Para-Bombay B phenotype: a rare ABH blood group variant at tertiary care hospital, Gwalior India

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Abstract
The H antigen is the precursor substance for A and B antigens formation on red blood cells of an individual, and its absence is termed as H deficient phenotype. The lack of H antigen on both red blood cell (RBCs) and secretions results in a classical Bombay phenotype with anti-H antibodies in serum. If the H antigen is absent on RBCs and present in secretions and plasma, the resulting blood group is the Para-Bombay phenotype. Although, the H gene is genetically absent in Para-Bombay (hh genotype), at least one Se (Secretor) gene is present. Para-Bombay or red blood cell (RBC) H negative secretor individuals may or may not have anti-H in their serum. In both cases, routine blood grouping is O. A blood sample from a 24-year-old female was sent to the blood bank, where the routine grouping revealed O RhD positive. Complete blood grouping by Gel technology revealed that her forward grouping was Oh and reverse grouping was B. Patient is secretor for B and H antigens. The adsorption-elution test is negative. Family grouping was also done to find out compatible blood and her family genesis. Patient blood group was Para-Bombay B. Complete blood grouping (forward and reverse), as well as saliva grouping and adsorption-elution test is advisable when there is a discrepancy in ABH grouping.

Introduction
The classic Bombay phenotype was first reported by Bhende YM et al. in 1952 in Bombay, India, and is associated with the ABO and H blood group systems.1 In the classic Bombay phenotype, both red cells and secretions (Non-secretor) are deficient in H, A, and B antigens. During the routine blood testing, cell grouping shows characteristics of the O group. Serum grouping reveals the presence of anti-H activity in the serum, in addition to the natural ABO antibodies. Para-Bombay individuals H antigen is absent on their red blood cells, but unlike those with the Bombay Phenotype, they have H antigen (and thus, A or B antigen) in their secretions and plasma.2 Therefore, Although, genetically, the H gene is absent in Para-Bombay (hh genotype), at least one Se (Secretor) gene is present.3 Para-Bombay’s may make a small amount of A or B antigen (depending on their ABO genotype) and H antigen in their plasma, some of which may adsorb to the RBC surface.4 In spite of this, Para-Bombay individuals can make a strong antibody against the H antigen (like present in Bombay Phenotype); consequently, they may require H-negative red blood cells blood for transfusion.5 Furthermore, in the Para-Bombay phenotype, the atypical antibodies in the serum react preferentially at lower temperatures (below 20°C to 22°C).6 Bombay phenotypes have a relatively higher incidence of 1 in 10,000 in India7 (1:4600 in Ratnagiri district8 and 1:7600 in Mumbai9) than Europe (1:1,000,000).10,11 In India, the Para-Bombay phenotype is extremely rare, and only a very few cases have been reported. No published study has reported the prevalence of Para-Bombay phenotype in India. However, in the Chinese population, more Para-Bombay phenotypes have been reported than the Bombay.12

Case Presentation
A 24-year-old female, full-term, primigravida with a hemoglobin of 7 grms% admitted to the Obstetrics and Gynecology Department of our Institute. A request for one unit packed Red Blood Cells (RBCs) comes to the blood bank. Her blood grouping and RhD typing were done by Gel Technology; Make-Tulip. Her forward

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grouping (cell) was Bombay (Oh) phenotype, and reverse grouping (serum) was B (Anti H is also absent in serum), while RhD status was Positive (Figure 1).

Further saliva grouping of the patient was performed to resolve the controversy of cell and serum grouping. Saliva grouping was done by using a neutral gel card with control. The patient was a secretor for B and H Substance. Adsorption-elution test was negative on the patient’s RBCs (Figure 1).

Finally, the patient’s blood group was determined as Para-Bombay B RhD Positive. The problem was to find out compatible RBCs for transfusion. Bombay and Para-Bombay RBCs were not available in stock or nearby centers. So detailed blood grouping of her accessible family members (mother, father, and her two brothers), as well as her husband, and later on, baby after birth, has been done, which is summarized in Figure 3. The striking feature of ABO grouping is that her mother and brothers have no H antigen on the RBC surface.

Now in excise to find out compatible Packed RBCs, cross-match is incompatible with allogenic random O and B cells at all the temperatures 40°C, 22°C, and 37°C, and all phases (Saline and AHG). It is more significant at 4°C in the saline phase, but cross-match is compatible with the cord blood (O and B cells), and patient’s mother and brother cells at all the temperatures 4°C, 22°C, and 37°C, and all the phase (Saline and AHG). An elective cesarean section was planned to keep her brother’s RBCs ready for transfusion, if required in an emergency. The policy is to avoid transfusion as far as possible. The patient delivered
a male baby. His blood group was B RhD negative, and transfusion was not required during and after the operation. Both mother and baby were alive and healthy.

Discussion
As H is the precursor substance for A and B antigens, it is present on all red cells except in the rare Bombay and Para-Bombay phenotype, where it may be absent or deficient. The ABO genes regulate the presence or absence of A and B antigens, whereas the H antigen results from α-1-2-fucosyltransferase (FUT) gene. H gene (FUT1) determines the presence of H antigen on the RBCs and Se gene (FUT2) in saliva and body secretions. FUT1 forms the H antigen, which is expressed in erythroid tissues and vascular endothelial cells by fucosylation of the type 2 chain oligosaccharides on red cell glycoproteins and glycolipids. FUT2 recognizes type 1 chain precursors to form H type I antigens in secretions and tissues such as secretory glands and digestive mucosa.14

Bombay phenotype is characterized by the lack of ABH blood group antigens on the surface of RBCs and in saliva, resulting in the inheritance of FUT1 (h/h) and FUT2 (se/se) genes.12 All the Bombay phenotype cases reported in India showed only the T725G mutation of FUT1 and the 10 kb gene deletion of FUT2, which are responsible for this rare phenotype, suggesting its unicusinic origin.13 Unlike Bombay, the Para-Bombay blood group individuals can express type I chain A, B, and H antigens in their plasma and secretions. The weak A and/or B antigen expression on red cells is due to passively adsorption2 and could only be detected by the adsorption and elution technique.12

In the present case, forward grouping is Oh, and reverse grouping is B. In saliva grouping, the patient is a secretor for H and B substances. The adsorption-elution test on the patient’s RBCs is negative. So ABO grouping of the patient is Para-Bombay B (Oh<sup>+</sup> secretor). The problem was to find a compatible packed RBC for transfusion. Bombay cells were not available in our blood bank and or at nearby centers. Cross-match was incompatible with allogenic random O and B cells at all the temperatures 40°C, 22°C, and 37°C, and all phases (Saline and AHG). It was more significant at 4°C in the saline phase, but the cross-match was compatible with cord blood (O and B cells), and the patient’s mother and brother cells at all the temperatures 4°C, 22°C, and 37°C and all the phase (Saline and AHG); because her mother and brothers have B antigen on RBC, but have no H antigen. Possible mother has small I activity on red cells (not converted to adult I antigen) which is carried in all the children. (Small amount of H converted to B antigen) and family has clinically significant Anti I/Anti HI/ Unidentified antibody in their serum. in their serum. Because of the fact that cross-match was compatible with ABO matched cord blood sample and with her family members excluding father.

Conclusion
The present case of Para-Bombay B phenotype, detected due to the discrepancy in cell and serum grouping, reveals the importance of complete blood grouping and use of anti-H reagent in Group O patients. In routine blood banking, besides blood grouping, detailed serological tests such as secretor status, adsorption-elution, and serum antibody titration at different temperatures should be performed, and molecular testing is recommended for further confirmation.

Conflict of Interest
Authors have declared that no conflict interests exist.

Ethical Approval
Ethical approval has been taken by appropriate ethical committee of Gajra Raja Medical College, Gwalior, India and research have therefore been performed in accordance with the ethical standards laid down in the 1964 declaration of Helsinki.

Author’s Contributions
This work was carried out in collaboration between all authors. Author Dharmesh Chandra Sharma designed the study, wrote the protocol and wrote the first draft of the case report. Author Sunita Rai and Sachin Singhah managed the literature search. Author Prikriti Gupta and Shailendra Sharma managed the experimental process. All authors read and approved the final manuscript.

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