CORRESPONDENCE

Passenger Lymphocyte Syndrome Following Minor ABO Mismatch Liver Transplantation

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Dear Editor,

Non-ABO identical liver transplantation (LT) is in growing trend in India due to limited availability of organ donors and the growing number of patients awaiting orthotopic liver transplantation. Recipients of minor ABO mismatched organ transplantation may experience delayed hemolysis mediated by donor lymphocytes contained in the graft. Donor lymphocytes produce iso-agglutinins capable of destroying the recipient's red cells, resulting in varying degree of hemolysis known as passenger lymphocyte syndrome (PLS) [1]. PLS is not an uncommon cause of anemia in non-ABO identical LT but often goes undiagnosed and not yet reported in India in ABO mismatch LT.

We present a case of 48 years old male, AB positive, with ethanol related end stage liver disease who underwent live donor liver transplant from a O positive donor without any intraoperative complications. He had history of multiple transfusions in past 2 years during episodes of gastrointestinal bleeds but no history of haemolytic transfusion reaction or red cell immunization. Intraoperatively, the patient was transfused with AB positive 4 packed red cells (PRC), 2 fresh frozen plasma (FFP), 3 units of cryoprecipitate and 1 unit of single donor platelets (SDP) and 2 units of FFP postoperatively. Injection Methylprednisolone 500 mg was given intravenously in the anhepatic phase and

then was changed to oral prednisolone. Cap tacrolimus 0.5 mg twice daily was started 12 h after the surgery and was adjusted as per tac levels during postoperative period. The postoperative course of the patient was uneventful and graft function was normal by postoperative day (POD) 5. However, POD 7 onwards, patient showed decline in hemoglobin (Hb) level from 10 to 6.9 g%. As per liver transplant transfusion policy, Crossmatch compatible O positive PRC was issued and transfused. However, the Hb was not raising in spite of transfusion of O positive PRC. There was no evidence of bleeding or sepsis and by POD-12, investigations showed peak bilirubin levels 14.53 gm/dl, reticulocyte count 9%, Serum LDH 708 IU/ml and peripheral smear suggestive of hemolytic anemia. On immune-hematological workup, repeat ABO and Rh typing (Gel method) showed AB positive with mixed field reaction with anti-A and anti-B in forward grouping, the reverse grouping showed no discrepancy in saline phase. On performing polyspecific direct anti-globulin test (DAT) using the LISS Coombs column agglutination technique (Bio-Rad GmbH, Cressier-sur-Morat, Switzerland), the patient's red cells were found to be positive (2+). Elution was performed using commercial acid elution kit (Diacidel, Bio-Rad GmbH, Cressier-sur-Morat, Switzerland) and the eluate showed the presence of anti-A antibody. Indirect antiglobulin test of the patient's serum and eluate using 3-cell panel of O group (Diacell, Biorad GmbH, Cressier-sur-Morat, Switzerland) was negative, ruling out the presence of any unexpected antibody. Anti-A antibody was probably IgG type as it was detectable in the serum only in AHG phase and was also confirmed by presence in RBC eluate. Serial titration of liver donor serum showed IgG anti A and anti B titres of 256 and 128 respectively. Hemolysin test was positive. A provisional diagnosis of PLS was made. Autoimmune hemolytic anemia was ruled

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Fig. 1 Progression of bilirubin and haemoglobin levels and RBC transfusions over post-transplant period

out by time of onset of hemolysis, its transient nature, absence of previous history of primary autoimmune disease, negative indirect coombs test on testing with patient serum and eluate and Crossmatch incompatibility with AB positive but compatible with O positive red cell units. A total of 6 O positive units were issued between POD-10 and POD-20 and the patient was serially monitored with DAT and the progression of bilirubin and Hemoglobin is shown in Fig. 1. 22 days postoperatively, his Hb rose to 9.1 g%. His condition improved gradually and was discharged in stable condition.

Liver transplantation can be associated with many hematological abnormalities such as PLS, graft-versus-host disease, post-transplant lymphoproliferative malignancies, thrombotic microangiopathy [1]. PLS can develop abruptly and ranges from mild to severe. Donor derived antibodies are short lived, typically develops 7–14 days post liver transplantation and resolves within 3 months post-transplant [2]. Most cases of PLS are due to ABO mismatch, but antibodies against Rh, Kidd, Kell, Duffy have also been reported to cause PLS [3]. In a recent study, the prevalence of PLS among minor mismatch LT was 20% with hemolysis in all patients [4]. Although the hemolysis is usually mild and self limited, substantial morbidity such as renal failure, DIC and multiorgan failure has been reported and require timely identification and management [5]. Definite diagnostic modalities includes flow cytometry and nested polymerase chain reaction which can diagnose the donor lymphocyte microchimerism. Treatment involves transfusion with Group O PRC or antigen negative RBC units. In rare cases, additional treatments such as stronger immunosuppression or red cell exchange required [2].

The case highlights the importance of monitoring patients receiving ABO or Rh mismatched transplants for

PLS, which is indicated by abrupt fall in hemoglobin without signs of bleeding, biochemical features of hemolysis, positive DAT and presence of relevant antibody (anti-A or anti-B or other clinical significant donor derived red cell antibody) in patient serum and/or RBC eluate. Donor compatible transfusion is also recommended as a prophylactic management against PLS in minor ABO mismatch LT.

Compliance with Ethical Standards

Ethical Approval All procedures were in accordance to ethical standards. Informed consent was taken from the patient before blood transfusions.

Conflict of interest The authors declare that they have no conflict of interest.

References

- Smith EP (2010) Hematological disorders after solid organ transplantation. *Hematology Am Soc Hematol Educ Program* 2010:281–286
- Audet M, Panaro F, Piardi T, Huang P, Cag M, Cinqualbre J et al (2008) Passenger lymphocyte syndrome and liver transplantation. *Clin Dev Immunol* 2008:1–4
- Petz LD (2005) Immune hemolysis associated transplantation. *Semin Hematol* 42:145–155
- Romero S, Solves P, Lancharro A, Cano I, Moscardo F, Carpio N et al (2015) Passenger lymphocyte syndrome in liver transplant recipients: a description of 12 cases. *Blood Transfus* 13(3):423–428
- Yazer MH, Triulzi DJ (2007) Immune hemolysis following ABO-mismatched stem cell or solid organ transplantation. *Curr Opin Hematol* 14(6):664–670