

Successful Heart Transplantation Despite Rhesus Blood Type Mismatch: A Case Report

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ARTICLE INFO Received July 7, 2023 Revised October 3, 2023 Accepted October 20, 2023

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Matching for the rhesus (Rh) blood group is currently not taken into account in the organ allocation system. However, in Rh-mismatched transplantation, the primary concern is the potential for RhD-negative recipients to develop sensitization and produce anti-D antibodies if they receive a transfusion of RhD-positive blood. It is estimated that over 80% of RhD-negative recipients may experience Rh allosensitization when exposed to RhD-positive blood, although this occurrence is less common in recipients of solid organs. In theory, RhD-negative recipients who receive organs from RhD-positive donors are at risk of alloimmunization and the production of anti-D antibodies, which could complicate future blood product transfusions. However, our understanding of the impact of donor-recipient Rh mismatch on transplant outcomes, particularly in heart transplantation, is limited. We report a case of successful Rh-mismatched heart transplantation, which was effectively managed through the use of preoperative RhD immunoglobulin and plasmapheresis.

Keywords: Rh blood group, Plasmapheresis, Blood type incompatibility, Case reports

Case report

A 72-year-old male patient, with blood type B and rhesus D (RhD)-negative, was diagnosed with end-stage heart failure resulting from hypertrophic cardiomyopathy. Due to ventricular tachyarrhythmia, the patient had previously been fitted with an implantable cardioverter-defibrillator. He was admitted to the emergency department experiencing chest pain. Transthoracic echocardiography revealed a significantly thickened interventricular septum (mid-septum thickness, 17 mm) and a reduced ejection fraction of 22%. A left ventricular assist device was not considered as a treatment option due to the patient's severe interventricular septal hypertrophy. As a result, the patient was referred for a heart transplant.

Initially, heart transplantation was deemed challenging due to the patient's high panel reactive antibody (PRA) level, which was measured at 74% using the Luminex beadbased immunoassay. The patient's Rh-negative blood type added to these difficulties. While waiting for a suitable heart donor, the patient underwent plasmapheresis five times, each time using 400 mL of 20% albumin and 4 units of fresh frozen plasma. Despite these interventions, the PRA levels continued to increase, eventually reaching 97%.

After a 13-month hospital stay, the patient underwent an orthotopic heart transplantation. Despite having an Rh-negative blood type, a heart from an Rh-positive, blood type B donor was successfully utilized in the procedure. To prevent Rh allosensitization, the patient was preoperatively given a single dose of RhD immunoglobulin (WinRho SDF 1,500 U, 300 µg; Kamada, Rehovot, Israel). Importantly, no adverse effects, such as hemolysis due to immune complex formation, were observed. Postoperatively, plasmapheresis was performed to monitor PRA levels and to detect any potential presence of anti-D antibodies. In accordance with our institutional protocol, the patient underwent immunosuppressive therapy, which included intravenous methylprednisolone, mycophenolate mofetil, and tacrolimus. Rh-negative red blood products were used for transfusions as needed. However, during the patient's stay in the general ward, no red blood cell transfusions were necessary, as there were no signs of bleeding. Immediately following the operation, 2 packs of fresh frozen plasma (approximately 260 mL) were administered.

The postoperative PRA level was found to be 81%, with no HLA-donor-specific antigen present. Following this, plasmapheresis was carried out 5 times during the postoperative period. Each session of postoperative plasmapheresis involved the use of 20% albumin (500 mL) and normal saline (2,500 mL). Echocardiography confirmed satisfactory allograft function. Regular endomyocardial biopsies were performed, and the patient has not had any instances of cellular or antibody-mediated rejections. Furthermore, there have been no instances of hemolysis up to 1 year after the transplantation.

The patient provided written informed consent for publication of the case details and clinical images.

Discussion

Theoretically, the presence of an Rh mismatch is not problematic if the transplanted organ does not contain the donor's blood cells, especially in patients who are immunosuppressed. As a result, the Rh blood group is not considered in the organ allocation system. However, it should be noted that in a small percentage of cases, Rh recipients can become allosensitized when the graft is sourced from Rh-negative donors [1]. Rh allosensitization has been documented in roughly 5% of Rh-incompatible liver and kidney transplants [2,3]. There have even been isolated instances of fatal graft-versus-host reactions leading to extensive hemolysis [4].

Although reports of immune reactions related to Rhmismatched transplantation are infrequent, when they do occur, they consistently involve severe and persistent hemolytic reactions, more so than those observed with ABO incompatibility. Hemolytic events resulting from Rh allosensitization are difficult to reverse using plasmapheresis and immunoglobulin treatments, and many cases ultimately prove fatal [5,6]. Given the lack of consensus guidelines for the prophylaxis of Rh mismatch transplantation [7], our strategy involved administering preoperative RhD immunoglobulin and performing perioperative plasmapheresis. The precise mechanism by which RhD immunoglobulin prevents isoimmunization remains unclear; however, it is thought to suppress the immune response and inhibit antibody formation in Rh-incompatible individuals [8]. Importantly, the patient in this case did not experience any side effects, such as hemolysis, which can result from the formation of immune complexes associated with RhD immunoglobulin.

Multiple plasmapheresis procedures were performed to eliminate any potential presence of anti-D antibodies and PRAs. Consequently, the patient underwent a successful transplant following the administration of preoperative RhD immunoglobulin and multiple plasmaphereses, with no instances of rejection or hemolysis observed.

In conclusion, Rh-negative recipients can effectively receive transplants from Rh-mismatched donors through the use of preoperative RhD immunoglobulin and perioperative plasmapheresis.

Article information

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Conceptualization: JHK. Data curation: JHK. Formal analysis: JHK, YRS. Methodology: YRS. Project administration: YRS. Visualization: JHK. Writing-original draft: JHK. Writing-review & editing: YRS. Final approval of the manuscript: YRS.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-forprofit sectors.

Acknowledgments

The authors thank Yu Rim Shin for providing the case.

References

- Ramsey G, Hahn LF, Cornell FW, et al. Low rate of rhesus immunization from Rh-incompatible blood transfusions during liver and heart transplant surgery. Transplantation 1989;47:993-5. https://doi.org/10.1097/00007890-198906000-00015
- Bolia R, Shankar S, Herd L, Hardikar W. Rhesus alloimunization occurs after Rh incompatible liver transplantation in children. Transplantation 2018;102:e1. https://doi.org/10.1097/TP.0000000000001976
- 3. Quan VA, Kemp LJ, Payne A, Andrews PA, Sacks SH. Rhesus im-



- munization after renal transplantation. Transplantation 1996;61:149-50. https://doi.org/10.1097/00007890-199601150-00028
- Sharma H, McAlister V. Fatal graft versus host hemolytic reaction from rhesus compatible mismatched liver transplantation. Hepatobiliary Surg Nutr 2019;8:186-8. https://doi.org/10.21037/hbsn.2019.01.05
- Cserti-Gazdewich CM, Waddell TK, Singer LG, et al. Passenger lymphocyte syndrome with or without immune hemolytic anemia in all Rh-positive recipients of lungs from rhesus alloimmunized donors: three new cases and a review of the literature. Transfus Med Rev 2009;23:134-45. https://doi.org/10.1016/j.tmrv.2008.12.003
- Gniadek TJ, McGonigle AM, Shirey RS, et al. A rare, potentially life-threatening presentation of passenger lymphocyte syndrome. Transfusion 2017;57:1262-6. https://doi.org/10.1111/trf.14055
- Ahn A, Yang JJ, Youk HJ, et al. Rh(D) Alloimmunization risk after Rh(D)-incompatible solid organ transplantations in Rh(D)-negative recipients. Am J Clin Pathol 2022;158:8-12. https://doi.org/10.1093/ aicp/agac002
- Crowther C, Middleton P. Anti-D administration after childbirth for preventing rhesus alloimmunisation. Cochrane Database Syst Rev 2000;1997:CD000021. https://doi.org/10.1002/14651858.CD000021