THE SYNDROME OF HEMOLYSIS, ELEVATED LIVER ENZYMES AND LOW PLATELETS IN THREE CASES

(Received 3 March, 1994)

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SUMMARY

This report consists of three patients with HELLP syndrome managed at the Marmara University Hospital Obstetrics and Gynecology Clinic between 1992-1994. The possible pathophysiology of this syndrome, the management of the patients and maternal and fetal outcomes are presented.

Key Words : Severe preeclampsia-eclampsia, HELLP syndrome

INTRODUCTION

Severe preeclampsia is diagnosed when one or more of the followings are present (1) Blood pressure of at least 160 mmHg systolic or 110 mmHg diastolic on two occasions 6 hours apart (2) proteinuria >5 gr/24 hours. (3) oliguria (<400 ml in 24 hours) (4) cerebral or visual disturbances, (5) pulmonary edema or cyanosis. A sixth criterion should be added to this list of findings in severe preeclampsia. This addition is to be called the HELLP syndrome, with the H for hemolysis, EL for elevated liver function test, and LP for low platelet counts (1,2).

This syndrome has been recognised for many years. According to Chesley some of these components had been reported in the obstetric literature for almost a century (3). Recognition of the clinical and laboratory findings (Table I, Table II) of the HELLP syndrome is important if early, agressive therapy is to be initiated to prevent maternal and neonatal death (4). The practicing obstetrician must be knowledgeable about this severe consequence of hypertension in pregnancy.

Table I- Diagnostic criteria for HELLP syndrome

1) HEMOLYSIS
- Abnormal peripheral blood smear
- Total bilirubin > 1.2 mg / dl
- Lactic Dehydrogenase (LDH) : > 600 U/l

2) ELEVATED LIVER FUNCTIONS
- SGOT > 70 IU / 1
- LDH > 600 U / 1

3) LOW PLATELETS
- Platelet count < 100 000 / mm^3

Table II- Laboratory differentiation of HELLP syndrome

HEMATOLOGIC :	
Platelet count	: Low
Fibrinogen	: Normal to increased
Prothrombin Time (PT)	: Normal
Partial Thromboplastin time (PTT)	: Normal
SERUM CHEMISTRIES :	
Glucose	: Normal
Uric acid	: High
Creatinine	: High
BUN	: Normal to increased

Table III- Management Outline of Antepartum HELLP Syndrome

1) Assess and stabilize maternal condition
   a: If DIC present, correct coagulopathy
   b: Antiseizure prophylaxis with magnesium sulfate
   c: Treatment of severe hypertension
   d: Computed tomography or ultrasound of the abdomen if subcapsular hematoma of the liver is suspected

2) Evaluate fetal well - being
   a: Nonstress testing
   b: Biophysical profile
   c: Ultrasonographic biometry

3) Evaluate fetal lung maturity if < 35 weeks' gestation
   a: If mature ..... Delivery
   b: If immature ..... Steroids ..... Delivery

CASE REPORTS

Case 1: A 22 year old primigravid woman at 27 weeks of gestation was referred with the diagnosis of severe preeclampsia. The main complaint was epigastric pain and vomiting. On admission blood pressure was 180/120 mmHg. Three-positive proteinuria and hyperreflexia were other important findings. Platelet count was 22000/mm^3. Serum transaminases were within normal limits. Mg SO_4 infusion and oral alpha-metyl DOPA 3x50 mg. were initiated. High blood pressure persisted and repeated laboratory results were as follows; Hb:10.7 g/dl, SGOT: 1380 IU/l, SGPT 530 IU/l, LDH:1880 U/l, BUN: 16 mg/dl, Creatinine: 0.9 mg/dl, Platelets: 13000/mm^3, Prothrombin time 13:1 seconds, Partial thromboplastin time: 40 seconds, Fibrinogen: 380 mg/l, Total bilirubin: 4.5 mg/dl. Triangular cells and burr cells were seen in peripheral blood smear. With the diagnosis of HELLP syndrome cervical prostaglandin was applied and 600 gr stillbirth infant was delivered. 2 units of fresh blood and 3 units of platelet suspension were transfused. Clinical and laboratory findings returned to normal levels within 3 days after delivery and the patient was discharged in postpartum 6 days.

Case 2: A 30 year old gravida 7 para 4 woman was found to have a blood pressure of 190/135 mmHg. in her first antenatal visit at 24 weeks' pregnancy. She had a history of eclampsia and delivery of a stillbirth infant in her previous pregnancy. Edema and hyperreflexia were not found on admission. The laboratory results were as follows; Hemoglobin: 15.2 g/dl, Plateles: 136000/mm^3, SGOT: 58 IU/l. There was 3+ proteinuria with the diagnosis of severe preeclampsia MgSO4 infusion and oral Alpha metyl DOPA and Hydralasin were administered. Ultrasonography revealed that fetal growth was appropriate with 20th gestational week. In the tenth hour of therapy repeated laboratory results were; Hemoglobin: 12.2 g/dl, Platelets: 33000/mm^3, SGOT: 500 IU/l, SGPT:471 IU/l, LDH: 5745 U/l, BUN: 9mg/dl, Creatinine 0.8 mg/dl, Prothrombin time: 12.8 seconds, Partial thromboplastin time: 38.3 seconds, Fibrinogen: 300mg/l, Total bilirubin: 4 mg/dl. Burr cells and schstocytes were seen in peripheral blood smear. There was persistant oliguria. HELLP syndrome was diagnosed and cervical prostaglandin was administered for the induction of labor. After six hours a 450 gr stillbirth infant was delivered. Three units of platelet suspension were transfused and IV diuretics were administered. Diuresis was achieved and blood pressure returned to 140/90 mmHg in the first postpartum day. Laboratory results were all normal in the postpartum tenth day.

Case 3: A 36 year old gravida 7 para 7 woman was referred because of jaundice after the delivery of a stillbirth infant at the 28 weeks' pregnancy . She was on the third postpartum day. The admission blood pressure was 160/110 mmHg. She was icteric, deep tendon reflexes were normal, and edema was not observed. Significant hepatomegaly was found on physical examination. Laboratory results were; Hemoglobin: 7.7g/dl, Platelets: 29000 / mm^3, SGOT

534 IU/dl, SGPT: 280 IU/dl, BUN: 20 mg/dl, LDH: 1334 U/1, Creatinine: 0.3 mg/dl, Fibrinogen: 400 mg/l, Prothrombin time: 13.8 seconds, Partial thromboplastin time: 30 seconds, Total bilirubin: 16.1 mg/dl. Peripheral blood smear was compatible with microangiopathic hemolytic anemia. With the diagnosis of HELLP syndrome supportive therapy was given and two units of fresh blood were transfused. Laboratory results returned to normal levels in the ninth postpartum day and she was discharged.

DISCUSSION

The incidence of severe preeclampsia-eclampsia complicated by HELLP syndrome has been reported to change from 2-12 % (4). Weinstein reports nausea, vomiting and epigastric pain as the most common symptoms (1,2). Right upper quadrant or epigastric pain is thought to result from obstruction of blood flow in the hepatic sinusoids which are blocked by intravascular fibrin deposition. In our cases, epigastric pain was seen as a main complaint in only one case but, nausea and vomiting were observed in all cases. On rare occasions hepatic involvement may result in intrahepatic hemorrhage and subcapsular hematoma, leading to rupture (5).

Hemolysis, defined as the presence of microangiopathic hemolytic anemia, is the hallmark of the HELLP syndrome (4). This anemia is thought to result from the passage of red blood cells through small blood vessels with damaged intima and fibrin deposition leading to the appearance of triangular cells, burr cells and echinocytes on peripheral blood smears (4,6). Bone marrow studies in patients with the HELLP syndrome show increased megakaryocytes, a feature which is compatible with either increased peripheral platelet consumption or destruction. It has been suggested that increased platelet agglutination is secondary to vascular endothelial damage and prostacyclin deficiency (6,7).

The patients studied in this report are a well - defined group with documented evidence of hemolysis, elevated liver enzymes, and low platelets. All patients had the abnormalities before delivery and each patient had true hemolysis proved by abnormal peripheral smear, elevated bilirubin values (mainly indirect), and marked elavations in lactic dehydrogenase. In addition, all patients had significant thrombocytopenia and marked elevations in serum glutamic oxaloacetic transaminase values. They had normal prothrombin time and partial thromboplastin time and normal fibrinogen value.

Pregnancies complicated by severe preeclampsia and HELLP syndrome are associated with poor maternal and fetal outcome (8,9). The reported perinatal mortality ranges from 7.7 % to 60% depending on the number of patients and the severity of the disease process. In addition, these patients are at increased risk for maternal mortality and morbidity in our cases, maternal mortality was not observed but these pregnancies were associated with poor perinatal outcome. The perinatal mortality rate was 100% which is much higher than that reported by others (10,11),

Pregnancies complicated by HELLP syndrome require a well - formulated management plan (Table III). Vaginal delivery can be accomplished in most cases, however if cesarean section is required, the use of general anesthesia, subfascial drains and preoperative platelet transfusions (if platelet counts were below 50.000/mm3) can reduce the incidence of complications (4).

Exchange plasmapheresis with fresh - frozen plasma has been advocated as a treatment by some authors in resistant cases (7,8) whereas prostacyclin treatment has been recommended by others (9). Martin et al recommended that a trial of plasma exchange with fresh - frozen plasma must be considered in HELLP syndrome which persists beyond 72 hours postpartum and if there is evidence of a life threatening microangiopathy (7).

Similar recommendations were made by Katz et al (8). On the other hand Sibai et al. recommended that virtually all such patients will have spontaneous resolution with supportive care alone (close observation of fluid intake and output, transfusions as needed) (10). In our cases, the patients required blood and/or blood product transfusions.

In summary, patients with severe preeclampsia and HELLP syndrome constitute a heterogenous group with wide range of manifestations and laboratory abnormalities. Management of such patients will depend on several obstetric and maternal variables including fetal gestational age and degree of laboratory abnormalities.

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