Title: Anti-Fy^a Hemolytic Transfusion Reaction in a Recipient of an Fy^a-positive Kidney

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Background:

The Duffy antigen system is determined by the gene ACKR1, which is found on chromosome 1 (1.q22-1.q23). The gene encodes a 336 amino acid acidic glycoprotein which determines the Duffy blood group system which consists of four codominant alleles, the two most common of which are FY*A and FY*B that encode for the 3 most common phenotypes Fy(a+b-), Fy (a+b+), and Fy(a-b-). Though most clinically relevant on reticulocytes and erythrocytes, it is also found in cerebellar neurons and venular endothelial cells. This unique feature of the Duffy antigen causes it to be found in large quantities in on Purkinje cells of the cerebellum, large pulmonary venules, endothelial cells of thyroid capillaries, and the post-capillary venules of some organs including the spleen, liver and kidney.

Anti-Fy^a is a relatively common antibody with IgG1 subclass of IgG predominating. Anti-Fy^a does not normally activate complement and mild acute or delayed hemolytic transfusion reactions are implicated which can also be fatal. Fy^a and Fy^b antibodies have also been implicated in HDFN.

In individuals of African ancestry, the Fy(a-b-) phenotype is the most common, caused by homozygosity for a silenced FY*B allele. A mutation in the GATA-1 transcription factor prevents expression in erythroid tissue; thus Fy(a-b-) people of African ancestry lack the FY glycoprotein on their red cells only. The implication of minor histocompatibility antigens, such as Fy^a, in renal allograft rejection has been established, however the specificity of these antigens is still unknown. Acute rejection of an allograft amongst African American renal recipients has shown similar rates despite varying Duffy blood groups, however delayed graft function has shown a strong association with decreased allograft survival. African Americans are at greater risk of end-stage renal disease (ESRD) than non-African Americans and make up at least one third of ESRD patients in the USA. They also have a 30% to 40% decreased kidney- graft survival after transplantation compared with white patients.

Case Report:

A 46-year-old African American male with sickle cell disease and end-stage renal disease presented to our institution for deceased donor kidney transplant (DDKT) on 2/22/2022. He had previously received care at outside hospitals, including previous blood transfusions. There was no previous blood type or additional information on file with our blood bank (no historical type and screen, red cell phenotyping, or antibody history). Type and screen and Check ABO samples were received in the blood bank immediately before renal transplant surgery. The patient's blood type was B Rh positive, the antibody screen was positive, and antibody identification was initiated. His pre-op Hb was 5.7 g/dl, and two RBC units were ordered for Emergency Release

before the antibody identification was completed. Once complete, anti-Fy^a was confirmed, and one of the two transfused RBCs was crossmatch incompatible and proved positive for Fy^a antigen. By post-op day two, the patient's Hb decreased from 7.7 g/dl to 6.1 g/dl, indicative of a delayed hemolytic transfusion reaction. Direct antiglobulin test (DAT) was negative.

Genotyping was then performed on a stored blood sample from the deceased kidney donor to determine the graft's Fy^a status. PreciseType Human Erythrocyte Antigen 1.2 BeadChip DNA array was performed which utilizes 24 known gene mutations to identify 35 red blood-cell antigens and three phenotypic variants from 11 blood groups simultaneously. The donor was determined to be positive for both Fy^a and Fy^b. Despite the concern for potential antibody-mediated graft rejection, the donor kidney functioned well and the patient was discharged on post-op day 7 without any acute complications.

Conclusions:

Although there is evidence of an immunologic role for Anti-Fy^a in graft survival, acute renal allograft rejection is not a current concern for allocation and matching of donor renal allografts. Non–major histocompatibility antigen immunity, regarding the Duffy system, is associated with chronic rather than acute graft loss. In the patient presented, their current renal allograft is reported to be functionally stable since transplantation on 2/22/2022.

References:

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