Blood group discrepancy: Is it Group I or Group III?

ABO blood group system is the most crucial blood group system in terms of blood transfusion and transplantation capable of causing fatal reactions. In the determination of ABO blood group, two methods – cell grouping and serum grouping – are performed as a double check. Discrepancies between these two methods often occur and are classified arbitrarily into Group I due to weak or absent antibodies causing problems in serum grouping (as may be seen in the elderly, new-born patients and immune-deficient or immune-compromised patients), Group II due to weak or absent antigens causing problems in cell grouping (weak antigens, subgroups of A and B), Group III due to abnormal plasma proteins causing rouleaux formation as in multiple myeloma and Group IV due to miscellaneous reasons like panagglutination.[1,2]

Whenever discrepancies occur, they need to be solved before proceeding for transfusion. Resolution of blood group discrepancy is performed by checking the reactions at different temperatures or using multiple saline washing of the red cells to clear abnormal proteins as may be seen with cord blood samples or multiple myeloma. Similarly, steps such as testing with acidified sera and use of lectins are done in certain cases.

A 54-year-old male patient presented to the Department of Medical Oncology and was diagnosed with multiple myeloma. A request was made to Transfusion Medicine Department for the determination of blood group. There was no historic blood group record for this patient. Cell grouping was performed with Commercial Antisera A, B, AB and D (Meril Diagnostics, Gujarat) and on observing agglutination only with anti-D antisera, the cell group was initially identified as O RhD positive. On testing with commercial anti-H lectin which is performed for all O group patients routinely, rare groups such as Bombay and Para-Bombay groups were ruled out, as 4+ agglutination was found with anti-H lectin indicating the presence of H antigen in abundance. On performing serum grouping with in-house pooled A, B and O cells, no agglutination was found, and serum group was found as AB and a discrepancy was noticed. Testing of both cell and serum grouping was performed at 37°C, 22°C and 4°C to resolve the discrepancy as stronger reactions occur at 4°C ideally; however, there was no potentiation, and the cell and serum grouping continued to be same. To rule out weak subgroups of A or B causing abnormal reactions in forward grouping, saliva secretor status was performed using standardised methods and controls,[1,2] and the patient was found to be non-secretor by the haemagglutination-inhibition method. Secretor status was confirmed to be non-secretor using in house anti-Lewis antisera. Haemadsorption and elution studies were performed to finally rule out weak A or B subgroups using in-house polyclonal sera from donors. Through these investigations, weak subgroups of A, B and Cis-AB were all ruled out. Hence, this patient's blood group was confirmed as O RhD positive with no isoagglutinins due to multiple myeloma with associated hypo/agammaglobulinemia.

The most common discrepancy found in multiple myeloma is Group III discrepancy causing false-positive reactions in reverse grouping with all cells requiring the use of multiple saline washes or saline addition techniques. M protein produced by multiple myeloma cells is a common cause of Group III ABO discrepancies resulting from elevated levels of globulin or light chains of immunoglobulin. Abnormally elevated paraproteins cause the rouleaux formation which is stacks or aggregations of red blood cells (RBC) finally giving the 'stacked coin appearance' due to a reduction in 'zeta potential' (charge on RBC membrane). The saline addition technique rids the RBC membranes of the paraproteins and frees the RBCs in the case of rouleaux formation in the reverse grouping. In true agglutination, red cells will continue to clump after addition of normal saline. It could even be mistaken for agglutination by medical technicians in the forward grouping which is removed by multiple saline washing of cells before the start of cell grouping. Sometimes, Group I ABO discrepancies can also occur when patients have depressed antibody production or cannot produce the ABO antibodies specifically. Weak agglutination reactions may be obtained with reagent or in-house A, B and O pooled RBC suspensions and are a result of weak expression of anti-A and anti-B in the serum. Group I ABO discrepancy should be suspected because RBC and serum grouping reactions are normally very strong and react well at room temperature and best at 4°C. IgM is the predominant isoagglutinin found in blood Group A or B individuals; although, small quantities of IgG antibody can also be detected at the anti-human globulin phase. The severe

deficiency of IgM would be responsible for Group I ABO discrepancies in multiple myeloma with blood Group A or B. There are only two case reports on the literature search, wherein similar Group I discrepancy was found[3,4] and one case report showing both Group I and III discrepancies.[5] In one of these case reports, genetic typing was performed to confirm ABO group of patient, and in the other report, group discrepancy was resolved and blood group was confirmed by performing tests at antihuman globulin phase and secretor status assessment.

To conclude, in scientific research, anything cannot be taken for granted and its best to keep an eye out for strange observations that occur from time to time to avoid life-threatening mistakes and for scientific progress. To resolve the ABO discrepancy and to provide compatible blood for transfusion, it is necessary to obtain relevant historical information from the patient wherever possible and to provide medical and technical expertise as well as education for the blood bank technologist in transfusion medicine-related testing, practice, risks and related areas, in addition to following total quality management and continuous quality improvement practices.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Access this article online	
Quick Response Code:	Website: www.jcsr.co.in
	DOI: 10.4103/JCSR.JCSR_40_19

How to cite this article: Chaitanya Kumar IS, Babu BS, Arun R, Babu KV, Praveen MD, Sriranjitha TV, *et al*. Blood group discrepancy: Is it Group I or Group III? J Clin Sci Res 2019;8:42-3.