Case Report

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Critical evaluation of donor direct antiglobulin test positivity: Implications in cross-matching and lessons learnt

Vandana Puri, Aruna Chhikara, Geetika Sharma, Shivali Sehgal, Sunita Sharma

Abstract

Direct Antiglobulin Test is a method of demonstrating the presence of antibody/ complement bound to red cell membrane by using AHG to form a visible agglutination reaction. DAT positivity is seen in immune mediated haemolytic anaemias, however rarely non immune mediate haemolytic anaemias also show DAT positivity. DAT positivity predictive of 83% of autoimmune haemolytic anaemia and 1.4% cases without haemolytic anaemia. Screening of blood donors for DAT is usually not recommended traditionally by any guidelines. However DAT positivity is reported in 0.008% of donors. On extensive search of literature we could find only very few studies on DAT positivity in donors. We report two cases of DAT positive donors with no clinical or laboratory evidence of hemolysis.

Keywords:

Direct antiglobulin test, donor, incompatibility

Introduction

Direct antiglobulin test (DAT) is a method of demonstrating the presence of antibody/complement bound to red cell membrane by using antihuman globulin (AHG) to form a visible agglutination reaction. DAT positive is seen in immune-mediated hemolytic anemia; however, rarely, nonimmune-mediated hemolytic anemia also shows DAT positivity. DAT positivity is predictive of 83% of autoimmune hemolytic anemia and 1.4% cases without hemolytic anemia. In few patients of hemolytic anemia, patients can have positive DAT and negative indirect antiglobulin test (IAT) if the strength of offending antibody is low and it is adsorbed on the red cells. Screening of blood donors for DAT is usually not recommended traditionally by any guidelines.[1] However, DAT positivity is reported in 0.008% of donors.[2] Mostly, blood donors with a positive DAT result appear to be perfectly healthy and have no obvious signs of hemolytic anemia. However, a careful evaluation may show evidence of increased red cell destruction.[3] Studies describe that these donors are at increased risk of hematological malignancies and suggest that DAT positivity may precede the clinical detection of cancer by several months.[1] On extensive search of literature, we could find only very few studies on DAT positivity in donors. We report two cases of healthy DAT-positive donors with laboratory evidence of hemolysis.

Case Report

During routine cross-matching, two blood units collected from healthy donors were found to be incompatible with several

Department of Pathology, Lady Hardinge Medical College, New Delhi, India

Address for correspondence:
Dr. Aruna Chhikara, Department of Pathology, Lady Hardinge Medical College, Cannaught Place, New Delhi - 110 001, India.
E-mail: arunachhikara123@gmail.com

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recipient patient samples. As a part of departmental policy, repeat blood group of the bags was performed by both forward and reverse grouping by tube method and gel card method. The blood group of both the bags was reconfirmed as B+. The DAT and autocontrol of both the blood unit were put up using microcolumn gel techniques which was found to be positive (2+). The IAT of donor units was repeated as is done routinely for all the blood units collected using gel technique Diacell 1-11-111 Asia, Biorad, Switzerland in Liss Coomb's phase at 37°C and saline phase at 22°C. The IAT for both the units was negative on antibody screening panel in both phases. All the components of these donor units were retrieved and quarantined. Retrospectively, the donor questionnaire forms of both the donors were reviewed to recheck if any history of hemolysis was missed during donor screening. One of the donors was a 42-year-old healthy male, who was donating for the first time. The donor was contacted telephonically, and a repeat fresh sample was taken. No history of hemolysis was elicited in the donor or his family. The complete hemogram, reticulocyte count, and liver function tests were within normal limits. No evidence of hemolysis was noticed on peripheral smear. No history of any chronic illness or drug intake was present. The repeat DAT and autocontrol performed with fresh sample were positive. Further DAT profile showed the presence of IgG with negative reaction with the control thus validating the test. His extended Rh kell antigen profile showed the presence of 'D', 'C,' 'c,' and 'e' antigens. The follow-up of this donor is awaited. The other blood unit was collected from a 20-year-old healthy male. His DCT was 2+ with a positive autocontrol. DAT profile showed the presence of IgG and absence of any complement. His extended Rh kell profile showed the presence of 'C' and 'e' antigens. No past history of any blood transfusion and hemolysis was elicited. The same donor visited again for donation after a span of 4 months. This time, his DCT and autocontrol were negative [Table 1].

Discussion

DAT in healthy individuals was first described by Weiner in 1965 with an overall incidence as 1 in 5000.[4] In 1980, Habibi *et al*. reported a positive DAT incidence of 1 in 10000, of which 97% had IgG antibody coating the red cells.[2] Various studies quote the incidence of DAT from 1:1000 to 1:14,000 in donor population.[5,6] In our institute, we found only two cases of DAT-positive donors in 20,000 donations over a span of 2 years.

Table 1: Details of units cross-matched

Case	Blood group	AHG	Compatible
Unit I	B+	2+	No
Unit II	B+	2+	No

AHG=Antihuman globulin

A positive DAT may occur because of immune causes such as immunoglobulins or complement binding to red cells *in vivo*/*vitro*. Clinically significant *in vivo* causes of DAT positivity include AIHA, either due to warm or cold reactive antibodies, drug-induced positive DAT with or without hemolytic anemia, hemolytic transfusion reactions, hemolytic disease of fetus or newborn, and autoimmune disorders such as SLE and certain malignancies.

All healthy individuals have some IgG on their cell surfaces, which might be involved in normal process of red blood cell (RBC) senescence. Furthermore, most healthy individuals with a positive DAT do not show clinical/laboratory evidence of hemolysis, and the strength of DAT is not necessary, an indication of presence or severity of hemolysis. The incidence of AIHA in population is variously reported to be in range of 1 in 1 million donations.[3] Garratty in their study found that of the individuals with positive DAT, 2/3 of individuals have IgG-coating red cells, of which about half have IgG only and other half have IgG plus complement. The remaining 1/3 have complement only.[7] In both of our cases, the red cells were coated with IgG only.

Since there is no well-defined policy of DAT testing in donors, most of the DAT-positive donors come to attention while cross-matching in AHG phase. We do cross-matching in AHG-coated gel cards which helps in picking up DAT-positive donors. These cases are frequently missed at centers where cross-matching is done in saline.

The DAT-positive donors have variable outcomes. In a study by Issitt and Anstee of blood donors with positive DAT and IgG coating the red cells, 3%–10% develop AIHA, 20%–25% become DAT negative over time, and 60%–70% remain DAT positive but hematologically normal.[8] Our donors did not show any laboratory or clinical evidence of hemolysis. Moreover, one of them became DAT negative over a span of 4 months.

Studies suggest that the risk of healthy donor with positive DAT in the absence of any underlying clinical symptoms progressing to clinically significant disease is very small. Rottenberg *et al*. described significantly increased risk of cancer, especially hematological malignancies, among blood donors with positive DAT and suggested that DAT positivity may precede the clinical detection of cancer by several months.[1]

All these postulations raise the question as to whether blood donors with a positive DAT should be allowed to continue donating blood or not. Evidences indicate that no immediate harm occurs to a transfusion recipient receiving RBCs from a donor with positive DAT, if

cross-matching can be done successfully. Furthermore, based on public data and clinical experiences, there is little reason to suspect that red cells weakly coated with IgG have a decreased posttransfusion survival.

There are no clear guidelines or established policies to deferral of DAT-positive donors and their referral to physicians. Review of regulatory requirements indicates that performance of DAT is not required as a test of record for blood donations. AABB standards of blood bank and transfusion services states that donors who have been found incidentally to have positive DAT at donation testing may remain as blood donors provided they continue to pass the health screening questionnaire and have normal hemoglobin.

Conclusion

DAT positivity in normal healthy blood donors is low. Such donors should be closely followed up to look for any clinical/laboratory evidence of hemolysis or development of malignancies in long run. DAT-positive blood units do not predispose the recipient to any adverse outcomes, and such donors can continue to donate blood provided they are medically fit.

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Conflicts of interest

There are no conflicts of interest.

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