

Overcoming the ABO Incompatibility Barrier in Pediatric Renal Transplantation

SIDHARTH KUMAR SETHI, *PRANAW JHA, *SHYAM BIHARI BANSAL AND VIJAY KHER

*From Kidney and Urology Institute; and *Renal Transplant Institute; Medanta, The Medicity Hospital, Gurgaon, Haryana, India.*

Correspondence to:

*Dr Sidharth Kumar Sethi,
Pediatric Nephrology, Kidney and Urology
Institute, Medanta, The Medicity Hospital,
Gurgaon, Haryana 122 001, India.
sidsdoc@gmail.com*

Received: December 18, 2014;

Initial review: January 27, 2015;

Accepted: May 28, 2015.

Background: ABO blood type incompatibility between a donor and recipient is generally considered a contraindication to kidney transplantation. **Case characteristics:** A 12-year-old boy presented with end stage renal disease (blood group B), with the only healthy available donor being mother (blood group AB). The child received renal transplant with mother as the donor, with a designed desensitization and immunosuppressive protocol. **Observation:** At 6 months, child is doing well, with stable graft function. **Message:** ABO-incompatible kidney transplantation is a valid alternative for children with end stage renal disease. This is the first report from India of a Pediatric ABO incompatible renal transplant.

Keywords: *Blood group, Kidney, Renal transplantation.*

Kidney transplantation is considered an optimal therapy for all children with end stage renal disease; there is better longevity, quality of life and cost-effectiveness in comparison to long-term maintenance dialysis. Due to a severe shortage of suitable cadaveric donors, most pediatric patients receive a kidney from their living relatives. If an appropriate living related donor is not available, a child may have to wait for a considerable period of time for a cadaveric donor. In such circumstances, blood group ABO incompatibility was regarded as a major obstacle in screening potential living donors. ABO blood type incompatibility between a donor and recipient is generally considered to be a contra-indication to kidney transplantation because of the risk of preformed antibody-mediated hyperacute rejection [1]. With significant advances in technology and improved understanding of the nature of the ABO antigens and their distribution, several series of successful adult and pediatric ABO-incompatible transplant have been reported [1-4]. We report a case of 12-year-old boy, who received a successful ABO incompatible renal transplant from his mother.

CASE REPORT

A 12-year-old boy presented to our hospital with Stage 5 chronic kidney disease (CKD) and severe hypertension due to reflux nephropathy. He was started on maintenance hemodialysis and supportive care. The options of renal transplantation were discussed. The blood group of the patient was B+, and no family member had the compatible blood group, despite an extensive search for 6

months. The patient's mother had blood group AB+.

His current weight was 36 kg, height 140 cm, and body surface area 1.18 m². His baseline viral serology status was cytomegalovirus (CMV) (IgG Mother +, Child +) and Epstein-Barr Virus (EBV) (Mother +, Child -).

After discussing the risk and benefits of ABO incompatible transplant, the mother was selected as the donor. A flow-cytometry cross-match was negative. His baseline anti-A antibody titer was 1:16. He received injection Rituximab (170mg/m²) two weeks prior to transplant, and regular immunosuppression (Tacrolimus 0.05mg/kg and Mycophenolate 600mg/m²/dose) was started a week prior to tentative date of transplant. He was planned for double filtration plasmapheresis (one plasma volume) two days before surgery. The first session of double filtration plasma-pheresis was followed by intravenous immunoglobulin (IVIG) 5 g (0.2 g/kg/dose) (**Fig. 1**). He received another session of plasmapheresis in view of rebound rise in anti-A titer. He required two units of fresh frozen plasma in view of deranged prothrombin time after the second plasmapheresis.

The dose of tacrolimus (0.1 mg/kg daily) was increased from a day before surgery. He was transplanted in October 2014, with pre-operative anti-A titers of 1:4. He was given induction with intravenous basiliximab 10 mg on days 0 and 4 and intravenous methylprednisolone 400 mg on day 0 followed by oral prednisolone 40 mg that was tapered to 20 mg daily. Target blood levels of tacrolimus in initial three months were 9-12 ng/mL, 4-6 months 6-8 ng/mL and 4-6 ng/mL thereafter. He is

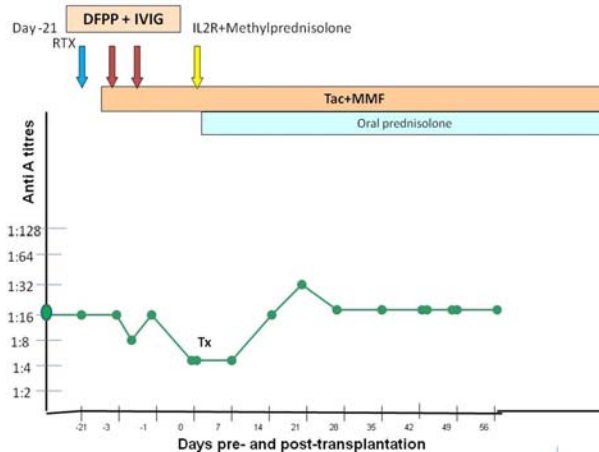


FIG. 1 The trend of antibodies with immunosuppression in the present case. DFPP: double filtration plasmapheresis; IVIG: Intravenous immunoglobulin; Tac: Tacrolimus; MMF: Mycophenolate mofetil; Tx: Date of transplant; RTX: Rituximab; IL2R: Interleukin-2 receptor antagonist Basiliximab. (See color image at website).

currently on twice daily dosing of Tacrolimus to maintain the required levels, and is on tapering prednisolone and mycophenolate mofetil.

Post-operatively, anti-A titers were monitored daily for a week, twice weekly for 4 weeks, and then weekly for 4 weeks, and then done only if there was a renal dysfunction. Initially, his anti-A titers rose to 1:32 on 15th postoperative day but then declined to 1:16 thereafter. Post-operatively, he had a progressive decline in serum creatinine to 0.5 mg/dL. There was no episode of graft dysfunction/rejection. The child has now completed 6 months of valganciclovir and trimethoprim prophylaxis. Currently, he is 6-months post-transplant with a stable graft function, serum creatinine 0.6 mg/dL with a normal urine microscopy and no proteinuria (urine protein/creatinine ratio 0.08), and negative for opportunistic infections.

DISCUSSION

Until recently up to one-third of potential kidney donors had to be excluded from living donation due to ABO incompatibility or had to undergo aggressive pre-conditioning protocols to overcome the immunological barrier and to enlarge the pool of potential living donation [2,3]. After introduction of rituximab, immunoabsorptive columns, and better understanding of biology in renal transplantation, ABO incompatible transplantation seems a feasible option, without the need for splenectomy, and with lower dosing of rituximab [3-5].

Our center earlier reported an 18-yr-old adolescent with ABO incompatible transplant [6]. Our departmental

threshold of anti-blood group antibody is 1:8, and the child achieved 1:4 anti-A pre-transplant titers (post plasma exchange), which is considered safe to transplant. There is no clear consensus on pre-transplant titer. Although some use the goal of a titer of 8 or less before surgery, there are centers that use higher-titer goals, and report excellent results.

Several investigators have demonstrated that lowering the titer of the offending anti-ABO antibodies pretransplantation, and maintaining such lowered levels for several weeks post engraftment, allows allograft survival even when antibodies later return to predepletion levels, and despite the presence of normal levels of complement. The apparent resistance of a vascularized graft to humoral rejection despite the presence of antibodies directed against the donor endothelium is called accommodation. There are several mechanisms involved in accommodation such as disruption of normal signal transduction, reduced cellular adhesion and prevention of apoptosis [7]. It has also been proposed that this may happen due to inactivation of glycosyltransferase enzyme during ischemia reperfusion injury. Hence, fewer blood group antigens are expressed on donor endothelium thereby reducing the immunogenicity [8]. Acute antibody-mediated rejection in an ABO incompatible renal transplant, almost always occur in first two weeks of renal transplant, which is the time taken for accommodation to set in [7-9]. Hence, most important requisite for successful ABO incompatible renal transplant is to achieve low antibody titer at the time of transplant and in two weeks post-transplant [9,10]. Therefore, the management of the child and the complications (including infections and acute rejection) does not differ from a normal transplant, as the body has accommodated the incompatibility.

There are reports of comparable results of ABO incompatible and ABO compatible renal transplantation in adults and children [1-4]. This report is to emphasize to pediatricians that ABO incompatibility does not always mean loss of hope for children with end stage renal disease.

REFERENCES

1. Shishido S, Hasegawa A. Current status of ABO-incompatible kidney transplantation in children. *Pediatr Transplant.* 2005;9:148-54.
2. Shishido S, Hyodo YY, Aoki Y, Takasu J, Kawamura T, Sakai KK, *et al.* Outcomes of pediatric ABO-incompatible kidney transplantations are equivalent to ABO-compatible controls. *Transplant Proc.* 2012;44:214-6.
3. Ohta T, Kawaguchi H, Hattori M, Takahashi K, Nagafuchi H, Akioka Y, *et al.* ABO-incompatible

- pediatric kidney transplantation in a single-center trial. *Pediatr Nephrol.* 2000;14:1-5.
4. Schaefer B, Tönshoff B, Schmidt J, Golriz M, Mehrabi A, Gombos P, *et al.* Bleeding complications in pediatric ABO-incompatible kidney transplantation. *Pediatr Nephrol.* 2013;28:327-32.
 5. Takahashi K, Saito K, Takahara S, Okuyama A, Tanabe K, Toma H, *et al.* Japanese ABO Incompatible Kidney Transplantation Committee. Excellent long-term outcome of ABO-incompatible living donor kidney transplantation in Japan. *Am J Transplant.* 2004;4:1089-96.
 6. Gupta PN, Pokhariyal S, Bansal S, Jain S, Saxena V, Sharma R, *et al.* Renal transplantation across ABO barrier. *Indian J Nephrol.* 2013;23:214-6.
 7. Park WD. Accommodation in ABO-incompatible kidney allografts, a novel mechanism of self-protection against antibody-mediated injury. *Am J Transplant* 2003;3:952-60.
 8. Takahashi K. Accommodation in ABO-incompatible kidney transplantation: why do kidney grafts survive? *Transplant Proc.* 2004;36:193S-6S.
 9. Sassi M, Maggiore U, Buzio C, Franchini M. Immunohaematological and apheretic aspects of the first kidney transplant from a living, ABO-incompatible donor carried out in Italy. *Blood Transfus.* 2011;9:218-24.
 10. Allen G, Simpkins CE, Segev D, Warren D, King K, Taube J, *et al.* Rapid accommodation of an A1 renal allograft after preconditioning for ABO incompatible transplantation. *Contrib Nephrol.* 2009;162:35-46.
-