J Nephropharmacol. 2017; 6(2): 134–137.

http://www.jnephropharmacology.com DOI: 10.15171/npj.2017.20

Journal of Nephropharmacology

Kidney transplantation in a patient with polycythemia vera

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ARTICLEINFO

Article Type:
Case Report

Article History:
Received: 25 January 2017
Accepted: 2 April 2017
ePublished: 12 April 2017

Keywords:
Renal transplantation
Polycythemia vera
Phlebotomy
Kidney transplantation

ABSTRACT

Polycythemia vera (PV) is a clonal over proliferation of hematopoietic stem cells, which increases red blood cell (RBC) mass and hematocrit, and is frequently accompanied with leukocytosis, thrombocytosis, or both. Few cases of renal involvement of PV have been reported to date. We present a case of PV based on *JAK2* (Janus kinase 2) mutation that did not need any treatment after unrelated kidney transplantation. According to the rarity of kidney transplantation in PV, more clinical evidence is needed to determine the frequency of its improvement after transplantation.

Case Report

Implication for health policy/practice/research/medical education:
Few cases of renal involvement of polycythemia vera have been reported to date. We present a case of polycythemia vera based on JAK2 (Janus kinase 2) mutation that did not need any treatment after unrelated kidney transplantation. According to the rarity of kidney transplantation in polycythemia vera, more clinical evidence is needed to determine the frequency of its improvement after transplantation.

Please cite this paper as: Akbari R, Sadeghi MV. Kidney transplantation in a patient with polycythemia vera. J Nephropharmacol. 2017;6(2):134-137. DOI: 10.15171/npj.2017.20.

Introduction

Polycythemia vera (PV) is a clonal over proliferation of hematopoietic stem cells, which increases red blood cell (RBC) mass and hematocrit, and is frequently accompanied with leukocytosis, thrombocytosis, or both. In PV, colony- and burst-forming units of bone marrow proliferation are formed without erythropoietin.

JAK2 (Janus kinase 2) mutation is associated with PV in more than 90% of cases, and it is the most important etiologic factor (1). Phlebotomy is the usual management of PV patients. Hydroxyurea in addition to phlebotomy is prescribed for those with a history of thrombosis or who are more than 60-year old. Renal diseases in PV are rare, and few cases of renal failure with glomerulonephritis have been reported (2,3).

Case Presentation

A 66-year-old Iranian man was referred to the nephrologist for renal replacement. Ultrasonography performed on December 29, 2012, revealed increased renal parenchymal echogenicity and decreased maximal dimension of both kidneys (right, 73 cm; left, 81 cm), with a 30-mm simple cyst in the right and 25-mm simple cyst in the left.

Serum analysis revealed a leukocyte count of 18700 × 10^9/L, hemoglobin content of 16.8 g/dL, and platelet count of 967 × 10^9/L. Serum urea nitrogen and creatinine (Cr) levels were 85 and 4.5 mg/dL, respectively.

Urine analysis revealed maximum amount of trace proteins and normal white blood cell (WBC) and RBC counts. Serum uric acid was 12.5 mg/dL, and thyroid test revealed high thyroid stimulating hormone (TSH) levels of 19 mIU/L. Serum Na levels were normal, but serum K^+ levels were high (5.5 mEq/L). Liver function, serum lipid profile, and glucose levels were in the normal range.

Based on para-clinical data and glomerular filtration rate (GFR) measurement by the modification of diet in renal disease (MDRD) formula, the patient was diagnosed with end-stage renal disease (ESRD). Eight years ago,

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polycythemia was diagnosed during routine investigation before coronary artery bypass grafting (CABG). At that time, plasma creatinine was 1.6 mg/dL based on his son's recall. The patient did not have any nephrology follow-up during that time. PV had been treated by phlebotomy and hydroxyurea. He reported several episodes of gout attack over the past years. Patient's laboratory data was shown in Table 1.

On examination, the patient was plethoric and his blood pressure was 160/80 mm Hg. The spleen was enlarged, and he had no symptoms and signs of uremia. He was referred to the hematologist for better control of polycythemia. His erythropoietin (EPO) level was 2.9 nm/mL (Reference value: 3.2–31.9), and *JAK2* mutation with polymerase chain reaction (PCR) was positive. Polycythemia was controlled with frequent phlebotomy and hydroxyurea.

Additional tests revealed Intact parathyroid hormone (iPTH) = 182 pg/mL, with electroluminescence study, and 24-hour urine protein test revealed glomerular proteinuria of 1.96 g/d. Secondary workup for proteinuria such as ANA, pANCA, cANCA, dsDNA, C3, C4, CH50, wright, 2ME, coomb's wright, VDRL, and PPD showed negative results and excluded secondary cause of proteinuria. According to the patient's refusal for other types of renal replacement therapy, we decided to perform preemptive transplantation. Finally, he received a kidney from an unrelated living donor on May 30, 2014. He had a good graft function after the transplantation, and plasma Cr was just under 2.0 mg/dL. Laboratory data and urinary output during the first 24 hours of transplantation are shown in (Table 2).

Graft ultrasonography and Doppler ultrasonography were normal. Cyclosporine and mycophenolate mofetil was prescribed. Laboratory data at discharge were as follows: Hb = 12.7 g/dL, WBC = 14200/µL, PLT = 307000/µL, Cr =1.1 mg/dL, Na = 137 mEq/Land K = 4.5 mEq/l. During the next 6 months of follow-up, serum creatinine remained in the normal range and phlebotomy was required only once to control polycythemia. Till August 1, 2016 he did not need for special treatment (phlebotomy, hydroxyurea), when his hemoglobin was 16.2 g/dL and phlebotomy was restarted.

Table 1. Laboratory tests before kidney transplantation

Date	HB (g/dL)	PLT×10^6/L	WBC×10^6/L	Cr (mg/dL)
2012.6.24	16.8	967000	18700	5.5
2012.10.17	16.2	437000	15700	4.1
2012.11.28	16.8	480000	18500	3.9

Discussion

There are only few studies on PV associated with renal disease in the literature. Jermanovich first reported about a patient who had PV and polycystic kidney on hemodialysis (4). Glomerulonephritis because of PV was reported by Plomely et al in 1938 (5).

Previous reports have shown that patients with PV were anemic with ESRD, and EPO was effective in correcting anemia as other ESRD patients (6).

Shih et al investigated the in vitro and in vivo responses of erythroid progenitor cells to EPO effect in sera of patients with ESRD because of PV and reported that autonomous progenitor cell growth persisted during the spent phase of PV and was characteristic of erythroid progenitor after development of end-stage renal failure (7). We presented the patient who needed frequent phlebotomy and hydroxyurea to control polycythemia during the spent phase of ESRD.

Only 23 patients of PV associated with renal disease have been reported in the literature. IgA nephropathy and focal segmental glomerulosclerosis were the most predominant histopathological features (3,5,8-16). Other histopathological features included membrano-proliferative glomerulonephritis and rapidly progressive glomerulonephritis (3,17).

In contrast to most reports, our patient had sub-nephrotic proteinuria with 1960 g/d (2,3,5,8-15,16). Microthrombi, glomerular capillary occlusion, and reduction in GFR because of PV associated with increased blood volume and viscosity can be considered to be associated with renal disease. In addition, factors associated with PV such as hypertension and hyperuricemia can affect renal microcirculation (16,18). Thrombocytosis and abnormal activation of megakaryocytes are other pathological factors for glomerular sclerosis (3,19).

Our patient was hypertensive, which is consistent with previous reports (2,3,5,8-10,14,16). He had a good graft function after transplantation, and serum creatinine

Table 2. Clinical status and laboratory tests after kidney transplantation

Date	BP (mm Hg)	Urine Output (cc/24 h)	Intake (cc/24 h)	Weight (kg)	WBC (×10^6/L)	HB (g/dL)	PLT (×10^6/L)	FBS (mg/dL)	BUN (mg/dL)	Cr (mg/dL)
2013.6.1	139/86	13150	13800	68	12300	12.2	558000	128	35	2
2013.6.2	130/80	7400	7000	70.5	10800	12.5	507000	90	23	1.1
2013.6.3	150/80	6600	6500	68.5	8100	10.9	394000	78	20	1.1
2013.6.4	130/80	4500	4650	68.5	8100	11.1	358000	119	21	1
2013.6.5	130/80	3350	2050	68.3	1200	13.2	458000	93	23	1
2015.3.4	110/70			70	7600	1405	250000	86	18	1.2
2016.2.6*	140/75			69	10/000	13.7	300000	80	15	1.2
2016.9.19				72	11600	16	696000	74	28	1.3

*He had not regular follow up after 2015.3.4.

was below 2.0 mg/dL 24 hours after transplantation. Graft ultrasonography and Doppler ultrasonography were normal, and he did not develop any thrombotic complications after the transplantation. Despite the necessity to treat polycythemia in the spent phase of ESRD, his hemoglobin was maintained at an acceptable level without the need for special treatment during 26 months after kidney transplantation.

Anemia after kidney transplantation is a known term in nephrology, its etiology may be a common cause seen in general population such as iron deficiency anemia or gastrointestinal bleeding, or may be a specific cause related to transplantation such as immunosuppressive drugs, acute rejection, infection, malignancies and chronic inflammation. Azathioprine, mycophenolate mofetil and specially sirolimus are drugs can suppress bone marrow (20,21). Decreased allograft function is the most important factor for post-transplantation anemia (22).

Post-transplant anemia due to immunosuppressive drugs, iron deficiency and chronic inflammation may be one explanation of good control of polycythemia for several months in the patient.

Conclusion

We report a rare case of PV was underwent renal transplantation with good control of PV during 26 months after transplantation without specific treatment. To the best of our knowledge, the present report is the first case of PV with no necessity for treatment for polycythemia after kidney transplantation. More clinical evidence is needed to determine the frequency of polycythemia improvement after transplantation in PV patients.

Acknowledgements

We would like to thank the Clinical Research Development unit of Rouhani hospital, Babol University of Medical Sciences for assistance in discussion of case and editing this article.

Authors' contribution

All authors contributed to write the manuscript. All authors read, revised, and approved the final manuscript.

Conflicts of interest

The authors declare no conflict of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

There was no source of funding for this publication.

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