Anti-D in RhD Positive Patient: Auto Anti-D or Anti-LW?

RhD Pozitif Hastada Anti-D: Otomatik Anti-D veya Anti-LW?

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ABSTRACT

Anti-LW and anti-D can be indistinguishable. Therefore, it is important to differentiate them since anti-D is a clinically significant antibody. ICAM4 and RHD genes encode the Landsteiner-Wiener (LW) and RhD antigens, respectively. However, the LW antigens expression requires an interaction with Rh proteins. Hence, LW antigen is being express more strongly by RhD positive (RhD+) than RhD negative (RhD-) individuals. We describe a 51-year-old male with underlying multiple medical problems. His blood group was O RhD+ with Rh phenotype R_1r (DCe/dce). The patient had been receiving regular packed cells (PC) transfusion for anemia due to underlying chronic kidney disease. Immunohematology workup showed antibody identification positive for auto-control with anti-D specificity which suggestive for the presence of autoantibody (anti-D or anti-LW). Cross-matching revealed incompatibility with all RhD+ but compatible with RhD-PC. Further investigations should be done to differentiate these two antibodies. The laboratory approaches in order to differentiate anti-LW and anti-D will be discussed and highlighted.

Key Words: Anti-D; anti-LW; alloantibody; autoantibody

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ÖZET

Anti-LW ve anti-D ayırt edilemez olabilir. Bu nedenle, anti-D klinik olarak önemli bir antikor olduğu için bunları ayırt etmek önemlidir. ICAM4 ve RHD genleri, sırasıyla Landsteiner-Wiener (LW) ve RhD antijenlerini kodlar. Bununla birlikte, LW antijenlerinin ekspresyonu, Rh proteinleri ile bir etkileşim gerektirir. Bu nedenle, LW antijeni, RhD pozitif (RhD +) tarafından RhD negatif (RhD-) bireylere göre daha güçlü ifade edilmektedir. Altında birden fazla tıbbi problemi olan 51 yaşında bir erkeği tarif ediyoruz. Kan grubu, Rh fenotip R1r (DCe / dce) ile O RhD + idi. Hasta, altta yatan kronik böbrek hastalığı nedeniyle anemi nedeniyle düzenli paketlenmiş hücre (PC) transfüzyonu alıyordu. İmmünohematoloji çalışması, otoantikor (anti-D veya anti-LW) varlığını düşündüren anti-D özgüllüğü ile oto-kontrol için pozitif antikor tanımlaması gösterdi. Çapraz eşleştirme, tüm RhD + ile uyumsuzluğu ortaya çıkardı ancak RhD-PC ile uyumludur. Bu iki antikoru ayırt etmek için daha fazla araştırma yapılmalıdır. Anti-LW ve anti-D'yi ayırt etmek için laboratuar yaklaşımları tartışılacak ve vurgulanacaktır.

Anahtar Sözcükler: Anti-D; anti-LW; alloantikor; otoantikor

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INTRODUCTION

ICAM4 and RHD genes encode the Landsteiner-Wiener (LW) and RhD antigens, respectively. However, Rh proteins were required for LW antigens expression and preferably is association with RhD (1-3). Thus, the LW and Rh antigens were phenotypically related which lead to difficulty in distinguishing anti-LW and anti-D (2-5). Therefore, it is important the differentiate between the two antibodies because D-negative and partial D individuals are prone to be alloimmunize and anti-D is a clinically significant antibody (1-3).

About 1-2 percent of the individual has reduced expression of the D antigen depends on the types of RHD gene mutation (1-3). The molecular basis of weaker D expression is primarily due to point mutations that cause amino acid changes and affect the quantity of RhD protein in the membrane lead to partial D (D mosaic) and weak D (Du) (1-3). Serological weak D test will be perform to detect partial D (D mosaic) and weak D but cannot differentiate them (1-3). Molecular method can be done to differentiate the type of mutation if clinically indicated (1).

The LW antigens are resistant to papain and chloroquine treatment but are denatured by treatment with 0.2m dithiothreitol (DTT), and D antigen is resistant to DTT (4-7). This DTT test can be done to differentiate between anti-LW and anti-D.

It is important to differentiate them, especially in RhD- childbearing age and pregnant ladies to prevent hemolytic disease of the fetus and newborn (5). Laboratory approaches in differentiating anti-LW and anti-D will be discussed and highlighted in this case report.

CASE REPORT

A 51-year-old male with underlying multiple medical problems; end-stage renal failure (ESRF), diabetes mellitus type 2, hypertension and epilepsy, was electively admitted for fistula creation. He had a history of regular uneventful PC transfusion for symptomatic anemia due to his underlying chronic renal disease. His hemoglobin level during the admission was 7.0 g/dL, with a total white cell count of 8.3 $x10^9$/L and a platelet count of 183 $x10^9$/L. His urea and creatinine were 49.5 mmol/L and 1921 µmol/L, respectively. This current pre-transfusion work-up revealed blood group O RhD+ with Rh phenotype R_1r (DCe/dce) and positive antibody screening. All documented previous antibody screening was negative. Antibody identification showed anti-D specificity with positive auto-control and direct Coombs test (DCT) (1+) as shown in Table 1. The elution study was not done. His plasma showed incompatibility with all RhD+ but compatible with RhD- PC. Repeat antibody screening a few days later showed the negative results. His hemoglobin level during current admission was 7 g/dL and there was no significant bleeding, packed cell transfusion was not given to him.

Table 1: Patient immunohematology results

Immunohematology Test	Result
Blood grouping	O RhD+
Rh phenotyping	R1r (DCe/dce)
Antibody screening	Positive at cell II and III
Antibody identification	Showed anti-D specificity
Autocontrol	Positive (+/-)
Direct Coombs test	Positive (+)
DTT treated RBC	Not done since repeated antibody screening was negative, indicate transient in nature of the antibody**.**

DISCUSSION

In RhD positive patient, it is usually uncommon to develop anti-D. Therefore if present need to consider auto anti-D, allo anti-D with partial D and anti-LW. Anti-D is indistinguishable with anti-LW antibodies (2-5). In this case, patient is RhD+ so auto-anti-D/-LW is considered due to antibody identification showed anti-D specificity with positive DCT. However, auto anti-D and anti-LW have not been confirmed due to repeated antibody screening later showed negative result. This most probably because of transient nature of auto anti-D or anti-LW.

Auto anti-D rarely cause hemolytic transfusion reaction and anti-LW is not clinically significant. Therefore, it is important to differentiate between the 2 antibodies. Some RhD+ patients may develop transient auto-anti-D with positive DCT after repeated blood transfusion of RhD+ blood as seen in this current presented case (4-6). While for auto anti- LW eventhough uncommon, it can be produced without apparent exposure during transient loss or suppression of LW antigens. The transient loss or suppression of LW antigens can occur in pregnancy and certain diseases, example Hodgkin's disease, lymphoma, leukemia, and sarcoma which can regain the normal or almost normal expression after delivery and treatment of the diseases (5,7).

For this patient Rh phenotyping showed R1r with strong reaction. However, determination of weak D and partial D is also required especially when D antigen phenotyping showed weaker reactions (4). Therefore, differentiating anti-LW antibody from anti-D is also required to prevent anti-D alloimmunization. Few methods are available to distinguish anti-LW from anti-D and suggested approaches of laboratory investigations to differentiate anti-LW and auto- or allo-anti-D were shown in figure 1. Treated RhD+ red blood cells with 0.2m dithiothreitol (DTT) should be able to distinguish between auto anti-D with anti-LW. Anti-LW will not react with DTT treated cells as LW antigens will be denatured but not RhD antigen. Another option is to test with red cells from the umbilical cord because the umbilical cord has a high expression of LW antigens (2). Therefore, the anti-LW reacts well with both RhD+ and RhD- cells, whereas anti-D will react just with RhD+ cells (4,7).

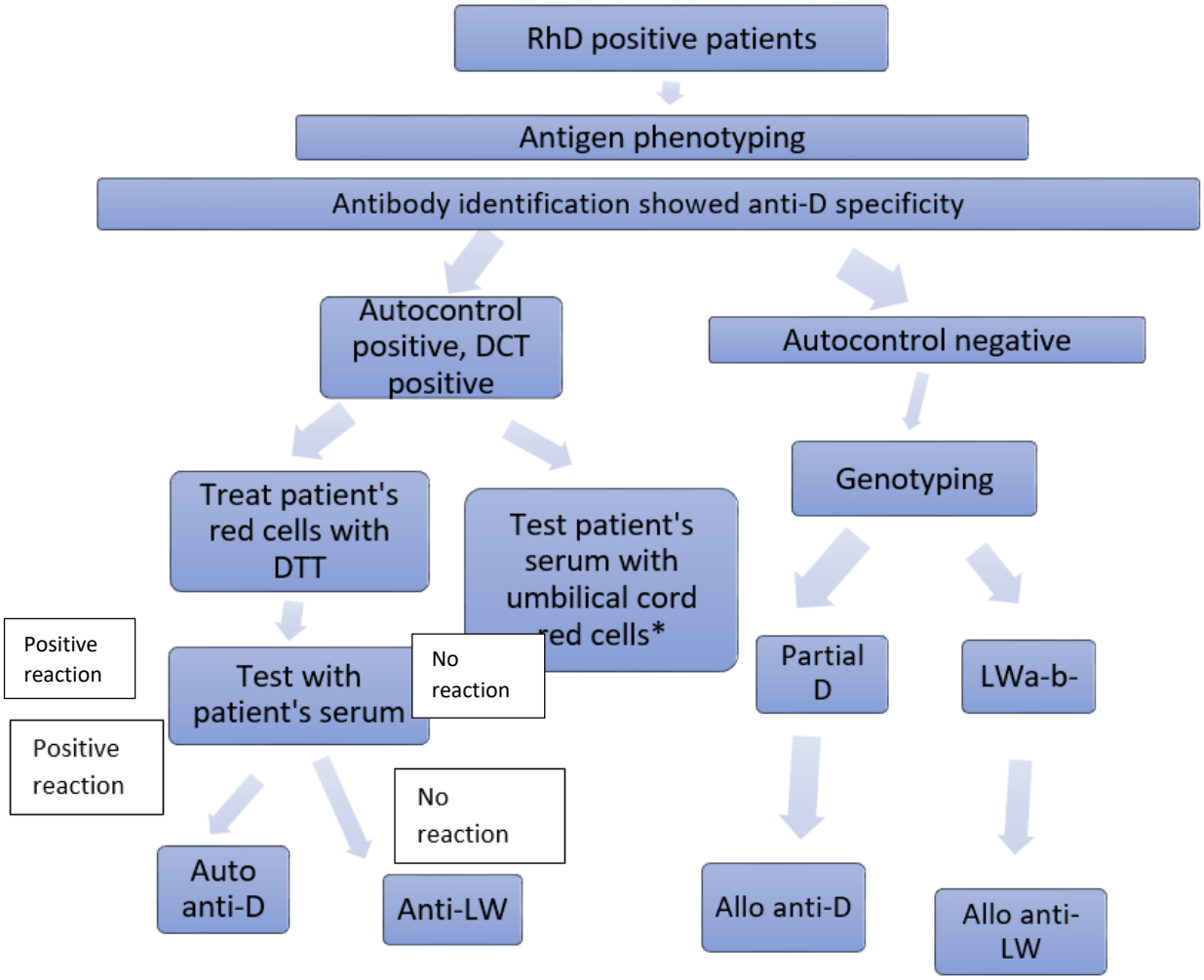

Figure 1: Suggested approaches of laboratory investigations to differentiate anti-LW and auto- or allo-anti-D. *umbilical cord presents a high expression of LW antigens. The anti-LW reacts well with RhD+ and RhD- cells.

CONCLUSION

Even though the anti-LW antibody has little clinical importance and no anti-LW has been reported for any serious hemolytic transfusion reaction or hemolytic disease of fetal and newborn it is still important to identify anti-LW and distinguished it with anti-D because anti-D is a clinically significant antibody.

Conflict of interest
No conflict of interest was declared by the authors.

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