Complement deficiency and susceptibility to autoimmune disease

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The complement system involves a cascade of proteins that recognise, bind and facilitate the elimination of invading pathogens. Complement is important for the identification, opsonization, and proper disposal of apoptotic cells, cellular debris and immune complexes. Inability to efficiently clear apoptotic cells could result in a source of autoantigens and drive autoantibody production. In addition, delivery of complement opsonised self-antigens to autoreactive B-cells contributes to anergy and diverts them from germinal centre reactions.

Deficiencies of early complement components (C1q, C1r, C1s, C4 and to a lesser extent C2) are strongly associated with increased risk of developing SLE or a lupus-like disease. Affected individuals with autosomal recessive disease tend to present in early childhood and experience severe morbidity with significant mortality.

This talk will concentrate on C1q deficiency, which is associated with high risk of lupus-like disease and infection, disease response to replacement via plasma infusions and the potential role of haematopoietic stem cell transplantation. HSCT is a viable option because unlike most other complement components in blood, the primary site of C1q biosynthesis is not in the liver, but in myeloid cells including macrophages, monocytes, and dendritic cells.