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Atypical hemolytic uremic syndrome

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Thrombotic microangiopathy (TMA) is defined by specific clinical characteristics, including microangiopathic hemolytic anemia, thrombocytopenia, and pathologic evidence of endothelial cell damage, as well as the resulting ischemic end-organ injuries. Among the TMA disease categories, atypical hemolytic uremic syndrome (aHUS) is caused by a genetic or acquired defect in regulation of the alternative complement pathway. The alternative pathway is spontaneously and continuously active on biological surfaces in plasma and in other bodily fluids and requires a unique system of regulation. Genetic variants leading to inappropriate activation of the alternative pathway cause predisposition to aHUS, with or without triggering factors. A variety of mutations in complement regulators have been reported as the causes of aHUS. It is important to consider the possibility of aHUS caused by genetic defects in all patients who exhibit TMA with triggering conditions such as infection, malignancy, pregnancy, transplantation, malignant hypertension, medications and autoimmune disease because of the incomplete genetic penetrance of aHUS. Therapeutic strategies for aHUS have been based on resolution of dysregulation in the complement system. Recently, eculizumab, a humanized monoclonal antibody directed against complement C5, has been proven to be effective against aHUS.

Based on this existing knowledge, the contents to be discussed in this lecture can be divided into the following three categories.

Firstly, the clinical practice guidelines and consensus regarding diagnosis and management of aHUS in Korea has been published by the expert group, and the main latest knowledge will be introduced.

Secondly, the genetic results of aHUS in Korea will be presented. Previously, in a multicenter study of 51 Korean children with aHUS, disease-associated variants were detected in 22% patients, and the prevalence of anti-CFH autoantibody was 29%. In the recent genetic study of Korean adult aHUS, 45% had at least one aHUS-related variants, and no patients had anti-CFH autoantibody. These findings suggest the age-dependent differences of genetic causes in aHUS.

Thirdly, since the introduction of eculizumab in Korea, it is necessary to estimate the current status of eculizumab administration and the efficacy of eculizumab in aHUS patients. Recently, the scope of use of eculizumab is expanding to transplant-associated TMA. It is possible that the genetic defects resulting in aHUS might coexist in transplant-associated TMA patients. Therefore, it is useful to examine the diagnosis and indications for administration of eculizumab when transplant-associated-TMA is associated with complement system activation.