

ERYTHROCYTOSIS AFTER KIDNEY ALLOTRANSPLANTATION: HAEMATOLOGICAL CHARACTERISATION AND COMPLICATIONS

G Keusch, H Jungbluth, K Mühlethaler, J Fehr, U Binswanger
University Hospital of Zurich, Zurich, Switzerland

Summary

Erythrocytosis (defined as a haematocrit of greater than or equal to 50 per cent) was observed in 15 patients 8.1 (range 1-30) months following kidney transplantation. No patient had undergone bilateral nephrectomy before transplantation. The average serum creatinine at the onset of post-transplant erythrocytosis was $113 \pm 34 \mu\text{mol/L}$. Haematocrit amounted to 54.3 per cent (range 50-72 per cent). Red cell mass was elevated in 14 of 15 patients amounting to $35.2 \pm 8.4 \text{ ml/kg}$ body weight, reflecting an increase of 40.4 (range 7-109) per cent as compared to normal values. Plasma volume was increased in four patients and decreased in 11. During an average observation period of 34 (range 9 to 80) months erythrocytosis persisted in 11 patients and resolved spontaneously in three. One patient developed anaemia during the course of a chronic rejection process. Despite therapeutic phlebotomies six thromboembolic events occurred in four patients at the presence of an haematocrit level of 55.9 ± 5.5 (49 to 65%).

Introduction

Following successful kidney transplantation haemoglobin concentration returns to normal within three to five months in the majority of patients. However, in nine to 21 per cent of kidney allograft recipients the haematocrit continues to rise resulting in post-transplant erythrocytosis [1-3], the aetiology of which remains speculative. Acute or chronic allograft rejection and transplant renal artery stenosis are the most frequently suggested aetiological factors [3,4]. Erythropoietin production by the native diseased kidneys has also been implicated [5]. The reported incidence of associated thromboembolic events is variable [1-3].

The purpose of this study is to report the clinical and haematological characteristics in 15 consecutive patients with post-transplant erythrocytosis, observed from January 1981 to July 1984 at the University Hospital of Zurich.

Patients and methods

Post-transplant erythrocytosis was defined as a haematocrit of greater than or equal to 50 per cent. The average age of the patients was 41.7 ± 8.7 (SD) years and the sex ratio was 10 males to five females. The underlying kidney disease was as follows: chronic glomerulonephritis in six patients; analgesic nephropathy in four; chronic pyelonephritis in two and lupus nephritis, diabetic nephropathy and bilateral cortical necrosis in one each. Thirteen patients had a first and two patients a second renal allograft. Unilateral nephrectomy prior to transplantation had been performed in two patients.

In addition to the routine haematological examinations the following parameters were determined: Red cell mass using ^{51}Cr -tagged erythrocytes; plasma volume using ^{125}I labelled human serum albumin; intraerythrocytic creatine and 2,3-diphosphoglycerate content; arterial blood gases and oxygen affinity in the venous blood. These measurements were performed at an average of 8.7 (0 to 41) months after the onset of erythrocytosis. To prevent thromboembolic events therapeutic phlebotomies were performed when the haematocrit was greater than 55 per cent.

Results

Erythrocytosis occurred between one and 20 months post-transplant (mean 7.4 months). The average maximum haematocrit (despite therapeutic phlebotomies for haematocrit > 55 per cent) was 54 per cent (range 50 to 72%) and the maximum haemoglobin concentration 17.4g/dl (range 15.9 to 21g/dl) respectively. The serum creatinine at onset of post-transplant erythrocytosis was $113 \pm 34 \mu\text{mol/L}$. Ten patients experienced one to three acute rejection episodes. Red cell mass was elevated in 14 of 15 patients amounting to $35.2 \pm 8.4 \text{ml/kg}$ body weight, reflecting an increase of 40.4 (range 7 to 109) per cent as compared to matched normal values. Plasma volume was increased in four patients and decreased in 11 (Figure 1). Diuretics were prescribed in five patients. In two of these five patients plasma volume was elevated by 23 per cent and 24 per cent, respectively. In the other three patients the decrease in the plasma volume varied from two to 19 per cent. The other haematological parameters (intraerythrocytic creatine and 2,3 diphosphoglycerate content), the arterial blood gases as well as the oxygen affinity in the venous blood showed no abnormalities. No patient had coincidental thrombocytosis and leucocytosis.

Post-transplant erythrocytosis during the observation period for an average of 34 months (range 9 to 80 months) in eleven patients. The serum creatinine at the last follow-up in this group was $111 \pm 19 \mu\text{mol/L}$. In three patients spontaneous recovery of post-transplant erythrocytosis was observed four, 10 and 21 months after onset. All these patients had a normally functioning allograft. One patient developed severe anaemia two months after onset of post-transplant erythrocytosis, during the course of a chronic rejection process with deterioration of kidney function.

Six peripheral thromboses were observed in four patients leading to pulmonary embolism in two. Thromboembolic events occurred in the presence of an haematocrit of 55.9 ± 5.5 per cent (range 49.2 to 65%).

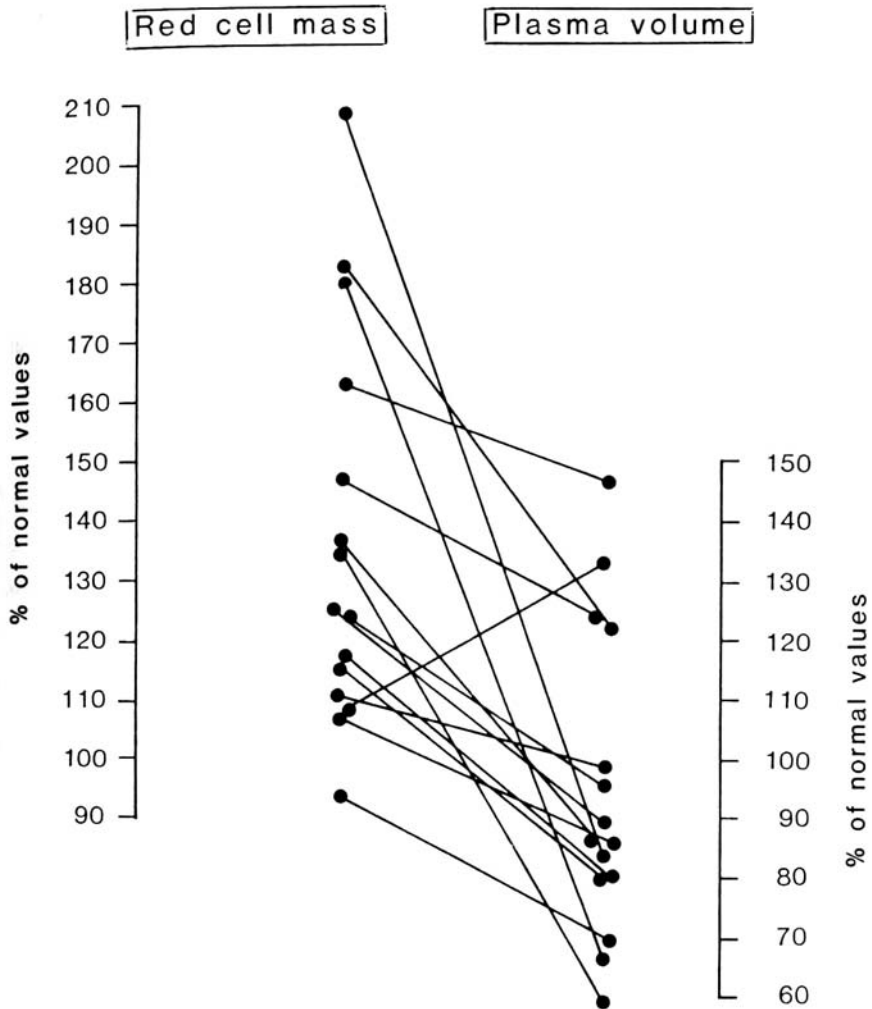


Figure 1. Red cell mass and plasma volume in 15 patients with post-transplant erythrocytosis. Values are expressed as percentage of matched normal values

Discussion

Our results show that post-transplant erythrocytosis was due to an elevated red cell mass in 14 of 15 patients and only in one case was raised haemoglobin and haematocrit secondary to reduced plasma volume. Because of the lack of leucocytosis, thrombocytosis and splenomegaly, polycythaemia vera was also an unlikely diagnosis in any of our patients. Since erythrocytotic patients in our series had excellent graft function and prognosis, allograft rejection did not seem to be a major aetiological factor. Selective venous catheterization of

native and transplanted kidney led to the suggestion that inappropriate erythropoietin production may originate from the diseased native kidneys [5,6]. The observation that none of our patients had a bilateral nephrectomy prior to transplantation and that post-transplant erythrocytosis disappeared in one patient of our series after removal of the native kidneys four and a half years after onset may support the role of the native kidney in developing post-transplant erythrocytosis.

It is apparent from our series that post-transplant erythrocytosis is not simply a laboratory abnormality since it was associated with significant morbidity. Six thromboembolic events occurred in four patients. The high frequency of thromboembolic complications has also been confirmed by other authors [1,3]. Because thromboembolic events occurred in patients with haematocrit levels of >51 per cent, therapeutic phlebotomies should be performed when the haematocrit reaches 51 per cent.

References

- 1 Wickre CG, Norman DJ, Bennison A et al. *Kidney Int* 1983; 23: 731
- 2 Herforth A, Binswanger U, Largiadèr F et al. *Schweiz Med Wschr* 1979; 109: 1293
- 3 Swales JD, Evans DB. *Br Med J* 1969; 2: 80
- 4 Bacon BR, Rothman SA, Ricanati ES et al. *Arch Intern Med* 1980; 140: 1206
- 5 Thevenod F, Radtke HW, Grützmacher P et al. *Kidney Int* 1983; 24: 227
- 6 Dagher FJ, Ramos E, Erslev AJ et al. *Transplantation* 1979; 28: 496