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Case Report

Role of Plasma Exchange in a Postpartum Case of Severe Thrombotic Thrombocytopenic Purpura with Acute Kidney Injury

Tulika Chandra*, Jyoti Bharti, Archana Solanki, Ashutosh Singh and Himanshu Reddy

Department of Transfusion Medicine, King George's Medical University, India

***Corresponding author**

Tulika Chandra, Department of Transfusion Medicine, King George's Medical University, Lucknow. India. Tel: 9415755536

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Keywords

- Therapeutic plasma exchange
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- Fresh frozen plasma
- TTP

Abstract

Introduction: Thrombotic thrombocytopenic purpura (TTP) is a life-threatening disease present with the classic pentad of microangiopathic hemolytic anemia (MAHA), fever, neurologic changes, thrombocytopenia, and renal dysfunction. In a diagnostic dilemma, therapeutic plasma exchange (TPE) choice of lifesaving intervention.

Aim: Aim to assess the efficacy of TPE in a suspected case of postpartum TTP.

Material and methods: 27 years old Female was admitted in an emergency, on Day 8th after a lower segment caesarian section (LSCS) with unresponsive behavior for 3 days and with TTP. She was normal 32 days back with her 2nd, 7-month pregnancy. Ultrasonography (USG) showed an umbilical cord around the neck of the baby. On the 5th postoperative day, shifted to emergency with fever, generalized anasarca, gastrointestinal tract (GI) bleeding, low platelet count, and low Hb, with a poor Glasgow coma scale (GCS) of 6. On the bases of serum urea and serum creatinine presented acute kidney injury with encephalopathy. At emergency, she was unresponsive to mechanical ventilation and supportive treatment, hence therapeutic plasma exchange was performed.

Results: After 8 TPE cycles patient presented with an improved hematological and renal profile with good GCS.

Conclusion: TPE is helpful and lifesaving for suspected TTP patients with AKI.

INTRODUCTION

Thrombotic microangiopathy (TMA) syndromes are characterized by MAHA, platelet clumping, and organ failure of variable severity for example, TTP, hemolytic-uremic syndrome (HUS), elevated liver enzymes, low platelets (HELLP) syndrome, acute fatty liver of pregnancy (AFLP), antiphospholipid syndrome (APS) and systemic lupus erythematosus (SLE) [1]. In this case, high suspicion of TTP due to severe thrombocytopenia, raised creatinine, elevated coagulation screen, and liver function test. TMA can feature several pregnancy-related disorders such as TTP / HUS, TTP, HELLP syndrome, or AFL. TMA is a life-threatening condition in pregnancy, due to delayed diagnosis, and in case of doubt, TPE should be started immediately as a lifesaving procedure. Pregnancy-related TMA can occur before or after birth or develops during the puerperium, typically about the 4th day postpartum. TMA from sepsis with disseminated intravascular coagulation (DIC) associated with prolongation of clotting time, prothrombin time and activated partial thromboplastin time (PTT, aPTT) due to consumption of clotting factors. TMA occurs by primary activation of platelets (ADAMTS13), and by primary endothelial injury (as with HELLP syndrome) [2].

CASE HISTORY

A 27-year Female, multigravida with two stillbirths ($G_2P_0L_0$; P_1 -male fetus 2kg normal vaginal delivery, P_2-male 2.5 kg cord around neck and low-lying placenta) presented 25 days back in emergency department with unresponsive behavior since 1 day on Day 8 post LSCS.. She was normal 32 days back with her 2nd ,7-month pregnancy. The USG at 7th month of pregnancy revealed cord around neck of the baby with low lying placenta, hence advised for LSCS under anesthesia. No history of post-partum hemorrhage (PPH) and blood transfusion. On 5th post operative day, she was unresponsive shifted to tertiary care center. No history of vomiting, seizures during the transport, urine output was normal, Vaccinated for both dose of tetanus toxoid (TT), on iron and folic acid supplementation. No history of cough, fever, chronic drug usage, bleeding or spotting per vagina (PV). Her blood pressure was higher than normal range. She was suffering from excessive vomiting during 1st trimester

along with constipation, diarrhea, orthopnea and burning during micturition. No previous history of hospitalization or surgical intervention. At the time of admission her HR-140/minute, BP-110/82 mmHg and SpO_2-70%. Respiration was gasping, Temperature was 98.6F, pallor and anasarca was present. Icterus was not present and lymph nodes were non palpable. Breast was bilaterally soft. GCS was $E_2V_2M_2$, with normal pupils, B/L coarse crepitation was present, S1and S2 present with no murmur and healthy abdomen. At emergency intubated and under mechanical ventilation with sedation; IV midazolam and fentanyl with drugs; inj. imipenem, inj. Teicoplanin, tab sodium bicarbonate, inj. Dexamethasone, inj. Enoxaparin was given.

At CCM, she was unresponsive for last 10 days with reduced urine output for 4 days. On examination: pallor (+), Anasarca (++), icterus (-), cyanosis (-), clubbing (-), Heart rate; 119/minute, BP; 124/80 mmHg, SpO_2; 100%, Respiratory rate; 24/minute, body temperature; 98.4F. On systemic examination central nervous system GCS 6. Her platelet count fell unexpectedly to 0.30 lac cells/mm^3 and with a falling Hb of 6.4 gm/dl she needed to transfused. After multiple transfusions her direct comb test, indirect comb test, auto control tests were respectively, 4+, 0, 4+. ssADAMTS13 test was not done. The results of the investigations were - Antinuclear antibody negative, IgG Cardiolipin negative, IgM Cardiolipin negative, protein C and protein S normal in range. Peripheral blood smear picture was predominantly microcytic hypochromic with hyper segmented neutrophils, schistocytes and some platelet clumps also seen. USG kidney showed grade 1 echogenic kidneys, urinary bladder partially distended with deranged liver enzymes, falling Hb and platelet count, high LDH level with unknown cause (Table 1).

MATERIAL AND METHEDOLOGY

One standard TPE procedure by fully automatic COM. TEC, Fresenius Kabi, Germany was preferred to used 1.5 plasma volume exchange using FFP as replacement fluid. Patient's informed consent was obtained before each procedure. Procedures were done on the double lumen femoral dialysis catheter under complete aseptic precautions. If any complication was seen during the procedure, it will managed by prophylactic administration of calcium gluconate (one ampoule diluted in 100 ml of 0.9% normal saline) was done for every 1000 ml of plasma removed [3]. We performed all the procedures @ 25-30 ml/minute blood flow and ACD (acetate, citrate, dextrose) as anticoagulant at 1:10 ratio. All cycles of TPE were successfully performed without any under and post procedural complications.

Treatment

She was unresponsive to steroids hence TPE therapy was performed. She was under sedation at 1st TPE cycle, exchanged 0.8 volume of plasma by 22 units FFP. After 10 days of 1st TPE cycle, her serum LDH level (1142 U/L) increased with decreased Hb. Per rectal examination showed internal bleeding. Next TPE cycles was performed at alternative days. At 2nd TPE cycle, patient's GCS was 8 without sedation. By 2nd and 3rd TPE cycle 0.8 volume plasma exchanged by 22 units FFP. At 3rd TPE cycle patient was fully oriented with person, place and time GCS 9. 4th, 5th, 6th, 7th and 8th TPE cycle, exchanged 1.0 volume plasma by 22 units FFP. After every TPE cycle her condition improved (Table 2). Measurement of effectiveness of TPE by platelet count, serum LDH, and serum creatinine after every alternate session [3].

Table 1: Blood investigations with no. of units, blood components transfused

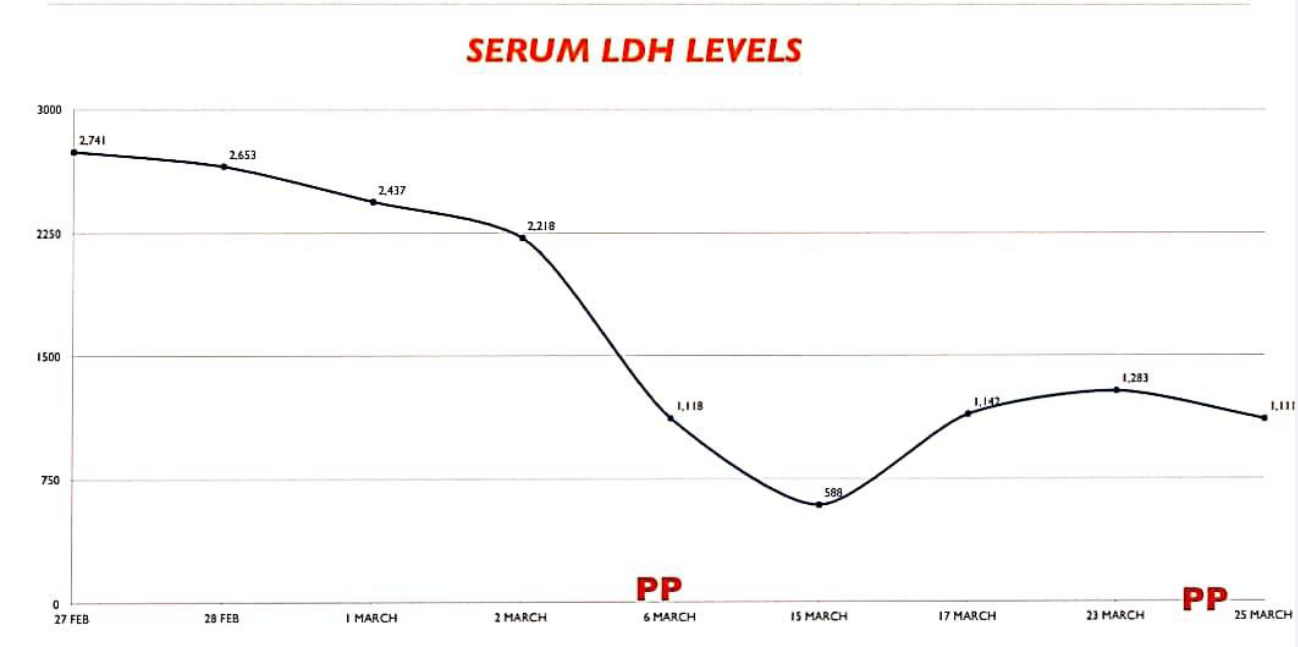
	12th March	13th March	14th March	15th March	16th March	17th March	18th March	19th March	20th March	21st March	22nd March
Hb%	6.7	7.8	6.5	6.7	-	8.6	7.8	6.9	7.2	7.5	9.4
Platelet counts	4.4	3.5	2.6	3.0	-	2.9	2.7	3.0	2.6	2.2	2.1
Blood products	1PRBC	-	1PRBC	-	-	-	-	1PRBC	1PRBC	1PRBC	-
Serum creatinine	3.4	-	1.5	-	-	1.3	1.4	2.4	2.3	1.6	1.6
Serum urea	65	-	40	-	-	27	26	40	43	27	23
Serum LDH	-	-	588	-	-	1142	-	-	-	-	-

Table 2: Pre and post procedural Laboratory (hematological and renal) profile for all TPE cycles:

No. of TPE	Hematological profile								Renal profile							
Cycle	Hb%		Platelet count		PT		aPTT		Serum creatinine		Serum urea		Serum LDH		Serum alkaline phosphate	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1st	6.44	8.4	0.80	0.60	18.1	20	9.8	1.5	2.14	3.01	45.6	96.4	1279.8	1289.9	241.7	
2nd	9.4	9.4	2.1	2.1	20	20	1.5	1.5	1.67	1.67	23.1	23.1	1283	1283	241.7	
3rd	7.5	8.6	2.2	1.2	20	16.1	1.5	1.2	3.45	3.67	29.8	77	1283	1527	241.7	
4th	8.6	6.5	1.5	1.6	16.1	18.1	1.20	1.35	3.89	3.49	77	79.3	1527	1196		
5th	7.29	7.3	0.80	0.60	18.9	78.9	1.34	3.98	3.89		89		1196.4	1063		
6th	6.5	7.6	1.6	1.6	18.1	14.3	1.35	1.06	3.49	3.17	79.3	67.1	1063	757		
7th	7.6	5.3	1.6	0.90	14.3	14.5	1.06	1.09	3.17	2.16	67.1	43.1	757	454		
8th	5.7	7.6	0.90	1.5		15.1		1.11	3.16	2.65	43.1	48.3	416	405		

Table 3: Differential diagnosis of patient

	Points Favour	Points against
PRE ECLEMPSIA (± HEELP)	Thrombocytopenia, anemia, Hemolysis AKI, Cerebral disturbance, Pulmonary edema	Liver enzymes normal no recovery after delivery AKI usually mild
THROMBOTIC MICROANGIOPATHY	Thrombocytopenia, Hemolytic anemia, Cerebral involvement, Fever present, PT, INR normal, Fibrinogen: normal pregnancy may trigger either TTP or C-TMA, TTP (associated with ADMAST-13 Def) 2nd or 3rd trimester. CMTAP: Usually post-partum, CMTAP: AKI usually sever	CM TMA: TPE may not be effective
RENAL COERTICAL NECROSIS	Abrupt onset of oliguria or anuria	Associated with catastrophic obstetric emergencies such as placental abruption with massive hemorrhage or amniotic fluid embolism, no hypoechoic area in renal cortex.
NSAIDs induced AKI, Acute pyelonephritis, Obstructive uropathy		
APLAS	Poor obstetric history	APLA: negative
ITP	Thrombocytopenia, Hemolysis, Any time pregnancy PT INR normal, Fibrinogen normal	No large platelets on PBS creatinine in raised
DIC/ Sepsis	Thrombocytopenia, mucosal oozing	Fibrinogen normal, PT aPTT normal
AFLP	Encephalopathy, Hypoglycemia, Elevated TLC, Elevated ammonia	Postpartum presentation, Bilirubin normal, SGOT normal



Graph 1 Serum LDH levels with days

DISCUSSION

TMA is a term used to describe a group of disorders characterized by thrombocytopenia, hemolytic anemia, and widespread thrombosis in the microvasculature, with HELLP syndrome, TTP, HUS, AFLP, SLE, APLS, and DIC resulting from severe sepsis, abruptio placentae or postpartum hemorrhage [4]. Diagnosis of this condition is not easy during pregnancy because the symptoms mimic, preeclampsia, HELLP, eclampsia or any acquired coagulopathy. Maternal death occurs due to acute renal failure, DIC or thrombocytopenia. TPE is the mainstay of treatment [5].

This case based on diagnostic dilemma.

N. Gonnade, A. Bajayee, A. Elhence et al. [3] stated that, 42% of the patients were not responded to TPE but 58% of patients gave adequate response with, complication like allergic reaction which was manageable.

M. Soffer, P. Bendapudi, D. Roberts et al. [6] stated that, TPE drastically decreased the rates of maternal mortality resulting from TTP, associated with pregnancies in the second trimester.

K. Artinger, G. Hackl, G. Schilcher et al. [7] reported, delayed recovery from HELLP syndrome and severe hypertension can clinically mimic primary TMA syndromes in the post- partum period. Immediate treatment with PEX and revisit the first tentative diagnosis decrease mortalities.

G. Ve, L. Trombotik, [8] stated in their study, thrombotic microangiopathies of pregnancy and postpartum period should be treated by TPE in tertiary care units promptly and correct steps should be followed to diagnose and treat these patients whatever the diagnosis.

M. Wind, A. Gaasbeek, L. Oosten et al. [9] stated that the counselling of patients on risks and benefits of TPE in pregnancy was issued based on the limited evidence that was found in literature, TPE procedures can be used safely during pregnancy with the appropriate preparation and experience of a multidisciplinary team.

P. Care, G. Ary, H. Ipscomb et al. [10] said In their study, that Early Plasma exchange is a relatively safe procedure during pregnancy which is unlikely to adversely affect the fetus. In addition to plasma exchange, corticosteroids, nonsteroidal ant inflammatory drugs, and transfusion with fresh-frozen plasma or packed red blood cells also be used in the treatment of TTP and HUS.

In our case, after every TPE cycle platelet counts increased and serum LDH was decreased. (Table 3) GCS improved with every TPE cycle; after 1st TPE cycle GCS 7 and after 2nd, 3rd GCS was 8. After 4th, 5th cycle her GCS became 10. After 7th TPE cycle her GCS was 12. Patient was well conscious and oriented with person, place and time on 8th TPE cycle. Patient was weaned off from IV drugs and stabilized on oral medicines. On regular follow up her bipedal edema disappeared totally. She was able to sit on her bed with support. Patient's vitals were stable, on examination and on investigation no sign of hemolysis was found. Patient was still under supervision in CCM unit with follow-up. After 8thcycle of TPE on post procedural investigation, serum LDH (Graph 1), serum urea, serum creatinine and platelet count were with a normal range. (Table 3) She was discharged after full recovery.

CONCLUSION

Basic screening methods in pregnancy like blood pressure monitoring and testing for proteinuria can identify and prevent potentially life-threatening complication for patients. Plasma exchange therapy should be performed without delay in suspected cases of during pregnancy and postpartum cases with carefully monitored platelet count and serum LDH level. In conclusion, both maternal and fetal survival depend largely on early diagnosis, early initiation of TPE, and close monitoring. In our case we cannot be sure about patient confirm diagnosis and after TPE the condition of patient was significantly improved. Thus, increased morbidity and mortality burden of pregnancy-induced microangiopathies can be decreased through the early management in pregnancy/postpartum with timely initiation of TPE therapy.

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