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LETTER TO THE EDITOR

Identification of a Case with Heterozygous Mutations in the *FUT1* Gene Leading to a Para-Bombay Phenotype

Chih-Lung Lin [1, 2] and Tze-Kiong Er [3, 4, 5]

[1] *Department of Neurosurgery, Asia University Hospital, Asia University, Taichung, Taiwan*
[2] *Department of Occupational Therapy, Asia University Hospital, Asia University, Taichung, Taiwan*
[3] *Division of Laboratory Medicine, Asia University Hospital, Asia University, Taichung, Taiwan*
[4] *Department of Health and Nutrition Biotechnology, Asia University, Taichung, Taiwan*
[5] *Department of Medical Laboratory Science and Biotechnology, Asia University, Taichung, Taiwan*

SUMMARY

Background: **A case of a para-Bombay phenotype caused by a compound heterozygous mutation in the *FUT1* gene was identified in this study.**
Methods: **We performed an agglutination examination of anti-H serum and secretor status to assess the presence of soluble blood group substances. Genotyping of *ABO* and *FUT1* genes was also performed.**
Results: **Our results showed the presence of A and H antigens in saliva. Based on these results, the patient in the present case was diagnosed with the para-Bombay A phenotype. Direct DNA sequencing of the *ABO* gene indicated A^{1v}/O^{1v}genotype. *FUT1* gene sequence analysis revealed that the patient harbored the compound heterozygous mutation, c.881_882delTT (p.Phe294Cysfs*40) and c.658C>T (p.Arg220Cys).**
Conclusions: **Improper identification of this phenotype may cause inappropriate transfusions because this particular blood group may be mislabeled as group O. Therefore, blood bank staff should be well trained to solve the discrepancy between cell and serum grouping in the para-Bombay phenotype.**
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Correspondence:
Tze-Kiong Er, PhD
Department of Medical Laboratory Science and Biotechnology
Asia University Hospital
222, Fuxin Rd.
Wufeng Dist., Taichung City 413
Taiwan
Phone: +886 4-37061668 ext 1297
Email: tzekiong92@gmail.com
ORCID ID: https://orcid.org/0000-0002-7068-1652

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A 70-year-old female patient presented at the hospital with spondylolisthesis. An MRI scan revealed degeneration of the intervertebral disc, narrowing of the intervertebral disc space at L2/3/4/5/S1 and mild scoliosis of the spine. Examination of the patient revealed hemoglobin levels of 9.2 g/dL, RBC counts of 2.93 x 10^6/μL, WBC counts of 10.9 x 10^3/μL, and platelet counts of 155 x 10^3/μL. The plasma levels of BUN and creatinine were all within the normal range, except for potassium and chloride, which were slightly lower than the normal range. A blood sample obtained from the patient was submitted to our division for blood typing and cross-matching, with a request to receive 2 units of leukocyte-

Table 1. Serologic and saliva test results of the patient.

Cell grouping			Serum grouping			Test for H antigen	Saliva secretor status	
Anti-A	Anti-B	Anti-D	A_1 cells	B cells	O cells	Anti-H	A_1 cells	B cells
0	0	4+	0	3+	0	0	0	2+

0 = no agglutination, 1+ = multiple small agglutinates with cloudy supernatant, 2+ = multiple large agglutinates with clear supernatant, 3+ = 2 - 3 large agglutinates with clear supernatant, 4+ = single large agglutinates.

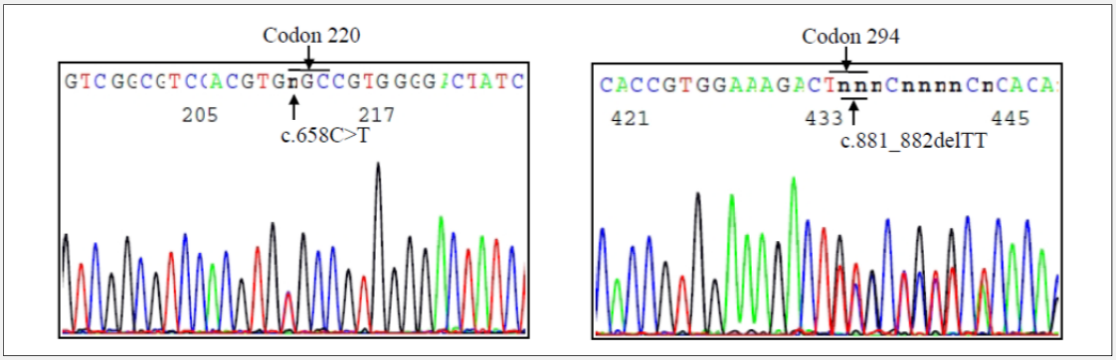

Figure 1. Direct sequencing revealed compound heterozygous type in the *FUT 1* gene (A) c.658C>T (B) c.881_882delTT.

poor packed red blood cells. ABO typing was performed using standard serological techniques after an immediate spin.

Testing the patient's red blood cells revealed no detectable ABO antigens on forward/cell grouping (group O blood type). In addition, reverse/serum grouping showed the presence of A antibodies in serum (group B blood type). To resolve the discrepancy between cell and serum grouping, we performed an agglutination examination of anti-H serum, and the red blood cells from the sample did not exhibit an agglutination reaction. Additionally, secretor status was determined in order to assess the presence of soluble blood group substances. Our results showed the presence of A and H antigens in the saliva. Based on these results, the patient in the present case was diagnosed with a para-Bombay A phenotype (Table 1).

Genotyping of *ABO* and *FUT1* genes was also performed. Direct DNA sequencing of the patient *ABO* gene indicated the A^{1v}/O^1 genotype. To examine potential mutations in the *FUT1* gene, we amplified and sequenced the full coding region of the gene. *FUT1* gene sequence analysis revealed that the patient harbored the compound heterozygous mutation, c.881_882delTT (p.Phe 294Cysfs*40) and c.658C>T, p.Arg220Cys) (Figure 1). The incidence of the para-Bombay phenotype was estimated to be 1 in 800 residents in Taiwan based on serological analysis [1]. Intriguingly, we have identified three cases of a para-Bombay phenotype in the Wufeng area, Taichung City in the past 2.5 years [2,3]. Awareness of the para-Bombay phenotype appears to be particularly important in our area. Although, a heterozygous mutation in *FUT1*, c.658C>T, has been identified in the Taiwanese population, c.881_882delTT and c.574AGdel account for the 85% of the para-Bombay individuals in the Taiwanese population [4]. In addition, two studies have reported heterozygous mutations in *FUT1*, c.658C>T, in Shanghai, Liaoning, and Zhejiang [5-7]. These studies showed a distinct geography between the different ethnic groups.

CONCLUSION

In summary, anti-H should be used routinely for blood grouping in our blood bank. Improper identification of this phenotype may cause inappropriate transfusions because this particular blood group may be mislabeled as group O. Therefore, blood bank staff should be well trained to solve the discrepancy between cell and serum grouping in the para-Bombay phenotype.

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Declaration of Interest:
There are no conflicts of interest associated with this paper.

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