A Case Report: Role of therapeutic plasma exchange in treatment of transplant associated thrombotic microangiopathy following renal transplantation

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Introduction: Transplantation-associated thrombotic microangiopathy (TA-TMA) in kidney transplantation is not an uncommon complication of Kidney transplantation and may be a cause of graft loss. It is characterized by hemolytic anemia, thrombocytopenia, and organ damage, especially manifesting as kidney dysfunction. TA-TMA occurs due to various reasons including viral infection, immunosuppressant drugs and antibody-mediated rejection (AMR), resulting in severe endothelial damage. Therapeutic interventions used to treat TMA include calcineurin inhibitor (CNI) dose reduction or temporary withdrawal, steroids, plasma exchange (PLex), intravenous immunoglobulin among other modalities. (**1-3**)

Case Report

A 49 year old male presented to the nephrology department with decrease in urine output and fluid retention. On examination he had hypertension. On Laboratory evaluation, his creatinine level was found to be 14.4mg/dl and urea was 203mg/dl. Abdominal ultrasonography of the patient revealed bilaterally small sized kidneys with increased cortical echogenicity with multiple cortical cysts. No other significant findings were noted. The patient was diagnosed as having end-stage renal disease (ESRD) of unknown aetiology as biopsy was not done in view of small sized kidneys. The patient was put on maintenance haemodialysis and was advised for the renal transplant as a definitive treatment. He remained on twice a week haemodialysis for 6 months and thereafter came for the renal transplant with his wife as the kidney donor.

Pre-transplant immunological work-up of the patient and the donor showed negative results for complement dependent cytotoxicity (CDC) crossmatch, T & B cell flow cytometry cross-match (FCXM) and donor specific IgG anti-HLA antibodies class I & II (MFI<500 by Luminex Flouro-beads X-Map). On high resolution HLA DNA typing by next generation sequencing patient was found to be 01/12 match at allele level with the donor at HLA class I and class II loci. The blood type of both the patient and the donor was O-Rh(D) positive. The patient was put on immunosuppressive induction regimen with tacrolimus, anti-thymocyte globulin and mycophenolate mofetil one day prior to transplantation. The patient underwent the renal transplantation without any intra-operative complications. The intra-operative urine output was observed in 2 minutes.

Post-transplant (day zero) his creatinine and urea levels were noted to be 4.2 mg/dl and 61 mg/dl, respectively. Post-transplant doppler ultrasonography on day-1 showed normal findings. The creatinine and urea levels being 2.0 mg/dl and urea 49mg/dl with adequate urine output @ 1 liter per hour. On post-transplant day 2 & 3 patient started showing slowly decreasing urine output and serum creatinine value got stuck at 2mg /dl. A drop in patient's hemoglobin was also noted with Hb being 5.8 gm/dl on day-3 as compared to 7.4 gm/dl on day-1. The Platelet count of the patient also decreased from 1.2 lac/µL on day-1 to 56000/µL on day-3. Serum LDH (>300 IU/L) was also found to be raised. In view of these findings, allograft biopsy was done and a diagnosis of moderate acute tubular necrosis with transplant associated thrombotic microangiopathy was made on day-5 post-transplant. Further testing to determine the exact aetiology of the condition could not be done due to unaffordability of the patient.

The patient was immediately started on IVIG and Therapeutic Plasmapheresis request was made to the Blood Centre. The patient under 5 TPE procedures on post-transplant day-5, 6, 9,10,11. After first two TPE procedures, the patient started showing improvement with creatine and urea levels being 1.8mg/dL and 39mg/Dl, respectively and normal ultrasonography findings. Patient's urine output was found to be improving. Thereafter, the patient 3 more TPE procedures on post-transplant day-9,10,11. Plasma exchange was done with albumin and fresh frozen plasma in the ratio of 1:3 as replacement fluid. On an average in each session, total blood processed was 5045 ml, total plasma processed was 3768ml and total replacement given was 3193ml. No adverse events were noted in the patient during TPE procedures.

Following the TPE procedures, the patient was discharged post-transplant day-12 with creatinine level of 1.2 mg/dL and normal urine output. On the last follow up 5 months post-transplant patient was doing well with creatinine level at 1.1 mg/dL.

Discussion: Post-transplant thrombotic microangiopathy has been reported with varied incidence ranging from 3 to 14%. (**4**)

In the present case study, the antibody mediated rejection, drug induced-TMA, atypical Hemolytic uremic syndrome and allograft hypo-perfusion were included in the differential diagnosis.

The exact cause of the post-transplant TMA in this case could not be made, as no further testing could be done due unaffordability of the patient. Plasma exchange is indicated as category-III treatment for transplant-associated TMA and as category-I in certain drug induced TMA and antibody-mediated rejection. In recent studies, plasma exchange along wit other treatments has resulted in allograft salvage rate of 80% in cases with Post-transplant TMA. (**5**)

Conclusion: In our case study, TPE was found to be an effective adjunctive treatment of TA-TMA and resulted in allograft salvage in the patient.

References:

1. Cho W, Jo S, Jung C, Kim M. Characteristics and management of thrombotic microangiopathy in kidney transplantation. Korean J Transplant 2023;37:11-18.
2. Karthikeyan V, Parasuraman R, Shah V, Vera E and Venkat K. Outcome of Plasma Exchange Therapy in Thrombotic Microangiopathy After Renal Transplantation. American Journal of Transplantation 2003; 3:1289–1294.
3. Ganesh K, Abraham A, Kumar J, Paul R, Simon S, Harshan N. Thrombotic Microangiopathies Post-renal Transplantation. Indian J of Transplantation 2020; 14:213-218.
4. Qutube S, Arun KG, Jayaram N, Ramakrishnan S, Dilip R. Post transplant thrombotic microangiopathy causing acute renal failure. Indian J Nephrol. 2009 Apr;19(2):74-6.
5. Connelly-Smith L, Alquist CR, Aqui NA, Hofmann JC, Klingel R, Onwuemene OA, et al. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice - Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue. J Clin Apher. 2023 Apr;38(2):77-278.