Thrombotic thrombocytopenic purpura in pregnancy

Thrombotic thrombocytopenic purpura (TTP), characterized by profound thrombocytopenia and microangiopathic hemolytic anemia, is a life-threatening syndrome. The incidence of TTP is reported to be one in 25,000 pregnancies. TTP may be associated with germ-line mutations in ADAMTS13 (A Disintegrin And Metalloprotease with Thrombospondin Type 1 Repeats, 13) gene. ADAMTS13 cleaves von Willebrand factor (VWF) that reduces its adhesive function. The mutations in ADAMTS13 gene result in retention of ADAMTS13 protein inside cells or secretion of non-functional mutant proteins, which leads to severe deficiency of plasma ADAMTS13 activity. TTP may also occur in pregnancy de novo, which is caused by acquired autoantibodies against ADAMTS13 protein, inhibiting plasma ADAMTS13 activity. Deficiency of plasma ADAMTS13 results in an accumulation of ultra large VWF multimers on stimulated or injured endothelial cells or in circulation, leading to exaggerated platelet aggregation and thrombus formation in small arteres and capillaries. TTP may present in the first, second, and third trimester or in postpartum. Without treatment, TTP is uniformly fatal. Plasma infusion or exchange therapy dramatically reduces maternal and infant mortality rate, but remains as high as 10-20%, especially when TTP occurs concurrently with preeclampsia. Clinical recognition and use of proper laboratory tests to diagnose TTP during pregnancy are crucial for reducing mortality rates. We have recently developed tests in the laboratory for assessment of plasma ADAMTS13 activity, antigen, inhibitors, and gene mutations. These diagnostic tests help confirm diagnosis and provide molecular basis for differential diagnosis with many pregnancy-associated complications including hemolytic uremic syndrome, preeclampsia, HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelets) syndrome, acute fatty liver, and disseminated intravascular coagulation (DIC). Plasma infusion and/or plasma exchange remains the mainstay of treatment for TTP. Immunosuppressive therapy including corticoid steroid, cyclosporine, and rituximab may be used for patients with inhibitors or patients who relapse. However, the safety of using the immunosuppressive therapy during pregnancy remains to be evaluated. In summary, significant progresses have been made in the last decade in the understandings of pathogenesis of TTP, development of diagnostic tools, and treatment of TTP in pregnancy.

Biography
Long Zheng completed his M.D. from Nanchang University in China and Ph.D. from Medical University of Vienna in Austria. He subsequently completed his residency in Clinical Pathology and fellowship in Transfusion Medicine from Washington University in St. Louis, Missouri. Dr. Zheng is currently an associate professor of pathology and laboratory medicine in the University of Pennsylvania Perelman School of Medicine and director of Hematology and Coagulation Laboratories at the Children’s Hospital of Philadelphia. He is an Established Investigator of American Heart Association and National Institute of Health with research projects on biology and chemistry of ADAMTS13 metalloproteinase and pathogenesis of TTP. Dr. Zheng is also a member of editorial boards of Hereditary-Genetics, Journal of Biotechnology and Biomaterials, and The World Journal of Stem Cell.