**Complement activation in hematological diseases – how innate immunity induces red blood cell destruction**

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As an efficient effector system of the innate immunity the complement system plays a crucial role in the defense against infectious agents, e.g bacteria. However, deficiency of complement factors, inadequate regulation and/or overwhelming activation of the complement system may be harmful to the host. Patients suffering from autoimmune hemolytic anemia (AIHA), paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS) are complement-mediated rare diseases treated by the hematologist. Until recently, these diseases could not or only inadequately be treated. However, with the availability therapeutic complement inhibitor these complement-mediated diseases can now efficiently be treated and hence outcome of these patients significantly improved. The comprehension of physiology of complement system is a “sine-qua non” to understand complement activation and its defective regulation in diseases, such as e.g PNH. Classical complement activation is crucially involved in the pathogenesis of AIHA mediated by IgM autoantibodies. Inhibitors targeting the classical pathway of complement turned out to inhibit hemolysis and improve red blood cell recovery upon transfusion in AIHA patients. The absence of GPI-linked complement regulators on cellular surfaces is the underlying cause of hemolysis induced by uncontrolled activation of the alternate complement pathway in PNH patients. Treatment with antiC5 inhibits intravascular hemolysis, prevents fatality and improves outcome. Other inhibitors targeting C3 activation seem to be efficient as well. Atypical HUS is characterized by inadequate regulation of the alternate pathway by dysfunctional or absent plasmatic complement regulators. Treatment with complement inhibitors or substitution of plasmatic complement regulators may halt hemolysis and improve renal function leading to a better outcome of these patients. Targeted therapy to inhibit complement activation or restore complement regulation are an established approach to treat complement-mediated disease in hematology.