Case Report

Report of two cases of anti-M antibody in antenatal patients

Joseph Philip, Neerja Kushwaha, Neelesh Jain

Department of Transfusion Medicine, Armed Forces Medical College, Pune, Maharashtra, India

Abstract

Anti-M is a relatively common naturally occurring antibody reacting optimally at 4°C and weakly or nonreactive at 37°C. It is usually clinically insignificant but can be active at 37°C because of thermal amplitude of IgM component or presence of IgG component. It can cause or delayed hemolytic transfusion reactions or hemolytic disease of newborn. At our center we have encountered two cases of anti-M antibodies- one presenting as crossmatch incompatibility and other as blood grouping discrepancy in the last 8 months.

Key words: Anti-M antibody, antenatal, hemolytic disease of fetus and newborn

Access this article online

Website: www.ajts.org

DOI: 10.4103/0973-6247.150963

Quick Response Code:

Correspondence to:
Dr. Joseph Philip,
Department of Transfusion Medicine, Armed Forces Medical College, Pune-40, Maharashtra, India.
E-mail: eoj_in@yahoo.com

Introduction

In adults, anti-M is a relatively common naturally occurring antibody reacting optimally at 4°C and weakly or nonreactive at 37°C.[1] It is usually clinically insignificant but can be active rarely at 37°C because of thermal amplitude of IgM component or presence of IgG component. It can cause or delayed hemolytic transfusion reactions or hemolytic disease of newborn. At our center we have encountered two cases of anti-M antibodies one presenting as crossmatch incompatibility and other as blood grouping discrepancy in the last 8 months.

Case Reports

Case 1

Demand for two units of packed red blood cells (PRBC) came to our blood bank for a 20-year-old female ($G_2P_1A_0L_1$) at 36 weeks of pregnancy. Her hemoglobin was 7.0 g/dl. The blood group of the patient was 'A' Rh 'D' +ve. However, all donor red cell units were incompatible by Indirect Antiglobulin Test (IAT) with both, gel technique (-ID Microtyping system) and conventional test tube method. The sample was referred to the Immunohematology lab (IHL) for workup. Direct antiglobulin test (DAT) was performed on patient's red cells using polyspecific antiglobulin reagents (anti IgG and C3d) and found negative along with negative autocontrol. Antibody screening was done using Low Ionic Strength Solution (LISS) - IAT screening test with commercially available three cell panel (Biomed, DiaMed GmbH, Pra Rond 23, 1785 Cressier FR, Switzerland). Results showed positive reactions with panel I and III while negative with panel II [Figure 1].

Anti-e, anti-Jka, anti-M, and anti-S were considered as differential diagnosis. For antibody identification, 11-cell panel (Biorad-ID Micro typing system) was used, which identified anti-M Ab [Figure 2].

Patients sera showed 3+ reaction with M+M+ homozygous cells, 2+ reaction with M+N+ heterozygous cells but negative with M-N- cells in LISS/Coombs cards at 37°C and NaCl cards at 4°C. No reaction was seen with enzyme treated cells in all panels. An extended phenotype showed that the patient was M-antigen negative. To determine the immunoglobulin class of antibody, reactivity was noted before and after treatment with dithiothreitol (DTT). The antibody persisted after serum was treated with DTT suggesting the presence of IgG component along with IgM. Fetal sonogram, however, did not reveal any evidence of hemolytic disease of fetus and newborn (HDFN). Patient was transfused with M-antigen negative compatible blood.

Case 2

A 22-year-old female, G5P2A2L0 at 28 weeks of pregnancy, Rh isoimmunized, to be taken up for intrauterine transfusion (IUT). Cell grouping of patient was AB negative while reverse (serum) grouping showed agglutination with A and B cells. To solve this ABO discrepancy IHL workup was done. Patient's DAT and autocontrol were negative. Antibody screening using three-cell panels gave a differential of anti-D, anti-k, anti- Kpb, anti-Jsb, anti-M, anti-Lub, anti-Fya, anti-Jka, and anti-P1 [Figure 3]. Antibody was identified using 11-cell panels as anti-M [Figure 4].

It was confirmed by repeating the reverse grouping with M-antigen negative A and B cells and no reaction was seen. Specificity of the antibody was determined as IgM after treatment with DTT. Although this antibody was clinically insignificant

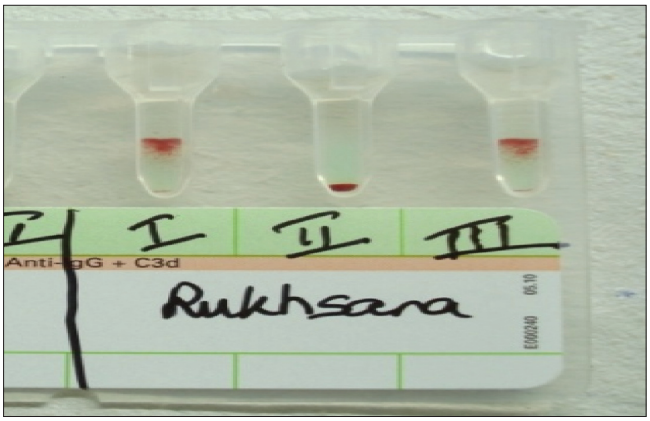

Figure 1: LISS Coomb's gel card showing three-cell panel antibody screening results at 37°C

Figure 3: LISS Coomb's gel card showing three-cell panel antibody screening results at 37°C

yet M-antigen negative 'O' Rh 'D'-ve unit, which was crossmatch compatible with the patient was issued. Successful IUT was performed.

Discussion

Anti-M antibodies are usually naturally occurring, cold reactive, and clinically insignificant antibodies. Anti-M is common in antenatal patients (even when the fetus is M-negative); however, there are few reports of potent IgG anti-M that is active at 37°C and causes HDFN.[1] This holds true for our first case. Although the anti-M antibody had IgG component which was reactive at 37°C it was not potent enough to cause HDN in the fetus. However, such anti-M is capable of causing acute or delayed hemolytic reaction in the recipient (mother).[2] Anti-M is generally thought of as an IgM cold-reacting antibody; however, most anti-M antibodies appear to be IgG or have an IgG component.[3] Anti-M, whether IgM or IgG, does not bind complement. Anti-M antibodies that react at colder temperatures (i.e., room temperature and 4°C) and dissociate at 37°C or in AHG phase of antibody testing, generally are not considered clinically significant.[4] Incidence of 'M' antigen is fairly common in the population, about 75% (worldwide).[2] Incidence of anti-M in donor sera was found to be 1 In 2500 when reacting with homozygous M+N- cells while incidence reduced to half i.e., 1 in 5000 when screened with

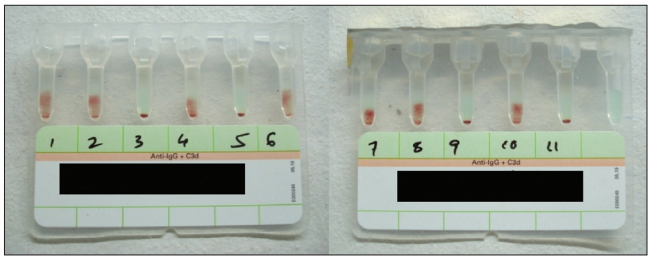

Figure 2: LISS Coomb's gel card showing one to 11-cell panel antibody identification results at 37°C

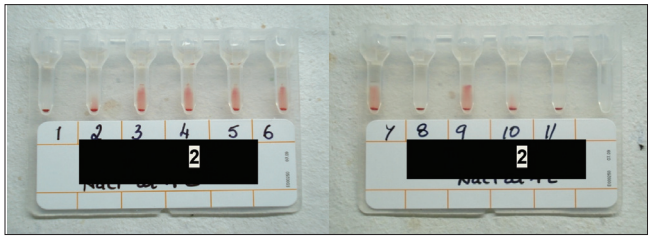

Figure 4: NaCl gel card showing one to 11-cell panel antibody identification results at 4°C

heterozygous M+N+ cells, indicating that some weaker examples of anti-M may be missed with heterozygous cells.[5] In our first patient there was stronger reaction with homozygous cells as compared to heterozygous M+N+ cells. MN antibodies are often pH dependent. IgM anti-M has an optimum pH of 6.5 and are mostly inactive at pH 7.5, becoming non-specific below pH 6.5.[5] Another feature of this antibody is its failure to react with ficin or papain-premodified cells. Proteolytic enzymes, such as ficin or papain, cleave red cell membrane sialoglycoproteins at well-defined sites.[6]

Cases of clinically significant anti-M antibodies have been reported by Tandon *et al*., and Justin *et al*.[4,6] Moreover 15 cases of patients with auto anti-M have been reported and reviewed by Sacher *et al*.,[7] According to him, 11 were non-significant while rest four gave some symptoms of cold hemagglutinin disease. A few cases of warm autoimmune hemolytic anemia (AIHA) caused by autoanti-N have been described, one of which had fatal outcome. However, autoanti-M, responsible for warm AIHA, has not been reported[2,5].

Anti-M causing HDN has been reported by Duguid J *et al*., Kanra T *et al*., Furukawa K *et al*.,[8-10] ranging from cases requiring exchange transfusions to intrauterine fetal deaths.

It is important to type specificity of anti-M antibody with accuracy as it can influence clinical outcome. Reactions can be falsely interpreted as positive in AHG phase if a high titer IgM-type antibody reacts at room temperature and agglutination is carried forward to AHG phase. Therefore strict warm conditions should be maintained during incubation and centrifugation; there should be no interruption during the procedure and results should be read immediately.

Although clinically significant anti-M antibodies are rare, once encountered, antigen-negative blood should be issued to prevent inadvertent adverse effects of transfusion.

References

1. Reid ME, Westhoff CM. Other blood group antigens and antibodies. In: Hillyer C, Anderson K, Silberstien L, Ness P, Roback JD, editors. Blood Bank. Transfus. Med. 2nd ed. New Delhi: Churchill Livingstone; 2009. p. 96-7.
2. Daniels G. Other blood groups. In: Roback JD, Combs MR, Grossman BJ, Hillyer CD, editors. Tech Man 16th ed. Bethesda: AABB; 2008. p. 414-7.
3. Leger RM, Calhoun L. Other Major Blood Group System. In: Harmening DM, editor. Mod Blood Bank Transfus Pract. 5th ed. New Delhi: Jaypee Publisher; 2008. p. 165-7.
4. Steinert JN, Kirkegaard J, Jigar S. Patel. Unusual Antibody Reactions in a 55-Year-Old Man Lab Med 2006;37:671-4.
5. Daniels G. Human Blood groups. 2nd ed. Oxford, UK: Wiley Blackwell; 2002. p. 146-7.
6. Tondon R, Kataria R, Chaudhry R. Anti-M: Report of two cases and review of literature. Asian J Transfus Sci 2008;2:81-3.
7. Sacher RA, Abbondanzo SL, Miller DK, Womack B. Auto anti-M. Clinical and serologic findings of seven patients from one hospital and review of literature. Am J Clin Pathol 1989;91:305-9.
8. Duguid J, Bromilow IM, Entwistle GD, Wilkinson R. Haemolytic disease of the newborn due to anti-M. Vox Sang 1995;68:195-6.
9. Kanra T, Yuce K, Ozcebe IU. Hydrops fetalis and intrauterine deaths due to anti-M. Acta Obstet Gynecol Scand 1996;75:415-7.
10. Furukawa K, Nakajima T, Kogure T, Yazaki K, Yoshida M, Fukaishi T, *et al*. Example of a woman with multiple intrauterine deaths due to anti-M who delivered a live child after plasmapheresis. Exp Clin Immunogenet 1993;10:161-7.

Cite this article as: Philip J, Kushwaha N, Jain N. Report of two cases of anti-M antibody in antenatal patients. Asian J Transfus Sci 2015;9:89-91.

Source of Support: Nil, **Conflict of Interest:** None declared.