Passenger Lymphocyte Syndrome after Renal Transplant: Case Report

Abstract

Passenger lymphocyte syndrome (PLS) is a rare cause of anemia resulting from immune-mediated hemolysis in the post-transplant recipient. We report a case of 26-year-old male who underwent renal transplant. His mother as donor was O positive while he was A positive. He developed anemia at 1-week post-transplant, which later turned out to be PLS. Laboratory findings included rapidly decreasing Hb level and intravascular hemolysis. Hemolysis was brief, because the lymphocytes passed on with the donor organ were able to proliferate only for a while. The case signifies the importance of PLS as a cause for anemia, specifically in the early period after solid organ transplant. It is usually self-limiting, and the treatment requires blood transfusion of donor's blood group.

Keywords: *Passenger lymphocyte syndrome, post renal transplant, hemolytic anemia*

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Background and Introduction

Passenger lymphocyte syndrome (PLS) is a specific type of graft-versus-host disease, resulting in an immune-mediated hemolysis in the post-transplant recipient.Viable donor B lymphocytes transferred with the organ during transplantation produce antibodies against recipient red cell antigens, leading to hemolysis.[1] This condition is known as passenger lymphocyte syndrome (PLS). Onset is between 1 to 3 weeks post-transplantation, and the course is self-limiting, as ABO antibodies clear out within a maximum span of 3 months.[2]

Case Description

A 26-year old male, a case of an end-stage kidney disease (ESKD) subjected to renal transplant, with mother as the donor having O positive blood group while recipient had A positive blood group. HLA loci match was 7/10 and CDC was negative. Single antigen bead testing was not done. Since it was an ABO compatible transplant, antibodies were not tested. The treatment was initiated with triple immunosuppressants i.e., prednisolone 20mg/day, tacrolimus 0.12mg/kg/day and Mycophenolate mofetil 2gm/day. No Induction agent was used. His renal transplant surgery went technically well. On the third postoperative day, his serum creatinine was 1.2 mg/dl. [Table 1] His graft Doppler was normal with good cortical flow at all poles and normal RI values (0.57-0.65). Tacrolimus drug doses were adjusted according to its plasma level.

He was discharged on the 8th postoperative day in stable condition. He was followed up on 12th, 15th, 19th and 21st day post-transplant during which his renal function remained stable but his Hb showed a declining trend. Hence, evaluation for the cause of anemia was initiated. There was no evident intra-abdominal collection on Ultrasonographic imaging. Stool for occult blood was negative on three consecutive days, thereby ruling out any gastrointestinal blood loss. The peripheral smear showed no evidence of schistocytes. His Serum B12, Iron, TIBC, Ferritin and bilirubin level were normal, while corrected retic count and LDH were elevated. [Table 2].

Due to lack of any evident reason, further workup for rare causes was initiated. 2D echocardiography did not show any evidence of endocarditis and even serum parvovirus B-19 IgM was negative. Further, auto-immune causes were assessed by conducting Direct and Indirect coombs test. While Indirect coombs test was negative, direct coombs test was positive, with low serum Haptoglobin levels. Hence, Antibody Elution test was conducted which showed that Immune Anti-A antibodies eluted from red blood cells. Reaction of elute with O cells was negative. Finally, his Anti-A antibody titre was done by gel

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Table 1: Changing clinical parameters by post-transplant days

Post operative day (POD)	Hb (gm)	TC (cells/cumm)	PC (cells/cumm)	S. creatinine (mg/dl)	Urine output (ml)	Tacrolimus level (ng/ml)
POD-0	11.0	8250	145000			
POD-1	10.4	8130	174000	1.63	33100	
POD-2	7.2	4410	121000	1.27	20200	12.7
POD-3	7.7	3450	110000	1.14	17600	
POD-4	8.5	4550	126000	1.10	17000	
POD-5	9.3	5670	159000	1.20	10750	12.9
POD-6	9.2	6090	165000	1.37	8700	
POD-7	9.0	6970	178000	1.60	8050	
POD-8	8.6	6840	195000	1.58	8240	
POD-12	10.1	9850	285000	1.48		
POD-15	9.0	10670	408000	1.36		
POD-19	6.2	8850	447000	1.40		
POD-21	5.6	7370	391000	1.34		
POD-22	4.8	6850	302000	1.38		10.4
POD-25	9.1	8360	303000	1.30		
POD-28	9.8	7650	374000	1.24		

Table 2: Important investigation at clinical presentation

Parameter	Value	Normal range
Serum Iron	145 µg/dL	50-160 µg/dL
Serum TIBC	320 µg/dL	250-450 µg/dL
Vitamin B12	680 pg/mL	190-950 pg/ml
Corrected Reticulocyte count	7.65%	0.5-2%
Total Bilirubin	1.1 mg/dL	0.0-1.4 mg/dL
Conjugated Bilirubin	0.3 mg/dL	0.0-0.3 mg/dL
Unconjugated bilirubin	0.8 mg/dl	0.2-1.2 mg/dL
Serum LDH	594 U/L	140-280 U/L
Serum Haptoglobin	<0.0763 gm/L	0.5-2.2gm/L
Anti-A titre	1:04	NIL
Heat elution test	Immune Anti-A antibodies eluted from RBC	
Peripheral blood smear	Dimorphic picture with macro/microcytosis and anisopoikilocytosis	

phase method, which was positive (titre-1:04). Therefore, hypothesis was formulated that anaemia was related to passenger lymphocyte syndrome. Evidence in favour of hypothesis was the presence of Anti-A antibodies with significant positive titre. Evidence against this hypothesis was absence of schistocytes. Considering the above results, it was proved that passenger lymphocyte syndrome prevailed.

The anemia was then treated with blood transfusion of donor blood group i.e., 'O positive'. Blood grouping and cross-matching was done and leuko-depleted two PCV were transfused without any transfusion reaction. Dose of prednisolone was increased from 15 mg to 30 mg while that of Tacrolimus and Mycophenolate were retained at the same level. His condition gradually improved with stable Hemoglobin and hence was discharged. On follow up too, his Hemoglobin gradually increased with good renal function.

Discussion

Passenger Lymphocyte syndrome is well known after ABO mismatch solid organ transplantation. It results from immune-mediated hemolysis, but even antibodies against Rh, Kidd and Lewis blood group have also been known to cause such syndrome. [3,4] Laboratory findings include rapidly decreasing Hb level, intravascular hemolysis of abrupt onset with hemoglobinemia and low Haptoglobin associated with raised LDH. Hemolysis is usually brief, because the lymphocytes passed on with the donor organ are able to proliferate only for a while and are not permanently embedded. The serum antibody is predominantly IgG, but it may also be IgM. Antibody production decreases gradually as the lifespan of the lymphocytes comes to an end.[5] The antibodies persist for a median of 5 weeks in kidney transplant recipients.[6]

The risk and degree of hemolysis is lowest in kidney (antibody in 17%, hemolysis in 9%), followed by liver (antibody

in 40%, hemolysis in 29%) and highest in heart-lung transplants (antibody in 70%, hemolysis in 70%).[6] Anemia is treated by transfusion with group-O RBCs, avoidance of ABO-incompatible plasma products and maintenance of adequate renal perfusion. Corticosteroids are often increased. In patients with more severe hemolysis, plasma exchange may be used to decrease antibody titre. Other strategies include an increase or change in immunosuppressant, intravenous immunoglobulin, red-cell exchange and usage of monoclonal antibodies such as rituximab.[1]

Conclusion

This case report signifies the importance of Passenger lymphocyte syndrome as a cause for anemia in solid organ post-transplant recipients, especially in ABO mismatch group. It occurs early after transplantation and diagnosis require evidence of intravascular hemolysis with immune antibodies (Anti-A or Anti-B) eluted from RBC. It is usually self-limiting, and treatment requires blood transfusion of donor's blood group.

Passenger lymphocyte syndrome, PLS, anemia, post renal transplant, hemolytic anemia, intravascular hemolysis, immune hemolysis, coombs positive, anti-a antibodies, haptoglobin, ABO mismatch, blood transfusion.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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