Case Report

Thrombocytopenia-associated multiple organ failure or severe haemolysis, elevated liver enzymes, low platelet count in a postpartum case

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ABSTRACT

Thrombocytopenia-associated multiple organ failure (TAMOF) is a thrombotic microangiopathic syndrome that includes thrombotic thrombocytopenic purpura, secondary thrombotic microangiopathy, and disseminated intravascular coagulation. We report a case of postpartum female who presented with TAMOF or severe Haemolysis, elevated liver enzymes, low platelet count (HELLP) which was managed with plasma exchange. This case report is to make clinicians aware that TAMOF, severe HELLP, and other differential diagnosis in a postpartum case have a thin differentiating line and plasma exchange can be considered as one of the management options.

Key words: Plasma exchange, postpartum, severe haemolysis, elevated liver enzymes low platelet count, thrombocytopenia-associated multiple organ failure

INTRODUCTION

Thrombocytopenia-associated multiple organ failure (TAMOF) is a thrombotic microangiopathic syndrome that includes thrombotic thrombocytopenic purpura (TTP), secondary thrombotic microangiopathy (TMA) and disseminated intravascular coagulation (DIC). This condition develops in patients with immunodeficient conditions like infection, transplantation, radiation, chemotherapy, cardiopulmonary bypass or autoimmune diseases.[1] Here we report a case after obtaining consent from the patient, diagnosed to have TAMOF with strong differential diagnosis of HELLP syndrome and its successful management with plasma exchange.

CASE REPORT

A 36-year-old female was admitted to the casualty department from another hospital with complaints of abdominal pain, constipation and jaundice. She had a history of hypertension and pre-eclamptic toxaemia two days previously for which she underwent emergency lower segment caesarean section (LSCS) at 35 weeks' gestational age in the previous hospital and delivered triplets. Discharge summary from the previous hospital revealed that her liver function tests were normal and she had a normal platelet count on admission to that hospital but on discharge, elevated alanine amino transferase (ALT) 228.1 IU/L and aspartate amino transferase (AST) 604.2 IU/L with hyperbilirubinaemia (356.7 umol/L with conjugated 241.43 umol/L and unconjugated 115.27 umol/L) were present. On admission to our hospital, she had tachycardia with a heart rate of 140/minute, blood pressure 176/100 mmHg and peripheral oxygen saturation of 92% on 4 L/minute oxygen. On systemic examination, she was conscious and alert with no neurological deficits. Respiratory examination showed tachypnoea with decreased air entry in bilateral lower lung fields. Abdomen was tender, distended and tense. She had developed oliguria. Chest X-ray showed right-sided consolidation with pleural effusion confirmed by ultrasound. Computed tomography abdomen revealed massive intraperitoneal collection with thickened bowel

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loops. Her initial haematological investigations showed severe thrombocytopenia (platelets 20×10^9/L) with haemoglobin of 10.2 g% and white blood cells 11.2×10^9/L. Her coagulation profile was normal. Diagnostic ascites tapping showed 480/mm^3 white blood cells and rest of the analysis showed transudative picture. She was evaluated by a gynaecologist and surgeons, and bowel injury was suspected. The patient underwent exploratory laparotomy and 5.7 L of ascitic fluid were drained with findings of haemorrhagic liver parenchyma. There was no bowel, uterus or abdominal organ injury. She received 12 units of platelets intraoperatively. She was intubated and shifted to the intensive care unit (ICU). Postoperatively, her arterial blood gases on ventilator with inspired oxygen concentration (FiO_2) 0.6 showed metabolic acidosis (pH 7.17, pCO2 5.1, pO2 8.4, HCO_3^- 13.9, BE −13.8). Cultures of urine, sputum and blood that were sent for septic screening before starting antibiotics, turned out to be negative. Hepatitis viral markers and HIV were found negative. Peripheral smear showed fragmented red cells, anaemia with dimorphic cells, some polychromatic cells with burr cells, thrombocytopenia and leucocytosis with absolute neutrophilia, suggestive of microangiopathic haemolytic anaemia. Her investigations postoperatively also showed hyperbilirubinaemia, elevated liver enzymes, hypoalbuminaemia and thrombocytopenia. To rule out autoimmune disorders, antinuclear antibodies (ANAs) and antineutrophilic cytoplasmic antibodies (ANCAs) were tested and found to be negative. Plasmapheresis was initiated 30 hours after presentation at the hospital. Plasmapheresis was done eight times for over two hours in a nine-day period and haemodialysis was done four times [Table 1].

She received five units of packed red cells on the second day and once on the sixth day of admission to the ICU. Thrombocytopenia, liver function tests, renal function and lung condition improved over 10 days [Table 2].

The patient was kept intubated due to right-side pneumonia with synpneumonic effusion and she was successfully extubated on the 11th day of admission. Urine output of the patient increased to 2.5 L/day by the 13th day and increased thereafter. She was shifted

Table 1: Plasmaphersis and haemodialysis

Day of admission	FFP used for plasmapheresis (litres)	Adjuvants in plasmapheresis	HD
2nd	4.5	H. Alb 20% 300 mL	
3rd	5.4		HD over 18 hrs: 3 L fluid removed
4th	6		
5th	3.6	H. Alb 20% 0.5 L	
6th	1.5	H. Alb 20% 1.5 L	HD over 24 hrs: 3 L fluid removed
8th	1.5	H. Alb 300 mL	
9th	3		HD over 24 hrs: 2.5 L fluid removed
10th	3		
12th			HD done over 24 hrs: 2.5 L fluid removed

HD – Haemodialysis; FFP – Fresh frozen plasma; H. Alb – Human albumin

Table 2: Blood investigations

Investigations	Normal value	Day of adm.									
		1st	2nd	3rd	4th	5th	6th	7th	8th	9th	11th
Platelets (×109/L)	150-450	20	18	16	21	25	29	26	47	82	185
Haemoglobin (g/dL)	11.5-14.5	10.2	5.7	7.7	11.1	8.5	7.5	8.1	10.4	10.2	9.2
Total bilirubin (umol/L)	3-18	327	264	209.7	274.9	247.2	178.4	143.4	160.3	111	39
Direct bilirubin (umol/L)	0-4	197	168	149.3	170.3	159.7	123	99.4	116.2	68.4	19
ALT (IU/L)	10-60	166	88	31	37	34	34	25	18	19	26
AST (IU/L)	10-42	410	225	41	75	68	71	31	32	45	39
LDH (IU/L)	100-190	2800	2475	400	579	479	243	175	321	347	201
Serum albumin (g/L)	35-50	24.9	9.9	20.2	25.9	27.7	31.3	29.7	28.8	24.0	28
Blood urea (mmol/L)	2.5-8.2	10.7	12	14.7	5.1	8.6	11.3	6.0	8.8	7.9	6.0
Serum creatinine (umol/L)	44-120	174	208	238.2	161.6	176.5	250	152.3	227.6	173.1	181
Prothrombintime (sec)	11-15	20	18.2	>120	18	15.2	13.7	14.5	13.6	13.9	14.5
INR		1.88	1.70		1.41	1.31	1.13	1.22	1.12	1.15	1.22
aPTT (sec)	24-36	68	50.8	>180	>180	32.9	38.6	31.1	31.7	34.6	30
Urine output (mL)		10	20	585	410	290	235	260	130	345	1195

Adm – Admission; ALT – Alanine aminotransferase; AST – Aspartate aminotransferase; INR – International normalized ratio; aPTT – Activated partial thromboplastin time

to the ward on the 15th day and discharged home on the 25th day.

DISCUSSION

Differential diagnosis in pregnant females or post delivery with multiorgan failure like in our case can be HELLP (haemolysis, elevated liver enzymes, low platelet count) syndrome. TTP-haemolytic uremic syndrome (TTP-HUS), sepsis, DIC or TAMOF.

HELLP syndrome occurs in 0.5 to 0.9% of all pregnancies, 10-20% cases with pre-eclampsia and occurs post partum in 30% of cases.[1] It is characterized by haemolysis, elevated liver enzymes and low platelet counts (lactate dehydrogenase (LDH) ≥600 IU/L, AST ≥70 IU/L, platelets ≤100·10^9/L].[2] As reviewed by Haram *et al.*,[1] HELLP syndrome is associated with complications of renal failure, pulmonary oedema and DIC. Plasma exchange is one of the multiorgan support therapies which shows favourable outcome in patients with severe HELLP syndrome not responding to conventional treatment.[3,4] The exact mechanism of the effect of plasma exchange in HELLP syndrome is not known, but in general, plasma exchange removes plasma factors and substitutes new elements by refreshing the patient's own plasma.

Septicaemia is also probable in postoperative cases. It can present with thrombocytopenia, multiorgan failure and DIC. The usual presentation of fever, leucocytosis or leucopenia, negative cultures and unremarkable laparotomy excluded a source of infection in our case. Ono *et al.* has reported an association of severe deficiency of ADAMTS 13 (ADAMTS 13: A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) in sepsis-induced DIC with the development of renal failure.[5] Plasma exchange has been used as adjunct therapy in severe sepsis with reduction in mortality.[6] Plasma exchange is believed to replace cytokines and other inflammatory mediators with fresh plasma. Combination of plasma filtration with dialysis was successfully employed for the treatment of septic shock.[7] TAMOF includes TTP, DIC and secondary TMA.[8] TMAs include TTP, HUS, autoimmune disorders, malignant hypertension and drugs. Von Willebrand factor cleaving protease ADAMTS-13, found to be deficient in TTP, has helped separate it from HUS which is caused by direct endothelial damage by bacterial toxins, whereas in familial cases, inappropriate complement activation through deficient factor H appears to be a major mechanism.[9] Deficiency of ADAMTS-13 is caused by genetic defects or by autoantibodies against it. Marked haemolysis can also inhibit ADAMTS-13.[10] The presence of schistocytes in peripheral blood smear, raised LDH and low haptoglobin levels in our case was consistent with haemolysis. Plasma exchange in TAMOF is superior to plasma transfusion alone as it helps in the restoration of ADAMTS13 and removal of ADAMTS13 inhibitors.[11] DIC is a component of TAMOF; it was diagnosed by DIC scoring which includes elevated prothrombin time (PT) and activated partial thromboplastin time (aPTT), low platelets, low fibrinogen levels, and elevated fibrin degradation products.[12] Plasma exchange has also been found beneficial in DIC alone due to cytomegalovirus[13] and meningococcal sepsis.[14] Plasma exchange increases the activity of ADAMTS 13 and reverses multiorgan dysfunction.[15] Acute renal failure in such cases is due to microangiopathy and DIC.

There is a thin line which differentiates TAMOF from severe HELLP. High levels of high-molecular weight von Willebrand factor in maternal serum reflect the virtual absence of the metalloprotease ADAMTS13 enzyme which is required to control the level of the factor. Specific tests for this hereditary condition are not available in our clinical laboratory. In our case, due to normal liver enzymes [Table 2] and abnormal peripheral smear with sudden onset of multiorgan failure, we considered it as a microangiopathic state and initiated plasmapharesis.

CONCLUSION

TAMOF and severe HELLP are microangiopathic states associated with thrombocytopenia, TMAs, DIC and multiorgan failure. Plasma exchange can be considered as one of the management options in addition to supportive therapy in severe or refractory cases of HELLP syndrome and TAMOF.

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I, Dr. S Bala Bhaskar hereby declare that the particulars given above are true to the best of my knowledge and belief.

Date: 1st March 2013 **Hemant Manjrekar** **Dr. S Bala Bhaskar**