Case Report

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Passenger Lymphocyte Syndrome in a Renal Transplant Recipient – A Case Report

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Abstract

Background: Passenger lymphocyte syndrome (PLS) is an immune-mediated hemolysis that usually occurs after a minor ABO mismatched solid organ transplant. The occurrence of PLS is far less in renal transplant recipients than in other solid organ transplants.

Case presentation: We report a case of a 35-year-old male (A –ve) underwent renal transplant with his mother (O +ve) as donor and developed passenger lymphocyte syndrome. His post-transplant period was uneventful and attained normal graft function on day 5. Around 10 days after transplant, our patient showed a rapid fall in blood haemoglobin level and clinical jaundice. Direct coombs test and anti-A antibody titre done was positive confirming a diagnosis of PLS. He was stabilised with packed cell transfusion and his immunosuppression was changed to tacrolimus from cyclosporine. His condition improved with supportive measures and he was on follow-up for one year with normal creatinine and haemoglobin levels. However, later he died of fungal sepsis with functioning renal allograft.

Conclusion: PLS is an important complication than occurs increasingly minor non-ABO mismatch transplants. Early diagnosis and appropriate treatment are important in at risk individuals.

Keywords: Passenger Lymphocyte Syndrome (PLS); Renal transplant; Immune hemolysis

Introduction

Passenger lymphocyte syndrome is a rare cause of immune hemolysis, affecting solid organ transplantation.

Viable Donor B lymphocytes transferred with the organ during transplantation produce antibodies against recipient red cell antigens, leading to hemolysis. Herein, we report a case of PLS in a renal allograft recipient [1].

Case Report

Clinical presentation

A 35-year-old male diagnosed with end-stage renal disease (ESRD) in October 2011 was treated with hemodialysis thrice weekly. He was a non-diabetic and had history of hypertension for three years. His native kidney was probably chronic glomerulonephritis. There was no other significant prior medical or surgical treatment. In February 2012, he received a live-related renal transplant from his mother. The blood group of the recipient was A negative and donor was group O positive. Complement dependent cytotoxic cross-match was negative. No induction therapy was given and maintenance immunosuppression continued with cyclosporine (6 mg/kg/day) twice daily, azathioprine 100 mg once daily and prednisolone 30 mg once daily. Surgery and immediate post-transplantation period was uneventful. Foley's catheter was removed on day 3 and drain was removed on day 5. His serum creatinine decreased (day 2 - 3.5 mg/dl, day 3 - 2 mg/dl, day 4 - 1.5 mg/dl) and was 1 mg/dl (normalized) on day 5. On day 8, he developed low grade fever. There was no history of blood transfusion prior to transplant [2].

Clinical examination

On examination, he was febrile (temperature 100°F); anemic and mild icterus was present. His heart rate was 99/min, blood pressure was 130/80 mmHg and respiratory rate was 16/min. Other systems examination was normal. Written informed consent was obtained from mother of the child for publication of this case report.

Laboratory findings

On day 2, his hemoglobin was 9.5 mg/dl, total count - 8800/cu.mm, and random blood sugar - 98 gm/dl. serum Hb A1C - 5.4%, total bilirubin - 2.8 mg/dl, direct bilirubin - 1.8 mg/dl, alanine transaminase – 28 U/L, aspartate transaminase - 20 U/L, serum total protein - 7 gm/dl and serum albumin - 3.9 gm/dl. On day 5, urine culture showed *Escherichia coli.* His serum creatinine increased to 2 mg/dl on day 10 and renal biopsy done on same day showed isometric vacuolization with

focal lymphocytic infiltrate with no evidence of rejection or thrombotic microangiopathy. His hemoglobin continued to drop from 8 gm/dl on day 8 gm/dl - 3 gm/dl on day 22. Peripheral smear showed hypochromic anisopoikilocytosis and few spherocytes. Coagulation profile tests were normal. Blood culture showed no growth and CMV pp65 was negative. Direct coombs test was strongly positive. Anti-A titre done by gel card test (column agglutination technique) was elevated (1:512).

Differential diagnosis

Provisional diagnosis of passenger lymphocyte was made. Differential diagnosis includes sepsis, infection associated hemophagocytic syndrome, graft versus host disease-passenger lymphocyte syndrome and thrombotic microangiopathy.

Management

He was treated with intravenous meropenem. Packed cell transfusion (O +) was given for severe anemia. Cyclosporine was changed to tacrolimus. Patient started improving and discharged on day 35 with hemoglobin 9 gm/dl and normal serum creatinine and bilirubin levels. Investigations done are given in **Table 1**. Patient was on follow-up for one year with normal creatinine (0.8 mg/dl), random blood sugar of 88 mg/dl, HbA1C of 5.3% and his hemoglobin level was 14.5 gm/dl. Later he died of fungal sepsis with functioning renal allograft.

Table 1 Laboratory data.

Urine	
Protein	Traces
RBC	2-3/hpf
Hemogram	
White cell count	8800/cu.mm
Differential count	
Polymorphs	69%
Lymphocytes	31%
Platelet count	2,70,000 cu.mm
Reticulocyte count	4.10%
Serum Biochemistry	
Urea	68 mg/dl
Creatinine	2 mg/dl
Sodium	136 meq/L
Potassium	4.1 meq/L
Uric acid	5.4 mg/dl
Calcium	9.1 mg/dl
Phosphorus	4.1 mg/dl
Total bilirubin	2.8 mg/dl
Direct bilirubin	1.8 mg/dl
Indirect bilirubin	1.0 mg/dl
Total proteins	7.2 g/dl
Albumin	4.0 g/dl
Globulin	3.2 g/dl
Sugar	98 mg/dl
Lactate dehydrogenase	1400 U/L

Discussion

Passenger lymphocytes in grafted kidney have been reported to result in immune hemolytic anemia in minor ABO incompatible transplants [3]. Passively transferred viable donor B-lymphocytes with the transplanted organ produce antibodies against A and B antigens and results in immune hemolysis [4]. This mechanism of immune hemolysis was initially suggested in 1971 by Beck et al. and later Stevens coined the term 'passenger lymphocytes'.

Donor-derived ABO antibody mostly develops 7-14 days after transplantation predominantly IgG, but it may also be IgM. These antibodies are short-lived, persisting for a median of 5 weeks in kidney transplant recipients [5]. The clinical features of PLS include drop in hemoglobin, signs of intravascular hemolysis, decreased haptoglobin, hemoglobinuria, renal failure, positive direct antiglobulin test (DAT) and in severe cases multiorgan failure [6]. Monitoring for at risk patients include DAT daily starting 3 days after transplant and complete hemogram daily.

Ramsey [7] reported that the frequency of passenger lymphocyte derived antibodies and hemolysis was highest, at 70% (for both), in heart lung transplant recipients; 40% and 29%, respectively, in liver transplant recipients; and 17% and 9% in kidney transplant recipients. It is suggested that the severity of hemolysis may be related to the total B lymphocytes transplanted together with the organ. The passenger lymphocyte syndrome is most likely to occur when the donor is group O and the patient group A, perhaps related to the fact that IgG anti-A and anti-B are more common in group O than in B or A subjects [8].

Meta-analysis by Nadarajah et al. [9] showed 99 cases of PLS following renal transplants. The median time of onset of hemolysis was 17 days after transplantation with the earliest occurring on day five and the latest at 3 months after transplant. Reported risk factors for PLS include:

- Previous red blood cell sensitization.
- Donor blood group O to recipient blood group A or B transfer.
- Cyclosporine treatment.
- Infection is in the immediate post-transplantation period. Poor outcomes have been reported, with one fatal case and two cases leading to graft failure.

In most cases alloimmune haemolytic anaemia is a self-limiting condition remitting spontaneously within 2 months [10,11]. High-dose corticosteroids and immunosuppressive regimen alteration (reduction in calcineurin inhibitor dose/ change of cyclosporine to tacrolimus) are tried but no treatment has been uniformly successful. Immune modulation (e.g., by IVIG) and specifically targeting B-lymphocytes using monoclonal antibodies such as rituximab has been successful in case reports and case series. In most cases PLS can be treated only with transfusions. Transfused red cells should be of organ donor ABO group to replace susceptible red cells with cells that would not be hemolyzed [12].

Conclusion

Alloimmune hemolysis remains a rare but important cause of anaemia in the early post-transplant period despite the increasing use of immunosuppressive drugs directed against B-cells. PLS is an important complication observed with every organ type and increasingly with non-ABO antibodies. No specific treatment is available for PLS. Early diagnosis with clinical suspicion and prompt treatment is needed in these individuals.

Competing Interests

We declare that we have no competing interests (financial and non-financial).

Author's Contribution

All the authors contributed substantially in conception and design, drafting and revising the manuscript, given final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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