Original Article

Detection of rare blood group, Bombay (Oh) phenotype patients and management by acute normovolemic hemodilution

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Abstract:

Background: Due to lack of correct blood grouping practices, the rare Bombay Oh phenotype may be missed, subjecting patients to the risk of severe hemolytic transfusion reaction. In the absence of blood donor registry, transfusion management of patients needing immediate surgery is a challenge. This study presents detection of rare Bombay Oh phenotype patients and their management by acute peri-operative acute normovolemic hemodilution (ANH) in a hospital from central India. **Materials and Methods:** Blood grouping of patients and blood donors with a standard tube method was carried out and samples identified as rare Bombay phenotype were confirmed by saliva inhibition test. Surgical management of cases needing transfusion was done by ANH, as per the British Committee for Standards in Hematology guidelines. **Results:** The incidence of Bombay phenotype was 0.002% or 1 in 51,924 in the study. Amongst three cases (patients) identified as Bombay phenotype, one was Bombay Oh, Rh negative. Two cases were missed in the first instance and one case actually did not require transfusion. In the absence of a blood donor registry for Bombay phenotype, the cases needing transfusion were successfully managed with ANH in the operation theatre. **Conclusion:** A simple test like blood grouping should be done with serious intention with incorporation of both forward and reverse grouping, so that no patient receives wrong blood leading to fatal hemolysis due to transfusion. ANH is a cost-effective transfusion option for suitable patients. Appropriate clinical decision making, use of strategies to decrease peri-operative blood losses and cost-effective country based planning could be more widely applied to improve clinical transfusion practice.

Key words:

Acute normovolemic hemodilution, Bombay Oh phenotype, hemolytic transfusion reaction

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Introduction

The last two decades have seen blood transfusion services in developed nations trying desperately to minimize the risks of blood transfusion through transfusion transmitted infections. The need to improve transfusion safety in the developing world has been understood and is evident through the introduction of a National Hemovigilance Program. The role of blood group serology (BGS) laboratory is equally vital in the provision of safe and compatible blood to patients. However, it is also evident from reports that the laboratory errors continue to be one of the main causes of incompatible or inappropriate blood transfusion, compromising patient safety and resulting in mortality or severe morbidity. Rare blood group patients need to be identified and their transfusion requirements managed by the blood centers in life saving situations. Individuals with the rare Bombay phenotype (hh) do not express H antigen (also called substance H), the antigen which is present in blood group O. The H antigen is the precursor of A and B blood group antigens. As a result, they cannot make A antigen (also called substance A) or B antigen (substance B) on their red blood cells, whatever alleles they may have of A and B blood group genes.[1] The serum of such individuals has strong anti-H in addition to anti-A and anti-B. If patients with anti-H in their circulation receive transfusions of blood that contains the H antigen (e.g., blood group O), they are at risk of suffering an acute hemolytic transfusion reaction. Since their red cells do not react with anti-A, anti-B and anti-AB antiseras, they can be recognized as the O blood group in cell typing. The individuals with Bombay blood group can only be transfused autologous blood or blood from individuals of Bombay Oh phenotype only which is very rare. We present our experience of detection of three rare blood group, Bombay Oh phenotype patients at our center in central India and their successful management, two of them with peri-operative acute normovolemic hemodilution (ANH) as per the British Committee for Standards in hematology (BCSH) guidelines.[2]

Materials and Methods

Blood grouping: Routine blood grouping of blood donors and patients was done in the BGS section of blood bank using tube technique for both forward and reverse grouping. Anti-A, anti-B, anti-A B for forward reaction was used and agglutination of plasma with A, B and O (H) red cells (reverse reaction) were also tested for the presence or absence of antibodies in the serum. Confirmation of Bombay phenotype: To confirm the Bombay phenotype, anti-H lectin was used in forward grouping and agglutination inhibition test for determination of secretor status was performed. ANH: The procedure was carried out as per the BCSH guidelines in Case 1 and 3. The standard operating procedure was followed and patients with hemoglobin more than 11 g/dl were evaluated by the anesthesia and blood bank consultants. With informed consent, blood collection was done in the 350 ml single blood bags issued from the blood bank to ensure a standard anticoagulant/blood ratio and approximate volume of blood to be removed (in liters) to achieve the desired hematocrit was calculated using the following formula:

$$V = EBV \times (H0 - Hf/Hav)$$

Where, V = Volume to be removed, EBV = Estimated blood volume (usually taken as 70 ml/kg body weight), H0 = Initial hematocrit, Hf = Desired hematocrit and Hav = Average hematocrit (mean of H0 and Hf).

Results

Incidence of Bombay group in our experience of last 12 years was found to be 0.002% or 1 in 51,924 as only three patients and none of the blood donors out of 1, 55,771 total tested were detected to be of the rare blood group, Bombay Oh phenotype. Detection and transfusion management of Bombay Oh phenotype patients.

Case 1

The first case report is about a young 11-year-old female patient who came to the hospital on a Saturday to the cardiothoracic unit out-patient department (OPD) and was diagnosed to be a patient of atrial septal defect. She carried a blood group report of a hospital where her preliminary testing was carried out as O (ABO), Rh positive. As the blood group was readily available at our center, she was advised admission on Monday and her cardiac surgery was scheduled on Tuesday. Her blood sample for cross matching arrived at the blood bank with the request for two units of blood. Her blood group was also reported as O positive in the pre-transfusion testing at our lab. The matching was initiated and more than 10 red blood cell units of O positive were found to be incompatible. On repetition of the blood group, it was found that the pooled O cells were giving positive agglutination in the reverse grouping. Her red blood cells gave no agglutination with anti-H lectin. The probability that the patient was having the rare blood group, Bombay Oh phenotype was raised and further confirmation of the blood group was done by saliva hemagglutination inhibition test and the sample was also sent to a reference serology laboratory of Indian Institute of Immunohematology (IIH) at Mumbai, India and the report received later also confirmed the same. On taking further history, it was found that she was a tribal girl originally from a tribal state of India. Since this was the first case of Bombay phenotype, we decided to do blood grouping of her family members, but none of them were of the same group. However, her hemoglobin was 11.8 g/dl and the surgeon was explained about the rarity of the blood group as well the unavailability, the option of ANH was considered. She was successfully operated and withdrawal of one unit autologous blood was done with simultaneous hemodilution (ANH) in the operation theater and her course of stay was uneventful until her discharge from the hospital.

Case 2

Blood request for O negative blood for an 18 year female patient admitted to a local Government medical college hospital, due to non-availability of blood, came to our center.

The patient had undergone a hand surgery after having suffered a crush injury in her village and the blood transfusion was ordered prior to the discharge of patient from the hospital. Her blood group was mentioned as the O Rh negative in the blood request form. The blood group was done (forward and reverse both) and the patient turned out to be the rare Bombay Oh phenotype, Rh negative, giving agglutination with O pooled red cells in the reverse grouping and no agglutination with anti-H lectin in the forward. Patient's brother was the only relative available and his blood group was found to be O Positive. The treating doctor was informed about the rarity of the blood group and need to transfuse blood was discussed. Her hemoglobin was 10.2 g/dl and was recovering. The consultant had planned to transfuse one unit prior to discharge. The treating doctor was explained that there was no urgency to transfuse blood and that the patient could be discharged without any transfusion. Her brother was counseled about the rarity of blood group of his sister and the need to preserve the blood group report to avoid any transfusion ofwrong blood unit later in her life.

Case 3

The third case report is about a 12-year-old female patient who attended the neurosurgery OPD with the complaints of gradually progressive loss of vision in both eyes and was subjected to imaging tests. She was diagnosed with suprasellar epidermoid cyst. Her surgery was planned and for routine investigation, her blood sample for blood grouping was received at the blood bank. Her forward and reverse grouping was done and she was diagnosed as Bombay Oh phenotype with the inclusion of anti-H in forward and O red cells in the reverse grouping. To confirm, saliva testing was done and it was conclusive of the same. The request for blood was received as the patient was to undergo surgery on urgent basis. The blood grouping of patients' parents and other available relatives was performed, but none of them were of Bombay phenotype. The patient was a suitable candidate for alternatives to allogeneic blood transfusion as the requirement was 350 ml and ANH was planned as per the BCSH guidelines due to non-availability of any official guidelines in India. The surgeon in charge was explained as well the informed consent obtained from the patient. Under the supervision of anesthesia consultant and medical officer from the blood bank, patient was operated and ANH was performed with one unit of autologous blood being transfused during the surgery.

Discussion

Bombay phenotype was first reported by Bhende in 1952 in Bombay, India.[3] More than 130 Bombay phenotypes have been reported in various parts of the world. Bombay phenotype is rare, since it occurs in about 1 in 10,000 individuals in India and

1/1,000,000 individuals in Europe.[1] It is rare in Caucasian with incidence of 1 in 250,000. In a study from Sundargarh district in North-Western Orissa, the Central-Eastern part of India three unrelated cases of Bombay (Oh) phenotype in Paudi Bhuyan (a primitive tribe) and Khandayat Bhuyan from Lahunipara and Hemgiri Blocks, respectively have been described. Regarding the distribution and spread of the Bombay phenotype in different states of India, it is apparent that the phenotype is more common in the states of Western and Southern parts of India when compared to other states.[4] However, from Bhopal, Madhya Pradesh no data has been published. In a more recent study from South India, 13 Oh phenotypes (0.048%) were detected of which 7 were males and 6 females. Among these 13 Oh phenotypes, only 3 were Rh-D negative and consanguinity among parents was observed in 10 cases (77%) in a study amongst Bombay phenotypes.[5] However, in our cases none of the parents had a history of consanguineous marriage. One study attributed Indian Bombay and para-Bombay phenotypes to an inactivating missense mutation at the H locus, accompanied by deletion at the SE locus in the case of Bombay individuals.[6] Although rare, the Bombay Oh phenotype patients can have severe or fatal hemolytic transfusion reactions if the blood group is missed.[7,8] Awareness amongst treating doctors is a very important issue in managing such patients. In a recent case report from Iran, transfusion reaction in a case of Bombay blood group patient has been described and the reason for missing out on Bombay group has been stated as, only forward grouping being performed in routine with crude slide method and inappropriate documentation of cross matching.[9] It is very important that a simple test like blood grouping should be done with serious intention and correct method of including both forward and reverse grouping (a practice still needs full implementation) so that no patient is missed out or receives wrong blood, which could lead to serious hemolysis due to transfusion. The Bombay Oh phenotype can be missed if O cells are not used in reverse blood grouping and moreover routine anti-H lectin not being used in forward grouping increases the possibility further. Implementing a quality system in the laboratory minimizes errors and ensures that the right test is performed on the right sample, the right results obtained and the right blood product provided to the right patient at the right time. In a study from Bangladesh, it has been suggested to incorporate "routine serum typing or reverse grouping confirmation" along with "O" cell control in the reverse grouping procedure in every transfusion medicine department or blood bank or blood donor centers and this practice should be mandatory to reduce the risk of fatal hemolytic transfusion reaction.[10] Although in India awareness about quality management systems and accreditation activities has increased, still there are a lot of blood centers which need to follow the correct blood grouping procedures. National AIDS control organization, blood safety division nationwide training programs for blood bank medical officers and laboratory technicians also aims toward the same. It is essential to obtain accurate results for BGS tests such as ABO/RhD typing of the donor and patient and compatibility testing and it is equally important that results are transcribed, collated and interpreted correctly so that compatible and appropriate blood products are issued. The errors in the laboratory can be due to technical failure in serological testing, inadequate procedures leading to misidentification of the patient or donor samples, or due to misinterpretation of results. There is often a combination of factors, with the original error being compounded by a lack of adequate checking procedures in the laboratory.[11] In India, the referral laboratory at IIH, Mumbai can confirm the blood groups and can also provide information about blood donors with Bombay Oh phenotype as they have maintained the registry. The difficulty is that the individuals with Bombay blood group (Oh) can either receive autologous blood or blood from an individual of Bombay phenotype only. If transfusion is required in such patients, ANH is an easily available, low cost option with the potential advantage of a reduction in blood viscosity as done in Case 1 and Case 3. Both patients were children suffering from diseases where surgery as treatment was the only option, the banked blood was not available for the rare blood group, surgeons adopted blood sparing operating and transfusing strategy and successfully managed the patients with the single autologous blood units collected and re-transfused to them.

There is a need for a central registry of Bombay Oh group blood donors and options like cryopreservation or calling donors for blood donation should also be considered. The feasibility and economics is still doubtful in a diverse population and the long distances the donors may have to travel. However, regional registries could be made. If ANH is not possible in such patients, then the other blood saving strategies and options for good blood management to avoid transfusion should be considered. The appropriate clinical decision making and ANH has also been applied more widely to improve clinical transfusion practice. In addition in developing countries like India, pre-donation questionnaire and screening of blood units is still not by the latest techniques such as nucleic acid amplification techniques, the risks of infections and other non-infectious complications of blood transfusion is still very high and the cost of acquiring any infection through transfusion or even properly tested blood unit would be much higher than the use of ANH. Strategies to decrease peri-operative blood losses are also important including meticulous surgical techniques, use of autologous blood salvage, ANH and avoidance of coagulopathy and hypothermia. The benefit of ANH is the reduction of blood loss as the whole blood is shed peri-operatively at lower hematocrit values achieved with ANH. Because blood collected by ANH is stored at room temperature in the operating room and is returned to the patient within 8 h of collection, platelets and coagulation factors remain functional. In addition, unit testing is not essential. ANH is cheaper but equivalent to pre-operative autologous donation in selected clinical settings (e.g., patients with a high pre-operative hemoglobin concentration undergoing a surgical procedure with a high expected blood loss such as a revision hip replacement) for reduction of allogeneic blood transfusions. Other outcomes including anesthesia and surgery times, intra-operative hemodynamic values and length of hospital stay were also similar for pre-operative autologous donation and ANH.[12]

When the cases were discussed with the treating doctors, the BCSH guidelines for ANH helped to convince them as initial apprehension about using a different protocol was there, as well they had no information regarding the existence of such a blood group type. It is equally important to inform patients the rarity of the blood group and the need to have a careful attitude in future. The reason the patients, especially the female patients, needs to be counseled is that the patients may require transfusion at the time of child birth and carry a risk of wrong blood transfusion. All blood group reports must explain and advice that transfusion should be avoided until matched donors are found or options of autologous transfusion preferably ANH are suggested. Saliva samples may be tested for further confirmation and transfusion trigger should be kept at 7 g/dl hemoglobin wherever possible. Although molecular research and advanced modern technology

is playing a very important part in blood banks in developing countries also, however, the matter of concern is that the patients of rare blood groups like Bombay phenotype are still missed and are at risk of being transfused wrong blood group causing hemolytic transfusion reactions leading to even death. All blood banks should strictly adhere to adopting quality standards in performing basic blood grouping tests, giving away the obsolete methods and should realize the responsibility and role in avoiding life-threatening situations for the patients. Programs for implementation of the standard methods in blood banking have been started through training on a national level but it seems that they still need the due attention. Establishment of the hemovigilance system could also be an answer to understand the gaps. Transfusion of blood by ANH is a very simple, cost-effective option for blood management of rare Bombay phenotype as evident from our cases, other than keeping in touch with the national referral laboratory which maintains the registry of rare blood group donors. There is a need for good blood patient management to avoid transfusion where ever possible.

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