Clin. Lab. 2025;71:XXX-XXX

CASE REPORT

Identification of a Bm^{h} in a Chinese Individual

Qing Li [1, 2], Guojin Ou [1, 2]

[1] *Department of Laboratory Medicine, West China Second University Hospital, Sichuan University, Chengdu, China*
[2] *Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, China*

SUMMARY

Background: **The Bombay and para-Bombay blood groups are rare blood types that are significant to clinical blood transfusions. Accurate para-Bombay blood group identification is important for the safety of transfusions.**
Methods: **Serological and molecular biology methods were used to detect one case of ABO blood type. Genotypes of the para-Bombay blood group in the Chinese population were searched and summarized, and the safety of blood transfusion for this group was discussed.**
Results: **The ABO genotype of the case was B101/O01 and the *FUT1* gene haplotype was c.649T and 881_882 delTT, while the phenotypes were Bm^{h}, h2/h649, Le(a-b-), and Se^{357}/Se^{357,716}.**
Conclusions: **The h649/h2 *FUT1* genotype is newly discovered and is responsible for the para-Bombay blood group in the Chinese population. Accurate identification of this blood group using serology and molecular methods is significant to ensure the safety of blood transfusions.**
(Clin. Lab. 2025;71:xx-xx. DOI: 10.7754/Clin.Lab.2024.240744)

Correspondence:
Guojin Ou
No. 20, Section 3, South Renmin Road
Chengdu
China
Phone: +86 02888570938
Email: jiaozhu327@163.com

Case Report accepted August 5, 2024

KEYWORDS

Para-Bombay blood group, ABO gene, *FUT1* gene, secretory type, blood transfusion safety

INTRODUCTION

The Bombay blood group [1,2] has a complete lack of H-antigen expression in red blood cells and secretory fluid caused by *FUT1* and *FUT2* gene mutations, resulting in the silencing of protein expression from both genes. The para-Bombay type refers to a lack of H-antigen in red blood cells and secretory fluid caused by diminished FUT1 and FUT2 protein expression that is also caused by mutations in the *FUT1* and *FUT2* genes [1,2]. Weak A and/or B erythrocyte surface antigen phenotypes can be detected via absorption and release tests. Related para-Bombay blood groups have been found in different countries and regions [3]. Because this blood group is so rare, it is difficult to accurately detect using serotype identification methods for conventional blood groups, which makes clinical blood transfusions difficult to administer to patients of this blood group. Therefore, the timely and accurate identification of blood type and blood supply are particularly important when de-

livering emergency blood transfusions to critically ill patients with this phenotype.

CASE PRESENTATION

Clinical feature and serologic investigation

A 26-year-old woman who was 38 weeks pregnant, with no prior pregnancy or blood transfusion history, was admitted to the hospital to receive treatment for abnormal liver function. Once there, she underwent preoperative preparation for a Cesarean section procedure.

ABO and FUT blood group genotyping

Genomic DNA was extracted from the patient's blood sample using a blood DNA kit (Tiangen Biotech Co.) and sequenced between exons 1 - 7 of the *ABO*, *FUT1*, and *FUT2* genes using PCR-SBT, after serological testing [4].

RESULTS

Serological results

Microcolumn card (Grifol, Spanish) results were inconsistent with the positive and negative serotypes of Le (a-b-) (Table 1), and screening for irregular antibodies was positive. Serological and molecular biology tests were performed to confirm these results. Conventional ABO typing showed inconsistent positive and negative results. We therefore proceeded to analyze the patient's *ABO*, *FUT1*, and *FUT2* blood group genes.

Screening results for irregular antibodies at different temperatures are shown in Table 1. All antibody identification cells of the 16 groups in the antibody identification test were 2+, and no specific antibodies were detected. The Lewis phenotype of the patient was Le (a-b-), which proved that she was a secretory individual with small amounts of substances B and H in her saliva.

Molecular *ABO* and *FUT* blood group results

Gene sequencing results revealed that the patient's *ABO* genotype was B101/O01; her *FUT1* gene haplotypes were c.881_882delTT and 649T (Figure 1); and her *FUT2* gene haplotypes were c.357T, c.357T, and c.716A. To understand the molecular characteristics of the para-Bombay blood group in the Chinese population, we set keywords: "Chinese" and "para-Bombay" and/or "Bombay" and "Blood group". After analyzing, we included 33 English studies and summarized 25 para-Bombay genotypes and 29 alleles, which provided references for the identification of para-Bombay blood groups in Chinese population (Table 2).

DISCUSSION

The *FUT1* gene encodes a (1,2)-fucosyltransferase Type II antigen expressed on the surfaces of red blood cells (RBCs), and *FUT2* encodes a (1,2)-fucosyltransferase H Type I antigen that is secreted. The H antigen is the precursor substrate of the A and B antigens, and the *ABO* gene encodes glycosyltransferases that catalyze the H substrate to produce the A and B antigens. In 1994, Kelly et al. reported that the Bombay-like type was caused by mutations of the *FUT1* gene [2]. The Bombay phenotype is characterized by the absence of ABH blood group antigens both on the surfaces of RBCs and in the saliva, which results from silencing mutations in both the *FUT1* (h/h) and *FUT2* (se/se) genes. The para-Bombay phenotype results from a silenced *FUT1* gene (h/h) but an active *FUT2* (Se/Se or Se/se) gene, which is still capable of synthesizing the H Type I antigen (and, as a result, the A and B antigens as well) in secretions. These can then be adsorbed onto RBC surfaces from the plasma, or from a mutated *FUT1* gene, resulting in significantly lower enzymatic activity producing low levels of H Type II antigen (and A/B antigens) on RBC surfaces, which can only be detected using absorption and elution techniques. The rarity of the Bombay and para-Bombay phenotypes varies across different regions [5-7], and both hold substantial significance for clinical blood transfusion.

In this case, the patient's blood type was positively serotyped as B antigen weakened, anti-serotyped as B, and anti-H weakened. The possibility of the Bombay B class, rather than the B subtype, was considered. The B-type substance was detected in the patient's saliva, indicating that she had the secretory Bombay B subtype. Gene sequencing confirmed that the patient's *ABO* genotype was B101/O01 Her *FUT1* gene was sequenced as two haplotypes: h2 and G649T. The h2 (881_882-delTT) haplotype is a common Bombay-type characteristic mutation that causes a frameshift of amino acids at positions 294 - 332 and introduces a premature stop codon at position 333. The G649T variant has been previously reported in the Chinese population [8]. The ISBT allele is currently named *FUT1**01W.24, and it has also been discovered in our population (although not in the same genotype), indicating that this allele may actually be less rare than previously thought.

The Bombay blood group represents a rare blood group for which no clinical guidelines have yet been issued; therefore, it warrants further study before an appropriate solution can be formulated. Current blood transfusion recommendations for this blood group are as follows. First, blood transfusion departments should promptly report to their respective clinics when patients are found to have the para-Bombay blood type. They should then suggest collecting autologous blood before surgery. Recommendations should be adopted by clinics to ensure the smooth operation of this procedure. Second, conservative drug treatment is preferred for patients with chronic anemia who require blood transfusions. Third,

Table 1. Results of ABO serological and antibody screening tests of the sample at different temperatures.

	Tem-perature	Antibody screening			Forward				Saliva blood group substances and absorption and release test	Reverse				Results
		I	II	III	Anti-A	Anti-B	Anti-AB	Anti-H		Ac	Bc	Oc	Self-CL	
Blood group	25℃	+	+	+	0	w	w	0		3+	0	0	0	Bm^h
	37℃	0	0	0	/	/	/	/		/	/	/	/	/
	4℃	+	+	+	/	/	/	/		/	/	/	/	/
									saliva blood group substances	4+	0	3+	B	4+
									sample red blood cell + human standard plasma	0	2+	0	B	0
									sample plasma + standard red blood cell	3+	0	0	B	3+

Table 2. Summary of para-Bombay blood groups in the Chinese population.

No.	FUT1 gene variants	FUT1 amino acid substitution (allele)	FUT1 genotype	Year	References (PMID)
1	881_882delTT, 649G > T	FUT1*01N.13, Val217Phe	*h2/h649*	2024	This study
2	932G > A, 551_552delAG	Gly311Asp, FUT1*01N.06	*h1/h932*	2024	38899850
3	289G > A, 575G > C	Ala97Thr, Arg192Pro	*h289/h575*	2023	37458720
4	325_414dup, FUT1*01	Arg109_ Arg138dup, FUT1*01	*H/h325_414dup*	2023	37318046
5	902 A > G, homozygote	Asn301Ser, homozygote	*h902/h902*	2023	37318046
6	896A > C, 749-765del	FUT1*01W.28, FUT1*01N.33	*h896/h749-765del*	2022	34799859
7	649G > T, 768delC	FUT1*01W.24, FUT1*01N.20	*h649/h768delC*	2022	34967725
8	c.229C > T and 302C > T, 551_552delAG	FUT1*01W.39, FUT1*01N.06	*h1/h896*	2022	34792200, 25858679
9	424C > T, 35C > T and 803G > A	FUT1*01 W.23, Ala12Val and Cys268Tyr	*h9/h35,803*	2022	34693534
10	422G > T, 35C > T and 803G > T	FUT1*01N.01, Ala12Val and Cys268Tyr	*h422/h35,803*	2022	36169162
11	c.658C > T homozygote	FUT1*01W.09 homozygote	*h3/h3*	2021	34655188, 30217757, 23560544
12	361G > A, 881_882delTT	FUT1*01N.28, FUT1*01N.13	*h2/h361*	2021	34539321
13	508dupT, 787A > C	FUT1*01N.31, FUT1*01N.34	*h508dupT/h787*	2020	33175455
14	551_552delAG Homozygotes	FUT1*01N.06 homozygote	*h1/h1*	2019	30217757, 23560544, 30186784, 25761312
15	551_552delAG, 658C > T	FUT1*01N.06, FUT1*01W.09	*h1/h3*	2019	30217757, 3018678
16	551_552delAG, 814A > G	FUT1*01N.06, FUT1*01W.38	*h1/h814*	2019	30217757
17	755G > C, 755G > C and 551_552delAG	FUT1*01W.36, 755G > C and 551_552delAG	*h755/h1(755)*	2019	30217757

Table 2. Summary of para-Bombay blood groups in the Chinese population (continued).

No.	FUT1 gene variants	FUT1 amino acid substitution (allele)	FUT1 genotype	Year	References (PMID)
18	881_882delTT, homozygote	FUT1*01N.13, homozygote	*h2/h2*	2018	30186784
19	896T > C, 551_552delAG	FUT1*01W.28, FUT1*01N.06	*h1/h2*	2018	23560544, 30186784, 12366770
20	958insG and 961G > A homozygotes	FUT1*01N.35 with 958insG homozygotes	*h958insG,961*	2017	28026021
21	881_882delTT, 658C > T	FUT1*01N.13, FUT1*01W.09	*h2/h3*	2015	23560544, 25761312
22	551-552delAG, 522C > A	FUT1*01N.06, FUT1*01W.08	*h1/h6*	2015	25761312
23	35T, 35T+682G	FUT1*01.02, FUT1*01W.33	*h35/h35,682*	2011	21988368
24	551-552delAG, 293C > T	FUT1*01N.06, FUT1*01W.01	*h1/h293*	2005	15847661
25	881-882delTT, 522C > A	FUT1*01N.13 FUT1*01W.08	*h2/h6*	2002	12366770

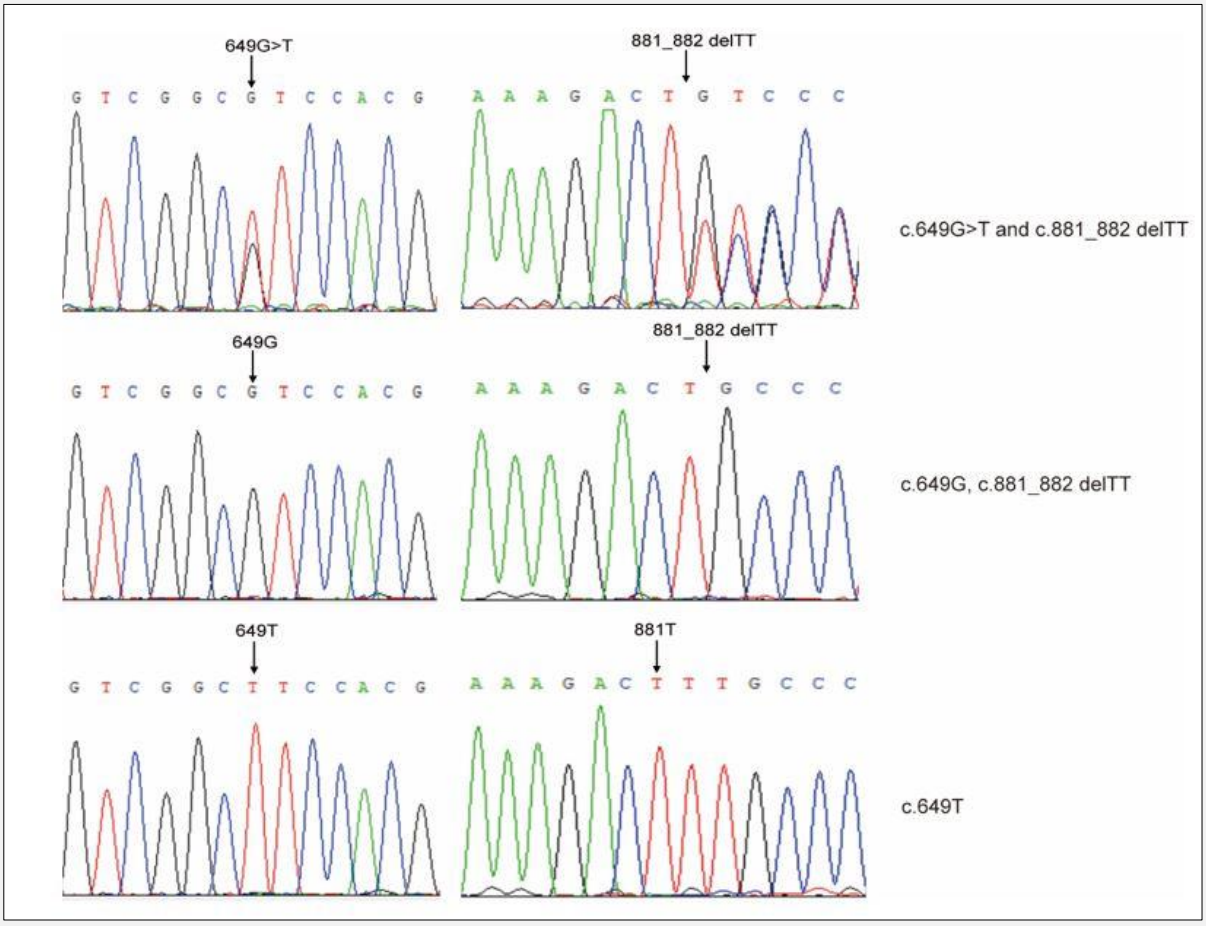

Figure 1. The sequences of FUT1 gene of the case.

when blood transfusion is necessary, there are two types of blood transfusion strategies: identical and compatible. Identical transfusion requires that the ABO and H phenotypes of the donor and recipient blood match, which is the safest transfusion strategy. Blood centers should establish rare blood-type donor blood banks and prepare frozen RBCs for emergency transfusions. Compatible infusion refers to the screening of blood suitable for transfusion under strict and robust laboratory conditions. Such transfusions of donors and recipients of ABO and H phenotypes must carry no possibilities of adverse transfusion reactions. This compatible method should be the main method used for blood group identification in special cases where patients with the para-Bombay blood type urgently require blood transfusions.

CONCLUSION

Overall, clinicians should first seek out homologous donor blood among the patient's immediate family members, then contact blood centers to find homologous donor blood, before finally screening for compatible blood types. Strict transfusion plans should be formulated before transfusions are needed, to avoid late treatment or death because of a lack of suitable donor blood to transfuse.

Declaration of Interest:
The authors have disclosed no conflicts of interest.

References:

1. Kaneko M, Nishihara S, Shinya N, et al. Wide variety of point mutations in the H gene of Bombay and para-Bombay individuals that inactivate H enzyme. Blood 1997 Jul 15;90(2):839-49. (PMID: 9226185)

2. Kelly RJ, Ernst LK, Larsen RD, Bryant JG, Robinson JS, Lowe JB. Molecular basis for H blood group deficiency in Bombay (Oh) and para-Bombay individuals. Proc Natl Acad Sci USA 1994;91(13):5843-7. (PMID: 7912436)

3. Soejima M, Koda Y. FUT1 variants responsible for Bombay or para-Bombay phenotypes in a database. Sci Rep 2023;13(1): 17447. (PMID: 37838738)

4. Liang W, Cai F, Yang L, Zhang Z, Wang Z. Four Non-functional FUT1 Alleles Were Identified in Seven Chinese Individuals with Para-Bombay Phenotypes. Iran J Public Health 2018;47(8):1128-36. (PMID: 30186784)

5. Luo G, Wei L, Wang Z, et al. The summary of FUT1 and FUT2 genotyping analysis in Chinese para-Bombay individuals including additional nine probands from Guangzhou in China. Transfusion 2013;53(12):3224-9. (PMID: 23560544)

6. Chen DP, Tseng CP, Wang WT, et al. Two prevalent h alleles in para-Bombay haplotypes among 250,000 Taiwanese. Ann Clin Lab Sci 2004;34(3):314-8. (PMID: 15487706)

7. Lin-Chu M, Broadberry RE. Blood transfusion in the para-Bombay phenotype. Br J Haematol 1990;75(4):568-72. (PMID: 2207009)

8. Sun X, Cai Y, Ni H, et al. Analysis of the molecular mechanism and pedigree investigation of para-Bombay phenotype caused by combined mutations at position h(649) and h(768) of FUT1 gene. Blood Transfus 2022;20(5):414-9. (PMID: 34967725)