Posttransplant Erythrocytosis in Renal Transplant Recipients at Jeddah Kidney Center, Kingdom of Saudi Arabia

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Objectives: **Posttransplant erythrocytosis is a well-known complication of renal transplant. It is a persistently elevated hematocrit level equal to or greater than 51%, or a hemoglobin level equal to or greater than 16 g/L, or both, in the absence of other causes.**
Materials and Methods: **We retrospectively reviewed this complication in patients who had received a renal transplant at our center between January 1991 and December 2005.**
Results: **Of 1655 renal transplant recipients, 159 patients (9.6%; 154 men, 5 women; mean age, 42 ± 9 years) developed posttransplant erythrocytosis. The mean follow-up was 96 ± 4 months. Posttransplant erythrocytosis appeared at an average of 8.2 ± 5 months after transplant (range, 3-40 months) and lasted an average of 10.3 ± 3 months (range, 7-35 months). In all 159 patients, the immunosuppressive medication regimen included prednisolone; in 144, cyclosporine was used, and in 108 patients, azathioprine was used, while in another group of patients, the latter 2 were changed to mycophenolate mofetil (n=38) and tacrolimus (n=13). Twenty-four patients (15%) were treated with phlebotomies, while 29 patients (18.2%) were given angiotensin-converting enzyme inhibitors. One hundred six patients were left untreated including 92 patients (57.9%) who received prophylactic anti-platelet medications. Remission of posttransplant erythrocytosis was seen in all treated and untreated patients. No thromboembolic complications occurred. Only 9 patients (5.7%) developed chronic allograft nephropathy during follow-up.**
Conclusions: **Our findings suggest that posttransplant erythrocytosis is a benign condition affecting males more than females, usually manifesting in the first year after transplant. Remission of posttransplant erythrocytosis can be seen in all patients; however, some patients may require treatment with phlebotomy or angiotensin-converting enzyme inhibitors. Posttransplant erythrocytosis has no adverse effects on renal graft function.**

Key words: *Polycythemia, Kidney transplant, Phlebotomy, Angiotensin-converting enzyme (ACE) inhibitors, Erythropoiesis*

Posttransplant erythrocytosis (PTE) is a common complication of renal transplant, estimated to occur in 10% to 15% of patients. Clinically, it is defined as a persistently elevated hematocrit (Hct) level equal to or greater than 51%, or a hemoglobin level equal to or greater than 16 g/L, or both, in the absence of other causes. We retrospectively reviewed this complication in patients who had received a renal transplant at our center between January 1991 and December 2005.

Materials and Methods

The medical records of 1655 renal transplant recipients attending regular follow-up at our center between January 1991 and December 2005 were reviewed. PTE was defined as a persistently elevated Hct level equal to or greater than 51%, or a hemoglobin level equal to or greater than 16 g/L, or both, in the absence of other causes, on 2 or more consecutive clinic visits. In all PTE patients, we reviewed their age; sex; original renal disease; presence of hypertension; antihypertensive medications; immunosuppressive regimen; date of onset and duration of PTE; complications; treatment modalities; and renal function at the onset of PTE, after 3 months, after 1 year, and at the end of follow-up.

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Results

PTE developed in 159 of 1655 patients (9.6%; 154 men, 5 women; mean age, 42 ± 9 years). Mean follow-up was 96 ± 4 months. Patients' original renal diseases included chronic glomerulonephritis, diabetes mellitus, hypertension, chronic pyelonephritis, and autosomal dominant polycystic kidney disease. In all 159 patients, the immunosuppressive medication regimen included prednisolone; in 144, cyclosporine was used; and in 108 patients, azathioprine was used; while in another group of patients, the latter 2 immunosuppressive medications were changed to mycophenolate mofetil (n=38) and tacrolimus (n=13). PTE appeared at an average of 8.2 ± 5 months after transplant (range, 3-40 months) and lasted an average of 10.3 ± 3 months (range, 7-35 months). Twenty-four patients (15%) were treated with phlebotomies, while 29 patients (18.2%) were given angiotensin-converting enzyme (ACE) inhibitors. One hundred six patients were left untreated including 92 patients (57.9%) who received prophylactic anti-platelet medications (either aspirin or dipyridamole). Remission of PTE was seen in all treated and untreated patients. No thromboembolic complications were seen. Hypertension (defined as blood pressure equal to or greater than 160/100 mm Hg) was seen in 55 patients (34.6%) and was well controlled with antihypertensive medications. During follow-up, nine patients (5.6%) developed chronic allograft nephropathy and 150 patients (94.4%) had normal renal graft functioning. Renal graft functioning was unaffected in most of the study groups. Mean serum creatinine levels were 116.7 μmol/L, 141.4 μmol/L, and 152.9 μmol/L at the onset of PTE, after 3 months, after 1 year, and at the end of follow-up, respectively.

Discussion

PTE is clinically defined as a persistently elevated Hct level equal to or greater than 51%, or a hemoglobin level equal to or greater than 16 g/L, or both, in the absence of other causes [1]. Its prevalence varies between 10% and 15% of all patients receiving a renal transplant (range, 2.5%-22.2%) [2, 3]. At our center, PTE occurred in 159 of 1655 renal transplant patients studied, a prevalence of 9.6%, which is similar to the reported prevalences of other centers [4]. PTE develops most frequently in males (97%), as confirmed in other studies [5]. Different effects and dosages of immunosuppressive agents have no effect on Hct or erythropoietin levels [6, 7], a finding that we observed since our patients were on differing immunosuppressive regimens. (We did not measure the erythropoietin levels in our patients.) PTE usually develops 8 to 24 months after successful renal transplant [1, 6]. At our center, PTE appeared at an average of 8.2 ± 5 months after transplant (range, 3-40 months) and lasted an average of 10.3 ± 3 months (range, 7-35 months). Although not fully understood, the pathogenesis of PTE appears to be multifactorial. Considerable evidence points to the participation of at least 3 hormonal systems: the erythropoietin, endogenous androgen, and rennin-angiotensin systems [7, 8]. Erythropoietin overproduction has been found to be 10 times higher in renal transplant patients with PTE than in their counterparts with normal Hct values [9], but other studies have shown that erythropoietin levels may be within normal limits [6]. In vivo administration of rennin or angiotensin II causes increased erythropoietin secretion [10]. Decreased concentrations of erythropoietin and Hct after ACE inhibition or angiotensin II receptor blockade have been observed in patients with PTE [11, 12]. In our series, 29 patients received ACE I or angiotensin II receptor antagonists, and their Hct levels decreased to within normal limits within 3 months after the onset of treatment. Androgens exert direct dose-dependent stimulation of erythroid progenitors and can promote erythropoiesis indirectly via their stimulatory effect on endogenous erythropoietins or via rennin-angiotensin system activation. This may explain the high prevalence of PTE in male patients, as reported previously [5] and as we have shown in our series. Thromboembolic complications with PTE develop in 10% to 30% of patients [2], but we did not observe any thromboembolic events in our series. Repeat phlebotomies in PTE patients is effective [13], and we treated 24 patients (15%) with phlebotomies. The prevalence of hypertension in patients with PTE is between 55% and 80% [11, 13]; in our series, we had only 55 patients (34.6%) with hypertension.

Conclusions

PTE is a benign condition affecting 9.6% of renal transplant recipients at our center. Males are affected more than females. PTE appears in the first year after transplant, remits in some patients spontaneously, but in other patients requires phlebotomy or ACE-I to control it. It does not affect graft function and has no complications.

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