Case Report

Postpartum thrombotic microangiopathy with acute kidney injury: A diagnostic challenge between TTP and atypical HUS

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Abstract

Background: Pregnancy-associated thrombotic microangiopathy (TMA) is a diagnostic challenge because postpartum thrombotic thrombocytopenic purpura (TTP), atypical hemolytic uremic syndrome (aHUS), HELLP syndrome, and secondary TMAs can overlap clinically. ADAMTS13 activity is central to distinguishing TTP from other TMAs, but borderline reductions may not be definitive in pregnancy.

Case Presentation: A 21-year-old primigravida at 33 weeks gestation presented with intrauterine fetal demise and developed postpartum anuric acute kidney injury, severe thrombocytopenia, and microangiopathic hemolytic anemia. She had no hypertension or neurological symptoms. Laboratory evaluation showed elevated LDH (2576 U/L), thrombocytopenia (30,000/μL), anemia (Hb 5.7 g/dL), schistocytes (1.6%), and ADAMTS13 activity of 23%. Liver enzymes were mildly elevated without features of HELLP syndrome.She was treated with hemodialysis and plasma exchange, with subsequent improvement in platelet count and renal function.

Conclusion: This case highlights the diagnostic challenge of postpartum pregnancy-associated thrombotic microangiopathy when ADAMTS13 activity is reduced but not severely deficient. Early recognition, prompt plasma exchange, and renal support were associated with haematologic and renal recovery, emphasizing the need for timely empiric treatment in similar cases despite uncertainty between TTP and aHUS.

Key words: Thrombotic microangiopathy (TMA); Thrombocytopenic purpura (TTP); Atypical hemolytic uremic syndrome (aHUS)

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1. Case Presentation

A 21-year-old primigravida with no known co-morbid illnesses had an intrauterine fetal demise at 33 weeks of gestation and underwent normal vaginal delivery with evacuation at a peripheral hospital. She had no significant antenatal events. She developed mild

postpartum hemorrhage and severe thrombocytopenia, with a platelet count of approximately 30,000/μL. There was a disproportionate drop in haemoglobin compared with the estimated blood loss. She became anuric immediately after delivery and was referred to our center for further management. Four days prior to delivery, she had an episode of malena. There was no history of fever, dysuria, loin pain, vomiting, or other infective symptoms. At presentation, she was found to have severe anemia and thrombocytopenia, with evidence of hemolysis and acute kidney injury. On examination, her blood pressure was 130/70 mm Hg, and there were no neurological deficits.

Laboratory evaluation revealed a hemoglobin of 5.7 g/dL, total leukocyte count of 22,000/μL, platelet count of 39,000/μL, blood urea of 50 mg/dL, and serum creatinine of 3 mg/dL. Lactate dehydrogenase was markedly elevated at 2576 U/L, and D-dimer was positive. She had mild transaminitis, with SGOT 270 U/L and SGPT 123 U/L, while bilirubin and alkaline phosphatase levels were within normal limits.

Her coagulation profile was near normal, with a prothrombin time of 17 seconds and an INR of 1.35. Peripheral smear showed schistocytes comprising 1.6% of red blood cells, along with normocytic normochromic anemia and thrombocytopenia. The PLASMIC score was 6/7.

Pro-calcitonin was markedly elevated at 50 ng/mL. Urine culture grew Enterococcus species, and she was treated with vancomycin. ANA was weakly positive, while complement levels (C3, C4) were normal, and anti-phospholipid antibody screening was negative. Given the clinical picture of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury, a thrombotic microangiopathy was suspected. As her PLASMIC score was 6/7, she was promptly initiated on hemodialysis, followed by plasma exchange. ADAMTS13 activity was found to be reduced to 23%. She required ongoing hemodialysis support. On days 1 and 2, she underwent two sessions of hemodialysis and received two units of packed red blood cells along with fresh frozen plasma. On days 3, 5, and 7, she underwent three sessions of plasma exchange. Further plasma exchange sessions were withheld due to rising platelet counts, improving urine output, and the development of a lower respiratory tract infection.

In total, she received nine sessions of hemodialysis, three sessions of plasma exchange, and two plasma infusions. Following plasma exchange, both urine output and platelet count improved, and dialysis was gradually spaced out.

On follow up, at 45 days postpartum, she is off dialysis, with a serum creatinine of 2.3 mg/dL and urine output of 1.8–2 L/day. Renal biopsy was not performed due to severe thrombocytopenia and subsequent improvement in urine output. Whole-exome sequencing did not identify any definitive pathogenic or likely pathogenic variants associated with an atypical hemolytic uremic syndrome phenotype. Incidentally, a pathogenic X-linked G6PD variant was identified.

2. Discussion

Pregnancy-associated thrombotic microangiopathy is an uncommon but potentially fatal syndrome that includes the 4 major forms:

- Thrombotic thrombocytopenic purpura,
- Complement-mediated thrombotic microangiopathy or atypical HUS
- HELLP syndrome is often seen in condition with pre-eclampsia, and

- TMA associated with APLA syndrome. [1] Other pregnancy-related complications such as sepsis, placental abruption, and postpartum hemorrhage can also present with features like thrombotic microangiopathy.[1]

TTP: Thrombotic thrombocytopenic purpura is caused by severe deficiency of ADAMTS13, the enzyme that cleaves ultra-large von Willebrand factor multimers. When ADAMTS13 is very low, (less than 10%), von-Willebrand factor is not cleaved and platelets aggregate excessively and form micro thrombi in micro circulation causing MAHA (micro angiopathic hemolytic anaemia), thrombocytopenia and specific organ involvement like CNS and kidneys.

Atypical hemolytic uremic syndrome is usually due to alternate complement pathway dysregulation. This leads to uncontrolled complement activation, endothelial injury, and microvascular thrombosis leading to MAHA, low platelets and organ involvement.

The major challenge is that these entities frequently overlap clinically in late pregnancy and the postpartum period, and early treatment often must begin before the exact subtype is confirmed. Reviews of pregnancy-related TMA emphasize that delayed recognition can lead to maternal acute kidney injury, multiorgan failure, placental infarction, and fetal death1 Fetal loss is a well-recognized complication of pregnancy-associated thrombotic microangiopathy (TMA). Both thrombotic thrombocytopenic purpura and other pregnancy-related TMAs have been linked to adverse obstetric outcomes, including intrauterine fetal death, stillbirth, and placental insufficiency. Recent literature further highlights that intrauterine fetal demise is not an isolated finding, but a relatively frequent complication reported across case series of pregnancy-associated TMA.

3. Differences between a-HUS and TTP

	TTP	**a-HUS**
Trigger	It can occur in pregnancy or postpartum, often as immune-mediated or congenital ADAMTS13 deficiency.	Pregnancy and postpartum are classic triggers/unmasking events.
Adamts13	Severe deficiency, typically <10%, strongly supports TTP.	Usually normal or mildly decreased (>10%)
Platelets	Often very low, sometimes profound	Can be low, but thrombocytopenia may be less dominant than in TTP.
Renal involvement	Mild to moderate	Severe dialysis requiring
Neurological involvement	More common (seizures and altered sensorium)	Rare
Fetal loss	Possible	More common than TTP
Response to plasma exchange	Usually dramatic if TTP.	May be partial or transient; definitive therapy is complementing inhibition if aHUS are confirmed

The clinical presentation in this case was most consistent with a pregnancy-associated thrombotic microangiopathy falling within the TTP–aHUS overlap spectrum. Features such as severe thrombocytopenia, microangiopathic hemolytic anemia, markedly elevated LDH, and a favorable response to plasma exchange pointed toward a TTP-like process. In contrast, the postpartum onset, anuric acute kidney injury requiring dialysis, and only moderately reduced ADAMTS13 activity (23%) argued strongly for a complement-mediated aHUS phenotype.

The patient's ADAMTS13 activity was 23%, which does not meet the classical threshold for a definitive diagnosis of TTP. In pregnancy, ADAMTS13 levels can physiologically decline, and borderline values are often difficult to interpret, particularly when samples are obtained after plasma therapy.

Current evidence distinguishes classical TTP from complement-mediated TMA by highlighting that TTP is typically associated with severe ADAMTS13 deficiency (<10%), whereas complement-mediated TMA generally shows preserved or only mildly reduced activity[2]. In this context, the present case falls into a diagnostic gray zone between pregnancy-associated TTP-spectrum disease and complement-mediated TMA.

Literature on pregnancy-associated TMA consistently shows that early plasma exchange improves outcomes when TTP is suspected, and a case series on pregnancy-induced TMA found better renal recovery when plasma exchange was instituted early. Hence plasma exchange shouldn't be delayed for diagnostic certainty.[3]

Renal biopsy was deferred due to severe thrombocytopenia and subsequent clinical improvement in urine output. This approach is justified, as performing a biopsy in the setting of unstable postpartum thrombotic microangiopathy carries a significant risk of bleeding and is unlikely to alter immediate management.

In most reported cases, the diagnosis is established clinically by integrating key features such as postpartum onset, hemolysis, thrombocytopenia, renal dysfunction, and ADAMTS13 activity, rather than relying on histopathological confirmation[1,2].

Normal C3 and C4 levels do not rule out complement-mediated TMA, as many patients with postpartum aHUS have normal complement profiles. In addition, a significant proportion of cases have no identifiable mutation on genetic testing. Therefore, a negative genetic workup should not lower clinical suspicion when the overall phenotype strongly suggests complement-mediated TMA.[4]

The Enterococcus urinary infection and elevated pro calcitonin may have acted as a trigger or confounder but are unlikely to fully explain the micro angiopathic haemolysis and severe thrombocytopenia.

Overall, this case is best framed as -Pregnancy-associated thrombotic microangiopathy with renal-predominant involvement, plasma responsiveness, and borderline ADAMTS13 activity, with differential consideration of TTP-spectrum disease and complement-mediated TMA. The intrauterine fetal demise, postpartum anuria, and severe haemolysis underscore the need for rapid recognition and empiric treatment in similar presentations.

4. Conclusion

Postpartum thrombotic microangiopathy is a high-stakes diagnosis that cannot be missed. Any woman presenting after delivery with severe thrombocytopenia, microangiopathic hemolysis, and acute kidney injury—particularly following fetal loss—should be treated as TMA until proven otherwise. Waiting for diagnostic certainty is a mistake; early initiation of plasma exchange and dialysis can be lifesaving and kidney-saving.

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