A Very Rare Case with Particular H-deficient Phenotypes

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Abstract Bombay phenotype, H partially deficient non secretor phenotype and Para-Bombay phenotype are rare blood groups with deficiency or absence of H antigen. A 52-year-old female with Chronic suppurative otitis media was referred to our hospital. The primary serologic results of ABO blood typing were discrepant in forward and reverse grouping. Further, the saliva secretion tests, the pedigree studies and the sequence analysis were performed to confirm the rare phenotype. The patient was diagnosed as a variant H-deficient phenotype, secretor (para-bombay). Red cells of the patient have no H antigens, and it's a very interesting thing that there were two opposite results in the saliva test by using different anti-H. The test showed that H substances were present in the saliva by using anti-H from Libo Biotechnology Co, while which were absent by using anti-H from Shanghai blood center. The patient's Lewis phenotype was Le (a–b+). Anti-HI was present in the sera of her. The sequence of the ABO gene of the patient was 261delG and 467C>T heterozygote by direct DNA sequencing and was assigned as A102/O01. There were two mutations of the patient's FUT1, 328G/A and 658C/T, which were identified by DNA sequencing compared with the reference sequence (GenBank, NG_007510.2). In this case, we report a patient with particular H-deficient phenotype, secretor, which showed opposite results in the saliva test by using anti-H from different sources. We suspect that it is a variant of para-Bombay phenotype.

Keywords Red cell · Blood group · H-deficient phenotypes

The ABH antigens are important to ABO blood group system. The H antigen, which was encoded by the FUT1 and FUT2 genes is the precursor of the A and B antigens [1, 2]. The correct expression of FUT1 was reported to be responsible for the expression on erythrocyte membrane of H antigen, while FUT2 be responsible for the presentation in secretory tissue of H antigen.

H-deficient phenotypes are rare blood group systems, in which the red cells are partially or totally deficient in H antigen. H-deficient phenotypes could be divided into three kinds of subtypes. One is Red cell H-deficient, non-secretor, named Bombay phenotype; another is Red cell H-partially deficient, non-secretor; and the third is Red cell H-deficient, secretor, named to para-Bombay [3]. The Bombay and para-Bombay phenotypes were reported from various parts of the world [4–10], while there were few reports of the H partially deficient non-secretor phenotype existing in the population of European origin [11]. In this case, we reported a particular phenotype, which is different from all the three kinds of subtypes of H-deficient phenotype.

Case Report

A 52-year-old female who presented with intermittent suppurative otorrhea of left ear for forty years was received at our hospital. The case was diagnosed with Chronic suppurative otitis media and referred for surgery. The pre-operative routine examinations of ABH blood type revealed that the patient has especial ABH blood group

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which is similar to para-Bombay phenotype. Further, the saliva secretion tests, the pedigree studies and the sequence analysis were performed to confirm the rare phenotype.

Serological Results

ABH serology was performed with standard serological techniques. The patient's RBCs showed 1 + strength of the agglutination with monoclonal human anti-A, and showed no agglutination with monoclonal anti-A₁, anti-B and anti-H. The patient's Lewis phenotype was Le(a–b+). Her serum reacted strongly with A, B and O cells at room temperature, yet the agglutination with O cells disappeared at 37 °C (Table 1). The saliva test showed that A substances were present in the saliva, meanwhile the H substances were present by using anti-H from Libo Biotechnology Co while which were absent by using anti-H from Shanghai blood center (Table 1). The serological characteristics showed that the patient has particular H-deficient phenotype, which is similar to para-Bombay phenotype. The serum of the patient contained anti-HI, which cannot be inhibited by H substance and can agglutinate adult cells only (Table 1). The titer of the anti-HI was 16 at 4 °C. The patient's brother and son showed normal phenotypes for ABO and H group systems.

ABO and FUT1 Gene Analysis Results

The sequence of exon 6 and exon 7 at the ABO locus of the patient was 261delG and 467C>T heterozygote by direct DNA sequencing and was assigned as A102/O01 (Fig. 1). There were two mutations of the patient's FUT1, 328G/A and 658C/T (Fig. 2), which were identified by DNA sequencing compared with the reference sequence (GenBank, NG_007510.2). 328G/A and 658C/T alone were

Fig. 1 Results of partial sequencing of ABO gene for the patient. **a** Heterozygous peaks of the exon6 261delG. **b** Heterozygous peaks of the exon7 467C>T

common reported comparatively [12–16] of para-Bombay phenotype, however 328G/A and 658C/T together were reported rarely, the frequency is about 0.9% among para-Bombay in China [17].

Discussion

The ABH antigens could be expressed both on erythrocyte membranes and in secretions. The H antigen is the precursor of the A and B antigens which were determined by FUT1 (H) and FUT2 (Se) genes [18]. H-deficient phenotypes are rare blood group systems which are characterized by the partial or total deficiency of H, A and B blood group antigens on the red blood cells. And the blood group

Table 1 Serological characteristics of the patient

Reaction condition	Forward grouping				Reverse grouping				Absorption-elution test				Lewis		Blood group substance		
	Anti-A	Anti-B	Anti-A ₁	Anti-H	A _C	B _C	O _C (adult)	O _C (cord)	Anti-A	Anti-B	Anti-A ₁	Anti-H	Anti-Le ^a	Anti-Le ^b	A	B	H
RT	1+	0	0	0	3+	4+	2+	0	4+	0	0	0	0	2+	+	–	–/+
4 °C	2+	0	0	0	4+	4+	3+	0	NT	NT	NT	NT	NT	NT	NT	NT	NT
37 °C	±	0	0	0	2+	4+	0	0	NT	NT	NT	NT	NT	NT	NT	NT	NT

NT not tested

Auto control—negative

^aAntigen Lewis is negative

^bAntigen Lewis is positive

Fig. 2 Results of partial sequencing of FUT1 gene for the patient. **a** Heterozygous peaks of the FUT1 328G/A. **b** Heterozygous peaks of the FUT1 658C/T

substance may or may not be present in secretions of the individuals with H-deficient phenotypes.

In this report, the weak A antigens can be detected on the red cells, and not be agglutinated by monoclonal anti-A₁, the A blood group substance can be found in the saliva, at the same time the anti-A can be detected in her serum, while the H antigens were only found in the saliva, the Lewis phenotype was Le(a–b+). Moreover, the serum of her contained anti-HI. All the results above suggested that this variant belongs to the A subgroup combine para-Bombay phenotype. Surprisingly, though, the H antigens of the patient showed up variability in the saliva, the H substance of her could inhibit the anti-H from Libo Biotechnology Co, while the anti-H from Shanghai blood center could not be inhibited. So we suspect that it may be a variant of para-Bombay phenotype in this case, but cannot be proved deeply by us. And to the best of our knowledge, this especial phenotype was reported for the first time. More interestingly, there was no new mutation in this particular case of FUT1 gene which plays an important role in H-deficient phenotype [19]. Gene expression regulation maybe play an important role for the variants.

In this case, Transfusion compatibility test was performed as usual though the patient did not apply for pre-operative blood preparation. The antibody detection test was negatively performed with three reagent RBCs in a gel-card format at 37 °C. Meanwhile O group RBCs were

found to be compatible with the patient by the same method. However, is it safe for blood transfusion? The anti-HI, a kind of cold autoantibody which would not react with H and I antigens at 37 °C, will confound the immediate-spin cross-match. Anti-HI as the cause of hemolytic reaction had been reported previously [20–22]. As a consequence, cross-match test and antibody selection test are not the guarantee for the safety of blood transfusion. Accurate blood typing is most important for blood transfusions.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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