

Challenges and Management of Thrombotic Thrombocytopenic Purpura During Pregnancy: A Case Report

Sumaiyah Adzahr^{1,*}, Adibah Daud¹, Nabilah Rameli², Nik Fatma Fairuz Nik Mohd Hassan², Nur Aini Syakirah Ahmad Shuyuti³



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ABSTRACT

Thrombotic thrombocytopenic purpura (TTP), a rare and potentially life-threatening blood disorder, poses unique challenges during pregnancy. It is characterized by microangiopathic hemolytic anemia, severe thrombocytopenia, and microvascular thrombosis. Pregnancy induces significant changes in hemodynamics and coagulation factors, complicating the already complex pathophysiology and presentation of TTP. TTP during pregnancy may be clinically challenging due to overlapping features with other thrombotic microangiopathies. Here, we report a 34-year-old woman at 12 weeks of gestation who presented with sudden onset of altered sensorium and fever. Initial investigations revealed anemia, thrombocytopenia, and numerous schistocytes in the peripheral blood smear. She was diagnosed with TTP based on clinical symptoms and laboratory findings. Ensuring correct diagnosis and management is critical because of the impact on fetal and maternal outcomes.

Key words: fresh frozen plasma, low platelets, plasma exchange, pregnancy, thrombotic thrombocytopenic purpura

¹Department of Pathology, Faculty of Medicine, Universiti Sultan Zainal Abidin, Kuala Terengganu, Terengganu, Malaysia

²Department of Pathology, Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan, Malaysia

³Department of Medicine, Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan, Malaysia

Correspondence

Sumaiyah Adzahr, Department of Pathology, Faculty of Medicine, Universiti Sultan Zainal Abidin, Kuala Terengganu, Terengganu, Malaysia
Email: srikandimaya11@gmail.com

History

- Received: Aug 28, 2023
- Accepted: Oct 08, 2023
- Published Online: Oct 31, 2023

DOI : 10.15419/bmrat.v10i10.837



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INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is a rare but severe complication during pregnancy that often occurs late in the third trimester or during puerperium. Before the development of therapeutic plasma exchange (PEX) and plasma infusion, pregnancy-related TTP caused significant maternal and fetal mortality rates as high as 80%. However, survival rates have dramatically improved after the development of these treatments¹.

CASE REPORT

A 34-year-old woman, gravida 8 para 3+4, presented to the emergency department at 12 weeks gestation with sudden onset of altered sensorium and fever. On examination, she was pale, jaundiced, febrile, and tachycardic. Laboratory investigations showed anemia with hemoglobin of 6.0 g/dL, thrombocytopenia with a platelet count of $11.0 \times 10^9/L$, and numerous schistocytes on a peripheral blood smear (**Figure 1**). Her lactate dehydrogenase (LDH) plasma level was very high at 2767 U/L, and her reticulocyte count was 10%. The renal function test was slightly abnormal, with blood urea of 7.5 mmol/L, total bilirubin of 31 $\mu\text{mol/L}$, and indirect bilirubin of 23 $\mu\text{mol/L}$. Levels of transaminases, prothrombin time, activated partial thrombin time, and international normalized ra-

tio were within normal limits. Based on her clinical symptoms and laboratory findings, she was diagnosed with TTP.

She was immediately started on PEX with fresh frozen plasma at 30 cc/kg daily for three days. Methylprednisone (500 mg) was also administered intravenously for three days. Despite continued PEX, her platelet count and hemoglobin remained unchanged. A regimen of 500 mg rituximab weekly was initiated to improve the curative efficiency of PEX since she might be refractory to PEX. The PEX procedure was maintained according to the established protocol. After three days of rituximab administration, the patient responded favorably by regaining consciousness. The patient's platelet count had returned to normal by the eleventh day. Disintegrin-like and metalloproteinase with thrombospondin type 1 motif, member 13 (ADAMTS13) activity was assessed as part of the comprehensive diagnostic workup for the TTP episode at the referral laboratory. The results showed low ADAMTS13 activity (1%), well below the normal range of 40%–130%, and elevated ADAMTS13 antibody levels (36.2 U/mL), exceeding the positive range threshold of 15. All the laboratory investigations are shown in **Table 1**.

Cite this article : Adzahr S, Daud A, Rameli N, Hassan N F F N M, Shuyuti N A S A. **Challenges and Management of Thrombotic Thrombocytopenic Purpura During Pregnancy: A Case Report.** *Biomed. Res. Ther.* 2023; 10(10):5956-5959.

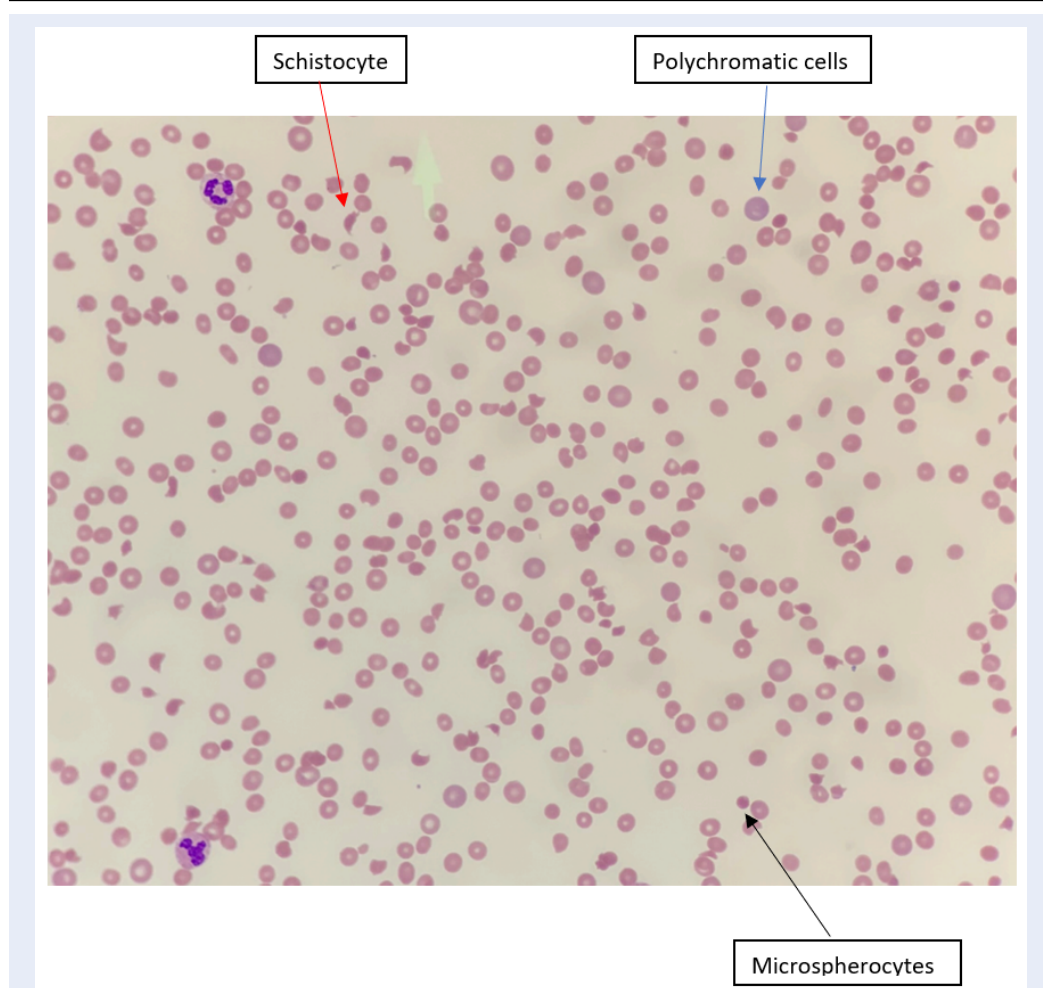


Figure 1: Peripheral blood examination showed numerous schistocytes (red arrow), some polychromatic cells (blue arrow), and some microspherocytes (black arrow). Magnification x40, Wright stain.

DISCUSSION

TTP is a life-threatening disorder characterized by microangiopathic hemolytic anemia (MAHA), severe thrombocytopenia, and microvascular thrombosis². It is caused by a deficiency of the ADAMTS13 enzyme, leading to the accumulation of ultra-large von Willebrand factor (vWF) molecules that bind to platelets and cause thrombotic occlusion in small blood vessels. TTP can be either acquired or congenital. Cases of acquired TTP show low ADAMTS13 activity and the presence of anti-ADAMTS13 antibodies. Cases of congenital TTP show low ADAMTS13 activity (<10%) and no detectable anti-ADAMTS13 antibodies³.

Pregnancy is one of the main triggers of acute TTP episodes, contributing to approximately 5% — 10% of all TTP cases in women². The challenges in diagnosing and managing TPP during pregnancy are due to its

atypical interaction with physiological changes. This correlation arises from the elevated levels of procoagulant factors, reduced fibrinolytic activity, diminished thrombomodulin function, loss of endothelial cell thrombomodulin, and a decline in ADAMTS13 activity accompanying pregnancy⁴. Pregnancy-related TTP has been associated with higher risks of maternal and fetal morbidity and mortality.

Clinical TPP presentations include thrombocytopenia, MAHA, altered renal function, fever, and neurological symptoms such as seizures⁵. Among patients, 24% have fever, 59% have renal abnormalities, and 63% have neurological signs. Renal involvement may present as proteinuria or increased serum creatinine levels. Neurological involvement may result in seizures, strokes, or confusion⁶.

TPP diagnosis requires the presence of both thrombocytopenia and hemolytic anemia. In the acute

Table 1: Laboratory investigations

Parameters	Day 1 (On admission)	Day 11 (After treatment with PEX and Rituximab)	Normal range
Hemoglobin (Hb)	6.0 g/dL	9.7 g/dL	12.0 -15.0 g/dL
White blood cell	10.1 x10 ⁹ /L	6.48 x10 ⁹ /L	4 - 10 x10 ⁹ /L
Platelet	11 x10 ⁹ /L	150 x10 ⁹ /L	150 - 410 x10 ⁹ /L
Reticulocytes	10.0%	1.5%	0.5 - 2.5%
Total bilirubin	31 μmol/L	27 μmol/L	1 - 17 μmol/L
Indirect bilirubin	23 μmol/L	10 μmol/L	< 7 μmol/L
Blood urea nitrogen	7.5 mmol	6.8 mmol	2.8 - 7.2 mmol/L
Creatinine	66	32	45 - 84 umol/L
Lactate dehydrogenase (LDH)	2767 U/L	-	140 - 280 U/L
ADAM TS13 activity	-	1%	40-130%
ADAMTS13 antibody levels	-	36.2 U/mL	Negative: < 12 U/mL Borderline:12-15 U/mL Positive: >15 U/mL

phase, the platelet count is often very low ($< 30 \times 10^9/L$), and there are signs of mechanical hemolytic anemia, including the presence of schistocytes, reticulocytosis, high indirect serum bilirubin, low serum haptoglobin, and negative direct Coombs test. LDH is usually significantly elevated due to red cell destruction and tissue necrosis, and routine coagulation parameters are usually normal⁷. Testing for ADAMTS13 activity is essential since the prevailing mechanism thought to underlie TTP is associated with ADAMTS13 deficiency. The TTP diagnosis is confirmed if ADAMTS13 activity is $< 10\%$. The differential diagnosis of TTP during pregnancy includes other thrombotic microangiopathies such as acute fatty liver of pregnancy, preeclampsia, atypical hemolytic uremic syndrome, and HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. Plasma treatment should begin as soon as possible when TTP is suspected, regardless of ADAMTS13 activity⁸. PEX appears more successful than plasma infusion. PEX eliminates ultra-large vWF multimers, anti-ADAMTS13 antibodies, and ADAMTS13 immune complexes while restoring ADAMTS13 activity. There is no specific PEX regimen that works best. Our standard of care, which follows the guidelines set by the British Committee on Standards in Haematology, involves initiating PEX with 1.5 plasma volume (PV) exchanges for the first three days, followed by 1.0 PV exchange the next day. PEX is maintained

until the platelet count reaches normal levels ($\geq 150 \times 10^9/L$ for two consecutive days). After attaining a steady response, many groups will discontinue PEX, while others suggest tapering the frequency of PEX to prevent exacerbations (recurrent TTP within 30 days of the last PEX)⁹.

Corticosteroids may be used in TTP to reduce the synthesis of ADAMTS13 inhibitors¹⁰. Rituximab (anti-membrane spanning 4-domains A1 [MS4A1/CD20]) also showed an excellent response with a reduced recurrence^{11,12}. In small case studies, other immunosuppressive drugs such as vincristine, cyclophosphamide, or cyclosporine were beneficial.

CONCLUSION

In our case, we had to administer rituximab as an immunosuppressive agent due to PEX refractoriness. This report highlights the complexities of managing TTP during pregnancy. Collaborative efforts are needed to refine treatment strategies, ultimately enhancing the prognosis for mothers and their infants in these challenging cases.

ABBREVIATIONS

ADAMTS13: A Disintegrin and Metallo-proteinase with Thrombospondin type 1 motif, member 13; **MAHA:** microangiopathic haemolytic anaemia **PEX:** plasma exchange **TPE:** therapeutic plasma exchange; **TTP:** Thrombotic thrombocytopenic purpura

ACKNOWLEDGMENTS

None

AUTHOR'S CONTRIBUTIONS

SA and NR are responsible for the writing of the article. NFFNMH and NASAS helped in data collection and interpretation. AD participated in sequence alignment. All authors read and approved the final manuscript.

FUNDING

None

AVAILABILITY OF DATA AND MATERIALS

Data and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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