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| RESEARCH ARTICLE

Beyond the Pentad: A Lethal Presentation of TTP with Multiorgan Involvement

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| ABSTRACT
This case report discusses a 41 year-old female with no significant past medical history who developed thrombotic thrombocytopenic purpura (TTP) presenting with severe hemolytic anemia, thrombocytopenia, acute kidney injury, and neurological deterioration. Despite aggressive plasmapheresis, corticosteroid therapy, and supportive care, the patient's condition rapidly worsened, culminating in multiorgan failure and death. This report highlights the critical importance of early diagnosis and intervention in TTP and discusses the clinical and laboratory parameters guiding management.

| KEYWORDS
thrombotic thrombocytopenic purpura; hemolytic anemia; acute kidney injury; plasmapheresis

| ARTICLE INFORMATION
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INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is a microangiopathic hemolytic anemia with its own pentad consisting of fever, thrombocytopenia, hemolytic anemia, and neurologic as well as renal dysfunction. TTP issues from either a congenital or an acquired decrease or absence of the von Willebrand factor-cleaving protease ADAMTS13. Yet again, it has to be noted that the deficiency of ADAMTS13 activity on its own does not result in clinically evident TTP. Individuals with hereditary ADAMTS13 deficiency remain asymptomatic until a triggering event such as a pregnancy or an infection takes place. TTP is well-known to be rare in its form with incidences reporting between 1 and 13 cases per million individuals depending on geographic location. It is also infamous to be more predominant in females than males (2:1 respectively), and the African and/ or the African American descent, with a tremendous mortality rate between 90% - 95% if left untreated, which decreases to a hopeful 10% - 15% if treated promptly (1). This case focuses on the optimized multidisciplinary approach that has been used to manage a patient with such a challenging prognosis.

CASE PRESENTATION

A 41 year-old female with no significant past medical history presented to the emergency room, with a 3-day history of persistent headache, dizziness, epigastric pain, vomiting, lethargy, and progressive fatigue accompanied by shortness of breath. There was no history of fever, bleeding, or prior neurological events. No blurring of vision or other visual disturbance, no chest pain, no palpitation, and no oedema. She had mild shortness of breath, but no cough. No change in bowel habit but, the patient was feeling nauseous. Her urine output and frequency was normal, no hematuria, no dysuria, but she stated that urine was dark in color. She also noted no muscle pain, weakness or numbness, and she appeared to be lethargic. She had visited an outside clinic where blood tests showed microcytic anemia and thrombocytopenia (Hb 6.9 g/dl and platelet count 11 10^3/ul), hence she was referred to our hospital. Patient was admitted in ICU for further evaluation and blood products transfusion.

On Admission: Day 1

- **Vital signs:** Temp. 37.1 °C, BP 107/75 mmHg, HR 88 bpm, RR 23/min, SpO2 100% on room air. RBS 119 mg/dL.
- **Physical examination:** Marked pallor, mild epigastric tenderness, no lymphadenopathy or hepatosplenomegaly noted, neurological exam normal, patient appears dehydrated.

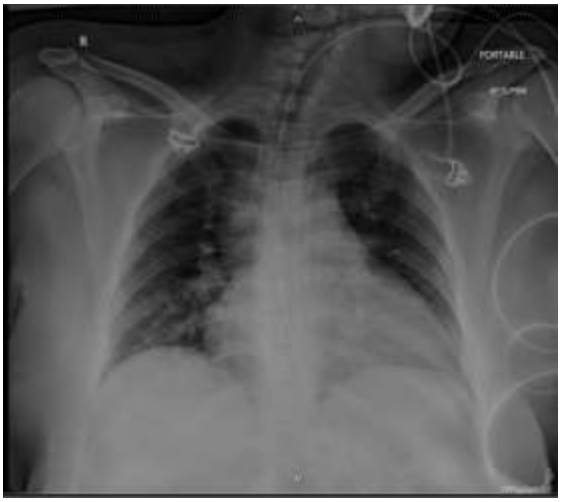
Management:

- Send baseline labs along with workup for anemia
- Arrange 8 units of Platelets and 2 units of PRBC for transfusion.
- Initially transfuse 4 or 6 units of platelets followed by 1 PRBC, IV fluids on slow rate till blood products transfusion starts, and, symptomatic treatment and close observation of vitals and clinical status.

Laboratory Investigations

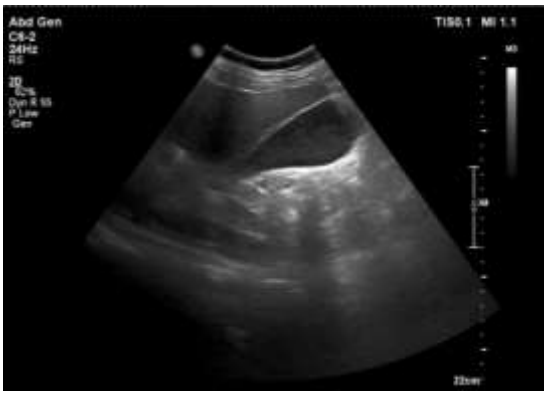
Parameter		Result	Reference Range	Notes
Hemoglobin (Hb)		6 g/dL	13.5–17.5 g/dL	Severe anemia
Platelets		10 $\times 10^3/\mu L$	150–450 $\times 10^3/\mu L$	Severe thrombocytopenia
Reticulocyte count		6.68%	0.5–2.5%	Elevated, indicating hemolysis
Ferritin		755.4 ng/mL	13–150 ng/mL	High Ferritin
Lactate Dehydrogenase (LDH)		>1200 U/L	140–280 U/L	Markedly elevated (hemolysis)
Haptoglobin		<0.06 g/L	0.3–2.0 g/L	Low, consistent with hemolysis
Vitamin B12		106 pg/mL	180-914 pg/mL	Critically low
Creatinine		1.37 mg/dL	0.6–1.2 mg/dL	Mild renal impairment
Urea		38.32 mg/dL	10–50 mg/dL	Within normal
AST		76 U/L	10–40 U/L	Elevated
ALT		80 U/L	7–56 U/L	Elevated
ALP		105 U/L	30 – 120 U/L	Within the normal range
Total Bilirubin		2.5 mg/dL	0.1–1.2 mg/dL	Elevated, hemolysis likely
Direct Bilirubin		0.52 mg/dL	0.1 – 0.3 mg/dL	
Indirect Bilirubin		1.99 mg/dL	0.2 to 0.8 mg/dL	
CRP		26.8 mg/L	<10 mg/L	Elevated inflammatory marker
Electrolytes	Ca^+	7.98 mg/dL	8.5 – 10.5 mg/dL	Hypocalcemia
	K^+	2.9 mol/L	3.5 – 5.0 mmol/L	Hypokalemia
Troponin I		1.51 ng/mL	<0.04 ng/mL	Mild myocardial injury
D-dimer		3610 ng/mL	< 500 ng/mL	Critically high
Peripheral Smear		Schistocytes present	N/A	Consistent with microangiopathic hemolysis
Direct Coombs Test		Positive	Negative	Autoimmune hemolysis
Indirect Coomb's Test		Negative	Negative	
ADAMTS13 activity		Pending	40-130%	To confirm diagnosis
Mycoplasma IgM		1.09	Negative / < 0.9 Equivocal / 0.9 – 1.1 Positive / > 1.1	Positive
Influenza A & B				Negative
Dengue NS1 Antigen				Negative
Dengue IgM				Negative
Malaria Antigen				Negative

- The patient was also found to be G6PD Negative.
- Chest X-ray showed bilateral alveolar infiltrates without effusions.



Hospital course: Day 2

- Patient became restless, increasingly lethargic with altered sensorium, requiring intubation for airway protection.
- Vitals at 6.30 AM: Temp. 36.8 °C, BP 121/81 mmHg, HR 87 bpm, RR 22/min, SPO2 99%, ventilated. RBS 166 mg/dL.
- Vitals at 13:10 PM: Temp 37.8 °C, 129/10 mmHg, HR 108/min, RR 12/min, SPO2 100%. RBS 260 mg/dL.
- Intake/Output: 640/250 ml overnight.
- GCS E2M4V2.
- ABG: pH: 7.49, PO_2: 78 mmHg, PCO_2: 32 mmHg, HCO_3: 24.4 mmol/L, Lactate: 1.2 mmol/L, Na^+: 139 mmol/L, K^+: 2.8 mmol/L. D-Dimer level was 3610.
- Patient was given 1 mg of Midazolam stat in view of restlessness
- Urgent 1 mega unit of platelets with 1 unit of PRBC transfusion. Low grade fever spike noted.
- After platelet transfusion patient was given injection furosemide 20 mg stat and Calcium gluconate. Advised to send PTH, Vitamin D levels, to do echo and get neurology consult for disorientation.
- Troponin - I increased dramatically from 1.51 ng/mL to 2.46 ng/mL within a day.
- ECG showed no acute ischemic changes.
- Urgent brain CT was done to rule out intracranial bleed and it was unremarkable.
- MRI brain without contrast findings are suggestive of no significant intracranial focal lesion.
- Ultrasonography of whole abdomen shows mild pelvic free fluid and minimal rim of fluid at Morrison's pouch.



- Plan to send LDH, urine and blood culture, urine microalbumin, ADAMTS-13 levels.

Labs Day 2:

Parameter		Result	Reference Range	Notes
Hemoglobin (Hb)		5.5 g/dL	13.5–17.5 g/dL	Severe anemia
Platelets		$15\times10^3/\mu L$	150–450 $\times10^3/\mu L$	Severe thrombocytopenia
Lactate Dehydrogenase (LDH)		> 1200 U/L	140–280 U/L	Markedly elevated (hemolysis)
Creatinine		1.61 mg/dL	0.6–1.2 mg/dL	Mild renal impairment
Urea		42 mg/dL	10–50 mg/dL	Within normal
AST		250 U/L	10–40 U/L	Elevated
ALT		229 U/L	7–56 U/L	Elevated
Total Bilirubin		3.5 mg/dL	0.1–1.2 mg/dL	Elevated, hemolysis likely
CRP		35 mg/L	<10 mg/L	Elevated inflammatory marker
ESR		65 mm/hr	0-20 mm/hr	Elevated inflammatory marker
Electrolytes	Na^+	133.6 mEq/L	135 to 145 mEq/L	Mild hyponatremia
	Mg	1.49 mg/dL	1.7 to 2.2 mg/dL	Critical hypomagnesemia
Troponin I		3.33 ng/mL	<0.04 ng/mL	Mild myocardial injury
Pt		13.1 sec	11 and 13.5 sec	Normal
INR		1.15 sec	0.8 to 1.1 sec	Mildly elevated
Direct Coombs Test		Positive	Negative	Autoimmune hemolysis
ADAMTS13 activity		Pending	>67%	To confirm diagnosis
Vitamin D, 25-OH		15.7 ng/mL	20-50 ng/mL	Low
Parathyroid hormone intact		253.6 pg/ml	5-65 pg/mL	High
Hep B		Negative	Negative	
Hep C		Negative	Negative	
HIV		Negative	Negative	
Covid-19		Negative	Negative	

- Management included:
    - Initiation of plasmapheresis via femoral catheter (with removal of plasma around 1.2 times of the plasma) uneventfully, 6 FFPs were transfused during plasmapheresis, 2 units PRBC transfusion done overnight.
    - High-dose methylprednisolone at 1 mg/kg/day to suppress autoimmune activity.
    - Packed red blood cell transfusions for severe anemia.
    - Broad-spectrum antibiotics (ceftriaxone and azithromycin) continued empirically.

Hospital course: Day 3

- Vitals at 06.15 AM: Temp 37.8 °C, BP 105/77 mmHg, HR 106/min, RR 14/min, SPO2 100%. RBS 220 mg/dL.
- Vitals at 21:16 PM: Temp 38.9 °C, BP 98/64 mmHg, HR 34/min, RR 12min. SPO2 100%.
- The patient developed persistent hypotension requiring norepinephrine support and persistent tachycardia. On high dose of norepinephrine: Temp 37.3 °C, BP 95/73 mmHg, HR 102/min, RR 18/min, SPO2 100%.
- Intake/Output: 3220/5175 ml, with urine output around 25 ml/hr, on the following infusions: fentanyl 30 mcg/hr, cisatracurium 3ml/hr, midazolam 2mg/hr, furosemide 5mg/hr, normal saline 60 ml/hr, and noradrenaline 10 ml/hr (double strength).
- Ceftriaxone was stopped antibiotics were escalated and meropenem and tazocin were started.
- Plan to do a 1 PRBC transfusion during sustained low-efficiency dialysis (SLED) followed by a second session of plasmapheresis. If no improvement noted clinically or hematologically then to give first dose of injection rituximab for severe TTP.

- Patient developed one generalized tonic-clonic seizure which was controlled with midazolam 4mg, muscle relaxant as well as and levetiracetam 1000mg stat followed by 500mg BD.

Lab Results Day 3

Parameter	Result	Reference Range	Comments
Hb	7.5 g/dL	13.5–17.5 g/dL	Further decline
Platelets	20 $\times 10^3$/µL	150–450 $\times 10^3$/µL	Worsening thrombocytopenia
WBC	17.6 x10^3/µL	4.0 – 11.0 x10^3/µL	High
LDH	>1500 U/L	140–280 U/L	Increased hemolysis marker
Creatinine	1.61 mg/dL	0.6–1.2 mg/dL	Progressive kidney injury
Urea	68.96 mg/dL	10–50 mg/dL	Markedly elevated
eGFR	35.2 mL/min/1.73 m^2	≥ 90 mL/min/1.73 m^2	Severe decrease
AST	625 U/L	10–40 U/L	Severe hepatic injury
ALT	229 U/L	7–56 U/L	Elevated
ALP	79 U/L	30 – 120 U/L	Within the normal range
Total Bilirubin	4.68 mg/dL	0.1–1.2 mg/dL	Rising hemolysis/cholestasis
Direct Bilirubin	3.75 mg/dL	0.1 – 0.3 mg/dL	
Indirect Bilirubin	0.93 mg/dL	0.2 to 0.8 mg/dL	
CRP	78.3 mg/L	<10 mg/L	Markedly elevated
PCT-Q	1.315 ng/mL	< 0.05 ng/mL	Moderate increase
PT	18.4 sec	11 and 13.5 sec	Elevated
INR	1.62 sec	0.8 to 1.1 sec	Elevated
Troponin I	3.33 ng/mL	<0.04 ng/mL	Progressive myocardial injury
Electrolytes Ca^+	7.63 mg/dL	8.5 – 10.5 mg/dL	Hypocalcemia

- Mycoplasma IgM negative after receiving treatment.
- ADAMTS13 activity reported at 3% (severe deficiency) confirming TTP diagnosis.
- Additional transfusions with platelets and FFP administered as clinically indicated.
- Patient suddenly developed bradycardia progressing to asystole. CPR was initiated however ROSC could not be achieved and the patient resuscitation was unsuccessful.

DISCUSSION

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening thrombotic microangiopathy characterized by microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and variable organ dysfunction, most often due to impaired ADAMTS13 enzyme activity (2). Although the classic pentad of TTP: thrombocytopenia, MAHA, neurological symptoms, renal dysfunction, and fever, is rarely observed in full, our patient exhibited most of these features throughout the course of her illness. She presented with severe anemia, thrombocytopenia, elevated lactate dehydrogenase (LDH), low haptoglobin, and schistocytes on peripheral smear, all strongly suggestive of TTP. Despite intensive care, her condition deteriorated rapidly, and she passed away before ADAMTS13 test results became available. This case highlights the aggressive progression of TTP and the critical importance of early empirical plasma exchange. Although ADAMTS13 deficiency confirms the diagnosis, treatment should never be delayed while awaiting these results, as early deterioration is common.

Cardiac involvement in TTP can range from silent elevations in cardiac biomarkers to heart failure, myocardial infarction, or sudden cardiac death. Currently, there is limited guidance on the optimal approach to cardiac assessment and management in TTP. Patients with cardiac manifestations should be closely monitored using telemetry, serial troponins, and echocardiography, with prompt initiation of both TTP-specific and cardiac-targeted treatments. Aspirin is generally recommended for all patients with TTP. Furthermore, cardiac injury evidenced by elevated troponin levels has emerged as a significant prognostic marker associated with worse outcomes, necessitating early aggressive intervention (3).

While another reported case of TTP secondary to pancreatitis and clopidogrel had a favorable outcome due to early recognition and intervention. (4) Another small retrospective study across six institutions found that delayed initiation of plasma exchange particularly beyond 24 hours after presentation was associated with significantly increased mortality (6). While plasmapheresis has dramatically improved survival, mortality rates still range between 7% and 22%, even with standard treatment (7). In our case, despite supportive measures including transfusions, ventilatory support, and dialysis, the patient's prognosis was poor due to multiple high-risk features: critical thrombocytopenia, confirmed ADAMTS13 deficiency, neurological decline with seizures, elevated troponin, and inflammatory markers (CRP, procalcitonin). A marked rise in liver enzymes and worsening coagulopathy

indicated systemic microvascular injury and multiorgan failure. The sudden onset of bradycardia and asystole, ultimately leading to death despite resuscitative efforts, illustrates the rapid and unpredictable nature of fulminant TTP.

Emerging data also suggest racial disparities in immune-mediated TTP (iTTP) outcomes, including higher relapse rates and poorer treatment response in Black patients, underscoring the need for timely, and aggressive management (5). In resource-limited settings where ADAMTS13 testing is not readily available, treatment decisions must rely on clinical presentation and tools like the PLASMIC score. This scoring system is especially valuable when diagnostic delays are expected, enabling clinicians to distinguish TTP from other mimicking conditions such as vitamin B12 deficiency and to initiate life-saving interventions like plasma exchange and corticosteroids without delay (8).

Caplacizumab, a nanobody targeting ultra-large von Willebrand factor (UL-vWF), has shown promise in improving outcomes in aTTP. In a recent study, caplacizumab significantly reduced the incidence of major thromboembolic events, aTTP exacerbations, and mortality compared to placebo (11.4% vs. 43.2%), emphasizing its potential clinical benefit (9).

CONCLUSION

TTP remains a hematological emergency requiring rapid recognition and initiation of plasma exchange. Despite current therapies, mortality remains high in severe presentations. This case underscores the necessity of prompt recognition and treatment initiation in TTP, as well as vigilant monitoring for multi-organ involvement, particularly cardiac and renal which are key prognostic determinants. The timely use of caplacizumab and early introduction of rituximab may improve outcomes in similar future cases. Ultimately, this case reflects the aggressive course of severe acquired TTP and highlights the critical role of early diagnosis, multidisciplinary management, and ongoing clinical vigilance.

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