CASE REPORT

A Possible Side-effect of Human Erythropoietin Therapy: Thrombosis of Peripheral Arterial Reconstruction

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Introduction

Because chronic renal failure is a known risk factor for atherosclerosis and longer survival for haemodialysis patients has been reported, the occurrence of chronic arterial disease and the need for peripheral arterial reconstruction are increasing in this group of patients. Human erythropoietin (rHuEPO) has been introduced to reverse the severe anaemia of end-stage renal disease and to improve life quality of chronic uraemic patients.

Several reports have recently focused on the risky side-effect of this therapy if haemoglobin concentration is normalised to levels of 13.5–16.5 g/dl. An increased thrombogenicity of prosthetic arterial access for haemodialysis and an increase in cardiac-related fatalities are possible side-effects of this therapy.

Case Report

A 53-year-old patient under recombinant human erythropoietin (rHuEPO) had recurrent thrombosis of an axillofemoral bypass graft. In 1981, he made two unsuccessful kidney transplants for chronic glomerulonephritis that resulted in end-stage renal failure. Thereafter, he started chronic haemodialysis on a 3-day basis. In 1995, he underwent a right axillofemoral bypass graft (externally supported Dacron, 8 mm in diameter) for contraindicated cause of multiple previous operations. Duplex scan and angiography showed occlusion of the common iliac artery, site of previous transplants, and mild atherosclerotic lesions in the infrainguinal vessels. The ankle–brachial index was 0.3. The reconstruction did well for 30 months. One month before re-admission he started a therapy based on rHuEPO (3000 IU 3 times/week) because of moderate anaemia (red blood cell count = 2.8 × 10^6/μl reference range: 3.9–5.5 × 10^6/μl – platelet count = 85 × 10^3/μl, reference range: 150–450 × 10^3/μl – haemoglobin = 8.8 g/dl, reference range: 14.0–17.5 g/dl – haematocrit = 27%, reference range: 41–50%). At presentation he was afebrile, blood pressure was in the reference values. Laboratory tests showed a red blood cell count of 4.26 × 10^6/μl, a haematocrit of 37.4%, a haemoglobin of 10.8 g/dl, a platelets count of 128 × 10^3/μl and a white blood cell count of 2.72 (reference range: 4.5–11.0 × 10^3/μl). Studies to assess the coagulative profile (PT, PTT, fibrinogen and AT-III) were within the reference range. The right lower limb was cold and no distal pulses were palpable. A thrombectomy of the occluded graft was successfully carried out. No signs of infection or myointimal hyperplasia were observed. Postoperatively all distal pulses were present and the ankle–brachial index was 0.8. The postoperative course was complicated by an episode of angina pectoris. rHuEPO therapy was continued at the same dosage. One month after discharge the patient was re-admitted for critical ischaemia of the right upper and lower limbs. The bypass was occluded and the ipsilateral upper and lower limb pulses were absent. Laboratory tests were comparable to those of the last admission. An emergency operation was planned, but the patient had a fatal myocardial infarction.

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Discussion

The benefits of rHuEPO therapy are widely accepted, but the present case elucidates some of the risks. Since rHuEPO was introduced, a great debate was present in the literature concerning the possible thrombogenic side-effects of rHuEPO therapy. At present an increased thrombogenicity of vascular prosthetic arterial access for haemodialysis, if haemoglobin levels are normalised, was observed. Furthermore, an increase in cardiac-related fatalities in patients under rHuEPO therapy was noted and a recent, large, controlled study stated that in patients with clinically evident congestive heart failure or ischaemic heart disease, administration of rHuEPO to raise haematocrit to 42% is not recommended. No data are available on peripheral arterial reconstruction.

Our case demonstrates that peripheral arterial grafts may undergo an increased risk of thrombosis in patients under rHuEPO therapy. However, we should consider that intradialytic hypovolaemia, hypotension or a decreased cardiac output might have also contributed to graft thrombosis. In conclusion, a balance between rHuEPO therapy of haemodialysis patients with anaemia and the potential risk for peripheral arterial reconstruction thrombosis should be achieved, either by reducing the dosage of rHuEPO or with the association of an anticoagulant drug.

References


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