Title:
Post-transfusion hyperhemolysis syndrome following gastrointestinal bleeding secondary to prehepatic portal hypertension

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Post-transfusion hyperhemolysis syndrome following gastrointestinal bleeding secondary to prehepatic portal hypertension

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Dear Editor,

Hyperhemolysis syndrome (HHS) is a rare, life-threatening complication and early identification is key to improve prognosis (1).

Case report
A 30-year-old woman with portal cavernomatosis secondary to postnatal omphalitis and two bypass surgical procedures during childhood experienced multiple bleeding events from gastroesophageal varices. These required multiple transfusions and the antibody analysis was consistently irregular. At age 28, progressive thrombosis was identified in the inferior vena cava and other areas which responded to hypo-coagulation therapy. Eleven days before admission, the patient presented with self-limiting “sentinel” bleeding which required three red blood cells concentrates (RBCCs). The origin could not be identified due to the diagnostic limitations as the patient was pregnant. Following a curettage procedure due to a miscarriage, the patient was admitted due to a new bleeding event secondary to aberrant collateral circulation
(duodenal pericholecystic varices on computed tomography and magnetic resonance imaging [CT/MRI], resulting in intermittent hemobilia). Five RBCCs were transfused with an almost null response. During admission, the patient had persistent severe anemia without re-bleeding, combined with fever, reticulocytopenia, hemolysis and a negative direct Coombs test. The patient started therapy with corticosteroids and immunoglobulin. She was discharged after two weeks on a descending regimen of oral corticosteroids (Table 1) and required no further transfusions.

Discussion
HHS develops with no hematologic underlying disease in exceptional cases (2,3). It manifests with paradoxical post-transfusion decreased hematocrit (lysis of both transfused and host red blood cells), reticulocytopenia (rather than the expected reactive reticulocytosis), fever and evidence of intravascular hemolysis. Direct antiglobulin is negative in acute forms. Basic treatment includes steroids and immunoglobulin (3). Subsequent transfusions are both dangerous and ineffective, and therefore are initially contraindicated and should only be used in life threatening situations (4). Early clinical identification allowed this patient to receive specific therapy. Transfusions were discontinued and post-bleeding anemia (5) was managed according to laboratory parameters.

References
1. Aragona E, Kelly MJ. Hyperhemolysis in sickle cell disease. J Pediatr Hematol Oncol 2014;36:54-6. DOI: 10.1097/MPH.0b013e31828e529f
Table 1. Time course of laboratory parameters according to treatment

<table>
<thead>
<tr>
<th>Day</th>
<th>0°</th>
<th>1°</th>
<th>2°</th>
<th>3°</th>
<th>5°</th>
<th>7</th>
<th>9</th>
<th>14°</th>
<th>32°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/l)</td>
<td>60</td>
<td>74</td>
<td>72</td>
<td>63</td>
<td>57</td>
<td>72</td>
<td>77</td>
<td>88</td>
<td>103</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>19</td>
<td>21</td>
<td>22</td>
<td>19</td>
<td>18</td>
<td>23</td>
<td>26</td>
<td>29</td>
<td>38</td>
</tr>
<tr>
<td>Reticulocytes (x 10⁹/l)</td>
<td>357</td>
<td>705</td>
<td>157</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total bilirubin (BR) (mg/dl)</td>
<td>4.1</td>
<td>1.9</td>
<td>3.5</td>
<td>1.3</td>
<td>0.6</td>
<td>0.5</td>
<td>0.4</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Indirect BR (mg/dl)</td>
<td>3.3</td>
<td>1.1</td>
<td>2.5</td>
<td>0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>LDH (IU/l)</td>
<td>1,824</td>
<td>951</td>
<td>2,178</td>
<td>1,444</td>
<td>1,131</td>
<td>548</td>
<td>328</td>
<td></td>
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<tr>
<td>Haptoglobin (mg/dl)</td>
<td>0</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Ferritin (µg/l)</td>
<td>604</td>
<td>137</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Pre-transfusion. #Post-transfusion, after five RBC concentrates. ¶Onset of IV methylprednisolone 1 mg/kg/12 hrs. φOnset of IV immunoglobulin 1 g/kg/24 hrs (five
days). Onset of IV iron sucrose (200 mg/48 hrs) and erythropoietin (EPO) 30,000 IU weekly. Hospital discharge on PO prednisone 60-0-30 mg, with descending dosage.

At 30 days after steroid therapy onset.