales in the lungs were heard when checking with a stethoscope. No abnormalities were reported in the ultrasonography of abdomen and pelvis. In the chest X-ray (CXR), a slight mild-to-moderate pleural effusion was reported in the left lung. There were no abnormalities in the echocardiogram. Ejection fraction (EF) was 71%. In the neurological examination, there were no symptoms of a cerebral hemorrhage.

Despite the intubation, the patient experienced a gradual loss of oxygen saturation with pulmonary rales. Also, evidence of non-cardiac pulmonary edema followed by acute respiratory distress syndrome (ARDS) was observed so that despite high Fio2, the oxygen saturation was nearly 50-60%. Due to the onset of fever, an infectious diseases consultation was requested and meropenem and vancomycin were prescribed with metronidazole. The patient gradually experienced a reduction in diuresis and lung sounds and an abdominal distension was started.

Tests carried out on the patient in ICU were as follows: hemoglobin 11.3 mg/dl, platelet 63000/NL, LDH=1665, ALT=155, AST=369, creatinine 2.2, and a peripheral

blood smear showed less than 1% of schistocytes again. All the coagulation tests were normal throughout the entire period of hospitalization.

The next day, after 28 hours of cesarean section, she suffered from hypotension and bradycardia. Finally, cardiac arrest occurred and the patient died after 20 minutes of cardiopulmonary resuscitation (CPR).

Discussion

HELLP syndrome is a life-threatening disorder presented as one of the most important causes of maternal death during pregnancy. Hemolysis and microangiopathic anemia are important features of this syndrome. The presence of schistocytes and burr tuberculosis in the peripheral blood strongly affirms this diagnosis. A decreased platelet counts, less than 100,000, is another diagnostic criterion **(6)**. In the mentioned patient, about 1% of schistocytes was observed in the peripheral blood smear. Most white women suffer from this multiparous syndrome **(6)**. This patient was also multiparous 2.

Clinical symptoms such as a headache, visual changes, epigastric pain, nausea, and vomiting, compared to laboratory symptoms, are better predictors of maternal outcomes **(18)**. In the present patient, these symptoms were recorded as the main complaints of the patient at the first visit.

Approximately, 20% of eclampsia cases occur at the gestational age of 20 to 30 weeks **(19)**. In this patient, eclampsia occurred at the gestational age of 28 weeks. More than 50% of eclampsia cases occur before delivery **(14)**. This was the case for the patient mentioned in the present study.

In a systematic review, the most common clinical symptoms before the onset of eclampsia were hypertension, headache, and epigastric pain **(14)**. In the present patient, all these three symptoms were present at the time of hospitalization.

The incidence of eclampsia in HELLP syndrome is greater in patients with higher LDH levels (>1290 U/L) who suffer from a headache **(12)**. In the current patient, the LDH level was over 1,600; however, she did not have headache.

In a study conducted in 2017, poor maternal outcomes of the HELLP syndrome were accompanied by high levels of liver enzymes (AST>316 U/L) and (ALT> 217 U/L), LDH levels higher than 1290 U/L, and platelets more than 50,000 m^2 **(12)**. In the present case, during the hospitalization, all the severe criteria were present; and unfortunately, this was accompanied with a very poor prognosis (maternal death). Severe morbidities of eclampsia include acute renal failure (ARF) and ARDS **(20)**, both of which were present in the present patient. The risk of maternal death followed by eclampsia is different (0% to 14%), which significantly reduces in patients with regular prenatal visits and those who are managed in third level hospital (0%-1.8%) **(16, 17)**. Unfortunately, the patient did not have regular pregnancy cares and, in addition, she was misdiagnosed at the time of her first visit.

The risk of death is higher for infants compared to mothers. This risk is reported to be 4.6%-34%, and infants born before the 32nd week of pregnancy are at the highest risk of perinatal mortality. In the present case, the birth of the 28-week premature fetus resulted in the fetal death. Fetal immaturity, placental insufficiency, intrauterine growth restriction (IUGR), and abruptio placenta are among the important causes of fetal death, and this mortality depends on the pregnancy age **(21, 22)**. In the present case, the premature infant also died shortly after delivery due to the severe prematurity (28 weeks).

Conclusion

Nausea, vomiting, and epigastric pain in the late second or third trimester of pregnancy are among the significant symptoms which should be seriously taken into consideration. Therefore, it is recommended that such patients be hospitalized and precise evaluation be performed to rule out the life-threatening differential diagnoses, like HELLP syndrome, and to prevent dangerous complications which can lead to maternal death.

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Conflict of Interest

Authors declared no conflict of interests.

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