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Rainbow of Hemolysis Associated With Acquired Thrombotic Thrombocytopenic Purpura

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Graphical Abstract

Keywords

hemolysis; TTP; plasma; plasma free hemoglobin; cell-free hemoglobin

Acquired thrombotic thrombocytopenic purpura (TTP) is a rare disease characterized by thrombocytopenia and microangiopathic hemolytic anemia. Autoantibodies directed against the von Willebrand Factor (vWF)-cleaving enzyme, ADAMTS13, result in ultra-large vWF multimers consuming platelets and forming platelet-vWF microthrombi. Hemolysis occurs as red blood cells (RBCs), thought to be innocent bystanders in the pathophysiology of TTP, are damaged while attempting to traverse the thrombi-narrowed microvasculature. Schistocytosis and biochemical markers of hemolysis, including worsening anemia, decreased haptoglobin, and elevated cell-free hemoglobin, subsequently appear. Circulating cell-free hemoglobin can cause a variety of deleterious effects, including nitric oxide sequestration, oxidative injury, and extravascular translocation into tissues [1,2]. The diverse hues of hemolysis in the image illustrate the severity of TTP.

The examples in the image are plasma specimens from 15 unique patients in our institution's TTP biosample repository, all of whom had severe deficiencies of ADAMTS13 activity (<10% of normal levels). These specimens have been collected from the aforementioned TTP patients during their initial presentations immediately prior to their first therapeutic

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plasma exchanges (TPE) with plasma replacement, which is first-line therapy [3]. Upon visual inspection, there is overt, but variable, cell-free hemoglobin attributed to intravascular hemolysis in the plasma of all of these TTP patients. With the increasingly recognized importance of cell-free hemoglobin and associated molecules in different conditions such as sickle cell disease, sepsis, acute respiratory distress syndrome, extracorporeal circuits, malaria, and RBC transfusion, the hemolysis in TTP may make RBCs less innocent than previously suspected [4]. While TPE with plasma replacement removes the pathogenic autoantibodies and replenishes ADAMTS13, it also decreases circulating cell-free hemoglobin and replenishes depleted haptoglobin reserves, all of which are beneficial. Though no specific therapies for mitigating the detrimental impacts of hemolysis are currently approved in the United States, cell-free hemoglobin may provide another target to optimize in the care of TTP patients [2,5].

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