Passenger Lymphocyte Syndrome After Single Lung Transplantation: Report of a Case and Literature Review

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Passenger lymphocyte syndrome (PLS) may occur when an organ from a blood group O donor is transplanted into a blood group A, B, or AB recipient. ABO-identical organs are used in the majority of transplants. However, because of the shortage of suitable donors, a minor ABO-mismatch may occur when using blood group O donor organs in A, B, or AB recipients. Induction of red blood cell destruction by graft-derived antibodies after minor ABO-mismatched single lung transplantation (SLT) is rare. We describe a blood group A recipient who had hemolysis of red cells, starting from day 8 and lasting up to day 11 after SLT, which necessitated transfusion from a blood type group O donor. **(Mid Taiwan J Med 2002;7:124-8)**

Key words

ABO-mismatch, passenger lymphocyte syndrome, single lung transplantation

INTRODUCTION

Since the first successful single lung transplant (SLT) in 1983 [1], 11,148 lung transplants have been reported to the International Lung Transplant Registry, and 58% of them have been SLT. The overall survival rate is above 80% six months after lung transplantation (bilateral or single) according to the registry [2]. Although ABO-identical organs are used in the majority of transplants, when a suitable ABO-identical donor is not found, universal group O donor organs may be used in A, B, or AB recipients. This may induce passenger lymphocyte syndrome (PLS), hemolysis of the recipient's red cells by anti-A antibodies and/or anti-B antibodies produced by grafted donor lymphocytes [3]. In addition to bone marrow transplants [4,5], PLS can occur after transplant of any type of organ, such as liver [6], kidney [7], heart and lung [3,8], and lung [9].

We describe a blood group A recipient who had hemolysis of red cells, starting from day 8 and lasting up to day 11 after SLT, which necessitated transfusion from a blood type group O donor. We reviewed the literature, and, to our knowledge, this is the first reported case of PLS after SLT in Taiwan.

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CASE REPORT

The patient was a 43-year-old man with

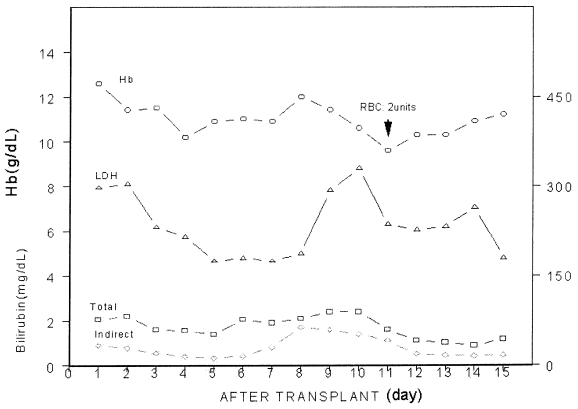

Figure. Flow chart shows hematologic and biochemical evidence for hemolysis. Two units of packed red cells were required to maintain the hemoglobin between day 11 and day 12 after operation.

end-stage emphysematous disease who underwent a left single lung transplant. His blood group was A, Rh-positive, and his human leukocyte antigen (HLA) serologic typing was A1101 A24 B54 B60 Cw7 DR4 DR12 DR52 DQ4 DQ7. There was no history of prior blood transfusion. Before surgery, hematologic values were within normal limits, and both the direct antiglobulin test (DAT) and red cell antibody screening were normal. The donor was a 16-year-old male with blood group O, Rh-positive, and HLA serologic typing A11 A24 B48 B75 Bw6 DR11 DR12 DR52, who died of intracerebral hemorrhage. No data on his red cell antibody screening could be obtained. The surgical procedure was uneventful, and the patient received left single lung transplantation (SLT). A cardiopulmonary bypass was used during operation because pulmonary artery pressure increased to 78/25 (50) mmHg when the left pulmonary artery was clamped. The ischemic time for the transplanted lung was 333 minutes. The bypass time was 70 minutes.

He received a routine immunosuppression regimen which included pre-SLT: azathioprine (2 mg/kg) and intraoperative 1 g methylprednisolone after vascular anastomosis; post-SLT: equine anti-human thymocyte globulin (2 mg/kg) was administered for five days, followed by prednisone (1 mg/kg/day). Cyclosporine A (adjusted to a whole blood level of 250–350 ng/mL) and azathioprine were administered intravenously in the immediate post-SLT period. The patient gradually received oral medication as tolerated. Antimicrobial prophylaxis, which included Vancomycin and Tienam was administered for five days, followed by cytomegalovirus prophylaxis with gancyclovir.

Postoperatively, jaundice developed (peak total serum bilirubin 41.0 μmol/L (2.4 mg/dL)), hemoglobin dropped from 120 g/L (12 U/dL) to 96 g/L (9.6 g/dL), and lactic dehydrogenase increased from 3.2 μKat/L (188 U/dL) to 5.6 μKat/L (330 U/dL) between postoperative day 8 and 11 (Figure). Acute hemolysis anemia was diagnosed. At the time of hemolysis, peripheral blood smear of the patient showed classic changes of immune hemolysis with spherocytes and polychromasia. However, subsequent DAT with anti-C3d and anti-IgG, and red cell antibody screening tests were normal. The patient was then given 2 units blood group O packed red cells which produced satisfactory hemoglobin increments. The patient was discharged on postoperative day 28. Nine months after transplantation, his clinical condition is excellent, pulmonary function test has improved significantly, and no evidence of hemolysis has been noted.

DISCUSSION

We have performed SLT on four patients, including three ABO-mismatched organs and one ABO-identical match. This patient was the only ABO-mismatched lung recipient who encountered PLS after SLT. According to the literature, PLS can occur after transplantation of bone marrow and any type of organ (Table) except cornea and heart, which probably reflects the successful removal of blood-borne lymphocytes at the time of transplantation and/or the absence of lymphoreticular tissue in the heart and cornea [3]. The reasons for PLS are explained by the fact that group O donor lymphoreticular tissue and circulating lymphocytes continue to

Table. Occurrence of passenger lymphocyte syndrome from solid organs and bone marrow transplantations in studied series

Author/Year	Organ/BMT	Cases reported	References
Bird/1982	Lung	1	9
Ramsey/1984	Liver	5	6
Mangal/1984	Kidney	3	7
Hows/1986	BMT	6	5
Hunt/1998	Heart-lung	6	8

BMT = bone marrow transplantation.

produce anti-A antibodies and/or anti-B antibodies after transplantation which mount a secondary immune response following antigenic stimulation by the recipient's differing ABO antigens [3]. It is possible that anti-A and anti-B antibodies may not be detected in the patient's RBC by DAT, as the findings in our studies and those of Hunt et al have shown [3].

In this study, we noted hemoglobin fall from 120 g/L (12.0 g/dL) to 96 g/L (9.6 g/dL) between postoperative day 8 and day 11. The occurrence of hemolysis due to PLS after transplantation varies. In the study group of nine heart and lung transplantation recipients, Hunt et al reported that a fall of hemoglobin of 5 g/L/day (0.5 g/dL/day) occurred for a mean of 13 days, starting from days 4–12 and lasting up to day 27 [3]. It has been reported that in renal and hepatic transplants with minor ABO incompatiblitily, hemolysis is usually short-lived; it can be seen as early as day 3 and can last up to three weeks, but there is no evidence of incompatible ABO antibody production persisting for longer than three months after transplantation [3,6-10]. Although the clinical problems usually can be solved successfully by transfusion, we think that PLS should be a differential diagnosis for anemia and/or jaundice after transplantation, especially in ABO-mismatched transplantation.

Concerning the management of hemolysis after a minor ABO-mismatched organ transplant, Hunt et al reported that one of the heart and lung transplant recipients had a maximal fall in hemoglobin of 5 g/L in 48 hours, and suggested that recipients of heart and lung transplantation should be closely monitored for signs of red cell destruction in the event of a hemolytic crisis due to donor ABO antibodies [3]. Furthermore, patients should be given group O red cell concentrates to prevent exacerbations of hemolysis as was done in this patient. Fresh frozen plasma should be of the recipient's group, and platelets can be from either recipient or donor group.

Interestingly, many studies have mentioned that cyclosporine may enhance, but not suppress, the production of anti-A and anti-B antibodies by donor lymphocytes [5,7,10]. Theoretically, cyclosporine is thought to inhibit the response of T lymphocytes to "new" antigens but not against antigens the immune system has already been primed to, such as the ABO antigens. Thus, cyclosporine will prevent the destruction and suppression of donor lymphocytes (new antigens), while allowing continued ABO antibody production from the already primed donor lymphocytes [3].

Due to a shortage of donor organs, it is inevitable to use ABO compatible, but not identical, blood group O donors in blood group A, B, or AB recipients. We think it is essential to monitor the patients for anti-recipient ABO antibodies after transplantation. If they appear, donor-type packed red cells should be given when needed throughout the period when the antibody is present [6].

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單肺移植後的過渡性淋巴球症候群：一病例報告和文獻回顧

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當血型O型的捐贈者器官移植給血型A、B或AB型的病患時，可能會發生過渡性淋巴球症候群，理想的情況下，大部份移植手術，採用血型ABO型完全相同的器官，有時，因爲器官的短缺，A、B或AB型的病患會使用O型捐贈者的器官，而造成輕微血型的不配合。在單肺移植手術中，因輕微血型不配合而由捐贈器官的抗體引起的紅血球破壞，較少被報告。我們報告一位A型血型病患，在接受一位O型捐贈者做單肺移植後8天到11天，造成紅血球溶血，而需要輸血的病例。（中台灣醫誌 2002;7:124-8）

關鍵詞

ABO血型不配合，過渡性淋巴球症候群，單肺移植

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