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# Liver Transplantation in a Case of Secondary Biliary Cirrhosis with Anti-M Antibodies

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**Abstract:**
Anti- M is a naturally occurring antibody of the MNS blood group system. This antibody is most reactive at temperatures below 37 ◦C, with an optimum temperature of 4 ◦C and is considered to be clinically insignificant.The antibodies can be of clinical significance causing hemolysis when reactive and hence M antigen negative blood should be transfused.We report the peri-operative management of a case of Liver Transplantation in a patient of secondary biliary cirrhosis with immunoglobulin (Ig)M anti-M antibody.

**Introduction**
Anti-M is a fairly common naturally occurring antibody originally described by Wolff and Johnsson in 1933.This case of secondary biliary cirrhosis came with jaundice, free fluid in abdomen and esophageal varices on upper GI endoscopy for liver transplantation.He was referred to the Immunohematology laboratory from the Cross match laboratory after he presented as Cross match incompatibility on ABO Rh crossmatching.
Case report: A 9-year-old male weighing 22kgs with B negative blood groups, operated for open cholecystectomy for common bile duct stone at the age of 6 years, had biliary stricture and recurrent cholangitis. He was managed conservatively till this time when presented again with progressive jaundice, itching,abdominal distension and mild ascites. On further investigation, he was found to have grade 2 oesophageal varices, intrahepatic biliary dilatation and enlarged liver with mildly coarse echotexture. He was then planned for Liver Transplantation for which on ABO Rh crossmatching, his blood reacted positivity on crossmatching with B negative and O negative blood groups.
Antibody screening and Identification and Resolution of ABO typing Discrepancies results indicated the presence of significant Anti- M alloantibodies in the plasma of pre-transfusion samples.Column agglutination test for ABO Rh determination showed B negative with the presence of IgM anti-M antibodies in plasma but the direct antiglobulin and elution tests were negative as shown in figure 1. Antibody hemolytic activity assay confirmed positivity on crossmatching caused by anti-M at and above 37° Celsius.

Diagnosis: NA
Previous Blood Transfusion (if any): NA

Sample Collected: NA
Lab Ref No. G2570
Sample Received: NA
Sample type: EDTA Samples
Comments: Samples were Ok

Test code: IH01, IH02
Test name: Antibody Screen and Identification, Resolution of ABO Typing Discrepancies

| Test | Interpretation |
|---|---|
| ABO/Rh determination (CAT) | B Rh (D) Negative |
| Antibody Screen (CAT) | Positive |
| Antibody Identification (CAT) | Anti-M |
| Auto control (CAT) | Negative |

Final Impression: **Clinically significant Anti-M allo-antibody identified in patient's plasma.**

Transfusion Advice: **Transfuse with M antigen and B Rh (D) Negative, AHG cross-matched compatible RBC unit.**

**Figure- 1 : Column Agglutination Test**

The child was worked up and posted for Living Donor Liver Transplantation with mother being the liver donor. The blood bank was requested to provide B or O negative blood and blood products with no M antigen in them.After arrangements of adequate number of blood and blood products,the patient was considered for a living donor liver transplantation ,the graft being donated by the mother.

General anaesthesia consisted of anti-sialogogue inj glycopyrolate, anxiolytic- inj Midazolam, Opioid-Fentanyl, induction agent Thiopentone Sodium and muscle relaxant Rocuronium.An endotracheal tube of 5mm cuffed was used for intubation and fixed at 16cms at the angle of the mouth. The right internal jugular vein was cannulated with two triple lumen central line catheters of 5.5 Fr 8cms for infusion of drugs, iv fluids, blood and blood products. A radial and a femoral arterial line was inserted for monitoring of invasive blood pressure and also a Flotrac monitor was used to assess beat to beat status of cardiac and clinical parameters of the patient.

The considerations of anaesthesia in paediatric liver transplantation are mainly related to the airway management, hypothermia, hypoglycemia, bleeding, hypotension, coagulopathy, fluid and electrolyte imbalance, arrhythmia, pulmonary oedema, renal failure, neurological compromise.

The child was operated for a living donor liver transplantation in 3 phases , the dissection phase, the anhepatic phase and the neohepatic phase.There requirement of first red blood cell transfusion came during dissection phase in which we transfused 300 ml of leucodepleted, Anti-M negative ,B negative red blood cells and 150 ml of single Donor platelet compatible for the child. Prophylactic inj Hydrocortisone 1mg/kg , inj Pheniramine 2mg/kg Stat have been injected to the patient for the prevention of any transfusion related reactions.The temperature of the patient was recorded 36.4 degree Celsius. On transfusion of the blood and products, no adverse events were noted. The patient demographic and intra-operative data are depicted in table- 1.

| | |
|---|---|
| Age | 9 years |
| Weight | 22 kgs |
| Blood Group | B negative |
| Cold ischemia time | 41 mins |
| Warm ischemia time | 28 minutes |
| Initial Hemoglobin | 9.2 g/dl |
| Graft weight | 374 grams |
| GRWR | 1.7 |
| Blood loss | 450 ml |
| Transfusions | 300ml LDPRBC, 150 ml SDPC |
| Urine output | 1800 |
| Duration of surgery | 13 hours |
| Last Hemoglobin | 8.4 g/dl |
| Last Lactate | 2.4 |
| Fluid balance | 280 ml positive |

**Table- 1 : Patient demographic and intra-operative data.**

The patient was given 220mg of Methylprednisolone as induction immunosuppressive agent and broad spectrum antimicrobials were used to prevent infection.Blood loss was replaced with blood and blood products with a target hemoglobin of 8-9 gm/dl. Coagulopathy was diagnosed based on Thromboelastogram , surgical site oozing and was corrected accordingly. Blood sugar was maintained at a range of 100- 150 mg/dl. Serial ABG analysis were done to monitor acidosis, electrolytes, trends of sugar and lactate. Correction of electrolyte imbalance, metabolic and respiratory acidosis were done accordingly. The patient was shifted to the post liver transplantation icu on ventilator and extubated the next day. The child was monitored according to the institutional post liver transplantation care protocol and was successfully discharged on the 10th post operative day.

**Discussion**

The International Society of Blood Transfusion has described 33 blood group systems presenting over 300 antigens with ABO-Rh as the largest system. The MNS antigen system was first described by Landsteiner and Levine in 1927 and is based on two genes: Glycophorin A and Glycophorin B. The blood group is under control of an autosomal locus on chromosome 4 and also under control of a pair of co-dominant alleles LM and LN [1]. The MNS system is a highly complex system that has 46 antigens.The anti-M antibody was first discovered by Wolf and Johnson in 19331. The common antigens in this system are M, N, S, and s [2]. The various blood group systems are described in Figure 2.

| Name | Symbol | Number of antigens | Gene name | Chromosome |
|---|---|---|---|---|
| ABO | ABO | 4 | ABO | 9 |
| MNS | MNS | 43 | GYPA, GYPB, GYPE | 4 |
| P | P1 | 1 | P1 | 22 |
| Rhesus | Rh | 49 | RhD, RhCE | 1 |
| Lutheran | LU | 20 | LU | 19 |
| Kell | KEL | 25 | KEL | 7 |
| Lewis | LE | 6 | FUT3 | 19 |
| Duffy | FY | 6 | FY | 1 |
| Kidd | Jk | 3 | SLC14A1 | 18 |

**Figure - 2 : Various blood group Systems**

The human plasma contains only two naturally inherent antibodies namely, Anti- A and Anti- B. All other antibodies are called “unexpected red cell antibodies” . The existence of unexpected antibodies will cause many adverse blood transfusion reactions in patients who receive normal blood transfusion treatment, such as fever, chills or rashes in mild cases, and hemolytic blood transfusion reactions in severe cases [3].Antibody detection plays a crucial role in blood transfusion medicine because it can detect irregular or unexpected antibodies, and unexpected antibody positivity is an important cause of hemolytic transfusion reactions.

The anti-M and anti-N antibodies are usually IgM types and are rarely associated with transfusion reactions. The IgM anti-M antibodies can be ignored if they are not reactive at 37 °C, but the patient should receive M antigen-negative red blood cells if the antibody is reactive at 37°C or if it is of IgG class.There will be cross positivity on testing the pre transfusion samples for ABO Rh and on further investigation ABO discrepancy that affected serum testing due to presence of additional antibody other than A or B would be found.

The significance for anaesthesia and transfusion medicine lies in preparing adequate volume of blood and blood products while conducting a case. When IgM anti-M antibodies are present but not reactive at 37°C, the selection of transfusion RBC units are matched or compatible with patients’ ABO and RhD. However, M antigen-negative RBC are necessary for transfusion when the antibody is reactive at 37 °C or is of IgM + IgG class[4]

Most of the anti-M antibodies are temperature-responsive, the strongest reaction at 4 °C, a weak reaction at room temperature, and a weak or even no reaction at 37 °C, which easily results in missed detection[5]. Anti-M antibodies in humans are divided into natural antibodies and immune antibodies, including the more common IgM properties, IgM + IgG properties, or IgG properties alone, however IgG antibodies are relatively rare [6]. Anti-M may be naturally occurring or immune mediated due to exposure in a previous pregnancy, transfusion, or transplantation[7].

In 2012, Kaur et al. reported two cases of clinically significant anti-M antibodies one presenting as a cross-match incompatibility and the other showed a discrepancy in blood grouping and concluded that if the antibody is reactive at 37 °C, the patients should receive antigen-negative red blood cells [8].

The preparation and conduction of a case of pediatric liver transplantation in itself implies for caution to be authorised at multiple levels starting from diagnosis of Liver disease, perioperative transfusions, fluid and electrolyte management, glycemic control, temperature management, reno-protection and airway control right from induction till extubation. With all these concerns around, the cross positivity on ABO-Rh grouping might cause more distress mainly in diagnosis and arrangements of blood and blood products in emergent situations of preoperative blood loss in the form of malena , hematemesis, epistaxis or trauma or in case of acute liver failure. Therefore prior diagnosis of cross reactivity, identification of the antibodies in the recipient and arrangements essential for adequate volume of blood and blood products are the cornerstone of management in such a case.

The occurrence of peri-operative hemolysis or acute transfusion related reactions in a case of pediatric liver transplantation can camouflage the diagnosis with anaphylaxis caused by drugs, TRALI, TACO, Febrile nonhemolytic reactions or sepsis. General anaesthesia might blunt the signs and symptoms of hemolysis due to the presence of M antibodies in the recipient and the subsequent reactions associated with transfusions.Close monitoring of vitals and subtle changes in hemodynamics, urine output or appearance of rashes or other signs of allergic reactions are very essential to conclude a diagnosis and treat it accordingly.

Mathur et al. reported an unusual case of a potentially significant anti-M antibody in a healthy male blood donor without any history of transfusion in which the antibody showed a pan-reaction during reverse blood grouping at 37 °C but not at 4 °C. The discrepancy was resolved by treating the reagent red cells with papain as this destroyed the M antigen on the surface of the red blood cells [9].

Conclusion: It is already known that anti-M is a naturally occurring antibody that may be IgM or IgG and can not only cause discrepancy in blood grouping but may also be of clinical significance if it is reactive at 37 ◦C. In all such cases an immunohematology card must be issued by mentioning the type and nature of the antibody and the patient advised about future blood transfusions. Patients with such antibody require blood transfusion with M antigen negative compatible blood and products.The accurate diagnosis of anti-M antibody-mediated acute hemolysis is essential for prevention of transfusion reactions and associated organ dysfunctions.

**References:**

1. Mitra R, Mishra N, Rath GP. Blood groups systems. Indian J Anaesth. 2014 Sep;58(5):524-8. doi: 10.4103/0019-5049.144645. PMID: 25535412; PMCID: PMC4260296.
2. Navkudkar, Anisha; Desai, Priti; Thakkar, Rajesh; Rajadhyaksha, Sunil. Management of transfusion needs in a case of immunizing anti-M antibody in a patient with acute myeloid leukemia. Indian Journal of Pathology and Microbiology 63(2):p 251-254, Apr–Jun 2020. | DOI: 10.4103/IJPM.IJPM_166_19
3. Wang J. Study on the test effect of irregular antibody test in clinical blood transfusion and its influence on patients' treatment prognosis. Electronic Journal of Clinical Medicine Literature 2019;6:161.
4. Sahin I, Reagan JL, Niroula R, et al. Refractoriness to red blood cell transfusion therapy due to hypersplenism. Transfusion 2018;58:2513-6. 10.1111/trf.14876
5. Wang S, Wang J, Mo X, Wang Z, Wu Y, Liu F, Qu L. Analysis of anti-M antibody status and blood transfusion strategy in Hunan, China. Ann Transl Med. 2022 Nov;10(21):1166. doi:10.21037/atm-22-4999. PMID: 36467339; PMCID: PMC9708473.
6. Fadeyi EA, Naal T, Green M, Simmons JH, Jones MR, Pomper GJ. Anti-M-Induced Delayed Hemolytic Transfusion Reaction. Lab Med. 2020 Jul 8;51(4):426-429. doi: 10.1093/labmed/lmz078. PMID: 31756244.
7. Yu M, Graham K, Pasalic L, Alahakoon TI. Recurrent fetal hydrops with maternal M alloimmunisation: not a benign condition. BMJ Case Rep. 2019 Jul 21;12(7):e230552. doi: 10.1136/bcr-2019-230552. PMID: 31331930; PMCID: PMC6664319.
8. Kaur G, Basu S, Kaur P, Kaur R. Clinically significant anti M antibodies--a report of two cases. Transfus Apher Sci. 2012 Dec;47(3):259-61. doi: 10.1016/j.transci.2012.07.023. Epub 2012 Sep 13. PMID: 22980914.
9. Mathur A, Dontula S, Jagannathan L. An unusual case of a potentially clinically significant anti-M antibody in a healthy male blood donor without any history of blood transfusion. Blood Transfus. 2011 Jul;9(3):339. doi: 10.2450/2011.0069-10. Epub 2011 Jan 13. PMID: 21251471; PMCID: PMC3136603.