What Killed Mrs. Jane Doe?: Overview to Vascular Microthrombotic Disease.

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Background:

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening condition affecting 2 persons/million/year. Clinical management of vascular microthrombotic disease is challenging because of defining clinical and pathologic abnormalities. Diagnosis is made by clinical features, thrombocytopenia, and microangiopathic hemolytic anemia (MAHA), without an alternative explanation. Assessment of these coagulopathies requires a meticulous evaluation of predisposing conditions, overall clinical status, and prompt action. We present two cases with similar features but different pathologies.

Case # 1:

A 33-year-old male, with no medical history, was evaluated for altered mental status, fever & malaise. His family history was non-contributory. Labs showed MAHA with thrombocytopenia. Peripheral smear revealed schistocytes **(Figure 1**). Direct Coomb's was negative with normal fibrinogen. Chemistries showed acute kidney failure. D-dimer, LDH, total-bilirubin, reticulocyte count, PT/INR (15.5 secs/ 1.3) and CRP (46 mg/dL) were elevated. The ANA was negative. The patient had PLASMIC score of 6, plasmapheresis was initiated. One week later, labs showed ADAMTS13 deficiency (<0.03 IU/mL), and presence of anti-ADAMTS13 inhibitor.

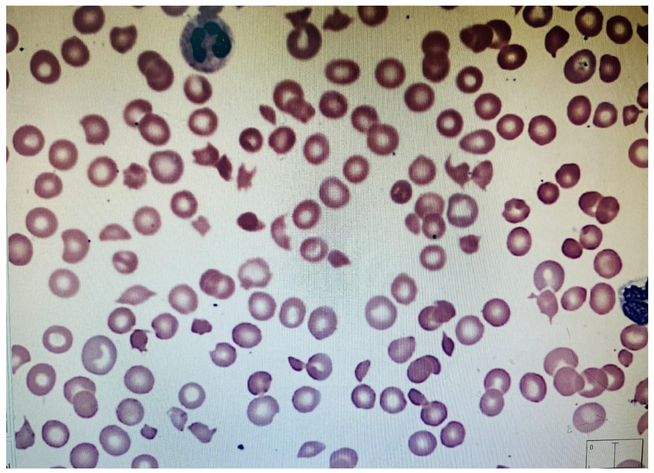
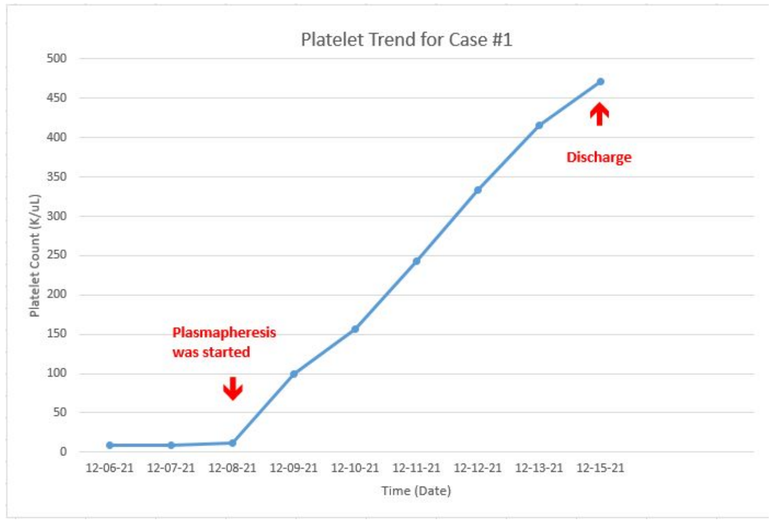
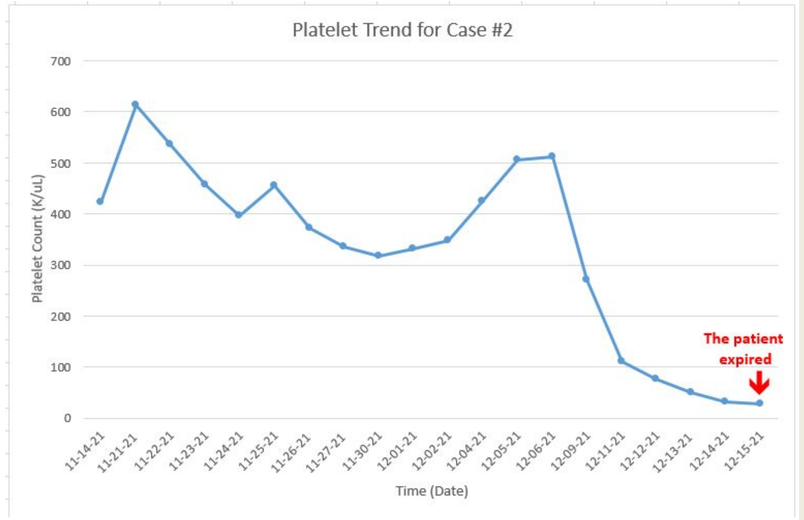


Figure 1: Peripheral blood smear showing microangiopathic hemolytic anemia with marked red cell fragmentation.



Case #2:

A 65-year-old female evaluated for altered mental status, sudden right-facial palsy, and hemiparesis. Her medical history is non-contributory. Thrombolytic therapy was administered for acute stroke and underwent thrombectomy. Labs showed MAHA with thrombocytopenia. Peripheral smear revealed 1+ schistocytes. Direct Coomb's was negative with normal fibrinogen. Chemistries showed acute kidney failure. D-dimer, LDH, total-bilirubin, reticulocyte count, PT/INR (13.0 secs/ 1.1), CRP, and ESR were elevated. The ANA titer was 1:40, negative SCL-70 Ab, with low C3. Given PLASMIC Score of 4, plasmapheresis was not indicated. However, due to worsening clinical course it was initiated. The patient expired before lab workup reported ADAMTS13 deficiency (0.52 IU/mL).



Conclusion:

Diagnosing TTP is challenging given the rarity, high-mortality, and precise cause. ADAMTS13 results may take days, leaving physicians to diagnose and treat based on clinical findings and routine labs. TTP is diagnosed based on the presence of thrombocytopenia and MAHA, with/without severe-end-organ damage. MAHA may be seen in other diseases including Hemolytic Uremic Syndrome (HUS), DIC, infection, severe hypertension, or malignancy. ADAMTS13 is important for effective diagnosis. In its absence, PLASMIC scores help determine ADAMTS13-deficiency.

PLASMIC SCORE		
Parameter	**Result**	**Score**
Platelet count	<30K	1
Creatinine	<2	1
INR	<1.5	1
MCV	<90	1
Presence of hemolysis variable	Either: - Reticulocytes >2.5% - Undetectable haptoglobin or - Indirect Bilirubin >2	1
Absence of active cancer		1
No prior stem cell or organ transplant		1

PLASMIC scores of 0-4, 5, and 6-7 are said to correspond to low, intermediate, and high probability of TTP, respectively.

Case 2 was "Complement-mediated atypical HUS (aHUS)" masqueraded as TTP. Complement-mediated aHUS is a thrombotic microangiopathy which mimics TTP. Diagnosis of aHUS is supported by the presence of thrombocytopenia, hemolytic anemia, renal failure, low C3, and ADAMTS13 >0.10, making TTP less likely. Ineffective response to plasmapheresis further supported the diagnosis of aHUS.

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