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Case Report

Timely Identification of the Anti-F Red Blood Cell Antibody Expedited the Procurement of 19 Crossmatch-Compatible Units of Red Blood Cells in Advance of Planned Simultaneous Liver and Kidney Transplants

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Abstract

We share the case of a 57-year-old male who presented for simultaneous liver and kidney transplants with history of alcoholic cirrhosis, non-alcoholic steatohepatitis, and end-stage renal disease who had the unusual antibody anti-f. Prompt identification of the anti-f antibody allowed the blood bank to provide 19 crossmatch-compatible units of red blood cells for the perioperative period. Fifteen of these were transfused, and 4 were returned unused. Our goal is to raise awareness of the rare anti-f antibody in order to prevent misinterpretations of the blood bank antibody panels of a patient with anti-f as simply the combination of anti-c and anti-e.

Introduction

The Rh system is clinically the second most important red blood cell (RBC) antigen system after ABO due to the high immunogenicity of Rh system antigens.1 As of 2023, the Rh system contains over 50 antigens with D, C, c, E and e as the most prominent ones. The blood group also consists of compound antigens that arise as a result of conformational changes in the RHCE protein. 2 One such example of a compound antigen is the f antigen. The f antigen was first reported after it was observed that c and e in cis were required for its expression.3 That is, the f antigen is expressed on RBCs with c and e on the same protein but not when c and e are on separate Rh proteins. Thus, f is expressed on RBCs with the ce and/or Dce haplotype but not on other RBCs.3 Anti-f is a rare antibody with clinical significance and may be missed if it is misinterpreted as the combination of anti-c and anti-e.4

Case Presentation

A 57-year-old male with alcoholic cirrhosis, non-alcoholic steatohepatitis complicated by hepatopulmonary syndrome, and end-stage renal disease on hemodialysis presented for simultaneous liver and kidney transplant. First, the liver transplant was performed successfully. The postoperative course was complicated

by hemorrhage that required a return to the OR for exploratory laparotomy and washout. Once the bleeding was controlled, the kidney transplant was completed without further complications. Both allografts functioned well. Prior to his liver transplant, his ABO/D typing was O+, and the antibody screen showed an anti-f. Consistent with previous case reports, we followed the recommendation that it is generally safe to provide RBCs that lack either the c antigen or the e antigen to patients with anti-f.5 In aggregate, the patient received 15 crossmatch-compatible units of RBCs during the perioperative period, as all of them were either c-negative or e-negative. In addition, 4 more units of c-negative or e-negative RBCs were ordered, crossmatched, and issued but were returned unused.

Discussion

The f antigen is present in 65% Caucasians, 92% Blacks and 12% Asians.3 It is expressed on RBCs having c and e antigens in the same haplotype. For example, RBCs with the genotype DCe/DcE express the c and e antigens but not the f antigen because the c and e genes are on separate haplotypes.3 Anti-f was first reported in 1953 in a polytranfused 30-year-old Caucasian male with history of hemophilia.6 An unidentified antibody was found in his serum alongside anti-B, anti-S, and anti-K. Absorption tests on red blood cells with different genotypes concluded that the antigen recognized by anti-f is part of the Rh blood group system.

The clinical significance of this antibody has been documented in the literature, albeit infrequently. In 1974, a case of hemolytic disease of the newborn was reported due to anti-f.7 It was also implicated in a delayed hemolytic transfusion reaction.8 Very rarely, anti-f can be an autoantibody. One example was a DCe/ce patient in whom an autoanti-f was detected only after doing an acidified antiglobulin test.9

Even though anti-f is expected to react with cells carrying the ce antigen, it has also been believed to react sometimes with cells expressing the D and c antigens even in the absence of the e antigen.3 This can be explained by the hypothesis that the D is dominant in this case and there is a reduced or different expression of c resulting in half the amount of f antigen production.10 Despite this occasional nuance of in vitro reactivity, we are not aware of any cases of a delayed hemolytic transfusion reaction after transfusion of RBCs that were f-negative yet e-positive. Thus, we used the previously reported strategy of providing RBC units that are either c-negative or e-negative with no additional restrictions.5

This last point may seem obscure, but it is critical because sometimes misconceptions can surround the f antigen and anti-f antibody. A common misconception is that a patient with anti-f has the equivalent of both

the anti-c and the anti-e antibodies. This is a tempting misconception because the antibody panels of a patient with anti-f may be misinterpreted as anti-c in combination with anti-e. A possible consequence of this misinterpretation is that one could conclude that the RBC units must be both c-negative and e-negative. This conclusion is sometimes drawn because a patient with multiple clinically significant antibodies should routinely receive RBCs that lack all the cognate antigens. For example, a patient with anti-E and anti-K should receive RBCs that lack both the E and K antigens.

However, this standard rule does not apply to anti-f for many reasons. First, as we discussed earlier, the anti-f antibody essentially recognizes the combination of the c and e antigens when they are on the same haplotype but not simply when the 2 antigens are present via any genetic mechanism. Second, there is no clinical evidence that dual negativity is required for a clinically safe transfusion. Third, RBCs that are dual negative for c and e are not readily available, as individuals with the genotypes DCE/DCE or CE/CE are vanishingly rare.3 In other words, this conclusion would impose a phenotype requirement that would be impossible to fulfill.

However, if anti-f is recognized, then a sensible and safe strategy is readily available. That is, about 20% of individuals in the United States are c-negative and about 2% are e-negative. Thus, it is usually possible to obtain several units of RBCs that are f-negative (usually from c-negative donors such as those who have the relatively common DCe/DCe genotype) within several hours to a day before a planned surgical procedure.

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