KSN 2021
FULLY VIRTUAL MEETING
September 02 (Thu) - 05 (Sun)

Abstract Submission No. : 9069

ABO-incompatible kidney transplantation. ~ Overcoming immunological barrier of ABO- carbohydrate antigen ~

Kazuhide Saito
Niigata University, Japan

Since 1960's, ABO-incompatible kidney transplantation (ABO-iKTx) has been recognized as an "immunologically contraindication". However, Slapak and Alexandre had opened the door in early 1980's utilizing plasmapheresis and splenectomy. Owing to the shortage of deceased donors, we have performed ABO-iKTx to expand the indication for living donor kidney transplantation since 1989. During the past three decades, more than 3,000 ABOi-KTx were performed in JAPAN.

We have been making a lot of efforts to improve the outcome from the clinical aspect and from translational research to elucidate the mechanism of acute antibody-mediated rejection in order to overcome the ABO barrier.

At first, we have abandoned splenectomy and utilized Rituximab, anti-CD20 monoclonal antibody with CNI/ MMF in preoperative "desensitization" since 2004. The success rate has reached 96.4% for 1-year, 91.2% for 5-year graft survival, similar to outcomes of ABO compatible kidney transplantation (ABO-cKTx). This dramatic improvement in results means that ABO-iKTx has become accepted as a therapeutic alternative for end-stage renal failure. Today ABO-IKTx accounts for approximately 30% of all living donor kidney transplantations performed in JAPAN.

Second, From careful and precise clinical observations, we have revealed that antibody mediate rejection(ABMR) after ABO-iKTx prone to occur from 2 to 14 days after surgery and cease after a few weeks. We named the former as " critical period" and the latter as " stable period". With an effective and appropriate " desensitization", Majority of recipients can get over the critical period and attain into stable period. In this stage, anti-donor type A/B antibody level become stable in the low titer and ABMR does not occur anymore. We have defined this stage as " immunological accommodation" which means that "the lack of reaction between ABO blood group antigens on the surface of endothelial cells within the graft and these antibodies in the blood of recipient, i.e. graft survival without ABMR."
Third, we have also made a lot of efforts to elucidate the mechanism of the induction and maintenance of "immunological accommodation" ABO carbohydrate antigens on the

endothelial surface of the graft remain stably expressing and its transferase are continuously produced. On the contrary, Anti-donor type AB antibody production would be decreased and remain suppressed both in vivo and in vitro. However, the incidence of microscopically thrombotic microangiopathy(TMA) likely to be observed in ABO-iKTx. These phenomenon shows the possibility of the underlining mechanism and switch which introduce the " immunological accommodation" and its maintenance. Other laboratory in Japan have reported the possible mechanism of AB carbohydrate antigen –A/B antibody reaction on the endothelial cell surface would suppress the complement activation by certain intracellular signal transduction.

Another problem is the anti-A/B antibody titration. As all of you know that pre- and post-operative antibody titer would be variable in a wide range and sometimes does not directly reflect the clinical outcome. Some patients with high titer does not develop ABMR, however, the other with low titer develop sever ABMR or TMA. Even though in patients who established the accommodation, anti-donor AB antibody titer sometimes versatile. One suspected reason of this would be the titration assay is still depend on the classical method of agglutination utilizing "standard red blood cell(RBCs). We have revealed by proteomic analysis, AB-carbohydrate blood group antigens in kidney endothelial cells are structurally different from those on the red blood cells(RBCs). From this fact and clinical variance, we have reached the hypothesis that the structural difference of ABO histo-blood group antigens and corresponding antibody production would be the key and keyhole of the development of acute ABMR in ABO-iKTx. In the next stage, we would like to develop the new system to identify the "truly reactive" antibody against AB carbohydrate antigen on the kidney endothelial graft.

In conclusion, ABO-iKTx has become the alternative choice of treatment of end-stage kidney disease. In near future, the true understanding of the induction and maintenance mechanism of "immunological accommodation" and achievement of detection / titration of the truly harmful anti-AB antibody against graft endothelial cells would establish the more safe, reliable and confident strategy of ABO-iKTx.