Case series investigation on the Lewis system antibodies encountered during a routine screening in a tertiary care hospital-based blood center

A. M. Gayathri, Debasish Gupta

Abstract:

BACKGROUND: Anti-Lewis antibodies, usually do not react at 37°C, hence are clinically insignificant. However, on rare occasions, these antibodies have been reported as the cause for hemolytic transfusion reaction (HTR).

AIM: We report our experience on the 6 cases of anti-Lewis antibodies that reacted at room temperature (RT) and at 37°C.

MATERIALS AND METHODS: Standard serological methods were employed in detection and identification of antibodies. Demographic and clinical details were obtained from the records on the subjects under study.

RESULTS: These were found among the patients and the blood donors of varied age groups and gender (21 to 65 years). Also, they were found among the patients with varied clinical diagnosis. The 2 patients in second trimester had anti-Le a or anti-Le b and other 2 male patients had anti-Le ab or anti-Le b with wide thermal amplitude were found during the course of pre-transfusion compatibility tests including antibody screening and cross-matching. Two male donors typed Le (a−b−) had anti-Le ab with wide thermal amplitude. Lewis antigen negative RBC units were provided for transfusion in the situation.

CONCLUSION: Although antibodies to Lewis blood group antigens often react at lower temperatures and therefore remain clinically insignificant, some of them, on rare circumstances, may react at higher temperature of 37°C and may produce hemolytic episode or at least yield reduced survival of incompatible red cells in transfusion recipients. On safer side, the antigen-negative unit may be used in transfusion. The donors’ registry with detailed phenotype profile may go a long way to provide blood for transfusion in emergency situations.

Keywords: Lewis antibodies, naturally occurring, phenotyping of donor

Introduction

The Lewis system was named after one of the first individuals to make the antibody.[1] Its antigens are not intrinsic to red blood cells (RBCs) but are passively adsorbed onto the RBC membrane from the plasma. There are two main antigens, namely Lea and Leb that give four phenotypes such as Le (a+b−), Le (a−b−), Le (a+b+), and Le (a−b−). The formation of these antigens is influenced by the interaction of three other genetically independent systems, namely ABO, H, and secretor at the phenotypic level. Phenotype Le (a+b−) is always nonsecretor for ABH, while Le (a−b−) is always ABH secretors as per the ABH gene present in the individual.[2] The individuals with phenotype Le (a−b−) RBC could either be secretor or nonsecretors.[3]
Gayathri and Gupta: Case series investigation on the Lewis system antibodies encountered during a routine screening in a tertiary care hospital-based blood center

Lewis antibodies are naturally occurring non-red cell immune, immunoglobulin M (IgM) reacting at lower temperature and usually made by Le (a−b−) persons. They often occur in pregnant women as they transiently exhibit the Le (a−b−) phenotype.[4] The antibodies may show an agglutinating as well as complement-mediated hemolytic property, and even if they fail to agglutinate antigen-positive red cells at 36°C, they may show the complement-mediated hemolysis.[4] Levine and Polayes[4] described an antibody that agglutinated 25% of red cell samples at 20°C and caused lysis at 37°C. Anti-Le Lewis antibodies, which are usually not reactive at 37°C, are mostly clinically insignificant. The clinically significant anti-Lewis antibodies to cause hemolytic transfusion reactions (HTRs) have been documented.[9]

Materials and Methods

Our institute performs antibody screening routinely as a part of national guidelines on all donated blood units as well as patients along with blood grouping. As a referral center, we receive clinical cases from outside hospitals for Rh screening in pregnant women, hemolytic disease of the fetus and newborn (HDFN) workup, abnormal antibody identification, etc. Serological tests include antibody identification using screening cells and 11 cell panel and titration of antibodies. The secretor status was carried out on subjects as Lewis antigens are found in secretions as ABH antigens.

Results

We had a total of 6 cases with Lewis antibodies, and among these six cases, two individuals were healthy voluntary blood donors, two were patients admitted in our institute for surgical procedures, and two referred cases from the local hospital for antibody identification [Table 1]. The six cases of anti-Lewis antibodies which include both patients and healthy blood donors were reactive at room temperature (RT) and at 37°C. There was no history of previous transfusions in all the six cases. All antibodies had both IgM and IgG components. The patients were issued antigen-negative compatible blood and the transfusion was uneventful.

Discussion

Lewis antibodies are naturally occurring antibodies and usually of IgM and clinically insignificant.[6] Anti-Lea is the most commonly encountered of the Lewis antibodies and is often detected in RT tests, but it sometimes reacts at 37°C and in the indirect antiglobulin test.[7] Anti-Lea is not as common or generally as strong as anti-Le and usually an IgM agglutinin and can bind complement. Hemodynamic changes in pregnancy may affect certain red cell antigen expression leading to the production of naturally occurring antibodies. The chances of HDFN are extremely rare since Lewis antigens are poorly expressed on fetal cells.[4] Lewis antibodies are rarely implicated in HTRs, as the most Lewis antibodies are not purported to be active at 37°C, and the Lewis antigens present in plasma of the transfused blood may neutralize the Lewis antibodies in the recipient.[9] Among the Lewis antibodies, anti-Lea is more frequently associated with acute HTRs[10] than is anti-Leb.[11] Cases of delayed HTRs have also been reported.[12] In our case series, none of the patients with Lewis antibodies developed any adverse events following blood transfusion. As a part of National and Institutional Policy, we discarded the donor units with Lewis antibodies to avoid untoward events since there are case reports of HTRs. Provision of RBC antigen phenotyped donor registry shall ensure the quick provision of antigen-negative blood for transfusion in emergency situations. Hemovigilance Program of India provides a perfect platform for reporting such unexpected transfusion reactions, thus adding onto the National and International Database.

Conclusion

Although antibodies to Lewis blood group antigens often react at lower temperatures and therefore remain clinically insignificant, some of them, on rare circumstances, may react at a higher temperature of 37°C and may produce hemolytic episodes or at least yield reduced survival of incompatible red cells in transfusion recipients. On the safer side, the antigen-negative unit may be used in a transfusion. The donors’ registry with detailed phenotype profile may go a long way to provide blood for transfusion in emergency situations.

Table 1: Case features on blood group and associated Lewis antibodies with a thermal range from 4°C to 37°C

| Cases       | ABO/Lewis phenotypes | Secretor Status | Antibody | Titer values |
|-------------|----------------------|-----------------|-----------|--------------|
|             |                      |                 |           | Immunoglobulin M+ | Immunoglobulin G | Immunoglobulin G |
| Primigravida| A, Le (a−b+)         | Secretor        | Anti-Lea  | 8            | 2             |
| G, P, L,    | O, Le (a+b−)         | Nonsecretor     | Anti-Leb  | 8            | 4             |
| Blood donor | A, Le (a−b−)         | Secretor        | Anti-Lea  | 4            | 2             |
| Blood donor | A, Le (a−b−)         | Secretor        | Anti-Leb  | 8            | 2             |
| Patient     | A, Le (a−b−)         | Secretor        | Anti-Lea  | 8            | 2             |
| Patient     | O, Le (a+b−)         | Nonsecretor     | Anti-Leb  | 4            | 2             |

Significance of a and b: types of antibodies in Lewis blood group system
Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. Mourant AE. A new human blood group antigen of frequent occurrence. Nature 1946;158:237.
2. Grubb R. Correlation between Lewis blood group and secretor character in man. Nature 1948;162:933.
3. Daniels G. Human Blood Groups. 2nd ed. UK: Wiley Blackwell; 2013.
4. Issitt PD, Anstee DJ. Applied Blood Group Serology. 4th ed. Durham, NC: Montgomery Scientific; 1998.
5. Mollison PL, Engelfriet CP, Contreras M. Blood Transfusion in Clinical Medicine. 10th ed. Oxford: Blackwell Science; 1997.
6. Harmening D. Modern Blood Banking and Transfusion Practices. 6th ed. Philadelphia: F A Davis Company; 2012.
7. Polley MJ, Mollison PL. The role of complement in the detection of blood group antibodies; Special reference to the antiglobulin test. Transfusion 1961;1:9-22.
8. Brendemoen OJ. Further studies of agglutination and inhibition in the Lea-Leb system. J Lab Clin Med 1950;36:335-41.
9. Roback JD, Combs MR, Grossman BJ, Hillyer CD, editors. Technical Manual. 16th ed. Bethesda, MD: AABB; 2008.
10. de Vries SJ, Smitskamp HS. Haemolytic transfusion reaction due to an anti-Lewis agglutinin. Br Med J 1951;1:280-1.
11. Jesse JK, Sheek KJ. Anti-Leb implicated in acute hemolytic transfusion reaction: A rare occurrence. Transfusion 2000;40 Suppl: 115S.
12. Contreras M, Mollison PL. Delayed haemolytic transfusion reaction caused by anti-LebH antibody. Vox Sang 1989;56:290.