TRAUMATIC HEMOLYTIC ANEMIAS: CASE REPORT AND REVIEW OF THE LITERATURE

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SUMMARY – Two patients with intravascular hemolysis are presented. One patient had traumatic hemolytic anemia after mechanical heart valve reimplantation, and the diagnosis was made rapidly and easily. In the other patient, the diagnosis was not so easy complex and time-consuming. This patient had both traumatic hemolytic anemia caused by orthopedic prosthesis, and neutropenia. Fragmentation was caused by interaction of red blood cells with altered intravascular surfaces or by direct physical trauma to the cells due to excessive shear forces in the circulation. The following findings are seen in intravascular hemolysis: decreased hemoglobin, increased reticulocytes and lactic dehydrogenase, decreased serum haptoglobin, and presence of shizocytes in peripheral blood smear. Patients are considered to have intravascular hemolysis when lactic dehydrogenase is >460, along with the presence of two established criteria. If not causal, therapy is supportive.

Key words: Anemia, hemolytic – etiology; Heart valve prosthesis, complications; Orthopedics, complications; Prosthesis, complications; Neutropenia, complications; Case reports

Introduction

Mild anemia is frequently found in individuals exposed to strenuous and sustained physical activity. The first clue to the pathogenesis of this anemia was provided in 1881 by R. Fleischer, an army physician, who studied a young Prussian soldier complaining of passing dark urine following strenuous field marches1. In 1964, Davidson provided a logical explanation for this phenomenon. He proposed that red cells were destroyed in the soles of the feet during running, and the runners were encouraged to change the stride and especially to wear soft linings in their shoes, whereafter hemoglobinuria disappeared2. The individuals involved in strenuous and sustained physical activity are frequently found to be mildly anemic3. The cause of this anemia is complex but appears to involve traumatic hemolysis with hemoglobinuria, iron loss in urine and sweat, dilution of the red cell mass by an increase in plasma volume, and possibly adaptation to the right-shifted oxygen dissociation curve4. Disturbances in the formed blood cells due to intravascular trauma are shown in Table 1.

We report on our two patients with hemolytic anemias, to refresh the concept of hemolysis in the differential diagnosis of anemias.

Case Reports

Case No. 1

A 53-year-old man, who had often suffered sore throat in childhood, was first told to have heart murmur at the age of 29. At the age of 34, he was hospitalized at a cardiology ward of our Department, when the diagnosis of major aortic valve dysfunction (stenosis and regurgitation) was established. An operation was proposed and he had a Björk-Shiley valve implanted in the same year. In the next year, systolic-diastolic murmur was detected by a cardiologist, and the patient underwent frequent controls. At the age of 47, a second operation was performed, because his end-diastolic diameter of the left ventricle was...
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Acta clin Croat, Vol. 41, No. 1, 2002

75 mm and aortic regurgitation 3+. A Carbomedics valve A-23 was implanted. Then, significant postoperative anemia developed. Ultrasonography of the heart showed minor dilatation of the left ventricle, end-diastolic diameter was 60 mm, and systolic gradient through the aortic valve was 5.3-6.6 kPa. Evaluation of this anemia was done at our Department of Hematology, where he was hospitalized. Ultrasonography showed no biliary tract calculi. Control ultrasonography of the heart, performed late in 1998, showed similar findings as after the second operation. Laboratory findings obtained in 1993 and on the last control in 1998 are shown in Table 2.

Table 2. Case No. 1: laboratory findings obtained in 1993 and on the last control in 1998

<table>
<thead>
<tr>
<th>Laboratory parameter</th>
<th>1993</th>
<th>1998</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes (x10^12/L)</td>
<td>3.01</td>
<td>3.57</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>91</td>
<td>83</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>87.1</td>
<td>69.2</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>30.2</td>
<td>23.2</td>
</tr>
<tr>
<td>MCHC (g/L)</td>
<td>347</td>
<td>336</td>
</tr>
<tr>
<td>Leukocytes (x10^9/L)</td>
<td>5.3</td>
<td>4.4</td>
</tr>
<tr>
<td>Platelets (x10^9/L)</td>
<td>407</td>
<td>138</td>
</tr>
<tr>
<td>Reticulocytes (%)</td>
<td>97</td>
<td>38</td>
</tr>
<tr>
<td>Bilirubin (mmol/L)</td>
<td>32.4</td>
<td>31.0</td>
</tr>
<tr>
<td>LDH (U/L)</td>
<td>3580</td>
<td>2440</td>
</tr>
</tbody>
</table>

Discussion

In case No. 1, the diagnosis was quickly and easily reached after transfusion incompatibility had been ruled as follows: L 5.9x10^9/L (immature 1%, segmented 15%, Ly 81%; Eo 1%; Mo 2%); E 4.1x10^12/L; Hb 128 g/L; MCV 90.5 fL; MCH 30.7 pg; MCHC 339 g/L; Pt 188x10^9/L; ESR 2; ferritin 128 (normal); Rtc 15%; bilirubin 15.0 mmol/L; LDH 237 U/L; total protein 74.5 g/L (albumin 59.9%, alfa 1 2.7%, alfa 2 2.5%, beta 10.6%, gamma 22.1%). Haptoglobin and free hemoglobin were normal. The patient’s history revealed he had lost both lower legs accidentally in childhood. Therefore he had orthopedic prostheses implanted. Then, other tests were performed. Micro IF antibodies for platelets and leukocytes were positive; IgG 3440 (normal 760-3260); IgM 3630 (normal 400-1620); hepatitis markers were negative; osmotic resistance was normal. Peripheral blood smear and bone marrow aspirate showed partly macroblastic and rich erythropoiesis and immature lymphocytes. Biliary tract ultrasonography showed no biliary calculi. Hemoccult done on three occasions was negative, and transferrin was normal. In 1993, the patient had low leukocyte count (2.8x10^9/L) for the first time, and he felt tired. In 1997, his haptoglobin was low, 420 (normal 790-2850), also for the first time. The patient had regular controls, and the last one, performed in 1998, yielded the following laboratory findings: E 3.22x10^12/L; Hb 103 g/L; MCV 93.6 fL; MCH 32.0 pg; MCHC 324 g/L; Pt 151x10^9/L; ESR 18; Rtc 19%; L 3.4x10^9/L (Gr 24%, Ly 72%, Mo 4%); LDH 492 U/L; bilirubin 25.6 mmol/L; the patient felt well.

Case No. 2

A 38-year-old man had initially visited a hematologist at the age of 29 for mild anemia. Laboratory findings were

Table 1. Blood cell disturbances due to intravascular trauma

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Fragments</th>
<th>Hemolysis</th>
<th>Thrombocytopenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>March hemoglobinuria</td>
<td>0</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Cardiogenic</td>
<td>+ to ++++</td>
<td>+/- to ++++</td>
<td>0</td>
</tr>
<tr>
<td>Blood vessel diseases(^a)</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TTP</td>
<td>++++</td>
<td>+++</td>
<td>++++</td>
</tr>
<tr>
<td>HUS</td>
<td>++++</td>
<td>+++</td>
<td>++++</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>++++</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Disseminated intravascular coagulation</td>
<td>++</td>
<td>+/-</td>
<td>++++</td>
</tr>
</tbody>
</table>

\(^a\)malignant hypertension, eclampsia, renal transplant rejection, hemangioma, immunologic diseases (scleroderma)

\(^b\)The table has been adapted from Harrison’s Principles of Internal Medicine, 11th Edition, 1987
out, because hemolytic anemia developed during the im-
mmediate postoperative course. In case No. 2, however, the
diagnosis was neither quick nor easy to reach. We believe
that his hemolytic anemia was caused by orthopedic pro-
theses that were functionally better but seemed to have
induced intravascular hemolysis. These orthopedic prosthe-
ses are unique for each individual patient. In aqueous sus-
pension, the red cell membrane can withstand shear pro-
ducing stress of up to 1.5 kPa. In patients with valvular
hemolysis, it is mild and rarely causes overt hemolytic ane-
mia, except for those with severe aortic or subaortic steno-
sis generating a pressure gradient across the valve of 6.3 kPa
or more. All prosthetic cardiac valves have an orifice size
smaller than the natural valve, and after implantation this
orifice is further reduced by tissue ingrowth and endothe-

alization. According to the literature, about 50% of pa-
tients with mechanical heart valve have intravascular
hemolysis, mostly mild, however, clinically significant in-
travascular hemolysis develops with thrombosis of the valve,
perivalvular leak, or fracture of the valve. Currently, hemo-
lytic anemia is considered a minor complication in reviews
of large series of patients after implantation of the mechani-

cal heart valve. Since the first description of march hemo-
globinuria, many additional cases of hemoglobinuria fol-

lowing long-distance running have been reported. Even
with well-designed padded insoles, there is still some trau-

amatic disruption of red cells by pressure on the soles dur-
ing running and walking. Similar traumatic red cell de-
struction with hemoglobinuria has been reported after
beating the head against the wall, hand-strengthening exer-
cises in a subject practicing karate, and in those play-
ning conga drums. We found no reports connecting ortho-

pedic prosthesis and intravascular hemolysis. Unfortunately,
there are many patients with lower-leg orthopedic prosth-

eses in Croatia, who sustained severe lower leg injuries
during the war in Croatia. In our case No. 2, his anemia was
in part considered functional pseudoanemia, although his
plasma volume was not determined. The gain in plasma
volume always exceeds the gain in red cell mass. A rea-
sonable comment is that we never found hemoglobinuria,
h owever, it is not obligatory for the diagnosis. Tests for
paroxysmal nocturnal hemoglobinuria (sucrose lysis test)
and paroxysmal cold hemoglobinuria (Donath–Landstine-
test) should be performed if any question arises. In case No.
2, neutropenia, possibly autoimmune, was also present,
however, it has been proven difficult to unequivocally dis-
tinguish cases of autoimmune neutropenia from cases of
chronic idiopathic neutropenia. Patients diagnosed as
having autoimmune neutropenia usually have selective
neutropenia and one or more positive tests for antineutro-
phil antibodies. Patients are considered to have intravascular
hemolysis when lactic dehydrogenase is >460, along with
the presence of two established criteria. Therapy for intra-

vascular hemolysis consists of vitamins (B12 and folic acid),
supplementation of iron according to ferritin level, eryth-
ropoietin and transfusion of washed red cells. A transfusion
of washed red cells was necessary in our patient No. 1, how-
however, on administering transfusion therapy one should al-
ways measure serum ferritin level to avoid hemosiderosis.

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er left-sided cardiac valve replacement with Medtronic Hall and
St. Jude medical prostheses, and influence of prosthetic type, po-


Sažetak

TRAUMATSKE HEMOLITIČNE ANEMIJE: DVA PRIKAZA SLUČAJA I PREGLED LITERATURE

F. Grubišić-Čabo i V. Stanić


Ključne riječi: Anemija, hemolitična – etiologija; Protetiki srčani zalistak, komplikacije; Ortopedija, komplikacije; Proteza, komplikacije; Neutropenija, komplikacije; Prikazi slučajeva