

Renal Transplantation in Human Immunodeficiency Virus-Seropositive Patient

Innocent Ijezie Chukwuonye^{1*}, Emmanuel Chukwuebuka Obi², Ernest Ndukaife Anyabolu³, Kenneth Arinze Ohagwu⁴, Miracle Erinma Chukwuonye⁵, Collins Ogbonna Nwabuko⁶

¹Division of Nephrology, Department of Internal Medicine, Federal Medical Centre, Umuahia, Nigeria.

²Division of Nephrology, Department of Internal Medicine, Federal Medical Centre, Umuahia, Nigeria.

³Division of Nephrology, Department of Internal Medicine, Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Awka, Nigeria.

⁴Department of Internal Medicine, Federal Medical Centre, Umuahia, Nigeria.

⁵Department of Family Medicine, Federal Medical Centre, Umuahia, Nigeria.

⁶Department of Haematology, Federal Medical Centre, Umuahia, Nigeria.

ABSTRACT

Kidney transplantation as a replacement therapy in HIV seropositive patients has always been challenging because of the need to strike a balance between the treatment of HIV with highly-active antiretroviral therapy (HAART) and concomitant administration of immunosuppressive drugs to maintain the graft. The key to achieving this is adequate pre-transplantation selection of subjects using specified guidelines. This is complemented by meticulous monitoring of the subjects post-transplant. A well-coordinated effort of the managing Physicians is required to achieve this goal. This case report is on our experience in managing an HIV-seropositive patient with ESRD that has living- donor kidney transplantation.

Keywords: HIV, End Stage Renal Disease, HAART, Renal Transplant, Immunosuppressants.

INTRODUCTION

The life expectancy in patients infected by the human immunodeficiency virus (HIV) has improved dramatically following the introduction of the Highly Active Antiretroviral Treatment (HAART) in the management of the disease.¹ The reduced acquired immunodeficiency syndrome (AIDS)-related mortality has resulted in the increase in complications such as kidney, liver and cardiac diseases.² These have largely replaced opportunistic infections as the leading cause of death in this group of patients.³ End Stage Renal Disease (ESRD) in HIV seropositive subjects usually results from a broad spectrum of disorders. These include, immune-mediated glomerulonephritis, HIV-associated nephropathy, drug induced renal disease or thrombotic microangiopathy. Human immunodeficiency virus-seropositive patients are also not immune to ESRD caused by diseases like hypertension and diabetes mellitus (DM).⁴

The management of ESRD involves three different modalities of renal replacement therapies viz. haemodialysis, peritoneal dialysis and kidney transplantation. One of these options must be adopted in the management of a patient with ESRD; failure to do this will lead to the patient's death. Kidney transplantation until recently had been considered as absolutely contraindicated in

*Correspondence to:

Innocent Ijezie Chukwuonye

Division of Nephrology,
Department of Internal Medicine,
Federal Medical Centre, Umuahia, Nigeria.

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HIV-seropositive subjects.⁵ However, with the introduction of HAART, it has become an acceptable form of renal replacement therapy in HIV-seropositive subjects with ESRD, in carefully selected cases.⁶ The management of HIV-infected subjects' pre- and post-transplantation is very complex and challenging. This is majorly due to drugs interactions, infection risks and associated co-infections. Renal transplantation is deferred in HIV-infected patients by many centers because of suspected poor outcome. This can be attributed to the fact that a synergy between the Nephrologist and HIV Physicians is very important for a successful transplantation. This coordination is usually very difficult in centers in resource-poor settings.

PATIENT AND OBSERVATION

The patient is a 37 year old female teacher who was first evaluated at a tertiary hospital in India in 2014 for possible renal transplant. She was initially diagnosed in a private hospital of having HIV. She was subsequently commenced on HAART (a combination of Abacavir, Lamivudine and Efavirenz). She was later diagnosed of Chronic Kidney Disease (CKD) a year later. Her CKD progressed to ESRD, despite intervention by a Nephrologist.

She was initially on haemodialysis while an arrangement for renal transplantation was being worked out with a centre in India.

Pre-transplant evaluation revealed CD4 cells count of 220cells/ μ l, HIV viral load of 25 copies/ml. screening for Hepatitis B and C viruses was negative. The abdominal ultrasound investigation showed evidence of kidney damage. Other investigations carried out on this patient were not remarkable.

The patient underwent live donor kidney transplantation in 2014. Triple immunosuppression therapy, comprising of Tacrolimus, Mycophenolate Mofetil (MMF) and Prednisolone, was initiated prior to transplantation. No antibody induction was given. She was also placed on Calcium Gluconate, Cotrimoxazole and Valganciclovir

She had features suggestive of acute graft rejection on day 4 post-transplantation and was given a high dose methylprednisolone with a good result. Tacrolimus blood level checks were normal. She was maintained on tabs Tacrolimus 1mg twice daily, Tabs MMF 360mg trice daily and tabs Prednisolone10mg once daily. She was later discharged from the hospital in India.

She is currently on follow-up management in our center, with occasional minor illness, that we normally treat promptly. Her performance after the transplantation about 30 months ago is remarkable. She keeps to regular clinic attendance and has been doing well on the same doses of immunosuppressants and HAART. Her investigation results including fasting blood sugar are usually normal and she is not hypertensive.

DISCUSSION

Recent studies in this era of HAART have shown results that suggest that renal transplantation is a viable option in properly selected HIV-seropositive subjects. Currently, the patient survival and renal allograft survival are found to be similar to those of non-HIV infected subjects.⁷ Death rates in HIV-positive ESRD patients are comparable to diabetic ESRD patients in this era.⁸

Our patient met the criteria for renal transplantation set by the British HIV association published guideline.⁹ The criteria included: CD4 cells count \geq 200cell/ μ l, HIV ribonucleic acid (RNA) viraemia < 50 copies/ml. She also adhered to her HAART regimen and was free from hepatitis B virus (HBV) or hepatitis C virus (HCV) infection and did not have any AIDS-defining illness.

However, using this guideline for the selection of HIV-infected patients for kidney transplantation, it has been found by some studies¹⁰ that only 20% of HIV-infected kidney transplant candidates were selected in the list or underwent transplantation.

This proportion is significantly low when compared to about 73% in HIV-seronegative patients evaluated during the same period. The criteria drastically reduced the number of HIV-seropositive subjects that can undergo a successful renal transplant.

Allograft rejection (AR) rates are higher in HIV-infected patients when compared with HIV-negative individuals.¹¹ The rate of acute rejection of renal transplants in HIV-infected patients ranges from 13% to 67%. This may be ascribed to immune dys-regulation or inadequate immunosuppression in the earlier period.¹²⁻¹⁴ Our patient had single episode of minimal feature of acute rejection which responded well to treatment with bolus methylprednisolone.

Co-administration of HAART and immunosuppressant therapy is usually complicated by drug-drug interaction. This is due to agents that induce or inhibit the p-glycoprotein 1 flux transporters and

cytochrome P450 3A (CYP3A4).¹⁵ This interactions can lead to unexpected increases or decreases in plasma level of drugs that are metabolized in this pathway e.g. Tacrolimus. This interaction can be ameliorated if appropriate pre-transplant trial is conducted with adequate therapeutic drug monitoring to establish the optimum doses of HAART and immunosuppressants. This was done in our patient and she has been doing well on the doses decided pre-transplant.

Contrary to the conventional belief that the HIV infection progression is enhanced by immunosuppression, the risk of opportunistic infection was not found in some studies. Some immunosuppressive agents (MMF, cyclosporine, Tacrolimus and Sirolimus) have been found to have antiretroviral properties and synergy with Abacavir.

This may explain why our patient tolerated immunosuppressive therapy with no deleterious effect on HIV disease and does not experience any major side effects. More than 30 months after renal transplant, she is currently free from any form of complications from the drugs, her routine investigations remains essentially normal.

CONCLUSION

This case report highlights the need to encourage patients being managed for HIV infection with ESRD especially in Sub-Saharan African countries that they should also consider renal transplantation as a viable option.

Careful monitoring of the patients pre- and post-transplantation, evaluating the drug dosages, the side effects, and patient clinical response as well as the adequate control of the HIV infection are keys to long term survival. Kidney transplantation in HIV-infected patient is an effective and safe treatment option for well-selected patients with ESRD.

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