Management of Coagulopathy in Acute Fatty Liver of Pregnancy

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Abstract:

A 31-year-old primigravida at 33 weeks of gestation with precious twin pregnancy was referred from a peripheral hospital with jaundice, malaise and hypoglycaemia. A clinical diagnosis of acute fatty liver of pregnancy progressing to coagulopathy was made. Emergency Caesarean section was performed and obstetric hysterectomy had to be done to control the bleeding. Timely management by obstetrician, anaesthetist and prompt component therapy by transfusion medicine specialist resulted in a successful outcome. The most advocated ratio of transfusing blood products in massive transfusion is 1:1:1 (packed red cells: fresh frozen plasma: platelets).

Key words: Blood Coagulation Disorders, Blood Platelets, Blood Transfusion, Fatty Liver, Pregnancy.

Introduction

“Acute yellow atrophy of liver” is a rare and fatal complication of pregnancy and it was first described by Stander and Cadden in 1934. This typically presents in the third trimester of pregnancy with maternal mortality rate of 18% and fetal mortality rate of 23% [1]. The mutation in long chain 3 hydroxyl acyl coenzyme A dehydrogenase leads to accumulation of fatty acids in the liver. Due to the risk of congenital deficiency, infants of affected patients should be closely followed up.

We present a case report of a 31 year old lady with acute fatty liver of pregnancy (AFLP) complicated by disseminated intravascular coagulation requiring prompt termination of pregnancy and apt component therapy.

Case Report

A 31 year old primigravida at 33 weeks of gestation with twin pregnancy presented with jaundice and malaise. There was no history of fever, vomiting, headache, abdominal pain, alteration in bowel or bladder habits. On the day of admission she was detected to have low blood sugar (random blood sugar 63 mg/dL). On physical examination, she was icteric with bilateral pitting pedal edema. Vitals were stable with a pulse rate of 90 beats per minute, respiratory rate of 20/minute and blood pressure of 160/100 mm Hg right arm sitting position. The patient was afebrile. She was oriented in person, place and time and her focal neurological findings were non-contributory. On systemic examination, abdomen was distended but non-tender. Respiratory, cardiovascular and nervous system were normal.
Ultrasonography revealed hepatomegaly with hypoechoic liver parenchyma and gallbladder wall edema. Growth of both fetuses corresponded to 30-32 weeks of gestation. Fibrinogen levels were too low to be detectable. Urine analysis revealed mild proteinuria. Serological tests for HIV, HBsAg, HCV were all negative. Laboratory findings on the day of admission are detailed in Table 1.

A presumptive diagnosis of ‘acute fatty liver of pregnancy’ progressing to disseminated intravascular coagulation was made in account of deranged liver function test, renal function test, hypertension, hypoglycaemia and coagulopathy. The patient was taken up for emergency lower segment Caesarean section under general anaesthesia prior to which she received 10 mg vitamin K and 2 units of fresh frozen plasma. Caesarean section was done and babies (both male) were fine with a satisfactory Apgar score. There was profuse bleeding intraoperatively and obstetric hysterectomy had to be done. The patient was started on rigorous component therapy and was transfused with 4 units of packed red cells, 12 units of fresh frozen plasma, 25 bags of cryoprecipitate, 6 units of platelets and 2000 ml crystalloids. The patient was hemodynamically stabilized. Post-transfusion prothrombin time on post-operative sample was 13 seconds (control 10.5 seconds), activated partial thromboplastin time 31 seconds (control 30 seconds), fibrinogen 274 mg/L (200-400 mg/L) indicating the correction of coagulopathy following component therapy. The post-operative SGOT (81 U/L), SGPT (61 U/L) and serum bilirubin (total 5.7, direct 3.2 mg/dL) were decreasing. She made a gradual recovery. Her LFT and RFT returned to normal and she was discharged on day 15.

**Discussion**

Pregnancy is a hyper-coagulable state with a relative increase in all coagulation factors except factor I (fibrinogen) and factor IX. Acute fatty liver of pregnancy is a rare life threatening obstetric emergency which if not managed promptly can progress to renal failure, clotting disorders, hypoglycaemia, coma and death. It is reported that being primigravida, having had multiple pregnancies, carrying male fetus and preeclampsia are high risk factors for acute fatty liver of pregnancy [2]. One should suspect the pathology particularly in presence of symptoms such as nausea, vomiting, jaundice and abdominal pain. Laboratory findings such as increase in bilirubin levels, hypoglycaemia, thrombocytopenia, mild to moderate elevation of serum transaminase levels, severe coagulopathy, hepatic encephalopathy are suggestive of acute fatty liver of pregnancy and distinguishes it from other causes of jaundice in pregnancy like HELLP (Haemolysis, Elevated Liver enzyme, Low Platelet count) syndrome, cholestasis of pregnancy.

| Parameters                      | Report | Reference Range |
|--------------------------------|--------|-----------------|
| Hemoglobin g/dL                | 12.5   | 12 - 14         |
| Total count cells/cu.mm        | 21,120 | 4000 - 11,000   |
| Platelet count cells/cu.mm     | 1,37,000 | 1,50,000 - 4,00,000 |
| ESR mm/hr                      | 56     | 0 - 29          |
| Total Protein g/dL             | 6      | 6.0 - 8.0       |
| S. Albumin g/dL                | 2.6    | 3.5 - 5.2       |
| S. Bilirubin Total, Direct mg/dL | 12,7.5 | 0.3 - 1.2 ; 0 - 1.2 |
| Aspartate aminotransferase U/L | 277    | 10 - 40         |
| Alanine aminotransferase U/L   | 257    | 7 - 56          |
| S. Alkaline phosphatase U/L    | 530    | 30 - 120        |
| S. Ammonia µmol/L              | 106    | 12 - 41         |
| S. Lactate dehydrogenase mg%   | 238    | 200 - 400       |
| S. Creatinine mg/dL            | 1.6    | 0.8 - 1.44      |
| Blood Urea mg/dL               | 39     | 10 - 45         |
| Prothrombin time (seconds)     | 30     | 10.5            |
| APTT (seconds)                 | 66     | 30              |
| INR                            | 3.3    | 1 - 1.5         |
| Blood Group                    | O Negative |

Table 1: Laboratory findings on day of admission.
(itching), acute viral hepatitis (severely elevated transaminases). Both the AFLP and HELLP syndrome are so alike in presentation that many may get confused in making a diagnosis. The symptoms of HELLP syndrome and AFLP frequently appear in third trimester. The incidence of HELLP syndrome is 1:5000 whereas AFLP is rarer (1:13000) [3]. The common symptoms associated with AFLP like nausea, vomiting, abdominal pain and altered sensorium were absent.

The definitive management of AFLP is rapid termination of pregnancy and prompt supportive care which was strictly adhered. The intraoperative profuse bleeding had to be managed by hysterectomy and massive transfusion. Component therapy was started with plasma when the INR was more than 1.5 times the control. The dose of plasma to be given is 15-30 ml/kg body weight [4]. Later the patient fulfilled the hospital criteria for massive transfusion and was initiated by the obstetrician. A ratio of 1:1:1 (packed red cells: fresh frozen plasma: platelets) was used for transfusion of blood components. Massive transfusion is defined as a transfusion requiring replacement of patient’s entire blood volume in 24 hours (10-12 units of packed red cells) [5] or replacement of 50% of the total blood volume within 4 hours (4-6 units of packed red cells) or need for at least 4 units of packed red cells within 4 hours with continued major bleeding or a blood loss exceeding 150 ml/min [6]. The decision to start and end the transfusion depends on the clinician. It’s ideal to send the blood sample for coagulation work up after completing the initial two cycles of transfusion and after every cycle thereafter. Cryoprecipitate was started when the fibrinogen levels fell below 100 mg/L [7]. A minimum of 10 bags can raise the fibrinogen levels to 75 mg/L. Ideally 4 to 6 grams or 50 ml/kg of cryoprecipitate should be given when the fibrinogen level falls below 100 mg/dL [8]. Platelets should be transfused when the platelet count falls below 50,000/cu.mm and adult dose of 4 to 6 units raises the platelet count to 20,000 to 30,000/cu.mm [9]. Four units of random donor platelets (RDP) were transfused during the massive transfusion and the other two units thereafter. Short term coagulation goals should be to keep hematocrit above 20% -24%, platelets above 50,000 cu.mm (> 1 lakhs cu.mm for CNS injury), fibrinogen more than 100 mg/dL, activated partial thromboplastin time less than 45 seconds and prothrombin time less than 18 seconds. Long term coagulation goals are to maintain hematocrit above 24%, platelets above 1 lakhs cu.mm, fibrinogen > 150 mg/dL, activated partial thromboplastin time less than 40 seconds, prothrombin time less than 17 seconds and fibrinogen more than 150 mg/dL [10].

Before 1980s the fetal and maternal mortality rate of AFLP was 85%. But at present with improved transfusion therapy and timely management, the mortality rate has been reduced to less than 10% [11].

| Parameters | Post-operative Day 7 | Day of discharge |
|------------|----------------------|------------------|
| Hemoglobin g/dL | 10.2 | 11.5 |
| Total count cells/cu.mm | 11420 | 6200 |
| Platelet count /cu.mm | 1,15,000 | 1,30,000 |
| Prothrombin time (seconds) | Test 11, Control 10.5 | Test 11, Control 10.5 |
| APTT (seconds) | Test 31, Control 30 | Test 30, Control 30 |
| SGOT U/L | 81 | 51 |
| SGPT U/L | 61 | 61 |
| Bilirubin Total, Direct mg/dL | 8.8, 5.71 | 1.2, 0.7 |
| B. Urea mg/dL | 36 | 35 |
| S. Creatinine mg/dL | 1.6 | 1.4 |
| Fibrinogen mg/dL | 270 | Not assessed |
Conclusion

AFLP is a rare complication of pregnancy and the management of the above mentioned case became more challenging due to associated coagulopathy. The case which could have been a life threatening condition was managed with the team work between the obstetrician, anaesthetist and the transfusionist. Formulating and establishing the hospital based massive transfusion protocol is helpful in coordinating the work of transfusionist and the surgeon.

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