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Clinical impact of complement binding assay

Myung-Gyu Kim
Korea University Anam Hospital, Korea, Republic of

Donor-specific antibodies (DSA) before and after transplantation are not only a major risk factor for poor transplant outcomes in the long term, but they also become important indicators in the diagnosis of acute or chronic antibody-mediated rejection (AMR). However, since the presence of a DSA in the blood is not necessarily associated with deterioration of renal function, careful interpretation is needed. In order to determine whether or not to treat DSA, it is necessary to discriminate the pathogenic DSA that causes AMR. Recently, several clinical studies have been reported to verify whether antibodies that react with complements such as C1q and C3d or antibodies with high mean fluorescent intensity (MFI) are associated with AMR. In 2013, Loupy et al. collected blood from 1,016 recipients at the time of transplantation, one year later, or during an episode of AMR, and analyzed antibodies that bind to C1q complement. They observed that patients with C1q binding DSA were at high risk of AMR and graft loss. In addition, several studies have demonstrated that DSA binding to the C1q or C3d complement is useful in predicting the desensitization response to AMR. However, it is not clear whether classification of DSA based on complement binding capacity could be an indicator of whether or how to treat AMR.
Although complement activation is important as a mechanism for AMR, non-C1q binding antibodies are found in patients with chronic AMR and complement-independent pathway can be an important mechanism of antibody-mediated graft injury. Therefore, further studies are needed to elucidate the clinical usefulness of the complement dependent assay in kidney transplantation. Developing diagnostic and therapeutic guidelines that combine complement binding capacity with other antibody-related indicators such as intensity, subtype of antibodies and clinical factors is an important challenge in overcoming AMR and improving long-term graft outcomes.