American Journal of Transplantation xxx (xxxx) xxx

Contents lists available at ScienceDirect

American Journal of Transplantation

journal homepage: www.amjtransplant.org

Case Report

Kidney transplantation across ABO-H incompatibility in a recipient with Bombay blood group: A novel report

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ARTICLE INFO

Keywords:
Bombay blood group
Renal transplant
ABO-H–incompatible transplant
H antigen
Anti-H antibody

ABSTRACT

The Bombay blood group is an exceptionally rare phenotype characterized by the absence of H antigen on red blood cells due to mutations in the *FUT1* gene and absence of H substance in secretions from concurrent *FUT2* deficiency. These individuals produce potent anti-H antibodies in addition to anti-A and anti-B antibodies, posing unique challenges in transfusion and solid organ transplantation. We report a successful ABO-H–incompatible renal transplantation in a patient with genetically confirmed Bombay phenotype. A 30-year-old man with end-stage kidney disease secondary to immunoglobulin A nephropathy was evaluated for transplantation with his mother as a potential donor. Serologic and molecular studies identified a *FUT1* homozygous missense variant (p.Leu242Arg) and a *FUT2* homozygous deletion consistent with the classical digenic Bombay phenotype. The patient underwent a structured desensitization protocol with rituximab, plasma exchange, and intravenous immunoglobulin prior to transplantation. The postoperative course was uneventful, with stable graft function. This ground-breaking case demonstrates that, with appropriate desensitization, anti-H antibodies can be safely managed, thereby expanding the feasibility of renal transplantation in recipients with the Bombay phenotype.

Abbreviations: FUT, fucosyl transferase; Ig, immunoglobulin.

Presented as an abstract presentation in World Congress of Nephrology, New Delhi, February 2025.

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https://doi.org/10.1016/j.ajt.2025.11.002
Received 19 June 2025; Received in revised form 5 November 2025; Accepted 5 November 2025
Available online xxxx

Please cite this article as: Raj TY et al., Kidney transplantation across ABO-H incompatibility in a recipient with Bombay blood group: A novel report, American Journal of Transplantation, https://doi.org/10.1016/j.ajt.2025.11.002

1. Introduction

The ABO histoblood group system remains one of the most clinically significant barriers to successful solid organ transplantation.[1] ABO histoblood group antigens are defined by specific oligosaccharide moieties synthesized from a common precursor, the H antigen.[2] Currently, there are 47 recognized blood group systems, comprising 392 red cell antigens that are determined by 52 genes.[3] The enzyme α(1,2)-fucosyl transferase (FUT), encoded by the *FUT1* gene, catalyzes the addition of fucose to form the H antigen, which subsequently serves as the substrate for A or B transferases.[4] The Bombay phenotype results from a homozygous loss-of-function mutation in *FUT1*, leading to complete absence of H antigen expression on red cells (Fig. 1). Concurrent *FUT2* inactivation abolishes H antigen secretion in mucosal and salivary secretions.[5]

First identified in Bombay, India, in 1952, by Dr Y.M. Bhende,[6] this phenotype is extremely rare, with a frequency of approximately 1 in 250 000 in White[7] and 1 in 10 000 in Indian populations.[8] Individuals with this phenotype possess naturally occurring anti-A, anti-B, and anti-H antibodies that can react with all non-Bombay blood types.[6] Consequently, renal transplantation in these patients is limited to donors with the same phenotype, making compatible transplantation virtually impossible. We present the case of a successful ABO-H–incompatible kidney transplant in a recipient with the Bombay blood group.

2. Case report

A 30-year-old man presented with hypertensive emergency and renal failure. Laboratory evaluation revealed serum creatinine of 11 mg/dL and nephrotic-range proteinuria. Ultrasound showed bilateral shrunken kidneys with increased echogenicity. Renal biopsy confirmed immunoglobulin (Ig)A nephropathy (M1E1S1T2C0). He was initiated on maintenance hemodialysis.

His mother, a 54-year-old woman with blood group B, was evaluated as a potential donor simultaneously. During pretransplant testing, the recipient's forward blood grouping showed no agglutination with anti-A or anti-B sera, suggesting group O. Reverse grouping revealed agglutination with A, B, and O cells. Direct Coombs test showed negative results. The unexpected agglutination with O cells raised suspicion for an unusual antibody directed against a common antigen.

Further testing with anti-H lectin showed no agglutination, confirming the absence of the H antigen. Extended red cell typing demonstrated a strong 4+ anti-H reaction with group O cells and absence of A, B, and H substances in both serum and saliva.

Genetic analysis identified a homozygous missense variant in exon 2 of *FUT1* (c.725T>G; p.Leu242Arg; chr19: g.48750557A>C), a known pathogenic mutation associated with Bombay phenotype. A contiguous 1.11-kb homozygous deletion involving the *FUT2* gene on chromosome 19 was also detected, confirming a nonsecretor status. Both findings established the classical digenic Bombay phenotype. Saliva inhibition testing showed negative results, supporting absence of H substance.

Antibody titration using the gel card (column agglutination) method revealed IgM anti-H and anti-B titers of 1:32; IgG anti-H and anti-B titers of 1:64. Complement-dependent cytotoxicity and flow cytometric crossmatch were negative for T and B lymphocytes. Donor-specific antibody testing using the LIFECODES (Werfen) Donor Specific Antibody Assay on the Luminex xMAP platform showed no detectable antibodies against donor HLA class I or II antigens.

A stepwise desensitization protocol was initiated, including rituximab (200 mg), oral tacrolimus, mycophenolate mofetil, methylprednisolone, and 3 sessions of plasma exchange, each

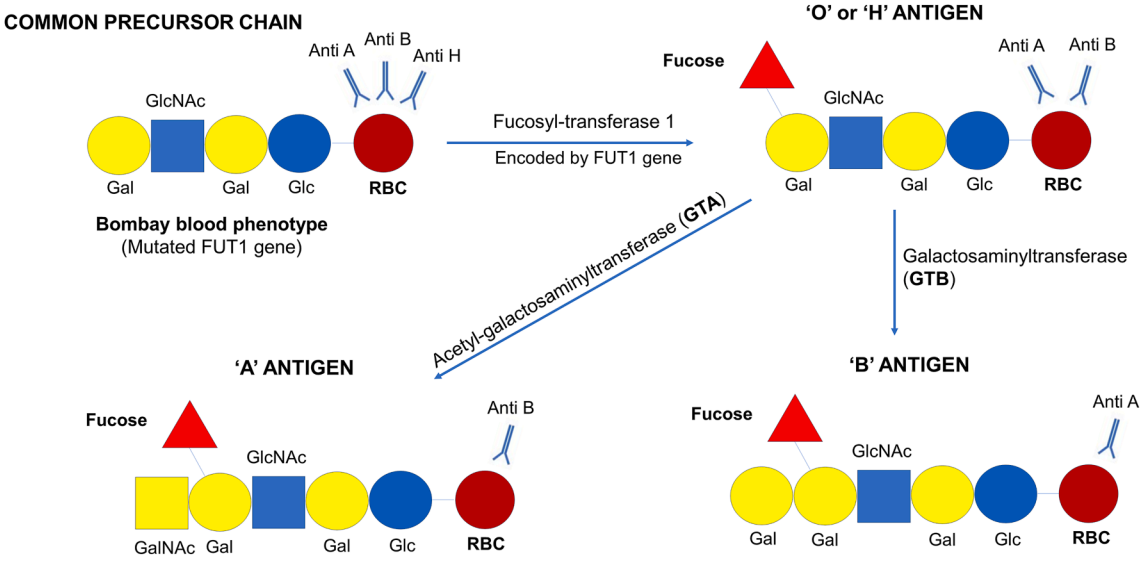

Figure 1. Blood group antigens and their corresponding antibodies. Gal, galactose; GalNAc, N-acetylgalactosamine; GlcNAc, N-acetyl glucosamine; Glc, glucose.

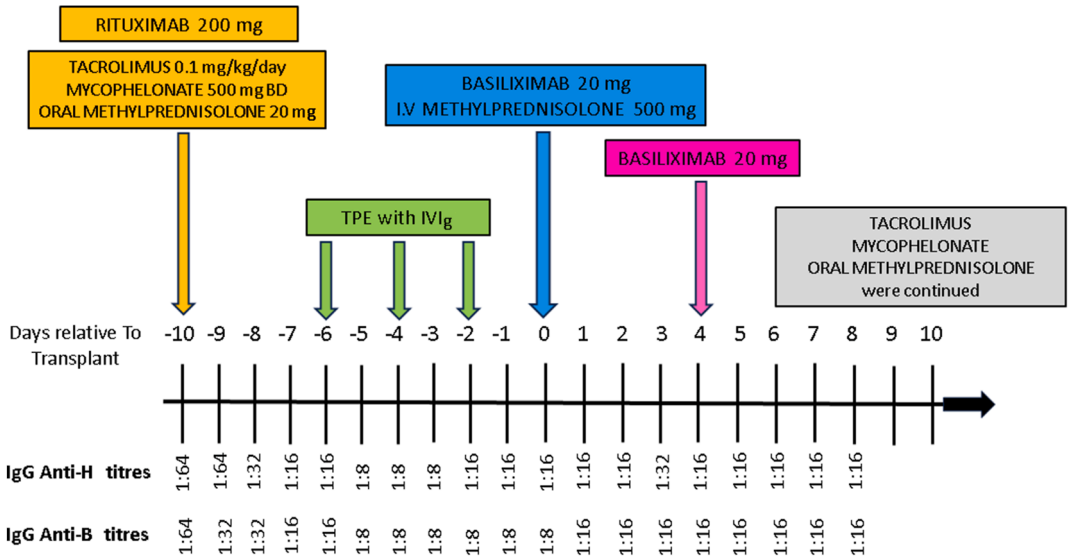

Figure 2. Desensitization protocol with dynamics of IgG titers. Ig, immunoglobulin; IVIg, intravenous immunoglobulin; TPE, therapeutic plasma exchange.

followed by intravenous Ig (5 g). By day of transplantation, IgG anti-H titers reduced to 1:16 and anti-B titers to 1:8 (Fig. 2).

Renal transplantation was performed with basiliximab induction. The perioperative course was uneventful. The patient achieved a nadir serum creatinine of 1.5 mg/dL, with good urine output. IgG anti-H and anti-B titers remained stable postoperatively.

Fourteen months posttransplant, his graft function has been stable with a creatinine of 1.6 mg/dL. The IgG anti-H titer was 1:8 and IgM was 1:4. His IgG anti-B titer was 1:8, and IgM was 1:4. At the time of writing, he was on tacrolimus (3 mg/d), mycophenolate mofetil (1250 mg/d), and oral methylprednisolone (4 mg/d).

3. Discussion

The Bombay phenotype represents a unique immune-hematologic challenge in solid organ transplantation because of the universal presence of anti-H antibodies that can react with virtually all donor tissues.[5] The *FUT1* gene encodes α(1,2)-FUT, essential for the formation of H antigen on erythrocytes and vascular endothelium, while *FUT2* governs H antigen expression in secretions. Mutations in both genes lead to total absence of H antigen expression, producing the classic digenic Bombay phenotype.[4,5]

In the context of renal transplantation, the absence of compatible donors with the same phenotype historically rendered such patients unsuitable for transplantation. The main immunologic barrier is the potential for anti-H–mediated hyperacute rejection, given that H antigen is ubiquitously expressed in vascular endothelium of most donors.[4,5,9] This risk parallels the hyperacute rejection observed in ABO-incompatible transplantation prior to the development of desensitization strategies.

The global experience with ABO-incompatible renal transplantation has demonstrated that, with appropriate desensitization, patient and graft survival are comparable with ABO-compatible recipients, confirmed by large meta-analyses.[10,11] Applying this paradigm to the Bombay phenotype, anti-H antibodies can similarly be reduced to clinically acceptable titers, allowing successful transplantation from a donor who expresses H antigen. In our case, achieving an IgG anti-H titer of 1:16 and IgM anti-H titer of 1:4 prior to surgery was considered a safe threshold to proceed.

One of the uncertainties in such transplants is whether graft accommodation also occurs with anti-H antibodies. The absence of published literature on successful organ transplants in recipients with Bombay phenotype significantly limits evidence-based guidance, making clinical decision making challenging. Although this mechanism has not been directly studied in Bombay phenotype patients, our patient's stable posttransplant antibody titers and sustained graft function suggest that accommodation may indeed extend to the anti-H system.

This case provides proof-of-concept that anti-H isoagglutinins behave similarly to anti-A and anti-B antibodies, being amenable to extracorporeal removal and capable of accommodation posttransplant. It demonstrates that, under stringent immunologic control and close monitoring, even recipients with the Bombay blood phenotype can safely undergo renal transplantation from conventional ABO donors.

4. Conclusion

This case establishes that renal transplantation in Bombay phenotype recipients, although once considered immunologically prohibitive, is feasible with appropriate pretransplant desensitization. Controlled reduction of IgG anti-H to $\leq$1:16 appears to permit safe transplantation with favorable outcomes. Broader reporting and long-term follow-up are essential to validate these findings and develop standardized desensitization protocols for ABO-H–incompatible transplantation.

Declaration of competing interest

The authors of this manuscript have no conflicts of interest to disclose as described by *American Journal of Transplantation*.

Data availability

No datasets were generated or analyzed for this case report.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajt.2025.11.002.

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