Cardiac Hemolysis and Anemia Refractory to Erythropoietin: On Anemia in Dialysis Patients

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Dear Sir,
A 74-year old priest was on regular hemodialysis treatment since 12/1989 due to end-stage renal disease of unknown origin. Because of an aortic stenosis with mitral insufficiency an aortic- and mitral-valve replacement with 2 Hancock bioprostheses was performed in 1/1990. Since then he did not reach hematocrit values above 30% despite 3 × 6,000 IU recombinant human erythropoietin (rHu-Epo 3 × 100 IU/kg) intravenously per week. He required 2 red cell transfusions every 6 weeks due to a slowly decreasing hematocrit with fatigue and weakness at 23%. In 10/93 anemia was normocytic (MCV 95 µl, MCH or HbE 32 pg, MCHC 33 g/l) with 2.8% reticulocytes, white cells were 8,200/ml and platelets 200,000/ml. Urea was 222 mg/dl, creatinine 12.9 mg/dl, bilirubin < 1 mg/dl, lactic dehydrogenase ranged between 200 and 240 U/l; serum iron was 54 µg/dl, transferrin 217 mg/dl, ferritin 215 ng/ml; parathyroid hormone 5.6 pg/ml and aluminium 33 ng/ml were normal. After a trial with iron 100 mg intravenously at each of 10 hemodialyses the persisting anemia was evaluated again: a slight reticulocytosis of 4.1% and mildly elevated lactic dehydrogenase of 252 U/l were found, and a hemolytic anemia was suspected which was confirmed by a depressed hapto-globin < 10 (normal 50–320) mg/dl. The patient had no splenomegaly and no drugs causing hemolytic anemia; Coombs’ test was negative. He had no indwelling catheter but a looped femoral sapheous polytetraflu-ethylene graft. Although fragmentocytes were not detected in the peripheral blood smear an association of hemolysis with a leak at the aortic prosthesis was most likely.

This is, to our knowledge, the first report of a dialysis patient with anemia refractory to rHu-Epo due to cardiac hemolysis. An association between traumatic hemolysis and artificial cardiac valve prostheses, especially if there is a leak, is well known [1]. The case may be of interest for clinicians dealing with dialysis patients as there is an increasing number of dialysis patients with cardiac valve replacement and hemolysis should be kept in mind as another possible cause of anemia refractory to Epo. Furthermore this report illustrates a step-by-step approach to anemia in dialysis patients (table 1):

Avoid blood loss and fill up iron stores. Although iron apparently was of no use in this patient, 10–20 × 100 mg iron intravenously may help to increase hematocrit in many other patients without Epo or without increasing its dosage. We prefer parenteral administration and try to achieve ferritin levels of 300 (100–500) ng/ml. However, iron overload should be avoided because patients may be more susceptible to infections at ferritin levels above 1,000 ng/ml [2].
If there is no response to iron and to Epo therapy treat common problems [3] such as severe hyperparathyroidism or aluminium overload and, if clinically indicated, give red cell transfusions during infections or postoperatively.

If there is no one of these problems, as in our case, anemia should be studied by reticulocyte count, red cell indices and peripheral blood smear as in any case of unexplained anemia. Additional laboratory tests should be considered after history and examination, e.g. haptoglobin for hemolysis, or hemoglobin electrophoresis for thalassemia [4]. Screening dialysis patients for folate and vitamin B12 levels is not rational [5] unless there is a macrocytic anemia.

A microscopic examination of the bone marrow is not useful in hemolytic anemia. However, in a case of unexplained anemia due to decreased production it may be diagnostic for sideroblastic anemia or plasma cell infiltration and can be informative about iron status.

Table 1. Approach to anemia unresponsive to Epo

Avoid blood loss and fill up iron stores
Treat other common problems
Infection
Aluminium overload
Hyperparathyroidism
Postoperative state
Classical anemia workup
Bone marrow examination

References