Life-threatening postpartum hemolysis, elevated liver functions tests, low platelets syndrome versus thrombocytopenic purpura – Therapeutic plasma exchange is the answer

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Abstract

The differential diagnosis of life-threatening microangiopathic disorders in a postpartum female includes severe preeclampsia–eclampsia, hemolysis, elevated liver functions tests, low platelets syndrome and thrombotic thrombocytopenic purpura. There is considerable overlapping in the clinical and laboratory findings between these conditions, and hence an exact diagnosis may not be always possible. However, there is considerable maternal mortality and morbidity associated with these disorders. This case underlines the complexity of pregnancy-related microangiopathies regarding their differential diagnosis, multiple organ dysfunction and role of therapeutic plasma exchange in their management.

Keywords: Cerebral venous thrombosis, life-threatening postpartum disorders, pregnancy-related microangiopathic disorders

Introduction

We present a case of postpartum female with hemolysis, elevated hepatic enzymes, low platelets (HELLP) with deranged renal function, and cerebral venous thrombosis, without a history of hypertension and proteinuria. Plasma exchange therapy was successfully used in reversal of organ dysfunction and resolution of hemolysis in this patient.

Case Report

A 20-year-old primigravida (36 weeks gestation) woman was admitted in the semi-urban private hospital in North India with generalized tonic clonic seizure (GTCS). She was given Inj. magnesium sulfate IV 4 g and 0.5 g/hour infusion. An emergency lower segment cesarean section (LCSs) was done and she delivered a 2.5 kg healthy male baby. The amniotic fluids were clear, with no signs of chorioamnionitis. After 6 hours of surgery, she became drowsy, blood pressure (BP) dropped to 70/38 mm Hg and had decreased urine output (20 ml for the last 2 hours). She was started on dopamine infusion and transferred to a higher level tertiary care hospital, 36 hours after the LSCS.

In our Emergency Department, she got repeat GTCS, was given 4 mg lorazepam and loaded with Inj. fosphenytoin 1 g intravenous (i.v.) followed by Inj. fosphenytoin IV 100 mg, eight hourly. She was intubated for airway protection and put on mechanical ventilation. Her BP was 100/74 mm of Hg on vasopressors (dopamine 12 µg/kg/min and norepinephrine 15 µg/min) and she had anuria for 6 hours. Her abdomen was distended, tense to palpation and there was per vaginal blood-stained discharge. The records of antenatal visits to urban health center were reviewed and there was no evidence of hypertension or proteinuria. Her arterial blood gas (ABG) showed severe metabolic acidosis, peripheral smear showed 3+ fragmented red blood cells (RBCs), reticulocyte count 3.4%, direct and indirect Coomb’s tests

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were negative besides other investigations [Table 1]. Her ultrasound abdomen showed free fluid and possibility of anterior uterine wall suture bleeding. A diagnosis of severe preeclampsia–eclampsia with differential diagnosis of thrombotic thrombocytopenic purpura (TTP) versus HELLP syndrome was made.

She was given four packed RBCs and platelets in view of active bleeding, 10 mg i.v. dexamethasone every 12 hourly for two doses, then 4 mg i.v. every 12 hourly, along with continuous renal replacement therapy. On Day 2, her abdominal distention further increased and her hemoglobin (Hb) was 5.2 g/dl, platelet count (PC) was 53 × 109/l, peripheral smear showed 3+ fragmented RBC and lactate dehydrogenase (LDH) was 4580 U/l. In view of persistent hemolysis and worsening platelets and multiorgan dysfunction, therapeutic plasma exchange was started with 100% volume replacement with Fresh Frozen Plasma (FFP).

On the next day, she was disoriented and not moving her limbs after stopping sedation. Her vasopressors were weaned off, and there was decreased per vaginal discharge. Her peripheral blood and urine cultures were negative. Her non-contrast computerized tomography (NCCT) scan head revealed cerebral venous thrombosis including inferior sagittal, left transverse, sigmoid sinuses and cortical veins thrombosis [Figures 1–3]. In view of altered mental status and anticipated prolonged ventilation, percutaneous tracheostomy was done on Day 9. Her renal functions improved and she was started on enoxaparin 60 mg subcutaneous (s.c.) twice a day. The dexamethasone was tapered off.

Patient’s neurological condition gradually improved; she started responding to verbal commands. She was then switched to warfarin on Day 19 to target International Normalized Ratio (INR) 2.0–2.5 and enoxaparin was stopped. Her tracheostomy was decannulated on Day 28 and she was discharged on the next day. On follow-up after 28 days, her weakness had further improved and she was ambulated with support and warfarin was continued for 1 year to target INR 2.0–3.0. The patient and her family were counseled regarding the possibility of recurrence of symptoms during pregnancy.

**Discussion**

The HELLP syndrome is usually associated with hypertension and proteinuria; however, it can present without preeclampsia in 10–20% patients. There are two main diagnostic criteria [Table 2] depending on the platelet counts, LDH and aspartate aminotransferase (AST) levels. The differential diagnosis of HELLP syndrome includes idiopathic thrombocytopenic purpura (ITP), acute fatty liver of pregnancy (AFLP), and TTP. The management of these life-threatening microangiopathic disorders differs; therefore, an accurate diagnosis is required.

| Table 1: Laboratory tests results | Before admission | On admission | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 8 |
|----------------------------------|-----------------|-------------|-------|-------|-------|-------|-------|-------|
| Variables (normal values)        |                 |             |       |       |       |       |       |       |
| Hb (g/dl) (11.5–15.5)            | 5.6             | 4.6         | 4.5   | 4.3   | 6.0   | 6.6   | 7.0   | 8.1   |
| PC (109/l) (150–450)             | 51              | 110         | 53    | 35    | 70    | 41    | 58    | 81    |
| Sr. bil. (mg/dl) (0.2–1.0)       | NA              | 1.55        | 1.9   | 1.76  | 1.23  | 1.3   | 1.1   | 0.9   |
| Direct bil. (mg/dl) (0.1–0.3)    | NA              | 0.2         | 0.3   | 0.3   | 0.2   | 0.2   | 0.3   | 0.3   |
| AST (U/l) (5–40)                 | NA              | 1927        | 1340  | 1200  | NA    | 430   | 87    | NA    |
| ALT (U/l) (5–40)                 | 391             | 1200        | 1953  | 1710  | NA    | 756   | 107   | NA    |
| ALP (U/l) (39–117)               | NA              | 282         | 375   | 192   | NA    | 112   | 108   | NA    |
| Sr. urea (mg/dl) (10–50)         | 68              | 130         | 108   | 128   | 100   | 58    | 108   | 118   |
| Sr. creat. (mg/dl) (0.5–1.3)     | 1.7             | 4.3         | 2.1   | 4.6   | 2.3   | 2.6   | 4.7   | 5.1   |
| PTT (seconds) (control 27.0)     | 29.2            |             |       |       |       |       |       |       |
| INR                              | 1.34            |             |       |       |       |       |       |       |
| FDP (µg/ml) (<10)                | <10             |             |       |       |       |       |       |       |
| d-Dimer (mg/dl) (<0.5)           | 12              |             |       |       |       |       |       |       |
| Fibrinogen (mg/dl) (200–400)     | 240             |             |       |       |       |       |       |       |
| DIC score (>5 overt DIC)         | 1               |             |       |       |       |       |       |       |
| LDH (U/l)                        | NA              | 4434        | 4580  | 5200  | 2600  | 780   | 560   | 909   |

PC: Platelet count, Hb: Hemoglobin, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, sr. bil.: Total serum bilirubin, sr. creat: Serum creatinine, NA: Not available, PTT: Partial thromboplastin time, INR: International Normalized Ratio, FDP: Fibrin degradation products, DIC: Disseminated intravascular coagulation
TTP shares pathophysiological characteristics of the HELLP syndrome and differentiation between the two is sometimes difficult.\(^5\)

The postpartum management of HELLP syndrome is mainly supportive.\(^2,3\) We started dexamethasone as recommended by Sibai et al., but the patient’s condition continued to deteriorate with conservative measures. There are few case reports of use of plasmapheresis or plasma exchange in postpartum HELLP syndrome.\(^2,3,6\) In our case, there was evidence of persistent hemolysis (fragmented RBCs, LDH > 600 U/l and anemia), thrombocytopenia and deranged AST/alanine aminotransferase (ALT). Our case thus fulfills the diagnostic criteria of HELLP syndrome, but due to the absence of clear history of hypertension and proteinuria and non availability of ADAMTS 13 test, we had difficulty deciding whether it was HELLP or TTP. Besides, the patient did not respond to expectant management for 72 hours. Thus, we took the decision of therapeutic plasma exchange. The patient responded effectively with resolution of hemolysis and reversal of organ dysfunction.

Life-threatening neurological complications of the HELLP syndrome are rare; there are few case reports of cerebral infarction after delivery.\(^7,8\) This is the first case to our knowledge, where we found cerebral venous thrombosis with non-hemorrhagic cerebral venous infarct. In our case, we used low molecular weight heparin, enoxaparin after resolution of hemolysis and thrombocytopenia, and switched her on warfarin to target INR 2.0–3.0 for 12 months as recommended by American College of Chest Physician (ACCP) 2008 guidelines.\(^9\)

### Conclusions

The distinction between preeclampsia-eclampsia, HELLP and TTP may not always be possible due to the various overlapping clinical and laboratory findings. The therapeutic plasma exchange therapy should be considered in persistent, life-threatening microangiopathy that is refractory to conservative measures.

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