Liaquat Medical Research Journal (LMRJ)
Open access, Peer review Journal OPEN ACCESS

Case Report

A RARE PHENOMENON OF ANTI-N ANTIBODY REACTIVITY AT 37°C: AN UNCOMMON DETECTION IN ROUTINE IMMUNOLOGICAL SCREENING

Muhammad Shayan Ashfaq, Muhammad Hasan

Section of Hematology & Transfusion Medicine, Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan

Correspondence:
Muhammad Shayan Ashfaq, Section of Hematology & Transfusion Medicine, Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan
Email: shayanthebest911@gmail.com

DOI: 10.38106/LMRJ.2025.7.2-07
Received: 16.04.2025
Accepted: 10.06.2025
Published: 30.06.2025

ABSTRACT:

Anti-N antibodies usually possess cold-reactive properties which make them clinically insignificant and are mostly classified as naturally occurring IgM antibodies. These antibodies sometimes trigger reactions at body temperature (37°C) or in the anti-human globulin phase resulting in serious medical outcomes such as delayed hemolytic transfusion reactions or hemolytic disease of the newborn. This case shows an extraordinary naturally occurring anti-N antibody which was detected in a 20-year-old male liver donor during standard antibody testing because of its unexpected reactivity at 37°C. The absence of any previous blood transfusions or medication use in the patient made this case stand out as particularly intriguing. The antibody identification was successful following the 'pre-warm' technique implementation while antigen phenotyping validated it as an IgG-type anti-N antibody. This medical case demonstrates the critical importance of recognizing unusual antibody responses during blood transfusions and organ transplants because uncommon reactions may lead to serious consequences.

Keywords: Anti-N antibody, MNS blood group system, Transfusion medicine, Serological testing, Delayed hemolytic transfusion reactions

INTRODUCTION

The MNS blood group system, discovered by Landsteiner and Levine in 1927, was the second to be identified after the ABO system. Among the antibodies in the MNS system, anti-M is a common "naturally occurring" antibody (1). The S antigen was identified in 1947 by Walsh and Montgomery after the development of the antiglobulin test (2). Most anti-M antibodies are cold-reactive and do not activate complement or react with enzyme-treated RBCs (3). They are rarely associated with hemolytic transfusion reactions (4).

Anti-N antibodies are less common than anti-M and are also typically naturally occurring, cold-reactive IgM or IgG agglutinins that do not activate complement or react with enzyme-treated RBCs (1). They are clinically insignificant unless reactive at 37°C and have been linked to rare cases of mild hemolytic disease of the fetus and newborn (HDFN) (5). Potent anti-N antibodies are more frequently found in individuals of African descent with a specific RBC phenotype (M+ N- S- s-) due to the absence of the N antigen (2). Immune anti-N antibodies are extremely rare (6). We report a case of naturally occurring anti-N that reacts at 37°C, identified during routine antibody identification testing (7).

CASE REPORT

A 20-year-old male from Karachi, who's healthy and without any remarkable medical history, decided to donate liver to his father. His father had been struggling with chronic liver disease because of a hepatitis B infection, so they set up a liver transplant at Dow University of Health Sciences, Karachi, Pakistan. The donor had never had a blood transfusion or taken any medication. For the usual pre-transplant checks, they sent a test request to Aga Khan University Hospital to identify any antibodies. The first blood tests came back showing a positive auto-control, which means his red blood cells reacted with his own serum at room temperature. However, when a Direct Antiglobulin Test (DAT) with anti-IgG + C3d, was performed it came up negative, ruling out any autoantibodies. Then three different antibody screening panels (ID-Diacell I-II-III, Biorad) were checked and found positive reactions in all of them (2+, 3+, and 3+). It was also noticed that the auto-control was positive right from the spin phase. So, it was decided to run the antibody screening again using a method where the sample was warmed everything up and the results were positive across all three panels. In order to further explore the Papain treatment

method (ID-Diacell Papain Kit), was used which came up negative for the red cell antibody screening. But when further evaluation was performed with the antibody identification using the warm technique, it was found that he had an anti-N antibody using this 11-cell identification panel (ID-Diacell, Biorad). The reaction was strong 3+, with homozygous N+ N+ cells (Panels 4, 10, and 11) and negative with heterozygous M+ N+ cells (Panels 1, 3, 7, and 8), plus also negative with N-negative cells (Panels 2, 5, 6, and 9). Then other antigens for N, S, s, and M were also checked and found that he was M-, N-, S-, and s-. Then his plasma was treated with dithiothreitol, which confirmed there was an IgG-type anti-N antibody present. The antibody titer was 1:2. This report emphasizes a naturally occurring anti-N antibody that reacts at 37°C, which could actually be important even though the donor hadn't had any blood transfusions before. It is therefore, highlights the need to check for these naturally happening antibodies during routine blood tests because their reactions at body temperature can affect blood transfusion practices.

DISCUSSION

Anti-N antibodies belong to the MNS blood group system and are usually naturally occurring and mainly cold-reactive IgM antibodies. These antibodies are often clinically insignificant unless they decide to react at 37°C or during the anti-human globulin (AHG) phase of testing. In this case, we found the anti-N antibody in a 20-year-old male liver donor who had a serological profile showing an uncommon blood group discrepancy. While anti-N antibodies are generally more of a cold-reactive type and don't usually bind complement, if they do react at 37°C, that's when raise the concern about their clinical significance.

Usually, anti-N antibodies do not cause major issues, as they are linked to non-pathological clinical outcomes. They typically do not lead to hemolytic transfusion reactions (HTRs) or hemolytic disease of the fetus and newborn (HDFN) unless they react at body temperature (37°C), like in this case (1). A transfusion reaction is more likely if these antibodies show strong reactivity at 37°C, but that's pretty rare. When it occurs, it can lead to delayed hemolytic reactions, which may result in certain transfusion-associated complications. Besides, while HDFN can be a concern in cases of maternal-fetal blood group incompatibility, instances of HDFN linked to anti-N are sporadic (2).

Interestingly, the IgM class of anti-N antibodies usually reacts in colder conditions and doesn't typically bind to complement or react with enzyme-treated red blood cells (RBCs). This is kind of similar to anti-M antibodies, which show the same cold-reactive behaviour and limited clinical relevance, unless they react at body temperature (3). However, in our case, the antibody was behaving unusually by reacting at 37°C, warning for atypical antibody behaviors in blood donors, especially when it comes to organ transplant recipients who might need careful cross matching and serologic evaluations.

The phenotyping results were non-significant since the donor's red cell antigen profile showed the absence of the M, N, S, and s antigens, which are usually part of testing in the MNS blood group system. In addition, after treating with Dithiothreitol (DTT), it was confirmed that the anti-N antibody was of the IgG nature, suggesting that it could have some clinical significance in certain transfusion scenarios (4).

Finding an anti-N antibody in a healthy individual with no prior blood transfusions is unusual, given that naturally occurring antibodies in the MNS system are typically IgM types and do not usually trigger immune responses. The titer of 1:2 suggests the anti-N antibody could be clinically important at 37°C (7). This goes to show how important it is to do a thorough antibody screening for blood donors; even naturally occurring antibodies might need attention in a clinical setting.

CONCLUSION

In conclusion this case really emphasizes the importance of rare blood group antibodies in organ transplantation and transfusion medicine. It's a reminder for clinicians and lab staff to keep a closer look at unusual antibody profiles, especially when there are discrepancies in routine serological testing. We need more studies and awareness about these antibodies to avoid adverse reactions in transfusions and organ transplant procedures.

Conflict of Interest

Authors declare no conflict of interest.

Ethical consideration

Informed consent of the patient was taken.

REFERENCE

1. Perrault R. Naturally-occurring anti-M and anti-N with special case: IgM anti-N in a NN donor. Vox sanguinis. 1973;24(2):134-49.
2. Harmening DM. Modern blood banking & transfusion practices: FA Davis; 2018.

3. Thakral B, Saluja K, Sharma RR, Marwaha N. Phenotype frequencies of blood group systems (Rh, Kell, Kidd, Duffy, MNS, P, Lewis, and Lutheran) in north Indian blood donors. Transfusion and apheresis science : official journal of the World Apheresis Association : official journal of the European Society for Haemapheresis. 2010;43(1):17-22.
4. Sancho JM, Pujol M, Fernández F, Soler M, Manzano P, Feliu E. Delayed haemolytic transfusion reaction due to anti-M antibody. British journal of haematology. 1998;103(1):268-9.
5. Ballas SK, Dignam C, Harris M, Marcolina MJ. A clinically significant anti-N in a patient whose red cells were negative for N and U antigens. Transfusion. 1985;25(4):377-80.
6. Klein HG, Anstee DJ. Mollison's blood transfusion in clinical medicine: John Wiley & Sons; 2013.
7. Kumawat V, Jain A, Marwaha N, Sharma RR. Anti-N antibody reacting at 37°C: An unusual occurrence interfering with routine testing: Two interesting cases. Asian journal of transfusion science. 2015;9(1):92-3.