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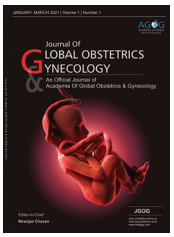
Case Report



From Crisis to Cure: Navigating Thrombotic Thrombocytopenic Purpura in Pregnancy

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ABSTRACT

Thrombotic thrombocytopenic purpura (TTP) is a rare but severe disorder characterized by low platelet counts, hemolytic anemia, and microvascular thrombosis, primarily resulting from a deficiency in the ADAMTS13 enzyme. Acute cases are often acquired, driven by autoantibodies that markedly reduce ADAMTS13 activity, while congenital TTP is identified through genetic testing and presents similarly without detectable antibodies. Pregnancy significantly increases the risk of acute TTP episodes due to heightened procoagulant factors and reduced ADAMTS13 levels. This article outlines management strategies for TTP in the context of pregnancy, emphasizing the importance of monitoring ADAMTS13 levels, platelet counts, and lactate dehydrogenase (LDH) levels. Pre-conception guidelines recommend a waiting period post-rituximab treatment, while management during pregnancy involves regular monitoring and potential plasma infusions or plasmapheresis, depending on the severity of the condition. Delivery recommendations vary based on ADAMTS13 activity, with close postpartum monitoring essential for early detection of relapses. The complexities of diagnosing TTP during pregnancy, due to symptom overlap with conditions such as pre-eclampsia and HELLP syndrome, are also discussed. Overall, these guidelines aim to ensure the safe management of pregnancies in patients with a history of TTP, prioritizing both maternal and fetal health

Key words: Thrombotic thrombocytopenic purpura, pregnancy, rare

INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) remained an enigmatic condition for more than 50 years until the discovery of the ADAMTS13 enzyme. ADAMTS13 is primarily synthesized in the liver, and it is a plasma protease responsible for the cleavage of von Willebrand factor (VWF), preventing the accumulation of ultra-large VWF (ULVWF) multimers that can spontaneously interact with platelets, causing microvascular thrombosis leading to thrombocytopenia and microangiopathic hemolytic anemia. Deficiency of plasma ADAMTS13 activity (<10%) resulting from mutations of the ADAMTS13 gene or autoantibodies against ADAMTS13 causes hereditary or acquired (idiopathic) TTP.[1] Pregnancy may be a precipitating factor in acute TTP, and there is a risk of relapse during subsequent pregnancies. TTP should be excluded in pregnancy-associated thrombotic microangiopathies.[2]

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Received: ***
Accepted: ***
DOI: ***

CASE SERIES

This is a case series of two siblings with known cases of acute gravid TTP with genetic predisposition with an acquired component.

Case 1

A 24-year-old Mrs. XYZ married for 5 years, Gravida 2 Para 1 and Death 1 with 20-week gestation, with diagnosed case of TTP in previous pregnancy in 2019, came with a fresh complete blood count (CBC) report of (hemoglobin [Hb] - 6.9 g/dL, TLC - $10*10^9$/L, platelet - $43*10^9$/L) as per the advice of local physician, with no clinical signs and symptoms (Table 1).

Reports dated 2019

She gives a history of multiple fresh frozen plasma (FFP) transfusion in previous pregnancy, which was followed by an emergency lower segment cesarean section at term in view of meconium-stained amniotic fluid with fetal distress. The maternal

outcome was uneventful; however, the infant succumbed to meconium aspiration syndrome.

She was then admitted to the medical ward and all routine investigations were done (Table 2).

She was transfused 1-pint packed red cells (PRCs) and 1-pint single donor platelets (SDP) and was started on tablet thyroxine 75 ug once a day. All other antenatal investigations were within normal limits. A targeted imaging for fetal anomalies (TIFFA) scan was done which showed no evidence of congenital abnormalities. The patient was serially followed up monthly with hemograms and was given multiple plasma infusions. She was also started on tablet prednisolone 20 mg once-a-day and tablet azathioprine 50 mg once-a-day. Serial fetal monitoring was done with doppler scans. The patient underwent an elective lower segment cesarean section at 37.6- week gestation and delivered a healthy fetus of 2840 g. She was transfused with 2 pint FFP post-partum. The maternal and fetal outcome was uneventful (Table 3).

Table 1: Reports dated 2019 of CASE 1

Lab parameters	Values	Normal range
Adamts 13 activity	37%	50–150%
Igg autoantibody level	12.5 g/L	<9.6 g/L
LDH	1110 U/L	140–280 U/L
Haptoglobin	<8 g/L	50–220 g/L
Schistocytes	3%	<0.5%

LDH: Lactate dehydrogenase

Table 2: Lab values on admission and after platelet transfusion of CASE 1

Lab parameters	Values	Post-transfusion values (1 PRC and 1 SDP)	Normal range
Hemoglobin (g/dL)	6.9	8.2	11–14
TLC (g/L)	$10*10^9$	$8*10^9$	$4*10^9$–$11*10^9$
Platelets (g/L)	$43*10^9$	$86*10^9$	$150*10^9$–$400*10^9$
PT (s)	10.6		11–13.5
INR	0.9		0.8–1.1
APTT (s)	29		30–40
T. Bili (mg/dL)	1.2		0.1–1
AST/ALT (IU/L)	36/15		<40
BUN (mg/dL)	8		<20
Creatinine (mg/dL)	0.5		<1.3
TSH	8		0.3–4.9
fT3	2.05		1.5–3.9
fT4	0.8		0.7–1.4
Fasting sugars (mg/dL)	90		86–92
Postprandial sugars (mg/dL)	100		<120
Urine routine	No evidence of proteins or glucose		

TLC: Total leukocyte count, PRC: Packed red blood cells, SDP: Single donor platelets, ALT: Alanine transaminase, AST: Aspartate transaminase, BUN: Blood urea nitrogen, TSH: Thyroid-stimulating hormone

Case 2

A 30-year-old Mrs. ABC married for 13 years, Gravida 2 Para 1 and Living 1 with 19-week gestation, with diagnosed case of TTP in previous pregnancy in 2019, came with a fresh CBC report of (Hb - 6.1 g/dL, TLC - $8*10^9$/L, platelet - $13*10^9$/L) as per the advice of local physician, with complaints of bleeding gums on brushing teeth. She gives history of loss of all previous papers proving diagnosis of TTP.

She gives a history of multiple FFP transfusion in previous pregnancy, which was followed by an elective lower segment cesarean section at term in view of transverse lie. The maternal and fetal outcome was uneventful.

She was then admitted to the medical ward and all routine investigations were done (Table 4).

The patient had persistently elevated blood pressure, suggestive of pre-eclampsia for which she was started on tablet labetalol 100 mg twice-a-day and tablet nifedipine 10 mg thrice a day. She was transfused 2-pint PRC and 8-pint FFP. All other antenatal investigations along with a 2D echo, renal artery doppler, and an ophthalmic examination were done which were within normal limits. A TIFFA scan was done which showed no evidence of congenital abnormalities. The patient was serially followed up monthly with hemograms and was given multiple plasma infusions. She was also started on tablet prednisolone 20 mg once a day and tablet azathioprine 50 mg twice a day. Serial fetal monitoring was done with doppler scans, with last USG done on March 20, 2024, suggestive of fetus of appropriate gestation age weighing 2100 g and raised pulsatile index of uterine artery (Table 5).

On March 22, 2024, the patient complained of severe headache with blurring of vision with persistent blood pressure of 200/110 mmHg in spite of full dose antihypertensives. She was undertaken for an emergency lower segment cesarean section in view of impending eclampsia, with peri-operative transfusion of 1-pint PRC and 2-pint FFP. The patient delivered a male child of 1900 g. The maternal and fetal outcome was uneventful.

DISCUSSION

TTP is a rare and severe condition that can be life-threatening. It is characterized by a combination of low platelet counts, hemolytic anemia, and the effects of microvascular thrombosis, all stemming from a deficiency in the ADAMTS13 enzyme. Most acute cases are acquired and driven by autoantibodies, resulting in very low levels of ADAMTS13 activity (below 10%) and the presence of anti-ADAMTS13 IgG antibodies. In contrast, a small number of TTP cases are congenital, with similarly low ADAMTS13 activity but

Table 3: Examination and findings during antenatal visits of CASE 1

Date of admission	Weeks of gestation	Clinical signs and symptoms	CBC	Values	Transfusion received	Values
December 25 2023	23 weeks	Bleeding gums	Hemoglobin (g/dL)	7.7	12-pint FFP	8
			TLC (g/L)	$10*10^9$		$5.8*10^9$
			Platelets (g/L)	$40*10^9$		$150*10^9$
January 25 2024	27 weeks	None	Hemoglobin (g/dL)	7.8	10-pint FFP	9
			TLC (g/L)	$5*10^9$		$8.5*10^9$
			Platelets (g/L)	$39*10^9$		$166*10^9$
February 25 2024	32 weeks	None	Hemoglobin (g/dL)	7.8	1 pint PRC 4-pint FFP	10.7
			TLC (g/L)	$8.4*10^9$		$8.4*10^9$
			Platelets (g/L)	$39*10^9$		$83*10^9$
March 20 2024	36 weeks	Petechiae over B/L upper and lower limbs	Hemoglobin (g/dL)	9.2	13-pint FFP	9.4
			TLC (g/L)	$8*10^9$		$5.8*10^9$
			Platelets (g/L)	$15*10^9$		$177*10^9$

CBC: Complete blood count, TLC: Total leukocyte count, PRC: Packed red blood cells, FFP: Fresh frozen plasma

Table 4: Lab values on admission and after platelet transfusion of CASE 2

Lab parameters	Values	Post-transfusion values (1 PRC and 1 SDP)	Normal range
Hemoglobin (g/dL)	6.1	8.8	11-14
TLC (g/L)	$8*10^9$	$8.9*10^9$	$4*10^9$–$11*10^9$
Platelets (g/L)	$13*10^9$	$121*10^9$	$150*10^9$–$400*10^9$
PT (s)	10.6		11–13.5
INR	1.05		0.8–1.1
APTT (s)	29		30–40
T. Bili (mg/dL)	1.2		0.1–1
AST/ALT (IU/L)	13/15		<40
BUN (mg/dL)	8		<20
Creatinine (mg/dL)	0.5		<1.3
TSH	3.95		0.3–4.9
fT3	2.74		1.5–3.9
fT4	0.75		0.7–1.4
Fasting sugars (mg/dL)	90		86–92
Postprandial sugars (mg/dL)	116		<120
Urine routine	No evidence of proteins or glucose		

TLC: Total leukocyte count, PRC: Packed red blood cells, FFP: Fresh frozen plasma, ALT: Alanine transaminase, AST: Aspartate transaminase, BUN: Blood urea nitrogen, TSH: Thyroid-stimulating hormone

without detectable antibodies, and are identified through genetic testing.

Pregnancy is a common trigger for acute TTP episodes. This is linked to increased levels of procoagulant factors, decreased fibrinolytic activity, reduced endothelial cell thrombomodulin, and lower ADAMTS13 activity during pregnancy.

ADAMTS 13 levels below 10% and no evidence of antibodies confirms the diagnosis of congenital TTP (cTTP). It is important to confirm the ADAMTS 13 results and proceed with mutational analysis during remission. In cTTP, plasma infusions (usually 10–15 mL/kg) should be initiated early in pregnancy and continued for 4–6 weeks after childbirth. The infusion frequency must be adjusted as pregnancy advances: initially, infusions are given every 2 weeks, but during the second or early third trimester, the frequency may increase to weekly or even every other day. The schedule should be further intensified if there are signs of clinical or laboratory worsening, such as reduced platelet counts or elevated lactate dehydrogenase

Table 5: Examination and findings during antenatal visits of CASE 2

Date of admission	Weeks of gestation	Clinical signs and symptoms	CBC	Values	Transfusion received	Values
January 04 2024	22 weeks	Bleeding gums	Hemoglobin (g/dL)	8.8	4-pint FFP	9.3
			TLC (g/L)	$7.1*10^9$		$9.6*10^9$
			Platelets (g/L)	$46*10^9$		$121*10^9$
January 23 2024	23 weeks	None	Hemoglobin (g/dL)	7.9	1-pint PRC 10-pint FFP	8.6
			TLC (g/L)	$10*10^9$		$11*10^9$
			Platelets (g/L)	$23*10^9$		$161*10^9$
February 15 2024	29 weeks	None	Hemoglobin (g/dL)	8.7	1-pint PRC 8-pint FFP	9
			TLC (g/L)	$10*10^9$		$9*10^9$
			Platelets (g/L)	$16*10^9$		$72*10^9$
March 04 2024	31 weeks	None	Hemoglobin (g/dL)	10.9	12-pint FFP	9.4
			TLC (g/L)	$8*10^9$		$8.4*10^9$
			Platelets (g/L)	$29*10^9$		$76*10^9$
March 18 2024	33 weeks	None	Hemoglobin (g/dL)	8.5	13-pint FFP	8.5
			TLC (g/L)	$9*10^9$		$7*10^9$
			Platelets (g/L)	$15*10^9$		$64*10^9$

CBC: Complete blood count, TLC: Total leukocyte count, PRC: Packed red blood cells, FFP: Fresh frozen plasma

(LDH) levels. In severe cases, particularly toward the end of pregnancy, daily plasma infusions may not prevent disease recurrence, and plasmapheresis (PEX) might be necessary to remove ULVWF multimers. Consequently, vaginal delivery is often induced at 36–37 weeks of gestation, and plasma infusions are continued for at least 3-week postpartum. In the case of acquired TTP with ADAMTS 13 levels below 10% and the presence of antibodies, further immunosuppression, such as steroids, may be necessary to achieve and maintain remission. During remission or subsequent pregnancies, if ADAMTS 13 levels remain low and antibodies are present, elective treatments such as rituximab could be considered before pregnancy.

Pre-conception and Early Pregnancy Management

Before conception

- Wait period: After rituximab treatment, it is recommended to wait at least 6–12 months before trying to conceive.

During pregnancy

- CBC monitoring: Perform monthly.
- ADAMTS13 activity testing: Check at least once per trimester (or monthly in your practice).
- Increased monitoring: If there are any signs of biochemical abnormalities (e.g., reduced platelet count or increased LDH levels), especially with decreasing ADAMTS13 levels, increase the frequency of checks.

Delivery Recommendations

Normal pregnancy

- ADAMTS13 activity >20–25%: A vaginal delivery at term is usually recommended.
- Post-delivery follow-up:
  - CBC: Monitor every other day for 3–5 days.
  - ADAMTS13 levels: Assess within 3 weeks after delivery.

Reduced ADAMTS13 Activity (<20–25%)

Without acute TTP symptoms

- Initial Treatment: Begin low-dose corticosteroids (oral prednisolone, 0.5 mg/kg daily) to decrease autoantibody production.
- If unsuccessful: If ADAMTS13 levels drop below 10% or corticosteroids do not suffice, start prophylactic plasma exchange (PEX), adjusting the frequency based on effectiveness (weekly or biweekly).

With acute TTP symptoms

- Treatment: Initiate daily PEX. Monitor maternal and fetal health closely with clinical evaluations, laboratory tests (platelet count and LDH levels), and fetal ultrasounds.

Handling severe cases and delivery decisions

Severe TTP with inadequate response to treatment

- Close surveillance: Monitor both maternal and fetal health meticulously.

- Delivery decision: If there is significant deterioration, consider early delivery or premature termination of pregnancy if needed.
- Post-partum monitoring: Essential to identify any signs of relapse.

These guidelines aim to ensure careful management of pregnancies in patients with a history of TTP, prioritizing both maternal and fetal health.

It is not usually recommended to start low-dose aspirin and/or thromboprophylaxis with low-molecular-weight heparin, except for women with a previous history of gravidic complications related to placental flow impairment and/or higher thrombotic risk.

Even diagnosis of this condition is not easy during pregnancy because the symptoms mimic those of pre-eclampsia, HELLP, eclampsia, hemolytic uremic syndrome, or any acquired coagulopathy.

CONCLUSION

Acute TTP is a critical medical emergency, particularly when it occurs during pregnancy or the postpartum period, requiring a multidisciplinary team approach. Accurate diagnosis and effective treatment rely on clinical evaluation alongside ADAMTS13 testing. Advances in therapies, including plasma exchange and immunosuppressive medications, have significantly improved outcomes for both mothers and babies affected by pregnancy-related TTP. Routine monitoring of ADAMTS13 levels, in combination with these treatments, helps ensure safe management and future pregnancy planning for women with this rare condition.

REFERENCES

1. Masias C, Cataland SR. The role of ADAMTS13 testing in the diagnosis and management of thrombotic microangiopathies and thrombosis. Blood 2018;132:903-10.
2. Scully M, Thomas M, Underwood M, Watson H, Langley K, Camilleri RS, *et al.* Thrombotic thrombocytopenic purpura and pregnancy: Presentation, management, and subsequent pregnancy outcomes. Blood 2014;124:211-9.

How to cite this article: Chavan N, Ajmera D, Kapote D, Trivedi T, Honrao S, Patel S, *et al.* From Crisis to Cure: Navigating Thrombotic Thrombocytopenic Purpura in Pregnancy. J Glob Obstet Gynecol 2024;4(3):25-29.

Source of support: Nil, **Conflict of Interest:** Nil.