AN ANALYSIS OF THE HAEMATOLOGICAL CHANGES IN POST RENAL TRANSPLANT PATIENTS AT A TERTIARY CARE CENTER

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ABSTRACT

BACKGROUND

Renal transplantation is considered as the surgical procedure used in renal replacement therapy. It has better patient survival. Common haematological changes in post renal transplant patients include anaemias, cytopenias, and rarely lymphoproliferative disorders. These changes are common adverse effects of immunosuppressive medications, infections due to immune suppression, transplant or immunosuppression-related co-morbidities.

MATERIALS AND METHODS

A retrospective study from the Upgraded Department of Pathology, Osmania General Hospital, Hyderabad was done. Haematological indices of 100 post renal transplant patients were collected. The whole blood samples were analysed on Sysmex-1000 automated cell counter. Indices included in the study are haemoglobin, RBC count, WBC count, Platelet count, Differential count, Reticulocyte count, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC).

RESULTS

There were 62% patients who had haemoglobin less than 9 gm/dl. 53% patients had leukocytosis. There was significant neutrophilic leukocytosis in 78% of patients. Thrombocytopenia was seen in 44% of patients.

CONCLUSION

Haematological changes post renal transplantation are multifactorial. Understanding how blood disorders develop will help cure these life threatening complications. Pharmacological treatment strategies for post-transplant blood disorders like tapering immunosuppressive therapy or replacing myelotoxic immunosuppressive drugs with lower toxic alternatives, recognizing and treating promptly the aetiological microorganisms attenuating bone marrow suppression will enhance kidney graft survival.

KEYWORDS

Renal Transplant, Anaemia, Leukopenia, Red Cell Indices.

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BACKGROUND

Renal transplant was the first solid organ transplanted successfully in 1954. In a solid organ transplant many immunosuppressants are used to increase the graft uptake. This in turn would cause immune modulation as well as expose the patient to many infections. This including the compromised non excretory function of the kidney results in a variety of medical conditions.

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The post renal transplant patients are faced with many haematological and non-haematological conditions. Our study aimed to analyse the post renal transplant haematological disorders. The haematological disorders encountered are, Post-transplant anaemia (PTA), post-transplant lymphoproliferative disorder (PTLD), Post-transplant erythrocytosis (PTE) and post-transplant cytopenias (PTC). Rarely hemophagocytic syndrome (HPS), thrombotic microangiopathy (TMA), therapy-related myelodysplasia (t-MDS), and therapy-related acute myeloid leukaemia (t-AML). A study of these conditions helps the pathologist and the clinician to understand how to approach.

MATERIALS AND METHODS

A retrospective study from the Upgraded Department of Pathology in Osmania General Hospital, Hyderabad was done. Haematological indices of 100 post renal transplant patients were collected from Sysmex-1000 from January

2015 to July 2017. The samples analysed were whole blood samples collected in potassium EDTA vacutainers and analysed in Sysmex -1000 haematology analyser. Indices included in the study are haemoglobin, RBC count, WBC count, Platelet count, Differential count, Reticulocyte count, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC).

The analysis of the quantitative data as the part of the research study was carried out with Microsoft Excel.

RESULTS

The study included haematological changes in 100 post renal transplant patients. There were 87 male patients and 13 female patients. Out of 87 male patients 65 received transplanted kidney from live donors whereas rest of 22 were cadaveric transplants. Among the 13 female patients, 11 received kidney from live donors and 2 from cadavers. (Table 1)

Sex	Total	Live Donor Transplant	Cadaver Transplant
Male	87	65	22
Female	13	11	2

Table 1. Type of Transplant Received by the Patients in the Study Group

Whole blood samples were collected from each patient in a potassium EDTA vacutainer and run on Sysmex -1000. various haematological parameters were analysed. Table 2 depicts the highest and lowest values of each parameter encountered in the study. The standard range of each variable was taken as fixed in the analyser and accordingly, number of cases above, within and below the normal ranges were noted (Table no. 2).

Variable	Maximum	Minimum
Hb g/dl	18	3.9
RBC (mill/cumm)	6	1.63
WBC /cumm	20,000	2,400
PLATELETS/cumm	3,75,000	30,000
RETICULOCYTE count%	4	0.1
MCV fl	100	60.2
MCH pg	33	20
MCHC	73	23
NEUTROPHIL count %	95	60
LYMPHOCYTE count %	38	02
MONOCYTE count %	15	01
EOSINOPHIL count %	05	00
BASOPHIL count %	01	00

Table 2. Maximum and Minimum Value of Each Variable Encountered in the Study Group

There were 62 (62%) patients who have haemoglobin less than 9 gm/dl. 53% patients had leukocytosis. There was significant neutrophilic leukocytosis in 78% of patients. Thrombocytopenia was seen in 44% of patients.

Red Blood Cells

Majority of the patients i.e. 44% had normocytic hypochromic picture. 28% showed microcytic hypochromic, 20% normocytic normochromic and 6% were with dimorphic anaemia.

Reticulocyte count in 60% of patients was in between 0.5%-1%. Neutrophilic leucocytosis was noted in 78% of cases where as lymphocytopenia was noted in 53% of cases.

Variable	Below Normal Range	Within Normal Range	Above Normal Range
Hb g/dl	62	28	10
RBC (mill/cumm)	52	46	2
WBC /cumm	6	41	53
PLATELETS/cumm	28	70	2
RETICULOCYTE count%	60	26	14
MCV fl	18	82	Nil
MCH pg	28	60	12
MCHC	24	74	2
NEUTROPHIL count	22	Nil	78
LYMPHOCYTE count	64	36	Nil

Table 3. Number of Cases Below and Above the Normal Values of Each Parameter

Bone marrow aspiration was done in 3 cases and bone marrow biopsy in one case. Bone marrow aspiration showed reduced haemopoiesis and erythroid hyperplasia.

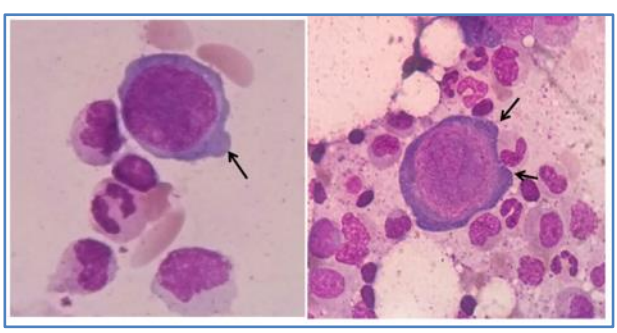

Figure 1. Bone Marrow Aspirate showing Intranuclear Inclusions in a Case of Parvo Virus B19

We had an interesting case of a 27 year old male patient receiving a live donor transplant presenting with intractable pancytopenia. He did not respond to transfusions, haematinics and reduction of immunosuppressants. Bone marrow aspiration showed hypoplastic marrow with erythroid hypoplasia and giant pronormoblasts with intra nuclear inclusions suggestive of Parvo virus B19 (Fig. 1) infection which was confirmed on PCR. On treatment with IV immunoglobulin the condition improved.

DISCUSSION

Blood disorders after renal transplant are frequently observed. Post-transplant anaemia, post-transplant

lymphoproliferative disorder, post-transplant erythrocytosis and post-transplant cytopenias are common haematological complications. Hemophagocytic syndrome, thrombotic micro angiopathy, therapy related myelodysplastic syndromes and acute myeloid leukaemia are uncommon but serious haematological complications in renal transplant recipients. Multiple factors including immunosuppressive drugs, allograft dysfunction, viral or bacterial infections, antibiotics, chemotherapy, decrease or increase in erythropoietin production, transplant rejection episodes and nutritional deficiencies are associated with the development of post-transplant blood disorders. According to the data and results in our study, all the indices were correlating with the post renal transplant changes with the patients who were studied in other articles.

In our study we observed neutrophilic leukocytosis as the most common finding (78%) which was not seen in other studies. More than half (62%) the patients had anaemia, most severe being 3.5 g/dl. This could be due to the immunosuppressive agents which cause direct suppression of bone marrow eryhtropoeisis[1] The spectrum of drugs used are usually antiproliferative drugs, calcineurin inhibitors, induction immunosuppressants, and antithymocyte antibodies. These drugs are known to cause increased incidence of PTA.[2,3] Post transplantation anaemia is associated with worse patient and graft survival and higher rates of acute rejection when compared with non-anaemic renal transplant recipients.[4] The mechanisms by which ACE (Acetyl choline esterase) inhibitors and ATII (angiotensin II) receptor antagonists cause PTA, include inhibition of endogenous erythropoietin production, inhibition of ATII-mediated stimulation of red blood cell precursors,[5] and the generation of an erythropoiesis-inhibiting protein by ACE inhibitors.[5,6]

PTLD is a well-recognized complication of both solid organ transplantation (SOT) and allogeneic hematopoietic stem cell transplantation (HSCT). In renal transplant recipients, PTLD is usually caused by EBV infection due to therapeutic immunosuppression after renal transplantation.[6,7] EBV infection is due to the usage of immunosuppressants[7] like Tacrolimus / FK-506 and Cyclosporin and mainly affects the B-lymphocytes[8,9] causing the unopposed proliferation of EBV infected B lymphocytes and hence lymphoma.[10] The patients with PTLD may develop infectious mononucleosis-like lesions or polyclonal polymorphic B-cell hyperplasia.[11] However we did not encounter any case of lymphoma in our study.

Transplant associated pancytopenia is almost always due to Parvo B virus infection in renal transplant recipients. As seen in our study the renal transplant recipient presented with life threatening pancytopenia and on bone marrow aspiration was found to have PVB infection. PVB19 infection also leads to various forms of glomerulopathy and allograft dysfunction.[12] Generally, post-transplant HPS is associated with a higher rate (53%) of death in renal transplant recipients.[13] Diagnostic criteria for HPS may include fever, cytopenia of two lines, hypertriglyceridemia, hypofibrinogenemia, hyperferritinaemia (>500 µg/L), hemophagocytosis, elevated soluble interleukin-2 receptor (CD25), decreased NK-cell activity, and hepato-splenomegaly.[14]

CONCLUSION

Pharmacological treatment strategies for post-transplant blood disorders should aim at tapering immunosuppressive therapy or replacing myelotoxic immunosuppressive drugs with lower toxic alternatives. Recognizing and treating promptly the aetiological microorganisms attenuating bone marrow suppression, restoring normal blood counts, retarding the progression of a blood disorder, enhancing kidney graft survival by treating underlying complications. By implementing all of the above strategies in patients with Post renal transplant we can decrease the incidence of blood disorders and improve long term kidney graft survival.

REFERENCES

[1] Winkelmayer WC, Chandraker A. Post transplantation anemia: management and rationale. Clinical Journal of the American Society of Nephrology 2008;(3 Suppl 2):S49-S55.
[2] Fang GX, Chan PC, Cheng IK, et al. Haematological changes after renal transplantation: differences between cyclosporin- A and azathioprine therapy. Int Urol Nephrol 1990;22(2):181-187.
[3] Jafari A, Najivash P, Khatami MR, et al. Cytopenia occurrence in kidney transplant recipients within early post-transplant period. J Res Pharm Pract 2017;6(1):31-39.
[4] Chhabra D, Grafals M, Skaro AI, Impact of Anemia after Renal Transplantation on Patient and Graft Survival and on Rate of Acute Rejection. CJASN 2008;3(4):1168-1174.
[5] Drueke TB, Locatelli F, Clyne N, et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med 2006;355(20):2071-2084.
[6] Yang Y, Yu B, Chen Y. Blood disorders typically associated with renal transplantation. Front Cell Dev Biol 2015;3:18.
[7] Newstead CG. Lymphoproliferative disease post-renal transplantation. Nephrology Dialysis Transplantation 2000;15(12):1913-1916.
[8] Comoli P, Cioni M, Basso S, et al. Immunity to polyomavirus BK infection: immune monitoring to regulate the balance between risk of BKV nephropathy and induction of alloimmunity. Clinical and Developmental Immunology 2013;2013:1-6.
[9] Scadden JR, Sharif A, Skordilis K, et al. Polyoma virus nephropathy in kidney transplantation. World J Transplant 2017;7(6):329-338.
[10] Kamaleshwaran KK, Rajasekar T, Shibu D, et al. Image findings of monomorphic non-hogdkin lymphoproliferative disorder in a post renal transplant patient diagnosed with fluorine-18 fluorodeoxyglucose-positron emission tomography

/computed tomography. Indian J Nucl Med 2014;29(3):189-190.
[11] Zimmermann H, Trappe RU. Therapeutic options in post-transplant lymphoproliferative disorders. Ther Adv Hematol 2011;2(6):393-407.
[12] Morrissey PE, Ramirez PJ, Gohh RY, et al. Management of thrombophilia in renal transplant patients. Am J Transplant 2002;2(9):872-876.
[13] Gurkan A, Yakupoglu U, Yavuz A, et al. Hemophagocytic syndrome in kidney transplant recipients: report of four cases from a single center. Acta Haematol 2006;116(2):108-113.
[14] Ponticelli C, Alberighi OD. Haemophagocytic syndrome - a life-threatening complication of renal transplantation. Nephrol Dial Transplant 2009;24(9):2623-2627.