Cardiac surgery and paroxysmal noctural hemoglobinuria

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Dear Sir,

We read with interest the report by Knobloch et al.[1] on the feasibility of cardiac surgery in a patient with paroxysmal nocturnal hemoglobinuria (PNH). Given the lack of literature in this area we would like to report on another patient with PNH who underwent coronary artery bypass grafting without perioperative complications.

Case summary. A 62-year old woman presented in October 2001 with angina pectoris and angiography revealed a grade two left ventricle and triple vessel coronary artery disease for which bypass grafting was recommended. She was diagnosed a year earlier as having PNH when presenting with severe intravascular hemolytic anemia, hemosiderinuria and a negative direct Coombs' test but no neutropenia or thrombocytopenia. At that time bone marrow examination showed erythroid hyperplasia, and decreased iron stores with normal cytogenetic analysis. Flow cytometry on peripheral blood for dual expression of CD55 and CD59 on granulocytes and red cells showed type I cells (both populations showing normal expression), and a second population of type II cells (CD59 expressing) represented 50% of red cells, 75% granulocytes. A small percentage was negative for both (type III cells). Management following diagnosis consisted of supportive packed red cell transfusions (11 units of Packed RBCs in the five months prior to surgery) and pulses of corticosteroids during hemolytic flareups, and low dose (81 mg) aspirin. Preoperative admission hemoglobin was 90 g/L, WBC 3.7x10^9/L, total bilirubin 61 μmol/L, LDH 2080 U/L, normal aPTT, INR/PT. She was given three units of packed RBCs and taken for triple coronary artery bypass grafting. The procedure was carried out with standard general anesthesia (pancuronium/rocuronium, propofol, sufenta) through a median sternotomy. Cardiopulmonary bypassing using a standard heparin protocol with protamine reversal was used (extracorporeal circulation discontinued after 80 minutes). Intraoperatively crystalloids but no red cells or inotropes were given (estimated blood loss ~ 705 mL). At the end of the procedure, the hemoglobin was 64 g/L and 3 units of packed RBCs were given in the recovery room. Postoperatively, unfractionated heparin 2,000 u IV q.4.h.x48 hours followed by enoxaparin 40 u s/c daily until discharge was given. In addition intermittent pneumatic compression of both lower limbs was maintained until the patient was ambulatory. Aspirin 325 mg OD was started six hours post-operatively. Other supportive measures included folate supplementation, hydrocortisone 50 mg IV q.8.h. x three days and prophylactic cefazolin x 48 hours post-operatively. Judicious use of crystalloid colloid and diuretic therapy was given to ensure satisfactory urine output. Extubation occurred on the evening of the day of surgery. Only one additional unit of packed RBCs was given two days post-operatively for a hemoglobin of 92 g/L. Otherwise the hemoglobin was maintained in the 92-106 g/L range. Platelets dropped to 82x10^9/L on the second postoperative day 1 thereafter increasing to 146x10^9/L on the day of discharge. Total bilirubin and LDH actually declined on the day post-surgery (37 μmol/L, 781 U/L) but remained elevated (34-45 μmol/L, 776-1088 U/L) until discharge. There were no other complications and the patient was discharged home six days post-operatively. She did well over the subsequent 25 months with her PNH being managed with supportive red cell transfusions as needed.

Discussion. PNH is a clonal hematopoietic disorder associated with a defect in expression of glycosylphophatidyl inositol-GPI anchored proteins on blood cells due to mutations in the X-linked PIGA gene.[2] This can lead to increased sensitivity to complement activation.[3] The principal clinical results include intravascular hemolytic anemia, venous thromboembolism and bone marrow failure. Cardiac surgery in PNH patients can, in theory, be associated with worsening intravascular hemolysis secondary to extracorporeal circulation, tissue injury and use of protamine as summarized previously.[1] In patients with pre-existing granulocytopenia and thrombocytopenia, infection and bleeding can become an issue, particularly as the latter can worsen post-operatively. Finally, venous thrombosis could result from platelet hyperactivity and microparticle generation conseguent to extracorporeal complement activation.[4, 5, 6] Our patient had an uneventful perioperative course despite evidence of ongoing hemolysis pre-operatively. The pre-operative course had been characterized by hemolytic anemia and absence of other significant cytopenias. We saw no evidence of worsening hemolysis following surgery. Moreover, with the use of an initial reduced dose of unfractionated heparin followed by prophylactic doses of enoxaparin plus intermittent pneumatic compression of both lower limbs, venous thrombosis was not a problem. As in the report by Knobloch et al, cardiac surgery with extracorporeal circulation is feasible in patients with PNH and in at least two cases was not associated with excessive complications that one might anticipate in this disorder.

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