Successful Renal Transplantation in a HIV Positive Nigerian Man: A Case Report

***Ekrikpo UE, Akpan EE, Udo AIA**

ABSTRACT

This is a 42 year old man, known hypertensive of 2 years with poor compliance to anti-hypertensiveswho presented with a 3 month history of generalized body weakness, progressive leg swelling, facial swelling, reduction in urinary output and clinial features of uraemia who was found to be HIV positive during work up for haemodialysis. His viral load at initial assessment was 6300 copies/ml with a CD4 count of 287cells/µL. Renal ultrasound showed reduced renal sizes with loss of corticomedullary differentiation. He also had proteinuria and haematuria. He had a successful renal transplant after 6 months on haemodialysis using an AV fistula as vascular access and developed New Onset Diabetes after transplant (NODAT). He has stable renal function 3 years after renal transplant and is on monthly renal clinic visits.

Keywords: Kidney transplantation, HIV, Nigeria

CASE PRESENTATION

Mr. S.U.A. is a 42 year old Petroleum products dealer who presented with a 3 month history of generalized body weakness, 2 months of progressive leg swelling and facial swelling worse in the mornings but reducing as the day progresses. He also noticed progressive reduction in urine volume. No dysuria, loin or suprapubic pain. He had a mild non-productive cough not associated with chest pain. He had lost about 5 kg of weight in the 4 months preceding presentation. He also complained of frequent hiccoughs. He gave a history of elevated blood pressure noticed 2 years prior to presentation but he was not compliant on antihypertensive medication. He was not diabetic and had no known family history of both conditions. No history of smoking but he takes alcohol occasionally.

Examination revealed a chronically ill-looking middle aged man, pale, afebrile (temperature 36.7^{0}C), anicteric, fair hydration status, no significant peripheral lymph node enlargement, had bilateral pitting pedal oedema up to mid-leg. He had a pulse rate of 86/min, normal volume regular, no arterial wall thickening, no radiofemoral delay. His blood pressure was 140/100mmHg, apex beat was not displaced but the fourth heart sound was audible and he had a loud A2. The respiratory rate was 28/min. He had fine crepitations in both lung bases. He had a liver span of 12cm with ascites demonstrable by shifting dullness, no palpable splenomegaly and no other palpable abdominal masses, no renal angle tenderness. No abnormality detected on Central Nervous System examination.

Renal Unit, Department of Internal Medicine, University of Uyo

*Corresponding Author: udekrikpo@yahoo.com

INVESTIGATIONS

- Serum E/U/Cr: Creatinine-1441µmol/L, urea-16.4mmol/L, K^+-5.1mmol/L, sodium-143mmol/L, bicarbonate-16mmol/L, chloride-104mmol/L, Ca^{2+}-8.3mg/dl, phosphate-5.4mg/dl; uric acid-5.0mg/dl. Corrected calcium-10.3mg/dl
- Anion gap-28.1
- Urinalysis-Proteinuria (+), haematuria-(++), no nitrites. No casts seen on urine microscopy.
- Ultrasound Scan: KIDNEYS-Right kidney measures 9.1 x 2.9 cm, left 9.1 x 3.2 cm. Increase in renal cortical parenchymal echogenicity seen in kidneys with loss of corticomedullary differentiation, no calculi seen. LIVER: mildly enlarged in size with diffuse increase in liver echogenicity suggestive of fatty liver. Portal and hepatic veins are normal in course and caliber.
- Liver Function Test-Total bilirubin-0.35mg/dl, direct bilirubin-0.1 mg/dl, AST-60 U/L, ALT-41 U/L, ALP- 86 U/L, albumin-1.5g/dl, total protein-7.7g/dl
- Glycated Haemoglobin-5.2%; fasting plasma glucose -5.3 mmol/L; 2 hours post prandial plasma glucose 5.8 mmol/L.

* FBC: Hb-7.2g/dl, haematocrit-22.2%, MCV-83.7fL (within normal range), MCHC-32.6g/dl, MCH-27.3pg, RCDW-16.1%, WBC-4,700/mm^3 (Neutrophils-68%, Eosinophils-2%, Lymphocytes-27%, Monocytes-3%).
* ESR-110mm (1^{st} hour Westergren)
* ABO blood group- O
* Rhesus positive
* Mantoux test-negative
* Stool M/C/S-normal GIT flora seen, no trophozoites, no red cells seen.
* HIV types I and II-positive
* HIV viral load-6300 copies/ml (patient on Abacavir (300mg bd)-Lamivudine (150mg bd)- Nevirapine which was changed to Tenofovir (300mg daily), Emtricitabine (200mg daily), efavirenz (600mg daily) on account of evidence of virologic failure.
* CD4 count-287 cells/Ul, absolute CD3+ Lymphocytes-1348 cells (716-2130 cells/uL), %CD3/CD8-60.7 (18-41%), %CD3/CD4-3.8 (26-48), absolute CD8 count-1004 (192-980), CD4/CD8 ratio-0.33 (0.57-2.03).
* HBsAg-negative.
* Anti-HCV-negative
* HCV RNA qualitative PCR-not detected
* CMV IgG - >20 U/ml (>1.2 immune).
* EBV (IgG) - >200 U/ml (>12 suggests EBV infection)
* Varicella Zoster IgG 12.7 IU/mL (=11 positive)
* VDRL test-non reactive
* Urine culture-no bacterial growth
* INR-1.21
* Chest X- ray did not show any abnormality.
* Doppler studies: Right common iliac, external iliac, common femoral, superficial femoral, profunda femoral and popliteal veins are patent, compressible and show spontaneous phasic flow with normal response to limb augmentation. The great saphenous vein was normal in course and caliber and was patent and compressible. Sapheno-femoral junction was competent.
* ECHO and ECG-normal findings.

DIAGNOSIS: HIV-RELATED NEPHROPATHY IN END-STAGE KIDNEY DISEASE

He had a left radiocephalic AV fistula created and commenced haemodialysis using a right temporary jugular catheter while awaiting maturity of the fistula. He was also commenced on Highly Active Antiretroviral therapy (HAART) combination of Zidovudine, Lamivudine and Nevirapine with twice weekly monitoring of his hematocrit. When anaemia persisted despite having 4,000i.u thrice weekly of erythropoietin and iron sucrose injections, Zidovudine was substituted with Abacavir for the patient. He failed to achieve virologic response to therapy and had his HAART regimen changed to Tenofovir, Emtricitabine andefavirenz. He was commenced on Hepatitis B vaccination schedule. He had twice weekly sessions of haemodialysis, oral Telmisartan (80mg daily) and Amlodipine (10mg daily), methyldopa (500mg thrice daily), Tab frusemide 80mg twice daily, Tab Brinerdin (one tablet daily), oral Co-trimoxazole, tab Atorvastatin 20mg daily, subcutaneous erythropoietin (4,000 i.u twice weekly) and Iron sucrose injection while awaiting renal transplantation, the prospective donor was the younger sister.

While being worked up for transplantation, he developed a right lobar pneumonia which was treated with IV Amoxicillin-clavulanic acid and oral Azithromycin and discharged after 2 weeks on admission. The patient asked to be referred to a hospital outside Nigeria where his transplant was to be done. His viral load at the time of leaving Nigeria was 1235 copies/µl and CD4 count was 224 cells/ µl.

After about 4 months on antiretrovirals, the viral load had reduced to 35copies/µl and CD4 count was at 319 cells/ µl and the patient was scheduled for renal transplant.

HLA Typing and Cross Matching

The patient and the donor both had O positive blood groups.

Table 1: HLA Typing Results

	A	B	DR	Others
SUA (patient)	A33, A30	B45, B42	DR13, DR14	Bw6, DRB3
AAU (Prospective donor)	A33, A74	B45, B57	DR13	Bw4, Bw6, DRB3

Lymphocyte cross match (NIH-CDC method) was negative with T and B cells at room temperature, 37^0C and 4^0C.

He had renal transplant done outside the country and returned back to Nigeria two months after the procedure to continue follow up in Nigeria. His immunosuppresants included Mycophenolate mofetil-1g twice daily, tab tacrolimus-2.5mg twice daily, tab prednisolone -10mg daily. One month after transplant, the patient developed high fasting and post prandial blood glucose (147mg/dl and 258mg/dl respectively) which is being managed with oral glibenclamide (5mg twice daily). His latest serum tacrolimus level is 6.2ng/ml. His serum creatinine 4 months after transplant has been between 76-108μmol/L, PCV-33 to 37% and fasting plasma glucose of 64 to 102mmol/L.

DISCUSSION

Renal diseases in HIV/AIDS patients could range from electrolyte abnormalities, acid-base dsorders, acute kidney injury to Chronic kidney disease including kidney damage caused by highly active anti-retroviral therapy (HAART) and antimicrobials used as prevention or treatment of opportunistic infections. These HIV-related nephropathy should be distinguished from HIV-associated nephropathy (HIVAN) which has unique, clinicopathologic and epidemiological features[1]. HIVAN predominantly affects Black African HIV patients, natural history improves with HAART, tends to present with oedema free heavy proteinuria with normal or large echogenic kidneys, normotension and CD4 count usually less than 200 cells/μL[1]. The pathologic features of HIVAN include collapsing focal segmental glomerulosclerosis (collapsing variant), microcystic dilatation of tubules and evidence of interstitial inflammation. The patient presented in this report does not appear to have HIVAN. Though he is Black, he had hypertension, relatively reduced kidney sizes bilaterally and his renal function did not improve with HAART. He also had developed kidney failure before commencing HAART suggesting HAART was not the cause of his kidney failure.

About 2 decades ago, most centers, even in the developed world, would not consider performing renal transplant on an HIV infected individual who does not have any other contraindication to the procedure[2]. The few centers that considered giving HIV infected patients a donor kidney did very few of this procedure. By 2002, an analysis of the US Renal Data Systems showed only 0.05% of the patients with end-stage renal disease (ESRD) starting on renal replacement therapy in the US being HIV positive at the point of transplantation[3]. The main factor militating against transplanting the HIV-positive was the perspective of waste of scarce donor kidneys due to the potential increase in morbidity and mortality of HIV-positive patients. For this reason, many consider an HIV-positive status a relative contraindication for renal transplant. HIV has been identified as rapidly becoming one of the commonest causes of ESRD in our environment[4] and documenting the comparable outcomes of HIV-infected renal ESRD patients after transplant will help local nephrologists make decisions about this modality of renal replacement therapy.

Studies in the USA and Europe suggest good graft outcomes in HIV-infected patients with 1 and 3-year graft survival rates of 90.4% and 73.7% in the USA[5], and 98% graft survival in 1 year in Europe[6]. This initial encouraging report has been dampened more recently by documentation of reinfection of grafts (especially podocytes and renal proximal tubular cells) by HIV which lead to higher rejection rates in these patients[7]. This has led to the invention of urine tests to check for HIV genetic materials that detect reinfection of the grafts[7] and may lead to interventions that will prevent rejection.

Electrolyte abnormalities and acid base disorders are frequent in HIV- related nephropathy[8]. In the pre-HAART era, many patients presented with hyponatremia[8] but this did not occur in this patient. He also did not have hypokalemia (usually from fluid and electrolyte depletion) or hyperkalemia (as a consequence of kidney failure). He appeared to have hypocalcemia but this must have been due to hypoalbuminemia as the calculated corrected calcium level was within normal limits. Medications like pentamidine, foscarnet and didanosine have been implicated as causes of hypocalcemia in HIV patients[8] but this patient was not on any of these drugs. He also had a high anion gap metabolic acidosis which may have been due to uraemia. Other causes of high anion gap acidosis include lactic acid accumulation during sepsis and long term use of Didanosine or Stavudine. He was not on these drugs.

This patient was using tacrolimus (a calcineurin inhibitor), Mycophenolate Mofetil and prednisolone. Tacrolimus has a number of dose-dependent adverse effects-hypertension, diabetes mellitus, nephrotoxicity, peripheral neuropathy, hirsutism, gingival hypertrophy and hyperlipidemia[9]. This patient already had elevated blood pressure and dyslipidemia before transplant and is currently on 4 anti-hypertensive medications and a statin. He has developed post-transplant diabetes which is being managed with glibenclamide. His serum creatinine is within normal limits and he has not developed hirsutism. He is also using mycophenolate mofetil (an antiproliferative agent) that suppresses B and T cell proliferation. The common adverse effects are nausea, diarrhea, leukopenia and thrombocytopenia[10]. After the initial diarrhea, our patient has not had a repeat episode. Full blood count during follow up has not suggested leukopenia or thrombocytopenia.

The patient now comes for monthly follow up at the renal clinic and has regular plasma glucose monitoring, monthly E/U/Cr, Full blood count and urinalysis and 3-monthly serum tacrolimus levels.

CONCLUSION

Improvement in medical care for HIV patients has made it possible to now consider renal transplantation for the increasing HIV positive ESRD patients. This successful case in Nigeria should be an encouragement to perform transplantation for HIV positive ESRD patients who can afford post-transplant care.

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