Short Report:
Cross Match Incompatibilities in blood bank - A Perplexing Scenario

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Abstract: A safe transfusion is the one which provides specific and effective components which have a reasonably normal length of survival in the patient, doesn't cause any immediate or delayed reaction and, doesn't jeopardize the safety of future transfusions or transmit disease. Cross match provides a final chance to check ABO compatibility and a second chance to detect clinically significant antibodies. Incompatible cross match results are not an uncommon occurrence in Blood Bank. Knowledge of the various causes of incompatible cross match may be useful in formulating a logical and stepwise approach so as to provide safe transfusion to the recipient.

Key Words: Cross Match, Incompatible, Blood Bank

Introduction:
A safe transfusion is the one which provides specific and effective components which have a reasonably normal length of survival in the patient, doesn't cause any immediate or delayed reaction and, doesn't jeopardize the safety of future transfusions or transmit disease. Cross match provides a final chance to check ABO compatibility and a second chance to detect clinically significant antibodies. Also by performing this it is possible to detect alloantibody against the antigens which are rarely present on the donor cells.

In this study, incidence and causes of incompatible crossmatch results by column agglutination method were evaluated. Steps were taken to resolve the cause of incompatibility to ensure safe transfusion to the patients. All cross matches performed in the blood bank during a period of one month were evaluated. The major cross match was performed by column agglutination technology using polyclinpecific (IgG+C3d) gel media and following manufacturer's instructions. A detailed history including history of previous blood transfusion, previous pregnancies and medications history was taken for patients in whom an initial incompatible cross match was detected. A repeat cross match with the same donor unit was performed along with two additional group specific donor units. Repetition would rule out possibility of technical errors like contamination, poor technique as well as clerical/transcriptional errors. If incompatibility persisted on these repeat tests, a further workup including serological investigations of the recipients' sample was performed.

The workup of recipients sample included DCT, autocontrol and antibody screening. Antibody identification was performed in antibody screen positive samples.

Results
A total of 4168 cross matches were performed in the blood bank by column agglutination technology during a period of one month. Out of these, 13 cases gave an initial incompatible crossmatch (0.31%). Four cases were found to have specific alloantibodies. All these patients were adults. There antibodies found were Anti-c, Anti-e, Anti-c+D and Anti-E respectively. For these patients, corresponding antigen negative compatible blood unit was issued. There were 4 cases which gave initial incompatible crossmatch but were not found to have any specific antibody on antibody screening and identification tests and available logistics. None of these cases had any recent history of transfusion in past 3 months. For these patients, group specific, extended Rh and Kell phenotype matched red cell units were reserved for transfusion. There was one case (neonate) with a positive DCT and gave trace incompatible reaction with the group specific bags crossmatched. Two samples which gave initial incompatible results were found to have fibrin threads. Fresh sample was asked for these cases, the cross match was repeated and the compatible bag issued. The remaining 2 cases gave incompatible results because of technical error in performance of the crossmatch procedure. When the procedure was performed again, the results were clearly negative (compatible).

Discussion
The causes of incompatible cross match are many and include both immune and non immune causes. Donor red cells may be incompatible to recipient cells because they may contain minor antigens against which the recipient may be alloimmunized or sensitized. Crossmatching of the donor cells with recipient's serum helps in picking up such cases. The immune causes of an incompatible cross match include non-specific cold agglutinins and cold agglutinins with specificity. Non-specific cold agglutinins are detected by reverse grouping of the non group O patients. Positive reaction is seen with all donor units tested including the A1 and B cells.
It is caused by performing a cross match with cold plasma. A cold antibody with specificity on the other hand will react with some of the units, possibly in varying strengths. It might not be picked up in the grouping or antibody screen. A passively acquired ABO antibody or new alloantibody may result in a weakly incompatible crossmatch. A passive ABO antibody occurs in non-group O patients only. It is formed after a recent transfusion of intravenous immunoglobulin or ABO mismatched platelets or mismatched solid organ transplantation. The Direct Anti globulin Test is positive, and eluate will react with AI and/or B cells. In such patients, transfusion is done with group O blood till the antibody disappears. If a new alloantibody is present, some donor units will be incompatible in varying strengths and patient may have a positive DAT. This requires antibody screening and identification and there might be a delay in providing blood until antigen negative cross match compatible units are obtained.

Antibody screening and identification helps in detecting the patients having clinically significant RBC alloantibodies. There were four such cases having Anti-c, Anti-e, Anti-c-D and Anti-E respectively in this study. Antibodies against low incidence antigens are likely to be missed. Few antibodies manifest a dosage effect dependent on the heterozygosity of genes controlling expression of antigens on reagent screening cells. Using different types of screening cells improves the chances of having all major RBC antigens present in their homozygous forms during testing. (1) Also, in some cases no specific antibody can be picked up even after detailed workup including adsorption and elution studies (4 cases in this study). For patients who screen negative for RBC alloantibodies, only an immediate spin crossmatch needs to be performed. For those with a positive alloantibody screening or those with a history of clinically significant antibodies, an AHG crossmatch must be performed. (1)

The issue of whether or not to omit AHG cross match for patients screened negative for RBC alloantibodies is controversial. (2) The decision should be made after considering factors like the possibility of incompatible crossmatches or haemolytic transfusion reactions due to RBC alloantibodies not detected by antibody screening; potential cost and labor-saving benefits of omitting AHG crossmatch and; the sensitivity of the antibody detection test used in the laboratory. (1) Studies have shown that there is very low risk of transfusing incompatible blood when the AHG crossmatch is eliminated for patients who have screened negative for alloantibodies. (3)

The non-immune causes of an incompatible cross match include fibrin threads and rouleaux formation. Fibrin threads mimic agglutination in the reaction tube. Centrifugation will deposit the fibrin plug at the bottom of the test tube and supernatant plasma can be used for a repeat crossmatch and testing. Rouleaux formation occurs because of excess of protein in the patient plasma. It can be picked up by reverse grouping and a false positive reaction with all donor units tested. Rouleaux formation disperses with saline replacement. Sometimes dirty saline bottles, dirty glassware and clotted segments result in false weakly positive cross match reactions. Clerical errors and technical errors in performance of the procedure may lead to altered reaction results. Stainsby et al have reported clerical errors as the common cause of incompatibility. (4) In pretransfusion testing, the importance of careful clerical checking cannot be overemphasized. The information on the label and on the transfusion request form should be identical. Patient’s serological and transfusion history must also be checked and results of current testing compared with those of previous tests. (1) Sample should be carefully checked for presence of clots and fibrin threads. ABO and Rh type must be determined for the blood of both the donor and the intended recipient diligently. The procedure should be performed by well trained and experienced technicians to avoid false incompatible results due to poor technique.

The reported incidence of incompatible crossmatches is variable, ranging from 0.21% (5) in Western India to 0.69% in a study from Eastern India. (6) Commonest cause of incompatible cross match reported previously is autoimmune haemolytic anemia. (5) Among alloantibodies, the most common antibody causing incompatibility is against the Rh system. (6) However, no such cases were seen in the duration of the current study. A longer prospective study would be useful for the detailed analysis of the causes of incompatible cross match and their incidence.

A logical stepwise approach is necessary to enable provision of safe transfusion to the patient. A thorough evaluation of the patients’ clinical history, clinical condition and underlying pathology should be done to identify the cause of an incompatible crossmatch.

References: