Background

Individuals with Bombay phenotype (H-deficient, non-secretor) are characterized by the absence of ABH blood group antigens both on the surface of red blood cells (RBCs) and in secretions resulting from silenced mutations in FUT1 (h/h) and FUT2 (se/se) genes, respectively. In contrast, para-Bombay phenotype retains some H antigen on RBCs either induced from a weakly active (H+weak/H+weak; H-deficient, non-secretor) or completely silenced FUT1 gene (h/h; H-deficient, secretor). The latter is mandatory linked with an active FUT2 gene (Se/Se or Se/se) enabling synthesis of ABH-antigens in secretions which may be adsorbed from the plasma onto RBCs surface (1, 2). The anti-H in para-Bombay individuals is usually weak and often does not react above room temperature.

Aims

A 61 year old Thai female with metastatic pancreatic cancer was hospitalized due to clinical deterioration with radiologically confirmed progression under palliative chemotherapy. A blood was transfused uneventfully and short-term stabilization was achieved. Due to the malignant primary disease her general condition further deteriorated and she died shortly thereafter under end-of-life care. In conclusion, we support the option to transfuse para-Bombay individuals with normal ABO blood group units, compatible by IAGT, when Bombay or para-Bombay blood in an emergency situation one can get.

Methods

Standard serologic techniques were used to detect ABH and Lewis (Le) antigens on RBCs (BioRad, Cressier, Switzerland; Biotest AG, Rupperswil, Switzerland). In addition, a very potent anti-A/B serum (Medion Grifols Diagnostics, Duedingen, Switzerland) was used to reveal traces of A and B antigens. Compatibility testing was performed using the indirect antiglobulin test (IAGT) at 37°C. Molecular ABO type was defined using a commercially available test kit (inno-train GmbH, Kronberg I.T., Germany). Sequencing was performed for coding exons of FUT1, FUT2 and FUT3 genes.

Results

The routine anti-A, -B and -A/B failed to detect the respective antigens and, most notably, no H-antigen was traceable. The RBCs showed only weak agglutination with the potent anti-A/B serum (Grifols). Only anti-H, but no anti-A or anti-B, was identified in the serum. Initial ABO genotyping by sequence-specific priming (PCR-SSP) resulted in AB genotype. In order to confirm serological H-deficient phenotype a more detailed analysis was performed including sequencing of FUT1 and FUT2 which revealed an active secretor status (Se/Se) but homozygosity for the FUT1*01W.09 allele (c.658C>T, p.Arg220Cys). Latter is common in Taiwanese population and allows only weak expression of ABH-antigen on RBCs (3), consistent with our observations. In the interests of completeness serological Le(a-b-) phenotype was confirmed by FUT3 sequencing (FUT3*le(59G) FUT3*le(59G, 508A)).

<table>
<thead>
<tr>
<th>Haemagglutination</th>
<th>Genotype</th>
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<tbody>
<tr>
<td>Anti-A*</td>
<td>Anti-B*</td>
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<tr>
<td>Thai patient</td>
<td>-</td>
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<tr>
<td>AB</td>
<td>FUT1</td>
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Table 1: Serological and molecular results of the para-Bombay patient.

Summary

In summary, our serological tests were in line with the characteristics of para-Bombay phenotype and confirmed by identification of the homozygous weakening mutation c.658C>T in the FUT1 gene. However, if low level of ABH-antigens on erythrocytes is determined by partially active FUT1 or normal secretor status is a matter of debate. Shortly after final diagnostics our patient developed acute gastrointestinal bleeding, requiring transfusion (Hb 53 g/l), fluid resuscitation and anticoagulation cessation. As we have no access to Bombay or para-Bombay blood in an emergency situation one A1B whole blood unit with negative cross-match was transfused uneventfully and short-term stabilization was achieved. Due to the malignant primary disease her general condition further deteriorated and she died shortly thereafter under end-of-life care. In conclusion, we support the option to transfuse para-Bombay individuals with normal ABO blood group units, compatible by IAGT, when Bombay or para-Bombay blood is not available (4).

References

(1) Storry et al., 2006
(2) Luo et al., 2013
(3) Yu et al., 1997
(4) Lin-Chu et al., 1990