

CASE REPORT

An Unusual Presentation of Partial Hemolysis, Elevated Liver Enzyme Levels, and Low Platelet Levels Syndrome in a Case of *in vitro* Fertilization-DEM Pregnancy

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ABSTRACT

Pregnancy in women with systemic lupus erythematosus (SLE) or autoimmune conditions is complicated by complement-mediated injury and is associated with increased risk of preeclampsia. Immunological intolerance between the mother and the fetus may play an important role in the pathogenesis of preeclampsia. The present case highlights the influence of susceptibility to preeclampsia/hemolysis, elevated liver enzyme levels, and low platelet levels (HELLP) syndrome due to preexisting autoimmune conditions. *In vitro* fertilization (IVF)-Donor embryo pregnancy (DEM) pregnancy is one such unique scenario where there exists partial immunological disparity between the native intrauterine environment and the implanted donor embryo that could predispose to autoimmune problems in pregnancy. This case illustrates a similar scenario in which a pregnant woman with IVF-DEM conception and antinuclear antibody (ANA) positive status manifested with a normotensive partial HELLP syndrome which was reiterated by the fact that there was clinical evidence of retroperitoneal hemorrhage intraoperatively during cesarean along with the neonate who was diagnosed to have L-carnitine deficiency, which is unique to fetuses with mothers of HELLP syndrome.

Keywords: Antinuclear antibody, Donor embryo, Hemolysis, elevated liver enzyme levels, and low platelet levels.

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INTRODUCTION

Hemolysis, elevated liver enzyme levels, and low platelet levels (HELLP) syndrome is a severe complication of pregnancy characterized by hemolysis, elevated liver enzymes, and a low platelet count.¹ The pathogenesis of HELLP syndrome remains unclear. Many investigators consider the syndrome to be a variant of preeclampsia, but it may be a separate entity. Hemolysis, elevated liver enzyme levels, and low platelet levels syndrome affects about 0.5 to 0.9% of all pregnancies.² It has been observed that mothers with preeclampsia do not always present with all clinical features of HELLP syndrome, but there are alterations in hematological indices and/or liver function that adversely affect fetomaternal outcomes. Some pregnant women develop only one or two of the characteristics of this syndrome. This category of women with at least two features of the complete HELLP syndrome is separately categorized as "partial HELLP syndrome" (PHS)³ that may progress to HELLP syndrome. Early diagnosis is critical because the morbidity and mortality rates associated with the syndrome have been reported to be as high as 25%. In the background of other risk factors like autoimmunity, laboratory parameters should be relied upon for the early diagnosis and management of HELLP syndrome.

CASE REPORT

A 34-year-old female primigravida at 32 weeks of gestation, booked with regular antenatal checkups, *in vitro* fertilization (IVF) donor embryo conception with subclinical hypothyroidism and gestational glucose intolerance on diet with antinuclear antibody (ANA) positive status, married since 7 years, nonconsanguineous marriage, presented with mild painless bleeding per vaginum and decreased fetal movements since 2 to 3 days. Physical examination was unremarkable. Vitals were normal. Fundal height corresponded to gestational age, uterus appeared relaxed, and fetal heart was good. Per speculum examination revealed mild brownish discharge. High vaginal swab for culture and sensitivity was taken. Urine albumin was nil. Non-stress test showed a reactive trace. Ultrasound findings were not contributory. (There was no obvious retroplacental hemorrhage and placenta was not low lying). Patient was admitted for observation and prophylactic steroids were administered in view of antepartum hemorrhage.

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Maternal surveillance for hypertension was performed and blood sugars monitored in view of gestational glucose intolerance. Lab investigations showed a platelet count of 1.2 lakh with lactate dehydrogenase (LDH) levels 527 IU/L, liver enzymes were within normal limits, and serum creatinine was 0.6 mg/dL. Repeat labs showed downward trend for platelet count, which dropped to 1 lakh and subsequently to 88,000 cells/mm³. There was a progressive rise in LDH levels to 623 IU/L. Dengue NS1 was found to be negative. Decision for emergency lower (uterine) segment cesarean section was taken in view of suspected PHS. Intraoperatively, a retroplacental clot of 100 mL was detected. Liquor was blood stained, which could have been suggestive of abruption. A 2-kg female baby was delivered and stabilized in the neonatal intensive care unit. One unit of packed cells was transfused to the mother in view of exaggerated blood loss due to uterine atonicity and retroplacental clot. Postoperative period was uneventful. Deranged lab values including platelet count and liver enzymes returned to normal. A diagnosis of "partial HELLP with abruption" was made postcesarean.

Neonatal Outcome

Postcesarean day 14, the baby developed apnea and convulsions for which she was ventilated. Extended metabolic profile was performed, which revealed L-carnitine deficiency typically associated with maternal Hemolysis, elevated liver enzyme levels, and low platelet levels syndrome. L-carnitine deficiency could present as neonatal apnea, which subsides with appropriate carnitine supplements.

DISCUSSION

It is often assumed that HELLP syndrome will always occur with preeclampsia, but there could be atypical manifestations of HELLP. Hemolysis, elevated liver enzyme levels, and low platelet levels can occur with subtle lab derangements without a background of hypertension.

Sibai³ proposed strict criteria for the diagnosis of the "true HELLP syndrome." But it has been observed that many women with severe preeclampsia may have laboratory abnormalities, such as isolated hemolysis or low platelet count or elevated liver enzymes, without the complete HELLP syndrome termed as "PHS."⁴

Partial HELLP syndrome can be as grave as HELLP syndrome. The rate of eclampsia in HELLP syndrome and PHS was found to be higher than that in preeclampsia. The incidence of HELLP syndrome has been reported as 0.5 to 0.9% of all pregnancies,² while that of PHS is not exactly known, with some literature reporting it as 21 to 24%.⁵

The pathogenesis of HELLP syndrome is not well understood. It is presumed that autoimmune mechanisms play a role in the pathogenesis of the HELLP syndrome

because the fetus acts as an antigen source for the mother and that transfer of fetal proteins to the mother may mediate autoimmunity, representing a subclinical rejection mechanism of the fetal allograft.^{6,7}

Gleicher⁷ described the occurrence of antiplatelet and cytotoxic antibodies in patients with HELLP syndrome. He reported immunoglobulin G antibody-mediated passive disease transfer to the fetus and also observed that up to 83% of infants born of mothers with HELLP syndrome show signs of hemolysis and that 26% were thrombocytopenic at birth.

Antinuclear antibodies were found to occur more often in patients with preeclampsia, fetal growth restriction, fetal death, or abruption placentae.^{7,8}

Immunological theory of preeclampsia in donor oocyte gestation was proposed recently by Levron et al,⁶ suggesting that immunological intolerance between the mother and the fetus may play an important role in the pathogenesis of preeclampsia.

Autoimmune theory of HELLP syndrome is reinforced by the fact that the rate of preeclampsia and fetal growth restriction has been significantly found to be higher in ovum donor recipients compared with women conceived with autologous oocytes.

Earlier studies have reported a 20 to 50% incidence of gestational hypertension in these pregnancies.⁹⁻¹¹ Explanations for the high rate of gestational hypertension in the donor oocyte pregnancies have been proposed to be related to the immune system, i.e., altered or inadequate immunoprotection of the fetoplacental unit in oocyte recipients.¹¹ It has been found that there is a higher frequency of preeclampsia in women with ovarian failure compared with those with functioning ovaries.⁹

L-carnitine deficiency in newborn has been shown to be associated with maternal, placental, and fetal complications.¹² A total of 62% of mothers carrying an affected fetus with long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency developed acute fatty liver of pregnancy or the HELLP syndrome during their pregnancies.¹³

CONCLUSION

This case illustrates that HELLP may present atypically. The vague nature of its presentation can make the diagnosis of HELLP syndrome difficult. The physical examination may be normal in patients with PHS. If HELLP syndrome is undiagnosed or untreated, it can result in life-threatening complications for both mother and baby. Because partial HELLP may progress to HELLP syndrome, any pregnant woman, especially with a history of donor oocyte or donor embryo conception, in the background of other autoimmune risk factors presenting with progressive fall in the platelet count and/or rise of LDH levels should be evaluated with caution, and a diagnosis of partial HELLP

should be considered. Typical features of HELLP syndrome like hypertension, headache, proteinuria, edema, visual disturbances may be absent in such patients, and hence, laboratory parameters should be relied upon for the early diagnoses and management of HELLP syndrome.

Early identification and prompt management of atypical HELLP syndrome which could be relatively common in IVF conceptions with donor gamete in the background of ANA positivity and history of premature ovarian failure are crucial to avert perinatal mortality and morbidity.

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