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Case Report

A-45-Year-Old Female, ABO Matched Living Related Kidney Transplant Recipient, Treatment Completed Hepatitis C Infection, Who Received Anti-Thymocyte Globulin as Induction Therapy Developed Pancytopenia and Acute Antibody Mediated Rejection Recovered with Plasmapheresis, Intravenous Immunoglobulin and Rituximab: Balancing Efficacy, Safety, and Cost!

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Case Summary

A-45-year-old female received kidney from her daughter, ABO matched. CDC cross match was 'AHG DTT treated B cell positive (1:1)'; 'Donor Specific Antigen'(DSA) was not done due to economic constraint. Therefore, 'Anti-thymocyte Globulin' (ATG) was given as induction therapy; she received methyl prednisolone, tacrolimus and mycophenolate mofetil according to protocol. Hepatitis C infection was treated for 6 months; the viral load was undetectable one month prior to transplant. She had macroscopic hematuria and oliguria 12 hours after transplant; slow reduction of serum creatinine; falling hemoglobin, total WBC and platelet count; pancytopenia on 'post-transplant Day 4 & 5'. Hemodialysis was initiated twice on 'post-transplant Day 3 and 5'. Graft biopsy done on 'post-transplant Day 7' after correction of platelet count was compatible with acute antibody mediated rejection. Therefore, plasmapheresis, intravenous immunoglobulin and intravenous Rituximab were initiated; she recovered gradually.

Keywords: Anti-thymocyte globulin, Acute antibody mediated rejection, Hepatitis C, Pancytopenia, Economic constraint

Introduction

Renal transplant becomes more successful with the advance of newer immunosuppressive therapy: mycophenolate mofetil, sarolimus. The donor with high immunological risks can be manageable with lymphocyte depletion therapy as induction agents. They are divided into two broad categories, based on their activity on T-lymphocytes, as lymphocyte-depleting antibodies and non-depleting antibodies. Lymphocyte-depleting antibodies are Rabbit Anti-thymocyte Globulin (rATG), Equine Anti-thymocyte Globulin (eATG), monomurab-CD3 (OKT3), and alemtuzumab; they have higher immunosuppressant effects and severe intense side effects like infection. Lymphocyte nondepleting antibodies are basiliximab and daclizumab; they have less intense adverse effects. Therefore, they are used in patients at lower risk of acute rejection. Possible benefits of intense immunosuppression must be balanced with increased risks of infection and malignancy. Advantages of ATG over basiliximab were highlighted in several studies. The chances of acute rejection were significantly reduced with ATG [1]. Moreover, tacrolimus and steroid requirements were reduced in ATG group than basiliximab group in elderly, low-risk kidney transplant recipients; furthermore, there was no differences in all-cause mortality, rejection, or infection in both groups [2]. The current kidney disease: Improving Global Outcomes guidelines recommend use of Rabbit Anti-Thymocyte Globulin (rATG) as induction therapy in renal transplant recipients at high immunologic risk for acute allograft rejection. Rabbit Anti-Thymocyte Globulin (rATG) is generally well tolerated in some reports. It is found to have severe side effects with varying intensity; however, they are manageable and reversible. Therefore, ATG is a better agent for induction of immunosuppression and is recommended for the treatment of acute cellular rejection [3].

Anti-thymocyte globulin (ATG) is a polyclonal antiserum introduced into clinical medicine more than 30 years ago; it induces a broad non-specific immunosuppression. In hematology, ATG from horses has been found to be superior to ATG from rabbits in treatment of aplastic anaemia [4]. Individualized dosing combined with therapeutic drug monitoring is recommended to improve outcomes of transplant cases [5]. A cost-effective approach is suggested in prescribing ATG; it should be balanced with not only efficacy but also safety [6-8].

Antibody-Mediated Rejection (ABMR) accounts for 20–30% of all acute rejection episodes following renal transplantation. The mechanism of damage in ABMR is mediated by Donor-Specific Antibodies (DSA). ABMR is generally less responsive to conventional anti-rejection therapy, resulting in poor allograft survival. Diagnosis of ABMR based on C4d immunostaining of renal allograft biopsies and the demonstration of donor-specific antibodies in the recipients. Diagnostic pitfalls in ABMR and its therapeutic challenges were mentioned in several reports [9,10]. Standard treatment for ABMR is evolving too [11]. Therapeutic options are plasmapheresis, intravenous immunoglobulin, immunoadsorption and rituximab or bortezomib, together with intensification of immunosuppression with a steroid/tacrolimus/mycophenolate mofetil combination. Regarding treatment of ABMR, the treatment recommendations were found to be largely based on expert opinion [12]. Therefore, therapeutic studies are required in renal transplant recipients presenting with ABMR to get better evidence [13-15].

Leukopenia and thrombocytopenia are commonly observed adverse reactions to administration of rATG; profound lymphocyte depletion is seen. Concomitant therapy with mycophenolate mofetil and valganciclovir drugs potentiates hematologic toxicity of ATG. Hence, daily monitoring of white blood cells, T-cell, and platelet counts is necessary; the dose adjustment mainly based on the level of depletion of each cell line. Previous reports proved that rATG induction in renal transplant recipients with high immunologic risk for rejection had more benefits than risks; however, more data were needed for special population like pediatrics, the elderly, and hepatitis C-positive and human immunodeficiency virus-positive renal transplant recipients [6]. This patient was hepatitis C-positive; treated well with undetectable viral load one month prior to transplant.

Case Presentation

The patient was DKM Cho, 53-year-old female, known Diabetes Mellitus for 20 years. She had diabetic kidney disease resulting in End Stage Renal Disease (ESRD); she had hemodialysis for 18 months. She got 4 units of whole blood transfusions for anemia; sensitized. She had 3 children, born with Lower Segment Caesarean Section (LSCS). Following LSCS in the youngest baby, left ureter was injured. It was again complicated by pyo-nephrosis of the left kidney; therefore, she underwent left nephrectomy.

She also had hepatitis 'C' viral infection; six months treatment with combination therapy of sofosbuvir and velpatasvir was completed 3 weeks prior to transplant. Fibro-scan was done 6 months prior to anti-viral therapy for hepatitis C was F4; then, its scoring decreased following treatment for hepatitis C. The liver enzymes were normal and hepatitis 'C' viral load was undetectable prior to transplant. Liver was normal in ultrasonogram; single gall stone with normal gall bladder was seen in pre-operative assessment for transplant. Upper GI scopy revealed erosive gastritis and duodenitis; they were treated accordingly. Serum tumor marker (Ca19.9) was raised; twice normal. CT abdomen and pelvis were normal. Colonoscopy showed multiple sessile polyps and biopsy confirmed that the lesion was benign. Therefore, 'raised Ca19.9' was possibly due to gall stone; she was asymptomatic.

Regarding immunological assessment, CDC cross match was 'AHG DTT treated B cell (1:1) positive'. Doing Donor Specific Antigen (DSA) and HLA typing would cause 60 Lakh Myanmar Kyats; it was more than 60% of total cost of renal transplant. Because of economic constraint, the patient and family decided 'not to send further testing' and they agreed to give induction therapy accordingly.

When choosing bacilizimab and Anti-Thymocyte-Globulin (ATG), they preferred ATG (high dose) in view of low rejection risk in long term. Therefore, 'ATG' was given as induction therapy; she received methyl prednisolone, tacrolimus and mycophenolate mofetil according to local renal transplant guidelines. The donor was the patient's daughter, 25 years old; their blood group ('A' 'Rh positive') were matched. The donor had one daughter; there was no history of blood transfusion or neonatal jaundice in her baby. Figure 1 reveals donor and her baby (Figure 1).

Figure 1: Donor and her baby.

Table 1: Clinical parameters till Day 9.

Parameter	Pre-T	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
Mean systolic BP (mmHg)		120	104	118	121	125	130	132	128	122	118
Mean diastolic BP (mmHg)		70	67	76	76	78	78	80	80	78	72
Mean HR (/min)		98	99	97	98	100	91	92	90	90	90
Intake (cc/ 24hr)		6,130	2,765	2,050	1,150	1,500	2,150	3,750	1,600	1,600	3,500
Output (cc/ 24hr)		4,270	1,220	1,830	1,860	2,025	700	4,250	250	570	3,400
Remark					Hemodialysis		Hemodialysis		biopsy		

The patient was hemodynamically stable during transplant surgery; total ischemic time was not long (cold ischemic time was 4 minutes and warm ischemic time was 39 minutes). Figure 2 shows recipient in immediate post-operative period. Her urine out-put (hourly) was 300-400 cc in immediate post-operative period for 14 hours; then, it dropped to 30-50 cc per hour later (1.0-1.5 liter per 24hour) (Table 1) (Figure 2).

Figure 2: Patient in immediate post-operative period.

Table 2: Biochemical parameters till Day 9.

Parame-ter	Pre- T	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
Remark					Hemo-dialysis		Hemo-dialysis		Biopsy		
Urea	31.6	31.8	41.8	58.7	92.4	132.9	163.8	201.2	96.5	165.8	197
(20-50 mg/dl)											
Creatinine (0.7-1.5 mg/dl)	3.3	2	2	2.3	2.5	2.5	3	3	2.6	3.7	2.7
Na	139	137	135	131	138	143	139	142	139	133	136
K	4.4	3.98	5.05	4.8	4.58	3.98	3.69	3.93	3.19	3.11	3.57
Cl	103.8	106.8	109.5	104.4	110	112.3	109.8	106.2	91.4	100.1	99.3
Total Bilirubin (0.2-1.0 mg/dl)						1.2	1.1	1.1	1.2	1	
Total protein (60-80 g/L)							52.8	55.7		51.4	
Albumin (40-60 gm/L)							31.7	34.5		31.1	
Globulin (20-40 g/L)							21.1	21.2		20.3	
ALT				22.5		22.7	17.2	16.9		14.6	
(5-49 U/L)											
AST				30.6		40.6	27.7	22		23.3	
(9-48 U/L)											
ALP (35-129 U/L)				73.6		91.8	76.1	64.9		69.1	

Intravenous infusion of frusemide and albumin augmented urine output to 1.5-2.0 liter per 24 hours; graft biopsy could not be done as she had thrombocytopenia. She had macroscopic hematuria oliguria and slow reduction of serum creatinine Table 2. Hemodialysis was initiated twice on 'post-transplant Day 3 and 5'. Oral therapy of 900mg Valganciclovir was given as prophylaxis to CMV infection; it was stopped due to pancytopenia (Table 2).

On Day '5', platelet count was 36X109/L; serum Tacrolimus level was 19ng/ml. Table 3 reveals hematological parameters. Therefore, Tacrolimus dose was reduced from 3 mg twice a day to 2.5 mg twice a day (1mg/dose reduction). On Day '7', platelet count rose to 94x109 /L after transfusion of 3 units of PRP; therefore, graft biopsy was done (Table 3).

Table 3: Hematological parameters till Day 7.

Parameter	Pre-T	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Hb (gm%)	8.5	9.8	8.7	9.1	8.5	8.7	9.7	9.7	9.7
PCV	25.4	28.4				24.9			
Total WBC	6.2	11.3		7.2	6.8	5.9	4.4	5	6.4
Neutrophil (%)	94.5	91.8		87.7	80.9		90	71.2	87
Lymphocyte (%)	3.4	4.8		8.4	12.5	16	8	16	16
Monocyte (%)									
Eosinophil (%)	2.1	3.4		3.9	6.6				
Platelet count	94	88		79	58	36	58	53	95
PT						11.3		13.4	
INR						1.13		1.35	
Tacrolimus level							18		
Remark					Hemodialysis		Hemodialysis	PRP 3 packets	Graft biopsy

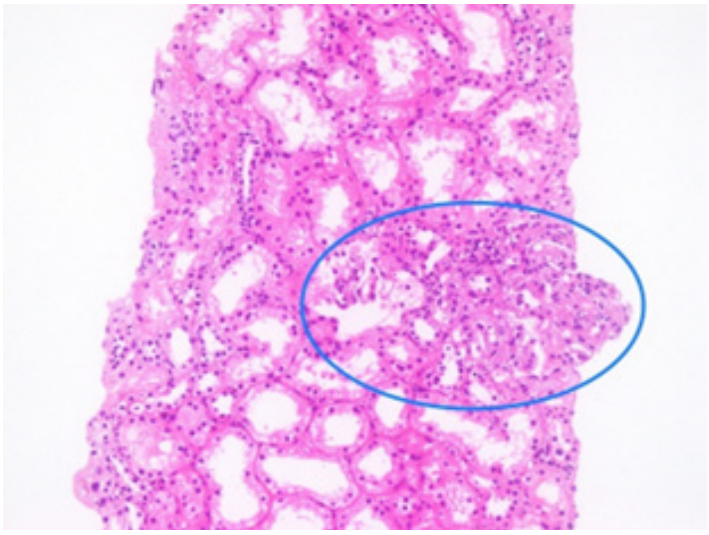

Figure 3: Histology of glomeruli and tubules showing the capillary loops of glomeruli is occluded with swollen endothelial cells and infiltrated mononuclear cells suggestive of glomerulitis (Blue circle indicates glomeruli) (H&E stain).

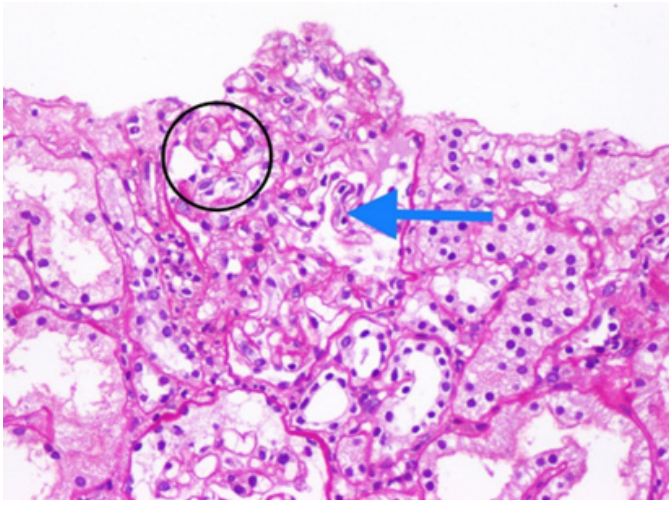

Figure 4: (a) Endothelial cell swelling (black circle) (b) Occlusion of capillary loop with mononuclear cell suggestive of glomerulitis (blue arrow) (PAS Stain).

In allograft biopsy, in H & E stain, the capillary loops of most glomeruli are occluded with swollen endothelial cells and infiltrated mononuclear cells suggestive of glomerulitis; it is shown in Figure 3. Figure 4 was PAS stain; it demonstrates endothelial cell swelling and occlusion of capillary loop with mononuclear cell suggestive of glomerulitis. Focal inflammatory infiltration in the intima indicating intimal arteritis is seen Figure 5, PAS stain. Figure 6 is Trichrome Stain; a fibrin thrombus is seen within the glomerulus. Figure 7,8 are Immunohistochemistry stain for C4d (IHC); peritubular capillaries show circumferential positive staining for C4d. All immunofluorescence stains were negative (IgG, IgA, IgM, C3c, C1q, Kappa and Lambda). The histology was compatible with anti-body mediated rejection (C4D positive +++); therefore, she was treated with plasmapheresis. Intravenous Immunoglobulin G was added on the third course of plasma pheresis. A total of 6 courses of plasmapheresis were done; and rituximab 500mg was given after final course of plasmapheresis (Figures 3-8).

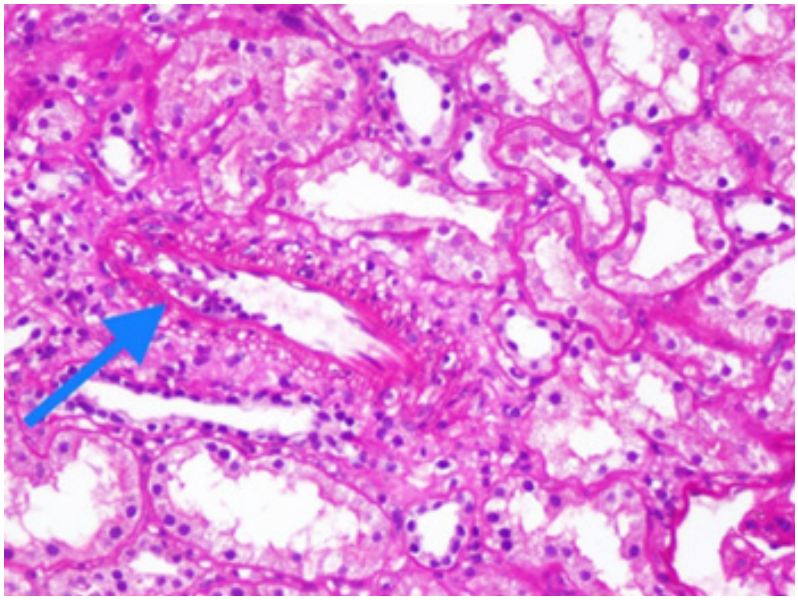

Figure 5: Focal inflammatory infiltration in the intima indicates intimal arteritis (Blue arrow indicates intimal arteritis) (PAS Stain).

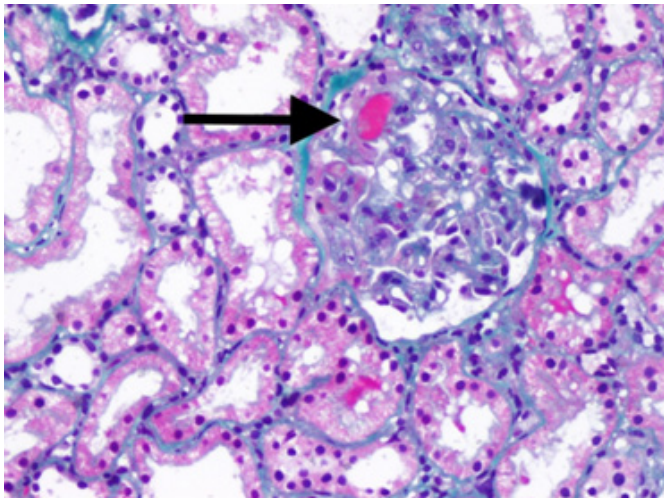

Figure 6: A fibrin thrombus is seen within the glomerulus (Black arrow indicates fibrin thrombus) (Trichrome Stain).

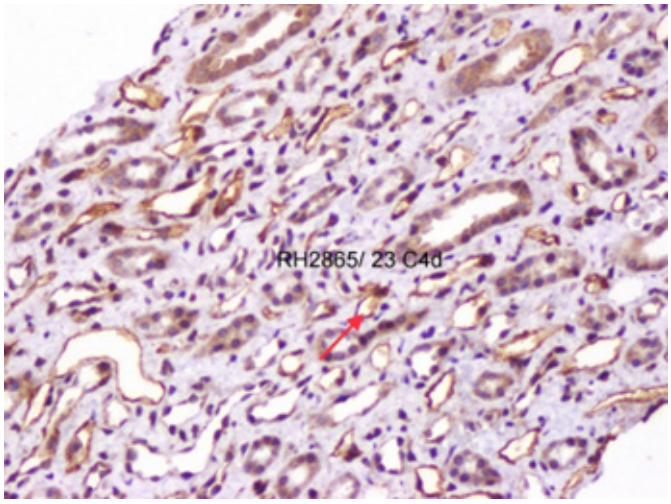

Figure 7: By IHC, peritubular capillaries show circumferential positive staining for C4d.

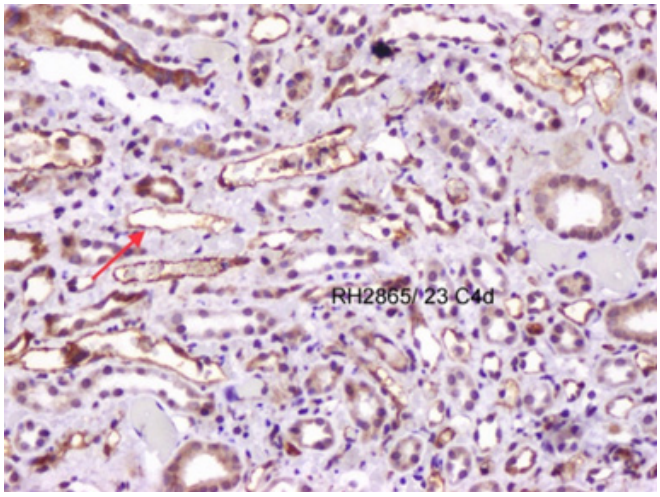

Figure 8: By IHC, peritubular capillaries show circumferential positive staining for C4d.

Table 4: Biochemical parameters from Day 10 to Day 20.

Parameter	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Day 19	Day 20
Plasmapheresis		1st		2nd		3rd		4th		5th	
IV Ig						5G		5G		5G	
Rituximab											
Urea	105.5	135.4	139.1	97.1	111.3	133.8	151.6	175.2	180.5	174.8	157.2
(20-50 mg/dl)											
Creatinine	2.9	4.3	4	3.4	3.5	3.4	3	2.9	2.1	1.5	1.3
Na	136	138	146	141	140	143	138	135	132	141	144
K	3.29	3.28	3.53	3.15	3.18	3.61	4.29	4.62	4.12	4.03	3.99
Cl	98.6	99.3	98.2	102.2	99.9	97.4	97.2	105.4	102.4	103.2	110.1
Total Bilirubin (0.2-1.0 mg/dl)			0.7		0.6				0.5		
Total protein (60-80 g/L)			44.6						48.8		
Albumin (40-60 gm/L)			31.7						34.9		
Globulin (20-40 g/L)	12.6		12.9						13.9		
ALT (5-49 U/L)			5.8		6.3				8.9		
AST			14.2		16.5				14.2		
(9-48 U/L)											
ALP (35-129 U/L)			44.6		41.8				14.7		

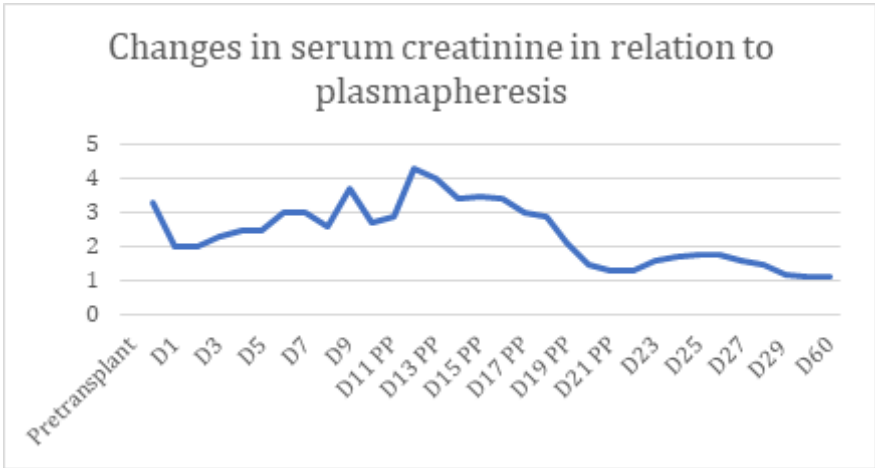

Figure 9: Changes in serum creatinine in relation to plasmapheresis.

As seen in Table 2 and 4 and Figure 9, there was no further rise in serum creatinine after third course of plasma pheresis; it became stable at 1.3mg%. And urine output increased to 2.0 liters per day. Now (31.05.2023), Day 60 after transplant, the patient was stable; serum creatinine was 1.1mg%; urine output was 2,500cc per day without diuretics; it was 1,500-2,000cc per day with frusemide 80 mg (Table 4) (Figure 9).

Table 1,5,6 show serial urine output in 24 hours. Figure 10 is taken on Day '30' post-transplant. Hematological parameters were stable; hemoglobin was 11.1gm%; total WBC was 5.3x109/L; platelet count was 121x109/L. Table 3,7,8 and Figure 11-13 demonstrate changes in each hematological cell line. Blood pressure was controlled well at 130/80 mmHg with carvedilol, nifedipine. She was on prednisolone 27.5mg OD (reducing by 2.5mg on every five days), mycophenolate mofetil 1G BD, tacrolimus 1.5mg BD (with Tacrolimus blood level 9.75ng/ml). Glycaemic control was maintained with linagliptin 5mg OD and insulin NPH 22 IU at 6Am. Valganciclovir was reinitiated on 'post-transplant Day 30' as platelet count was stable over 100x109/L (Tables 5-8) (Figure 10-13).

Table 5: Clinical parameters from Day 10 to Day 19.

Parameter	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Day 19
Mean systolic BP (mmHg)	108	110	106	110	114	120	130	122	120	126
Mean diastolic BP (mmHg)	68	68	64	62	66	75	74	70	72	70
Mean HR (/min)	90	94	94	95	92	92	93	93	91	91
Intake (cc/24hr)	1,800	3,200	1,700	2,200	2,000	1,400	1,300	1,300	800	700
Output (cc/24hr)	400	400	3,770	500	600	800	700	800	1,150	1,000
plasmapheresis		1st		2nd		3rd		4th		5th
IV Ig						5G		5G		5G

Table 6: Clinical parameters from Day 20 to Day 29.

Parameter	Day 20	Day 21	Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28	Day 29
Mean systolic BP (mmHg)	128	128	128	132	128	128	130	135		130
Mean diastolic BP (mmHg)	74	75	78	72	74	74	78	78		80
Mean HR (/min)	93	94	92	93	94	92	91	92		
Intake (cc/24hr)	600	600	500	500	600	600	700	1,000		
Output (cc/24hr)	720	720	2,300	2,350	2,165	2,900	2,650	2,700		2,500
plasmapheresis		6th								
IV Ig		25G								
Rituximab		500mg								

Table 7: Hematological parameters from Day 8 to Day 17.

Parameter	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17
Hb (gm%)	8.8	11.3	10.4	9.2	9.7	8	8.5	7.8	8.5	8.2
PCV						24.3	25.1	22.6	25	24.3

Total WBC	5.2	5.2	7.2	6.4	9.3	6.3	8.1	5.9	5.5	5
Neutrophil (%)	80	78	79	80	83	84	80	78	82	80
Lymphocyte (%)	18	18	21	19	16	17	13	17	11	16
Monocyte (%)										
Eosinophil (%)	3.4		3.9	6.6						
Platelet count	57	74	69	103	96	84	70	53	88	82
PT	15.2	14.1		12.6			11.3			
INR	1.5	1.4		1.25			1.11			
Tacrolimus level		19								
Plasmapheresis				1st		2nd		3rd		4th
IV Ig								5G		5G

Table 8: Hematological parameters from Day 18 to Day 60.

Parameter	Day 18	Day 19	Day 20	Day 21	Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 30	Day 60
Hb (gm%)	7.4	8.9	8.8	7.5	7.1	7.1	7.7	7.9	7.1	8.4	11.1	10
PCV	22.1	26.2	26.9	23.4	21.8	19.9	22.9	23.4	21.2	25.6		
Total WBC	3.5	3.9	4.1	2.8	1.7	1.7	1.8	1.9	1.7	2.7	5.3	2
Neutrophil (%)	71	69	73	67	82	76	78	79	76	78		75
Lymphocyte (%)	26	18	19	28	18	24	22	21	24	19		10
Monocyte (%)												
Eosinophil (%)	3.4		3.9	6.6								
Platelet count	56	96	104	64	85	65	82	94	107	100	121	58
PT	12.6											
INR	1.26											
Tacrolimus level	9.75											
Plasmapheresis		5th		6th								
IV Ig		5G		25G								
Rituximab				500mg								

Figure 10: Patient in Day 30 post-transplant period prior to discharge from hospital.

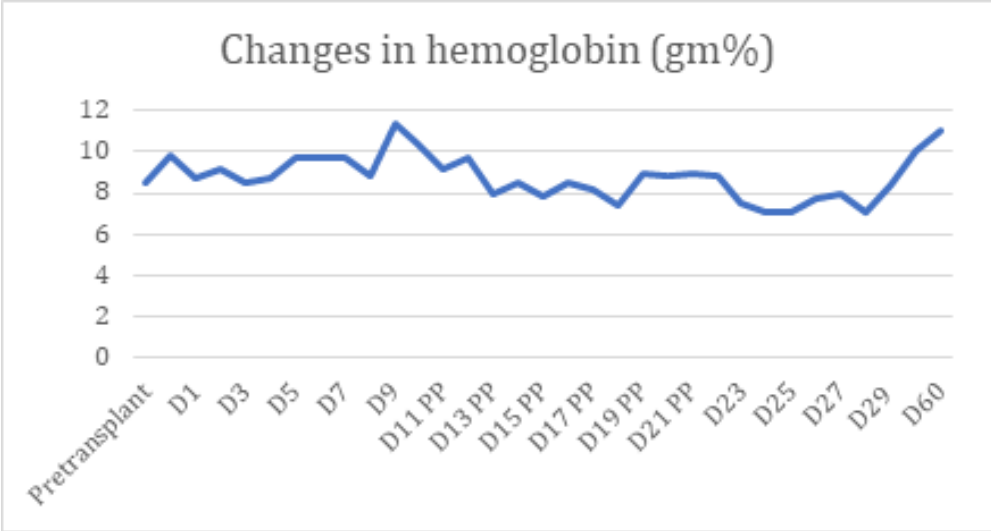

Figure 11: Changes in hemoglobin level.

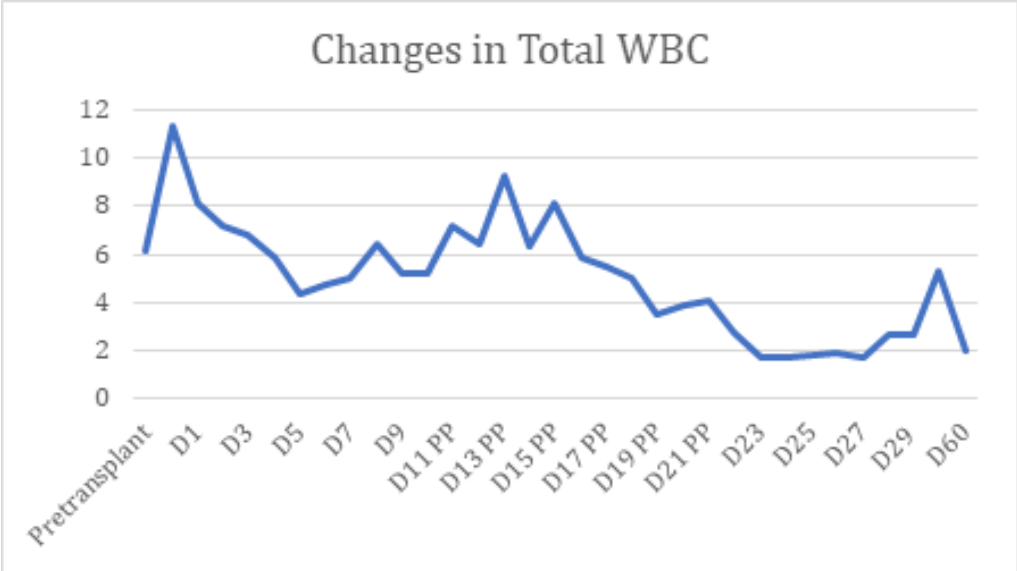

Figure 12: Changes in total WBC count.

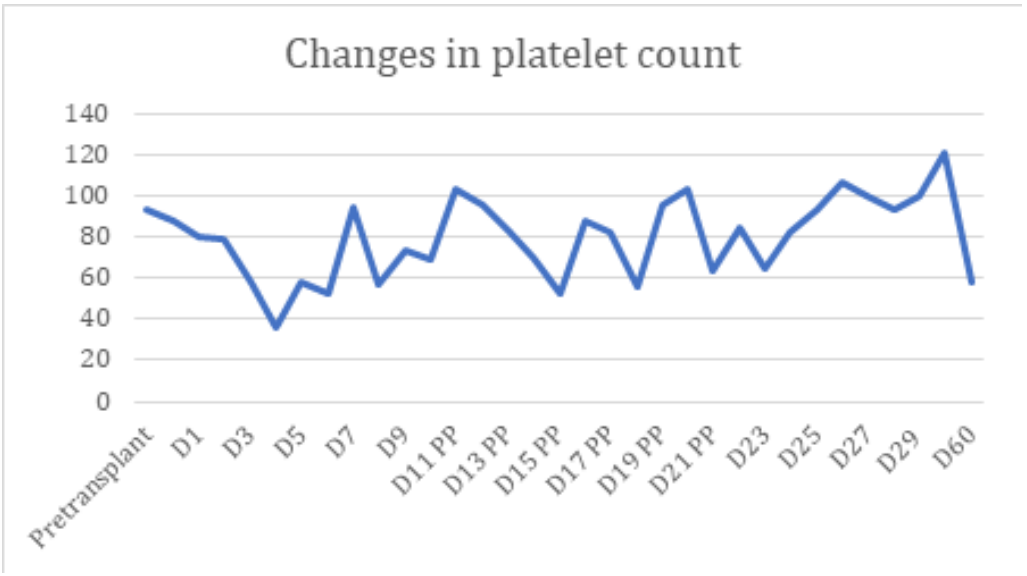

Figure 13: Changes in platelet count.

Discussion

Immunological screening of living donor is a big economic challenge for those who are planning for renal transplant in Myanmar. As immunological tests cannot be done at home; they must be sent to neighboring countries. The total cost of 'CDC cross match' and 'Donor Specific Anti-body' is USD 2,000 to 3,000; and, the inflation in US dolor exchange rate causes more difficulties. In this patient, CDC cross match was 'AHG DTT B cell (1:1) positive'; further testing 'Donor specific ant' was not done due to economic constraint. The patient and family accepted high risk of rejection without knowing the exact chances of rejection from the results of 'Donor specific antigen'. The expenses for immunological screening would be reduced if it was done at home- Myanmar. It highlighted the need for improvement in immunological field in Myanmar.

Testing 'Donor specific antigen' (DSA) was one of the recommended tests in immunological screening in both living donor and deceased donor renal transplant. On the other hand, one study on simultaneous liver and kidney transplant (SLKT) involving 135 patients reported that SLKT is associated with excellent long-term patient and allograft survival with a relatively low rate of rejection; testing for DSA does not impact SLKT outcomes [16]. The point considered retrospectively was that 'it would be better to postpone the donor if 'AHG DTT B cell positive' in CDC cross match result'. This case report gave challenges on doing immunological tests in low-income countries.

Next point is living donor issue. 'Ethical board for renal transplant' in our center generally allows kidney donation among close family members. Although the patient has 3 children, the daughter has the same blood group among all siblings. If the 'deceased donor renal transplant program' was fully developed in Myanmar, the patient would get well matched kidney. Therefore, we should put facts to higher authorities for development of the 'deceased donor renal transplant program' in Myanmar.

The patient and family agreed to take Anti-thymocyte globulin'(ATG) after counselling; however, the patient developed acute rejection in the first 12 hours after surgery. Lymphocyte-depleting antibodies, including Rabbit Anti-Thymocyte Globulin (rATG), Equine Anti-Thymocyte Globulin (eATG), monomurab-CD3 (OKT3), and alemtuzumab, are generally recommended in patients at high immunologic risk of rejection. Excellent immunosuppressive action of 'ATG' is beneficial in patients at high risk for acute allograft rejection; nevertheless, its benefits should be balanced with potential risks". The clinicians have to judge the possible benefits of intense immunosuppression with increased risks of infection and malignancy. The treating team made shared decision with the patient and family members. 'The current Kidney Disease Guideline' recommend the use of rabbit anti-thymocyte globulin as induction therapy in renal transplant recipients at high immunologic risk to prevent acute allograft rejection. Therefore, choosing ATG as induction therapy in this patient was in accordance with international guidelines. Developing ABMR in this patient after giving 'ATG" was uncommon; one reason for reporting the case. It provided additive information to former report [17].

It was reported that 'rATG is generally well tolerated, with adverse reactions ranging in severity but most often manageable and reversible'. This patient had leucopenia on 'Day 5 after transplant'; total WBC count was persistently low from 'Day 18' till 'Day 29'. Her platelet count was low till 'Day 30'. Anaemia, leukopenia and thrombocytopenia were commonly observed adverse reactions to administration of rATG, found in other studies [18]. The hematological side effects may be aggravated by mycophenolate mofetil and

valganciclovir. Luckily, the patient did not have infection problem or septicaemia.

Having thrombocytopenia in this patient delayed the timing of graft biopsy; it can be done only on 'Day 7' after correction with platelet transfusion. The biopsy was compatible with ABMR, and it was treated with plasmapheresis and IVIg. If there was no problem with platelet, the graft biopsy would have been done earlier; hence, early treatment. Subsequently, better and earlier response to treatment may result in longer graft survival. This case report supported the fact "balancing the risks and benefits in giving ATG".

Moreover, the patient was on mycophenolate mofetil and valganciclovir (Valcyte) according to protocol. They are well known to cause hematologic toxicity; therefore, they potentiate the risk of pancytopenia. Valganciclovir was omitted temporally till the recovery of white blood cell and platelet counts. It emphasized the importance of close monitoring of hematological parameters particularly in renal transplant recipient with 3 haemato-toxic drugs: ATG, mycophenolate mofetil and valganciclovir.

The patient had falling urine output in the first 24 hours after transplant. The question of 'whether the patient was having drug toxicity or rejection' can be solved by graft histology and drug level of tacrolimus. Therefore, both drug level and graft histology were important for timely treatment in saving kidney [9,10]. The exact nature of rejection can be seen with several special stains by expert renal histopathologist; management protocol depends on histological diagnosis [19]. Binding of donor-specific HLA antibody (DSA) and A/B blood type antibody on graft endothelial cells causes complement-dependent tissue damage. C4d, a product of the complement cascade, has long been an indicator of graft tissue damage in graft endothelial cells. In this patient, anti-body mediated rejection was confirmed in histology with various stains; H & E stain, PAS stain, Trichrome Stain, Immunohistochemistry stain for C4d and immunofluorescence stains (IgG, IgA, IgM, C3c, C1q, Kappa and Lambda). They were shown in different Figures. Therefore, we congratulate the renal pathologist and his effort in the background of resource poor setting. This is another reason for reporting cases.

Regarding platelet count in this case, the patient had low normal platelet count prior to transplant; it was related with old hepatitis C infection though the viral load was undetectable. Hepatitis C infection was reported to have extrahepatic manifestations such as bone marrow, joints and skin. In this patient, platelet and WBC were also influenced by old hepatitis C infection [20-22]. This case gave the effect of ATG on platelet and WBC in recipients with hepatitis C infection receiving mycophenolate mofetil and valganciclovir [6].

Regarding rituximab induction, it significantly increased the risk of leukopenia; nonetheless, no significant risk of infection was reported [23]. In this patient, ABMR was treated with plasmapheresis, IV Ig and riruximab. The patient did not have a severe infection. Total WBC did not significantly fall following rituximab; one reason for reporting.

Conclusion

This patient had high immunological risks; 4 units of blood transfusion; mother of 3 children; and 'AHG DTT treated B cell positive (1:1)' in CDC cross match. She developed acute ABMR though she received high potency lymphocyte depleting agent 'ATG'. Combination of ATG, mycophenolate mofetil and valganciclovir lead to torrential pancytopenia. Efficacy, safety, and cost of induction agent (ATG) as well as the cost of immunological screening should be considered in living donor related renal transplant particularly in low resource setting. Close monitoring of clinical and laboratory parameters and individualized handling of immunosuppressants are essential.

Ethical Approval

Our institution does not require ethical approval for reporting cases.

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Informed Consent

The informed consent for publication in this article was obtained from a patient.

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Declaration of Conflict of Interest

The authors declared no potential conflicts of interests with respect to authorship and publication of this article.

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