Case Report

DISSEMINATED INTRAVASCULAR COAGULATION IN A PATIENT WITH HELLP SYNDROME

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SUMMARY
HELLP (Hemolysis Elevated Liver enzyme Low Platelet) syndrome an atypical form of severe pre eclampsia, and if not treated is potentially fatal for both mother and fetus. Mostly presentation of HELLP syndrome is after 34 weeks of gestation but presentation may be between 20 weeks of gestation to few days after delivery. It is estimated that up to 10% of pregnancies are affected by HELLP syndrome. Only treatment option available to date is delivery of fetus and products of conception. In this case report patient was diagnosed having HELLP syndrome with DIC while initial presentation being thrombocytopenia and hypoxia.

KEY WORDS: HELLP syndrome, Disseminated Intravascular coagulation in pregnancy, Thrombocytopenia, Preeclampsia/eclampsia.


CASE REPORT

A 30 year old lady G6P3A2 presented in the department of obstetrics and gynecology of Fatima Memorial Hospital, at 27+ weeks of gestation with complaints of shortness of breath, drowsiness, right upper quadrant and epigastric pain and blurring of vision for last 12 hour. She had two abortions previously each at third month of gestation for which she did not consult a doctor. There was no other significant past medical history. General physical examination revealed afebrile patient having BP 200/120 mm Hg, Pulse 88/ minute regular, cyanosis, edema feet +ve. Her obstetrical examination revealed normal fetal move-ments with small for dates fundal height. Medical department was consulted for her shortness of breath and consulting physician observed drowsy, cyanosed, tachypneic patient having slight calf tenderness. Systemic examination revealed harsh vesicular breathing with coarse crackles in right lower part of chest. Patient was maintaining Oxygen saturation just over 80% at 16 liter of O2 supplementation as detected on pulseoximetry. Blood glucose level was 30 mg/dl, corrected with intravenous 25% dextrose water. Arterial blood gases showed respiratory alkalosis and severe hypoxia and patient was ventilated.

Baseline investigations revealed: Hb 12.4 g/ l; WBC 8000/mm3; Platelets 122000/mm3; Sodium 140mEq/L; Potassium 4.21 mEq/L; Blood Urea 23 mg/dl; Serum Creatinine 0.6mg/dl; Serum Total Bilirubin 3.7mg/dl; AST 475 U/L; ALT 233 U/L; Total Proteins 6.85 mg/dl; Prothrombin Time 15 sec (control: 14 sec); Activated Partial Thromboplastin Time 32 sec (control: 33 sec) Uric Acid 5.2 mg/dl. Lactate dehydrogenase 5113 I.U./L. Peripheral smear showed Anisocytosis ++, Microcytosis +, Macrocytosis + and fragmented RBCs +.

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Retic count 0.5%. Fibrinogen level was 3.61mg/dl (Normal 2 - 4 mg/dl). The urinalysis showed albumin 3+ and many RBCs. Blood negative for culture and sensitivity. The chest radiograph showed diffuse bilateral basal infiltrates. Later on ANA was done which was negative.

Next day abdominal ultrasonography showed single alive intrauterine pregnancy with severe intrauterine growth retardation and diffuse fatty infiltration of liver. Compression ultrasound of both legs did not show any evidence of Deep Vein Thrombosis. Termination of pregnancy was tried with intravaginal prostacyclin but failed and any surgical intervention was delayed due to critical condition of the patient.

M-mode and two dimensional echocardiography which showed normal left ventricular end diastolic volume, normal contractility, Left ventricular ejection fraction 55-60%. Left atrium 4.5 cm (mildly dilated normal 4 cm). Right sided chambers normal, valves structurally normal. Color and conventional Doppler showed Mild mitral regurgitation. Patient’s condition stabilized over next couple of days and was successfully extubated on third day of admission. Patient expelled spontaneously 0.8 Kg baby girl with Apgar score 5/10 at birth and 6/10 at 5 minutes and which expired in intensive care unit on second day. Repeat laboratory tests on day 4 showed: platelet count of 78,000/ mm3. On day 6 following reports were received: Platelets 93,000/mm3, ALT 37 U/L, Fibrinogen level 4.64 mg/dl, Fibrinogen degradation products > 20 ug/ml (Normal < 0.5ug/ml, Serum Uric acid 7.7 mg/dl. Patient remained stable and was discharged home on 9th day.

**MANAGEMENT**

Blood pressure was controlled initially with intravenous hydrallazine and oral amlodipine and Aldomet was started. Patient was put on assisted ventilation. Blood for culture and sensitivity was sent and intravenous Ceftriaxone and metronidazole started. Supportive care was provided with maintenance of blood sugar level, intravenous fluids and nasogastric feeding.

**DIFFERENTIAL DIAGNOSIS**

Based on initial assessment following were included in differential diagnosis:

1. Pulmonary embolism
2. Acute respiratory distress syndrome (ARDS).
3. Acute fatty liver of pregnancy (AFLP).
4. HELLP Syndrome.

Pulmonary embolism was suspected due to hypoxia, calf tenderness and cyanosis. Later on this diagnosis was not entertained due to abnormality in chest x-rays, compression ultrasonography negative for any evidence of DVT and no evidence of right ventricular strain on echocardiography. ARDS thought initially was not supported by maintenance of oxygen saturation on low FIO2 (45%) on ventilator and early weaning from ventilator.

AFLP and HELLP syndrome are conditions difficult to differentiate in late pregnancy. In this patient evidence of hemolysis (raised bilirubin 3.7 mg/dl, fragmented RBCs on peripheral smear and raised LDH 5113 IU/L), raised liver enzymes (ALT 233 U/L), and low platelets (initially122,000/mm3 later on 78,000/mm3 and recovering further later 93,000/mm3), strongly favored HELLP syndrome. Blood positive for DIC screening near the end of patient’s stay in hospital reflected reported association of DIC and HELLP syndrome as discussed below.

**DISCUSSION**

Waterstone et al have redefined HELLP syndrome as hemolysis (abnormal peripheral smear or raised total bilirubin concentration more then 20.5 umol/L), raised liver enzyme activity (elevated Aspartate aminotransferase >70 IU/L or raised glutamyltransferase >70 IU/L), and low platelets (<100,000/ml). HELLP syndrome is a variant of severe pre eclampsia. The complete spectrum of HELLP syndrome...
syndrome is seen in approximately 10% of pregnant women and 15% of women with preeclampsia-eclampsia. Mostly presentation of HELLP syndrome is after 34 weeks but may be diagnosed between 20 weeks of gestation to a few days after delivery. It is generally agreed that pregnancies complicated by preeclampsia and HELLP syndrome are at even higher risk for maternal and/or fetal complications. Factors contributing to the disease spectrum include the onset of vasospasm, activation of the coagulation system, oxidative stressors, increased inflammatory response, and ischemia.

Typical presentation of HELLP syndrome is with epigastric or right upper quadrant pain (65% to 90% of patients), malaise (90%), nausea or vomiting (36% to 50%) and headache (31 percent). Only 5% of the patients may have jaundice. On general physical examination 80% of patients show right upper quadrant tenderness and weight gain with edema in 60% of patients. Hypertension may be absent in 20 percent of patients. It is an atypical form of thrombocytopenia and microangiopathic hemolytic anemia and is associated with pregnancy.

Thrombocytopenia and microangiopathic hemolytic anemia in a young woman may suggest a variety of conditions, including thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, disseminated intravascular coagulation, systemic lupus erythematosus, HELLP syndrome, severe preeclampsia without HELLP syndrome, and acute fatty liver of pregnancy. The last three of these conditions are exclusive to pregnancy and differentiation between these three is difficult. In late pregnancy presentation of AFLP, preeclampsia or eclampsia with hepatic involvement, and the HELLP syndrome is almost similar and progression to severe liver dysfunction may occur.

Thrombocytopenia and microangiopathic hemolytic anemia are more severe in HELLP syndrome than in preeclampsia, and acute fatty liver of pregnancy. The last one manifests itself primarily as severe liver damage.

It is even tougher to differentiate between acute fatty liver of pregnancy and HELLP syndrome. Maternal mortality with AFLP is 18% to 85% while fetal mortality is 23% to 85%. AFLP is diagnosed on high degree of suspicion in third trimester of pregnancy with hepatic failure or hepatic encephalopathy and confirmed by micro vesicular fat on liver biopsy. HELLP syndrome is differentiated from AFLP by normal levels of: prothrombin time, partial prothrombin time (prolonged in AFLP) ammonia (high in AFLP) fibrinogen, glucose (low in AFLP). Uric acid and creatinine levels are high in both conditions. Liver enzymes, serum bilirubin and lactate dehydrogenase are elevated in both conditions more so in AFLP. Peripheral smear of blood shows normal picture in AFLP while mechanically damaged RBCs in HELLP syndrome. Additional biochemical abnormalities associated with both AFLP and pre-eclampsia include disseminated intravascular coagulation.

DIC occurs in preeclampsia 7% of the time, in HELLP syndrome 30% of the time, and in acute fatty liver of pregnancy 90% of the time. It is difficult to decide which of these three syndromes is causing the jaundice and DIC in the patient. Hypertension usually precedes the DIC associated with preeclampsia and HELLP syndrome. Thrombocytopenia below 100,000/µl almost always occurs with HELLP syndrome. Thrombocytopenia is the most common hematological abnormality of severe preeclampsia. Microangiopathic hemolytic anemia may also occur. Changes in the coagulation cascade and in the fibrinolytic system may result in the syndrome of disseminated intravascular coagulopathy. The cause of these changes remains uncertain, but a hypothesis involves vascular endothelial damage that causes activation of platelets and the coagulation cascade.

Risk factors for preeclampsia includes: 1st pregnancy, 1st pregnancy with new partner, preeclampsia in previous pregnancies, maternal age less than 20 years or more than 35 years, multiple pregnancies, preexisting hypertension.
The only effective way of treating severe preeclampsia/eclampsia is delivery. Maguire in 1909 first described the treatment of severe eclampsia with cesarean section and more than 90 years later delivery is still the best option available. Management of preeclampsia includes hospitalization of the patient, rehydrate and correct electrolyte imbalance, control raised blood pressure and delivery if gestation age is more than 36 weeks. However, delivery is must at any gestational age if eclampsia, HELLP syndrome or renal dysfunction is impending. Treatment of HELLP syndrome at less than 34 weeks has been controversial. In well controlled hypertension and absence of seizures 24 to 48 hours may be allowed for fetal lung maturity with administration of corticosteroids. Recent trial of 51 carefully selected cases has shown that under close supervision pregnancy can be continued to get fetal maturity in women with eclampsia or severe preeclampsia. Marked improvement in maternal platelet counts and liver function after the administration of corticosteroids, along with a trend toward improved fetal outcome has been shown in two studies but this treatment had only a marginal effect in delaying delivery.

Steroid use may help to expedite the improvement in laboratory parameters and shorten the hospital stay and major maternal complications may be prevented. Due to small amount of evidence proving its benefit steroid use is not yet endorsed in American College of Obstetrics and Gynecology practice guidelines on HELLP syndrome management. But this promising therapy may revolutionize the management of syndrome and large controlled trial is needed to better elucidate the risk and benefit of therapy.

Prevention of preeclampsia and its consequences had largely been disappointing but recent trials have shown beneficial effect of Antiplatelet drugs particularly aspirin. Review of recent trials in over 32,000 women with high risk pregnancy have shown reduction of 15% in preeclampsia, 14% reduction in perinatal mortality and 8% reduction in delivery before 37 weeks by the use of low dose aspirin. It is still to be decided which women be benefited more from low dose aspirin.

CONCLUSIONS

It is concluded that DIC can be associated with severe preeclampsia like HELLP syndrome in this case. Management is mainly conservative along with delivery of fetus as early as possible resulting in decreasing maternal and fetal mortality. Steroids and aspirin may have a role in future but further studies are required. Further more that close collaboration and interaction between different departments results in better care of the patient and life threatening conditions can be dealt with decreasing mortality and preventing significant morbidity.

REFERENCES