Faculty Abstract:

Diagnostic Workup and Management of Monoclonal IgM-related Cold Agglutinin Disease

Introduction: Cold agglutinin disease (CAD) is an autoimmune hemolytic anemia mediated by monoclonal cold agglutinins (CA). CA's are able to agglutinate erythrocytes at low temperatures as well as cause complement mediated hemolysis. CA are usually of the IgM isotype, and produced by clonal B-lymphocytes/plasmacells in the bone marrow. While CA's may also occur in WM patients, the CAD clone has distinct properties. CA's can result in heterogeneous clinical and hematologic presentation, where hemolytic anemia and cold induced peripheral symptoms may both be present, or only one of the two.

Main points that will be discussed:

- The diagnosis of Cold Agglutinin Disease, including erythrocyte serology testing, bone marrow pathology, including the new WHO entity CAD-LPD and the distinction from WM
- Current treatment options for CAD, including anti-CD20 antibodies, immunochemotherapy and complement inhibitors
- Management of fulminant/severe CAD
- Novel development and future perspectives for CAD treatment

In conclusion, the pathological properties of the IgM paraprotein that behaves as a cold agglutinin may lead to hemolytic as well as non-hemolytic (circulatory) symptoms. Treatment can be clone directed or complement directed. Correct diagnostic classification of the underlying B-cell disorder can be challenging, but MYD88 mutational testing may help make the distinction from WM.