

The Management for Thrombotic Thrombocytopenic Purpura in Pregnancy

Wang A, Martin E, and Weinstein L

Background:

- Thrombotic thrombocytopenic purpura (TTP) is a rare life-threatening disorder with the classic triad of microangiopathic hemolytic anemia, thrombocytopenia, and thrombosis
- Pathophysiology:
 - Deficiency in ADAMTS13
 - Acquired (most common):
 - Autoantibodies against ADAMTS13 leading to an immune mediated breakdown
 - Risk factors: Autoimmune disorders, HLA subtypes, female gender, and African Americans
 - Hereditary:
 - Gene mutation in ADAMTS13
 - vWF will form multimeric complexes which is regulated by ADAMTS13
 - ADAMTS13 is a protease that is responsible for the cleavage of large multimeric vWF complexes
 - Deficiency of ADAMTS13 leads to excessive formation of large multimeric vWF complexes inducing a prothrombotic state
- Precipitating factors:
 - Pregnancy: Increase gestational age leads to a decrease in ADAMTS13
 - Inflammation/ infections/ sepsis
- Symptoms
 - Initial symptoms: easy bruising, fatigue, and dyspnea
 - Neurological symptoms (~60%): headache, coma, stroke, seizures, and death
 - Mesenteric ischemia (~35%)
 - Heart ischemia (~25%)
 - Renal involvement is usually mild: proteinuria and hematuria
 - acute renal failure is rare
- Prognosis:
 - Without treatment, mortality rate is ~95%
 - With plasma exchange therapy, survivability is ~85%

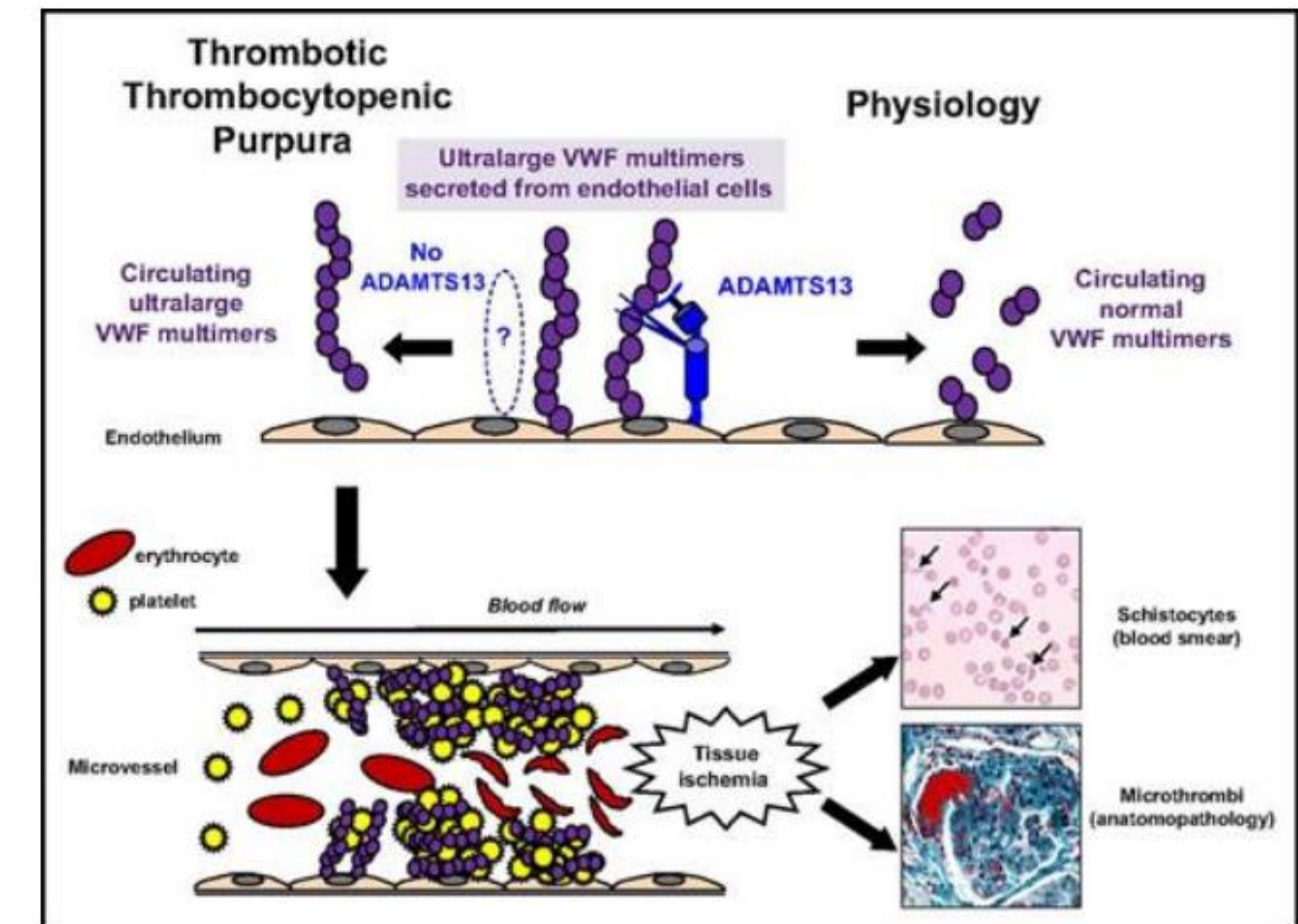


Fig 1: Pathogenesis of TTP caused by ADAMTS13 deficiency
Adapted from "Thrombotic thrombocytopenic purpura," by B.S. Joly, P. Coppo, A. Veyradier, 2017, Blood, Volume 129, Number 21, P. 2835-2844. Copyright 2017, American Society of Hematology.

The Management for Thrombotic Thrombocytopenic Purpura in Pregnancy

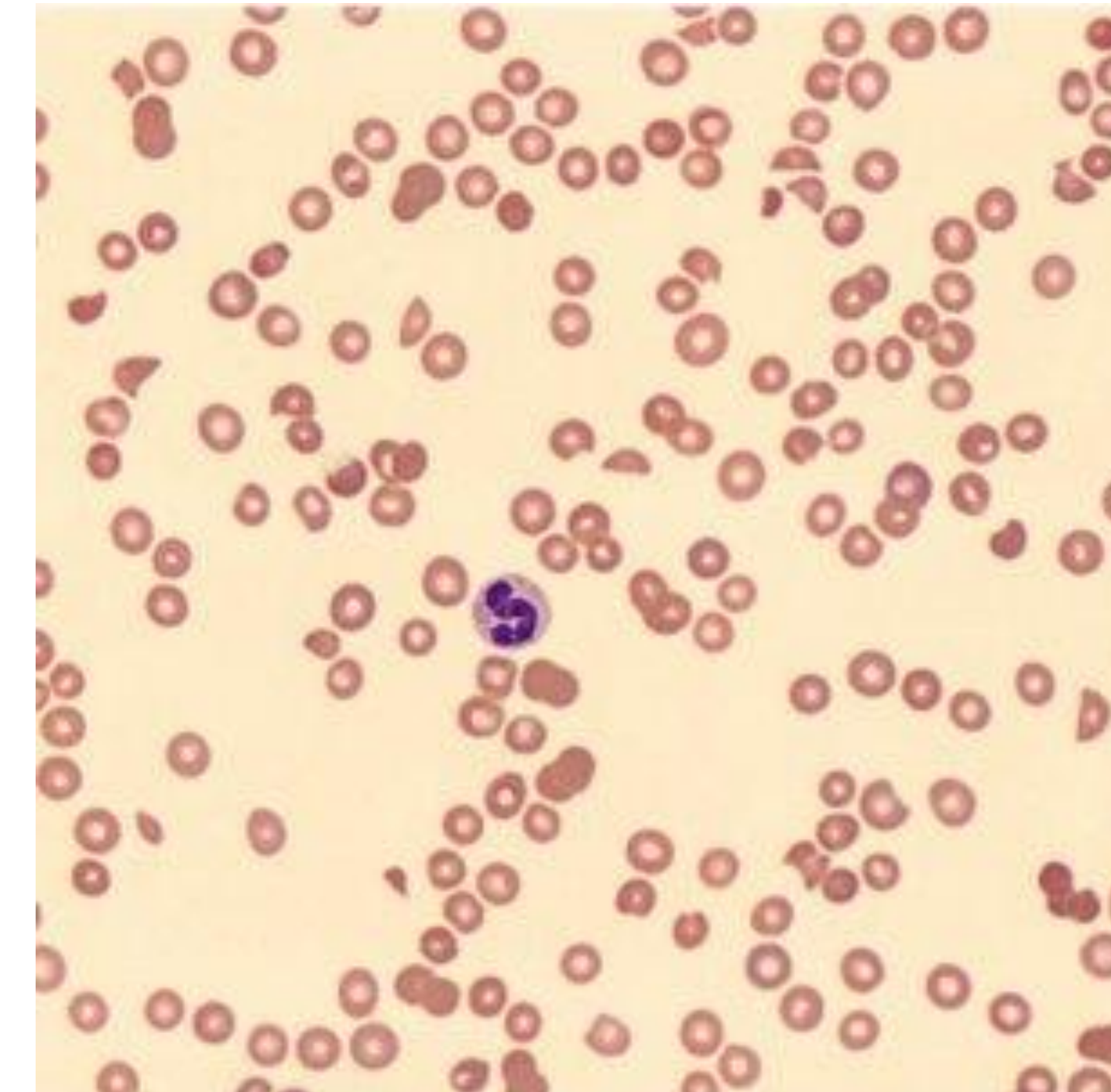
Wang A, Martin E, and Weinstein L

Case:

- 24 yrs. old G2P1 at 30 weeks and 0 days of gestation presented for diffuse bruising and hematuria.
- PMH: Asthma, previous cesarean delivery, and currently on treatment for pyelonephritis
- Initial laboratory test:
 - Hgb 5.7, platelets of 9000 microL
 - Creatinine of 1.18.
 - Lactate dehydrogenase 1289 Iu/L and reticulocyte count of 8%
 - Peripheral blood smear demonstrated an abundance of schistocytes
- Multidisciplinary approach: intensivist, hematologist, nephrologist, perinatologist, and anesthesiologist were formed to discuss the management of the complex parturient.
 - Initial differentials included ITP, TTP, HUS, and HELLP syndrome
 - TTP was higher on the differential due to an elevated PLASMIC score of 6 and ADAMTS13 activity level pending.
 - A right internal jugular dialysis catheter was inserted, and the parturient underwent 3 rounds of plasma exchange therapy. Initiation of high dose steroid and received multiple blood transfusions
- During her hospital course, the parturient developed severe range blood pressures unresponsive to antihypertensive treatment
 - She was diagnosed with pre-eclampsia with severe features and was delivered via urgent cesarean delivery at 30 weeks and 3 days of gestation

Intraoperative course:

- A preinduction arterial line was placed
- General anesthesia with an endotracheal tube was performed.
- The neonate was born successfully with an APGAR score of 5 (1 minute) and 8 (5 minutes)
- Significant intraoperative bleeding occurred with an estimated QBL of 1500cc
 - Uterotonics: Oxytocin bolus
 - Blood products: 1U PRBC, 1U FFP, and 8U platelets
 - Others: 1g tranexamic acid
- Hemostasis and hemodynamic stability was achieved, the patient was extubated and brought to the post-operative care unit on Labor and Delivery



Peripheral blood smear demonstrating schistocytes

PLASMIC Score

- Presumptive diagnosis of TTP, while ADAMTS13 activity level pending
- Each category is given +1 point
 - Platelet count <30,000/microL
 - Hemolysis
 - No active cancer
 - No solid organ or stem cell transplant
 - MCV <90 fL
 - INR <1.5
 - Creatinine <2.0mg/dL
- Likelihood
 - High probability: 6 to 7 points
 - Suggest ADAMTS13 activity <10%
 - Intermediate probability: 5 points
 - Low probability: 0 to 4 points

The Management for Thrombotic Thrombocytopenic Purpura in Pregnancy

Wang A, Martin E, and Weinstein L



Postoperative course:

- Parturient underwent another round of plasma exchange therapy
- Discharged on post-operative day 6 and the neonate was discharged home after several weeks
- During her hematology follow-up:
 - The initial ADAMTS13 activity resulted with <5% activity and negative ADAMTS13 antibody
 - Follow-up laboratory results were concerning for another TTP flare, and she was readmitted to the hospital for another round of plasma exchange therapy
 - She was diagnosed with congenital TTP

Learning points:

1. Congenital TTP can be exacerbated by pregnancy and can occur even after an uncomplicated prior pregnancy
2. Initiation of plasmapheresis should occur early and has significantly improved survival for patients experiencing TTP
3. A multidisciplinary team is essential to improve both maternal and fetal outcomes

Reference:

- Bérangère S. Joly, Paul Coppo, Agnès Veyradier; Thrombotic thrombocytopenic purpura. *Blood* 2017; 129 (21): 2836–2846. doi
- Scully, Marie, et al. “Thrombotic Thrombocytopenic Purpura and Pregnancy: Presentation, Management, and Subsequent Pregnancy Outcomes.” *American Society of Hematology*, American Society of Hematology, 10 July 2014,
- Soffer, Marti D, et al. “Congenital Thrombotic Thrombocytopenic Purpura (TTP) with Placental Abruptio despite Maternal Improvement: A Case Report.” *BMC Pregnancy and Childbirth*, U.S. National Library of Medicine, 15 June 2020,