Case Report

A Case Report on Post-Transplant Erythrocytosis

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Abstract

Post-transplant erythrocytosis is defined as persistently elevated haemoglobin and haematocrit levels that occur following renal transplantation and persist for more than six months in the absence of thrombocytosis, leukocytosis or other potential causes of erythrocytosis. Here, we report the case history of a 35-year-old male, who underwent live related kidney transplantation ten months ago, presented with high haemoglobin level and high haematocrit. It is an uncommon complication of kidney transplant recipient,whichprompted us to report the case.

Key words: *Post-transplant erythrocytosis, live related kidney transplant.*

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Introduction

Post renal transplant erythrocytosis (PTE) is defined as persistently elevated haemoglobin and haematocrit levels that occur following renal transplantation and persist for more than six months in the absence of thrombocytosis, leukocytosis or other potential causes of erythrocytosis.[1] A haematocrit level greater than 51 percent in renal graft recipient has been generally used as a cut off value for definition of PTE.[2] PTE occurs in 10-20% of the recipients of renal allografts, most often during the first 2 years following transplantation. After renal transplantation and successful engraftment, PTE has been found to develop within a period of 8 to 24 months.[2] Predisposing factors include male gender, presence of native kidney, smoking, transplant renal artery stenosis, type of immunosuppressant used (more frequently in cyclosporine-treated patient), rejection free course with well-functioning renal graft and adequate erythropoiesis prior to transplantation.[2-5] Thromboembolic accidents were reported in 10-30% cases of these of PTE patients, which may lead to death in 1-2% of them.[2,4,5] Considering the relatively high incidence of PTE and its potential fatal outcome, the early diagnosis and treatment would play an important role in preventing those complications.

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Case Report

A 35-year-old non-smoker and non-diabetic police officer, a live related kidney transplant recipient, presented during his regular follow-up with high level of haemoglobin with haematocrit. He is a known case of hypertension for seven years and chronic kidney disease for one and half years. He was on maintenance haemodialysis for 6 months. His transplantation was done on January, 2018. Donor was his spouse. His pre- and post-operative period was uneventful. He received basiliximab and methyl prednisolone as induction therapy. His maintenance immunosuppressive regime consisted of prednisolone, tacrolimus and mycophenolet mofetil. His daily urine output was around 4-5 liters per day with normal renal function (serum creatinine level in between 0.8 to 1.21 mg/dl).

On his routine follow-up after 6 months, he was asymptomatic with normal urine output (2.5-3 lt/day) and found to have high haemoglobin levels which was

Table I Level of haemoglobin, haematocrits and renal function of the patient with post-transplant erythrocytosis

Date	Hb (gm/dl)	PCV (%)	TC of WBC (/cmm)	Platelet count (/cmm)	Urea (mg/dl)	Creatinine (mg/dl)
(Pre-transplant) 14/1/2018	7.0	20.8	5400	100000	73	5.5
(Post-transplant) 21/1/2018	8.0	23.6	7580	128000	45	2.7
(During discharged) 29/01/2018	9.7	28.9	8430	302000	32	0.8
(1st follow-up) 2/2/2018	13.3	30.2	14070	394000	32	1.1
(2nd follow-up) 4/3/2018	12.4	29.6	9040	276000	28	1.0
(5th follow-up) 8/7/2018	15.7	52	12370	232000	34	1.2
(6th follow-up) 9/9/2018	18.1	54.6	8600	306000	35	1.1
(7th follow-up) 6/10/2018	19.4	58.9	7950	221000	27	1.0
(8th follow-up) 7/11/2018	18.5	56	9060	211000	21	09

persistent. He had no history of headache, dizziness, epistaxis, blurred vision, diarrhea, vomiting or polyuria and he was not on any diuretic medication prior to this episode. His blood pressure was within normal limits with antihypertensive medication (amlodipine and prazosin).

Investigation reports showed haemoglobin 18.1 gm/dl, haematocrit 56%, mean corpuscular volume 85.2 ft, mean corpuscular haemoglobin 28.2 pg, mean corpuscular haemoglobin concentration 33.0 g/dl, total white cell count 8.60×10^9 /l, platelet count 306×10^9 /l, random blood glucose 5.4 mmol/l, normal liver biochemistry, urea 30 mg/dl, creatinine 1.1 mg/dl, tacrolimus levels 6.0 ng/ml, urine routine examination-protein trace, pus cell 0-2/high power field (HPF), epithelial cell 0-2/HPF, red cells 2-4/HPF, abdominal ultrasound showed normal transplanted kidney with good vascular flow up to periphery and resistivity index (RI) was < 1. His haemoglobin level was persistently raised (in between 18.4-19.4 gm/dl) with raised haematocrit (in between 56-58.9%) for three consecutive visits within previous 3 months (Table I).

Despite of his high haemoglobin and haematocrit, he remained asymptomatic. He was advised for regular follow-up and report if headache and dizziness occurs.

Discussion

Erythrocytosis following renal transplantation has been recognized since 1965,[5,6] The published prevalence of PTE in kidney transplant recipient ranges from 6.5 to 38.4%. [7] The threshold haematocrit used to define PTE is variable and ranges between 51-54 percent; most clinician use 51 percent (corresponding to haemoglobin concentration of approximately 17 gm/dl). [2] The incidence of PTE appears to be decreasing. Erythrocytosis defined as haemoglobin >17 gm/dl was reported in 19 percent of those transplanted between 1993 to 1996, but only 8 percent of those transplanted between 1997 to 2005.[8]

Almost all cases of PTE develop in transplant recipients who have retained native kidneys.[4, 10] Patients with polycystic kidney disease (PKD) and glomerulonephritis were more likely to develop PTE in some studies.[11] Renal artery stenosis of the native or transplanted kidney was suggested as a risk factor for PTE in early case reports.[2,5]

The pathogenesis of PTE is multifactorial and not well understood. The following hormonal systems and growth factors have been implicated in the pathogenesis of PTE: erythropoietin, hematopoietic growth factors such as insulin-like growth factor-1 (IGF-1) and its binding proteins and serum-soluble stem cell factor (sSCF), renin-angiotensin system (RAS) and endogenous androgens.

PTE usually occurs 8 to 24 months after transplantation.[2] In the absence of treatment, PTE spontaneously remits in one-fourth of patients within two years from onset. In the remainder of patients, PTE persists for a number

of years, after which it may remit in association with deteriorating renal function due to chronic rejection.[12] Approximately 60 percent of patients with PTE experience malaise, headache, plethora, lethargy and dizziness; 10 to 30 percent develop thromboembolic events; and 1 to 2 percent eventually die of associated complications if untreated and if erythrocytosis does not spontaneously remit. Thromboembolic events may involve both veins and arteries and are manifested as thrombosis of digital or branchial arteries, thrombophlebitis, stroke or pulmonary embolus.[13] Platelet and leukocyte counts are normal and arterial blood gases are normal in patients with PTE.[2]

The diagnosis of PTE is made by clinical feature and laboratory finding and by the exclusion of common causes of nontransplant-associated erythrocytosis, including malignancies and in selected patients, chronic obstructive pulmonary disease (COPD). An ultrasound with Doppler waveform analysis of renal arteries of the native and transplanted kidneys and assessment of cytology of three morning urine samples in order to exclude renal artery stenosis and an underlying renal carcinoma respectively are useful. The measurement of erythropoietin concentrations is not helpful among transplant recipients, since high and low concentrations have been demonstrated among PTE patients. Measurement of renin-angiotensin system (RAS) activity, goralatide or insulin-like growth factor-1 (IGF-1) concentrations are also not helpful in making the diagnosis or direct treatment and are not performed among transplant recipients.

The preferred initial treatment for patients with PTE who have a hemoglobin concentration <18.5 g/dL is an angiotensin receptor blocker (ARB) or angiotensin-converting enzyme (ACE) inhibitor since these agents are effective in the majority of patients, are reasonably safe and among many patients, provide a necessary antihypertensive effect.

Patients who present with hemoglobin concentration >18.5 g/dL are generally treated with phlebotomy, along with the ARB or ACE inhibitor. Patients in whom an ARB or ACE inhibitor is ineffective in reducing the hemoglobin concentration are treated with serial phlebotomy. Although theophylline has been shown to be effective in treating PTE, it is rarely used, except in selected patients, because of the requirement for monitoring serum concentrations and because of undesirable side effects including tremor and insomnia. Similarly antiproliferative agents such as azathioprine or mammalian (mechanistic) target of rapamycin (mTOR) inhibitors may decrease erythrocytosis, but altering the immunosuppressive regimen to include such agents is not commonly done in the absence of other indications. The optimal haemoglobin among patients with PTE is not known. A target haemoglobin level <17.5 g/dL and continued therapy for PTE indefinitely since relapse of erythrocytosis is common and since the majority of renal transplant recipients are hypertensive and these drugs may slow the rate of progressive renal dysfunction.[14] Relapse of erythrocytosis is common if treatment is discontinued.[14]

Conclusion

PTE should be borne in mind when kidney transplant recipients present with high haemoglobin and haematocrit levels. Early diagnosis and appropriate actions may reduce the complication and fatal outcome of PTE.

Conflict of interest: Nothing to declare.

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