Letter to the Editor
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A Case of Bidirectional ABO- and RhD-Incompatible Liver Transplantation in a Mongolian Patient With Asian-Type DEL

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Dear Editor,

The DEL phenotype is a rhesus D (RhD) variant with extremely low RhD antigen expression [1-3]. It appears as RhD-negative in routine serological tests [1-3] and requires genetic tests to distinguish alleles [2-4]. Among the 50 described DEL alleles [2], *RHD*1227A* (*RHD*01EL.01*), known as Asian-type DEL [1-6], has a synonymous point mutation, c.1227G>A [1-6], near the exon 9–intron 9 junction [4]. Owing to splicing disruption [4], Asian-type DEL red blood cells (RBCs) exhibit a markedly reduced but complete RhD epitope repertoire [1-3, 5-7]. Unlike true RhD-negative and certain other DEL individuals [3], Asian-type DEL individuals do not produce anti-D alloantibodies upon RhD-positive blood component transfusion [1-7].

In East and Southeast Asian countries, RhD-negative individuals are rare (0.15–0.5% of the population) [1, 2, 4-7], whereas DEL individuals account for 10%–33% of RhD-negative cases [1-3, 5, 6], and Asian-type DEL individuals for 95%–98% of DEL cases [1-3, 5, 6], in Korean, Chinese, Japanese, and Thai populations [1-7].

To the best of our knowledge, Asian-type DEL has not yet been reported in the Mongolian population, and there is no report of liver transplantation in an Asian-type DEL recipient. We report the first case of bidirectional ABO- and RhD-incompatible living-donor liver transplantation in a Mongolian patient with Asian–type DEL accompanied with the transfusion of large amounts of RhD-positive blood components, in which the patient did not develop anti-D alloimmunization. This study was approved by the Institutional Review Board of Korea University Anam Hospital, Seoul, Korea (IRB No. 2024AN0309), and the need for informed consent was waived.

In July 2023, a 57-yr-old man from Mongolia with chronic hepatitis B and D virus infection was referred to Korea University Anam Hospital, Seoul, Korea. Computed tomography revealed two liver masses, liver cirrhosis, and grade 3 ascites. A complete blood count revealed anemia (Hb, 98 g/L) and thrombocytopenia (platelets, 91×10^9/L). Total bilirubin was 0.1109 g/L, albumin, 27 g/L, prothrombin time, 1.98 (international normalized ratio), and serum creatinine, 0.0177 g/L. Liver biopsy confirmed hepatocellular carcinoma. Liver transplantation was indicated, with a Child–Pugh score of 12 and a Model for End-stage Liver Disease score of 29.

The patient's ABO group was A. The patient tested RhD-negative

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with anti-D Bioclone MAD2/polyclonal (Ortho-Clinical Diagnostics, Raritan, NJ, USA), anti-D SIHDIA TH-28/MS-26 (Shinyang Diagnostics, Siheung, Korea), and anti-D Novaclone D175-2/D415 1E4 (Dominion Biologicals, Dartmouth, NS, Canada) IgM/IgG clone reagents. The RhCE phenotype was Ccee using anti-C, -E, -c, and -e reagents (Diagast, Loos, France). In *RHD* genotyping, the *RHD* promoter, intron 4, and exons 7 and 10 were amplified in allele-specific PCR, and sequencing of *RHD* exon 9 revealed c.1227G > A, indicating Asian-type DEL. The living liver donor was a B RhD-positive Mongolian. Following rituximab administration, preoperative plasmaphereses with AB RhD-positive fresh-frozen plasma (FFP) were performed for five days to lower the anti-B IgM titer from 1:256 to the target titer of ≤1:8 (Table 1).

During hospitalization and surgery, the patient was transfused with A RhD-negative RBCs (11 units), A RhD-positive RBCs (8 units), AB RhD-positive single-donor platelets (3 units), AB RhD-positive FFP (65 units), and AB RhD-positive cryoprecipitates (6 units). The liver graft (0.574 kg) was estimated to contain 166 mL of RhD-positive residual blood [8]. RhIG was not administered. While the postoperative immunosuppressants, basiliximab, mycophenolate mofetil, and prednisolone, were administered for a certain duration, tacrolimus and everolimus were maintained. After being discharged, the patient was followed for over a year without complications, isoagglutinin titer elevation, or evidence of antibody-mediated rejection. Subsequent antibody tests were negative, with the last test performed 90 days after surgery (Table 2).

While rare, anti-D alloimmunization can occur in immunosuppressed transplant recipients; therefore, RhIG administration is considered in RhD-incompatible transplantation [9, 10]. Our Asian-type DEL patient did not develop anti-D alloimmunization despite massive RhD-positive blood component transfusion without RhIG administration, which is in line with previous findings [1-7]. A previous study conducted in Korea also showed the absence of anti-D alloimmunization in RhD-incompatible solid organ transplantations [10], presumably because of the predominance of Asian-type DEL in the RhD-negative Asian population and immunosuppression [10].

Identifying Asian-type DEL would improve blood supply management, ensure patient safety in countries with limited RhD-negative blood supplies, and be beneficial when large amounts of blood transfusion are required, such as in liver transplantation.

Table 1. Allele-specific PCR and sequencing primers used in this study

Method	Target region	Forward primer sequence	Reverse primer sequence	Product size (bp)
Allele-specific PCR	*RHD* promotor	TCCACTTTCCACCTCCCTGC	GCAGCCAACTTCCCCTGTG	256
	RHD intron 4	CCTATTTTGGGCTGTCTGTGG	GAACCTGCTCTGTGAAGTGCT	298
	RHD exon 7	GTTGTAACCGAGTGCTGGGGATTC	TGCCGGCTCCGACGGTATC	123
	RHD exon 10	GATTTTAAGCAAAAGCATCCAAG	ATGGTGAGATTCTCCTCAAAGAG	191
	*HBB**	GAAGAGCCAAGGACAGGTAC	GGAAAATAGACCAATAGGCAG	408
Sequencing	*RHD* exon 9	GGTCCAGGAATGACAGGGCT	GTTTCTTCCAGCTTTTGCATTGT	589

*The β-globin (*HBB*) housekeeping gene was used as the reference.

Table 2. Transfused blood components

Transfused blood component	Preoperative	Intraoperative	Postoperative
Packed RBC (A RhD-negative)*	2		
Pre-storage leukoreduced RBC (A RhD-negative)*		9	
Pre-storage leukoreduced RBC (A RhD-positive)		7	1
Single-donor platelet (AB RhD-positive)		3	
FFP (AB RhD-positive)	50†	15	
Cryoprecipitate (AB RhD-positive)		6	

The table result presents the number of units of transfused blood components.
*Initially, RhD-negative RBCs were prepared as requested, and issued preoperatively and intraoperatively; however, because of a shortage of RhD-negative RBCs and the recipient's identification as being Asian-type DEL, RhD-positive RBCs were used in subsequent transfusions.
†FFP was used as a replacement fluid in plasmapheresis.
Abbreviations: RBC, red blood cell; FFP, fresh-frozen plasma.

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AUTHOR CONTRIBUTIONS

Kang T collected the data and wrote the manuscript. Choi R performed immunohematological tests and provided blood components. Kim DS participated in clinical evaluation and provided clinical feedback. Cho D interpreted *RHD* genotyping and revised the manuscript. Kim DW supervised the study and revised the manuscript. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST

None declared.

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