Case Report

Peripartum Sepsis Induced Thrombotic Microangiopathic Hemolytic Anemia: A case report with clinical dissection

Talib SH[1]*, Amjad SA[2], Sachin P[2], Pranita B[2]

[1]Department of Medicine, MGM Medical College, Aurangabad, India, [2]Department of Medicine, Resident in Medicine, Aurangabad, India

Corresponding author:
Dr. S.H. Talib,
Professor Emeritus,
Department of Medicine,
MGM Medical College,
Aurangabad, India,
E-mail: sftalib@gmail.com

Received: 05-Apr-2022,
Manuscript No. AMHSR-22-62783;
Editor assigned: 07-Apr-2022,
Pre QC No. AMHSR-22-62783(PQ);
Reviewed: 22-Apr-2022,
QC No. AMHSR-22-62783;
Revised: 28-Apr-2022,
Manuscript No: AMHSR-22-62783(R);
Published: 03-May-2022,
DOI: 10.54608.annalsmedical.2022.43

Abstract

A case of microangiopathic hemolytic anemia with peripartum TTP in a 24 yr old female patient who developed E.coli sepsis presented with unusual features of leukemoid reaction, anemia and thrombocytopenia. TTP was suspected on finding 3-4/hpf of schistocytes on peripheral blood smear. The importance of peripheral examination for schistocytes in peripartum period for evidence of Microangiopathic Hemolytic Anemia (MAHA) is discussed and described.

Keywords: MAHA; TTP; Schistocytes; Peripartum; *E. coli*; Sepsis

Introduction

A 24 yr old girl presented to the hospital for full term vaginal delivery. She denied history of hypertension, diabetes and tobacco chewing, alcohol or use of any illicit drugs or any medical illness. She had visited the hospital couple of times for ANC checkups and for bilateral pedal edema. The systemic examination was unrevealing. Neurological examination was unremarkable. She was hospitalized as a case of pre-eclampsia with blood pressure was 140/80 mm Hg with mild to moderate pedal edema and puffiness of face. Documents revealed hemoglobin 10.5 g %, TLC 11450/cumm, platelets 107000/cumm, normal kidney function, HbA1c 5.2%, urine albumin 1+, serum sodium and potassium within normal range.

Normal vaginal delivery with episiotomy undertaken. A baby girl of 2.7 kg was delivered. Her condition was described healthy. The patient was discharged on 6th day of hospitalization with advice to take supplemental medications. At the time of discharge, her Hb was 8 g %, platelets counts was 91000/cumm, electrolytes and kidney function were normal within limits. Details of investigation are shown in Table 1.

Two days later post discharged, she was rehospitalized with high grade fever with chills. The patient was toxic, drowsy, but responsive and arousable to deep pain stimulation. Glassgow coma scale was 8. Her pulse rate was 112/min regular low volume, respiration rate was 40/min, SPO2 70% on room air, BP was 90/60 mm Hg, temperature was 101 F. Patient had no meningeal signs, petechial hemorrhages or any rashes over the body.

On examination, the patient had generalized edema with moderate pedal edema along with signs of failure (Pro BNP of >35000 pg/dl). She had signs of dehydration with decreased urine output. X-ray chest was normal. Her PV examination revealed a large abcess at incisional site of episiotomy, incised and 200 ml of pus drained. Blood culture and pus culture were sent. The patient was intubated on emergency basis and was put on ionotropic support and Piperacillin-Tazobactam provided initially and later meropenem as per sensitivity.

Laboratory examination at this stage revealed urine albumin-3+ (300 mg/dl), urea-313 mg/dl, creatinine-9.1 mg/dl, Na+-124 meq/dl, K+-7.3meq/dl, Hb-7.1 g %, TLC-34460/cumm, Platelet-106000/cumm, serum bilirubin (total) -1.6 mg/dl, direct-1.5 mg/dl, SGOT-61U/L, SGPT-47U/L, ALP-110U/L, lactate-9 mmol/L, procalcitonin 22.3. Urine output was nil suggestive of acute kidney injury with sepsis.

Pus culture and blood culture showed the presence of E.coli. The peripheral blood smear showed presence of schistocytes 3-4/hpf (Figure 1). Other laboratory parameters revealed depleted complement levels of C3, C4, decreased haptoglobin levels,

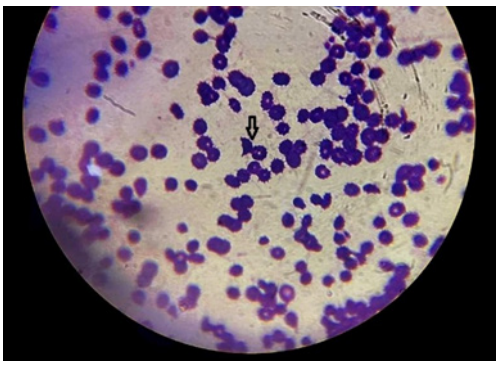

Figure 1: Legends to figure I-Peripheral smear showing presence of Schistocytes (black arrow).

How to Cite this Article: Talib SH, et al. Peripartum Sepsis Induced Thrombotic Microangiopathic Hemolytic Anemia: A case report with clinical dissection. Ann Med Health Sci Res. 2022;12:183-186.

Table 1: Pre and Post labor investigations undertaken during hospitalization.

Sr. No.	Investigation	02-09-2021 Pre Labour (Before Delivery)	16-09-2021 At Delivery	19-09-2021 Post-delivery on Discharge	25-09-2021 Peripartum Re-hospitalization	28-09-2021 to 13-10-2021	15-10-2021 Investigation done a day prior to death
1	Hb g% (N=11-13g%)	10.4	7.08	8	7	07-Apr	6.3
2	TLC /cumm (N=3500-9,000)	11450	12560	11180	34460	47870 -11610	8590
3	Platelet /cumm (N=165000-415000)	107000	85000	91000	1,06,000	11,9000 -35000	65000
4	PS (SCHISTOCYTES)	Not Seen	Not Reported	Not Done	2-3 /hpf	2-3/hpf	3-4/hpf
5	Blood urea (N=7-20 mg/dl)	17	17	18	303	270-125	169
6	Serum Creatinine (N=0.5-1.2 mg%)	0.9	0.5	6	9.1	7-2.6	4.8
7	Serum .Na^+ (136-146meq/L)	139	139	140	124	127-134	135
8	Serum .K^+ (3.5-5.5meq/L)	3.6	4	5.2	7.3	5.9-3.5	3
9	LDH (140-280 mg/dl)	201	293	220		894-450	
10	PT/INR (N 10 tO 13.5)	10.20/0.85	10.5 /0.9	106 /1.0	10.6/088	10.8 / 0.9	10.9 / 1.12
11	Serum Fibrinogen (N=200-400mg/dl)	Not Done				280mg/dl	
12	Urine albumin	Nil	+	+	+++	++	
13	Urine sugar	Nil	NIL	NIL	Nil	Nil	
14	HbA1C (5.7%-6.2%)	5.2	5.6		5.7	6	
15	Serum Bilirubin Direct (0.6-1.2 mg/dl)	0.4	1.5		1.9	0.9	
17	LFT enzymes	WNL	WNL		WNL	WNL	
19	Total protein (6.7-8.8 mg/dl)	6.1	5.5	5.8	5.8	5.0 -6.4	
20	Serum Albumin (3.5-5.5 mg/dl)	3.8	2.5	2.7	2.7	1.9 – 2.6	
22	Blood Culture				E.coli		
23	Pus Culture (episiotomy site)				E.coli		
23	C3 (N=80-178 mg/dl)				65		
24	C4 (N=12-42 mg/dl)				10		
25	Coombs Test Direct And Indirect				Negative		
26	Haptoglobulin (N=41-165 mg/dl)				20		
27	Lactate (N=0.5-1.6 mmol/L)				9	7 to 0.8	
28	Procalcitonin (N=<0.1 ng/dl)				22.3		
29	Pro BNP (age adjusted) (N<125 pg/dl)				>35000		

increased LDH, negative direct and indirect Coomb's test.

Emergency hemodialysis was initiated. She received multiple cycles (11) of hemodialysis. Multiple PCV transfusions were provided for her declining Hb.

During hospitalization 28/09/2021 to 13/10/2021, her Hb declined 7 g % to 4 g %, platelet counts declined seen from 119000 up to 35000, other investigations are shown in Table 1.

The calculated Plasmin score was 6, the value is considered as a high risk group.

Clinical and laboratory findings supported evidence of septic thrombotic MAHA with AKI. Plasmapheresis in this sepsis induced thrombotic microangiopathy case was advised and during treatment with plasmapheresis, the patient developed fatal cardiac arrhythmia, despite resuscitative measures patient succumbed to death.

Discussion

We describe our initial approach of thrombocytopenia associated with pregnancy that deteriorated during peri-partum period. The progression of the patient to pre-eclampsia (hypertension,

edema feet with albuminuria) were present. The features were prominent at term and progressed near delivery. The peripheral Smear revealed schistocytes 3-4/hpf suggesting the entity of Thrombotic Microangiopathic Hemolytic Anemia (TMA). MAHA is considered in clinical settings when presence of demonstrable schistocytes in the peripheral blood film are seen.

The causes of thrombocytopenia in pregnancy varies with duration of gestation and clinical status. Gestational thrombocytopenia is a benign, self-limiting condition. It doesn't require additional evaluation of thrombocytopenia because it gets resolved within 6 weeks of post-partum period.

In the present case, thrombocytopenia worsened during pre-eclampsia. The patient condition deteriorated as she developed abscess at episiotomy site which was excised and drained. Immuno thrombocytopenia occurs in 1-3 cases in 100000 pregnancies with 10 fold greater incidence than general population. ITP is an another cause, and autoimmune condition where antiplatelet antibody interfere with platelet production and causes destruction of circulating platelets observed in any trimester. 10% of patients of ITP known to be associated with HUS/TTP [1]. Other possibilities associated with pre-eclampsia with severe features and HELLP syndrome may have hypertension, headache and visual abnormalities along with thrombocytopenia and such patients may also present with MAHA with schistocytes in peripheral smear, raised LDH and decreased haptoglobin levels. All such features may also be found in thrombotic microangiopathic syndrome such as TTP. The present case has evidence of hemolysis, low platelets, hypertension and proteinuria, but failed to reveal elevated liver enzymes which rules out possibility of HELLP syndrome in this case.

Pre-eclampsia is common, seen in approximately 5% of pregnancy which is present with new onset hypertension, proteinuria and/or end organ dysfunction. After 20 weeks of gestation, low platelet counts are observed in 7% of cases with severe thrombocytopenia in 3% of cases [2].

DIC is yet another cause related to this entity in which coagulation and fibrinolysis become activated within vasculature. Peripheral blood smear often show depleted platelets and crescented RBCs associated with depletion of protein factors and platelets leading to bleeding as well as risk of thrombosis. There may be MAHA with schistocytes of PBS with aPTT, PT prolongation, low fibrinogen and increase plasma D-dimer levels. In the present case, PBS show schistocytes, has not shown prolongation of PT, aPTT nor shown decrease in fibrinogen. Also, there was no evidence of bleeding diathesis. Hence, DIC possibility was not considered.

The possibility of Acute Fatty Liver of Pregnancy (AFLP) which is uncommon form of liver injury observed in third trimester. This possibility is ruled out because of presence of normal liver function tests and normal PT, aPTT.

The case under discussion has evidence of a septic focus observed in peripartum period at episiotomy site. The culture revealed the presence of E.coli. Many systemic infections, bacterial, viral and fungal are known to trigger MAHA and thrombocytopenia. However, our patient who was having thrombocytopenia in pregnancy and the said infection was combated with higher antibiotics. Though, improved clinically but had persistent thrombocytopenia ,and reduced urine output (AKI) needing multiple hemodialysis.

Primary TMA can have multiple presentations with rapid onset illness or gradual onset with minimal symptoms. May have anuria (AKI) or normal kidney function. Once thrombocytopenia and MAHA are confirmed, main goal remains to identify primary TMA. It is essential as specific treatment are available for TTP and complement mediated TMA. When complement mediated TMA suspected, anticomplement therapy like Eculizumab should be started within 24-48 hours to limit kidney injury. The possibility of TTP is high in this case as plasmic score is 6 that belongs to high risk group and 72% risk of deficiency of ADAMTS13 $\leq$ 15%. It is to be emphasized that schistocytes $\geq$ 2/hpf in consultation with clinical scenario is highly suggestive of MAHA [3,4].

The complements are implicated in etiology of TMA which has been classified as primary TMA when genetics and acquired defects are observed as primary derivatives. In the secondary TMA; infections, auto-immune disease and pregnancy are recognized as co-factors. This case has shown reduction in complement C3 and C4.This patient has evidence of E.coli infection at local site as well as found in blood culture, such infections imply granulocytes, cytokines, elastase which are produced in sepsis and enclave the factors metalloprotease with thrombospondin, reducing ADAMTS13 levels in sepsis. The mechanism may contribute in development of MAHA. Sepsis induced thrombotic microangiopathic hemolytic anemia are reported in western literature. However, there is scarcity of such cases in Indian literature [5].

Sepsis is a condition with very high mortality rates >20% and the systemic review and meta-analysis done in 2014, does not show any benefit of plasmapheresis in sepsis. However, other studies denoted the fruitful efficacy of plasmapheresis in sepsis and septic shock with acute renal failure demonstrated a fourfold increase in survival compared to historic controls [6,7]. Unfortunately, our patient who was in septic shock with acute renal failure succumbed to death while on plasmapheresis developed fatal ventricular arrhythmias.

Enterotoxigenic E.coli is considered grade 3C recommendation for plasmapheresis. Some serotypes of E.coli cause direct damage to kidney epithelial, mesangial and vascular endothelial cells causing clinical manifestations of thrombotic microangiopathies with acute kidney injuries in adults [8]. Other gram negative infections resulting in TMA may not extrapolate the same results with use of plasmapheresis. In Indian scenario, gram negative organisms induced TMA and benefits of plasmapheresis need more extended studies..

Conclusion

Peripartum sepsis induced thrombotic microangiopathic hemolytic anemia should be suspected in patients with especially gram negative sepsis when the case depicts rapidly falling platelets and hemoglobin. Importance should be attached to blood smear peripheral examination for detecting schistocytes. Repeated PBS examinations for suspecting of

MAHA is warranted. Timely consideration for plasmapheresis is beneficial in septic TMA.

References

1. George JN, McIntosh JJ. Thrombocytopenia in pregnancy. 2021.
2. Perez Botero J, Reese JA, George JN, McIntosh JJ. Severe thrombocytopenia and microangiopathic hemolytic anemia in pregnancy: A guide for the consulting hematologist. Am J Hematol. 2021;96:1655-1665.
3. Oliveira DS, Lima TG, Benevides FLN, Barbosa SAT, Oliveira MA, Boris NP, et al. Plasmic score applicability for the diagnosis of thrombotic microangiopathy associated with ADAMTS13-acquired deficiency in a developing country. Hematol Transfus Cell Ther. 2019;41:119-124.
4. Burns ER, Lou Y, Pathak A. Morphologic diagnosis of thrombotic thrombocytopenic purpura. Am J Hematol. 2004;75:18-21.
5. Pene F, Vigneau C, Auburtin M, Moreau D, Zahar JR, Coste J, et al. Outcome of severe adult thrombotic microangiopathies in the intensive care unit. Intensive Care Med. 2005;31:71-8.
6. Rimmer E, Houston BL, Kumar A, Abou-Setta AM, Friesen C, Marshall JC, et al. The efficacy and safety of plasma exchange in patients with sepsis and septic shock: A systematic review and meta-analysis. Crit Care. 2014;18:699.
7. Gårdlund B, Sjölin J, Nilsson A, Roll M, Wickerts CJ, Wikström B, et al. Plasmapheresis in the treatment of primary septic shock in humans. Scand J Infect Dis. 1993;25:757-61.
8. Schwartz J, Padmanabhan A, Aqui N, Balogun RA, Connelly-Smith L, Delaney M, et al. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the writing committee of the american society for apheresis: The seventh special issue. J Clin Apher. 2016;31:149-62.