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Post Renal Transplant Segmental Allograft Infarction from Multiple Vessel Anastomosis

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INTRODUCTION

Segmental allograft infarction is a poorly characterized complication following renal transplantation. In contrast to total graft thrombosis, segmental infarction is uncommonly recognized. Focal perfusion defects following renal transplantation have been the subject of only a few previous reports. The incidence in these studies has varied from 4–42%, reflecting heterogeneity in the patient populations and small study number [1-3]. Although an association with rejection, prolonged ischemia, and multiple renal arteries is reported, the condition remains poorly defined. There are few case reports of delayed graft function as a result of vascular anastomosis in Nigeria [4].

This is a case of a 41-year-old Police Officer with multiple vessel anastomosis transplantation presenting with post-transplant segmental infarction.

CASE REPORT

He was a 41-year-old Police officer; known hypertensive patient diagnosed 7 years prior to presentation and was managed for end stage renal disease secondary to chronic glomerulonephritis with hypertensive heart disease. He had been on thrice weekly maintenance haemodialysis.

His genotype was AA, not a known diabetic, asthmatic or epileptic patient. He had no previous history of surgery and blood transfusion. He had no known drug allergy, occasionally used herbal remedies and was on antihypertensive medications. His medications included tab telmisartan 80mg daily, frusemide 40mg bd, nifedipine 20mg bd, methyldopa 500mg 8 hourly, metoprolol succinate 100mg daily, vitamin D 0.25mg bd, calcium carbonate 600mg bd, S/c erythropoietin 4,000 i.u twice weekly and I.V iron sucrose 100mg weekly.

He was married with two children. His father had history of hypertension. He stopped alcohol consumption 3months prior to presentation (usually take 2-3 bottles /week), and smoked cigarette (10 sticks per day for 10 years).

Physical examination revealed a young man who was not in respiratory distress but severely pale with periorbital and bilateral pedal oedema. Cardiovascular examination revealed a pulse rate of 88bpm and blood pressure of 160/100mmHg with a displaced apex beat and S1, S2 and S3 heart sounds. The abdomen was full, soft and moves with respiration. He had mild epigastric tenderness and tender hepatomegaly of about 4cm below the right costal margin. The spleen and kidneys were not palpably enlarged.

Investigation results included FBC: PCV - 13.6%, Hb - 4.2g/dl, WBC - $3.4X10^9$/L, neutrophil - 70%, lymphocyte - 21%, monocyte - 8%, eosinophil - 1%, platelet - $167X10^9$/L, ESR - 82mm/hr, E/U/Cr: Na - 135, K - 3.6, Cl - 101, HCO_3 - 22, Urea - 305.4mg/dl, Cr - 26.1mg/dl, eGFR - 2.45ml/min, serum albumin - 31g/L, total protein - 51g/L. Abdominal ultrasound showed bilaterally shrunken kidneys (right kidney measured 7.5 by 3.0cm, and left kidney measured 7.3 by 3.0cm) with loss of

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corticomedullary differentiation. Echocardiography showed concentric left ventricular hypertrophy, good global systolic function. There was no regional wall motion abnormality and dilated left atrial size, while the right atrium and ventricle was normal. There was no obvious intra-cardiac clot or vegetation seen. Trace circumferential pericardial effusion was seen, with intact inter-atrial and interventricular septum, ejection fraction (EF%) was 55%. HIV, HBV, HCV screening were all negative. Positive EBV-IgG, and EBV NA IgG, with positive CMV IgG. Urinalysis showed pH - 5, protein was 3+, and others were normal.

He was enrolled into the Renal Transplant programme. His work up for surgery included HLA typing which was a complete match (0/6 mismatch), while complement mediated cytotoxicity assay with dithiothreitol (DTT) treatment was negative for T and B cells cross match at 4^0C and room temperature and luminex assay for donor specific antibody was negative. Both donor and recipient were blood group B. Donor renal CT angiogram revealed multiple renal arteries, as shown in figure 1.

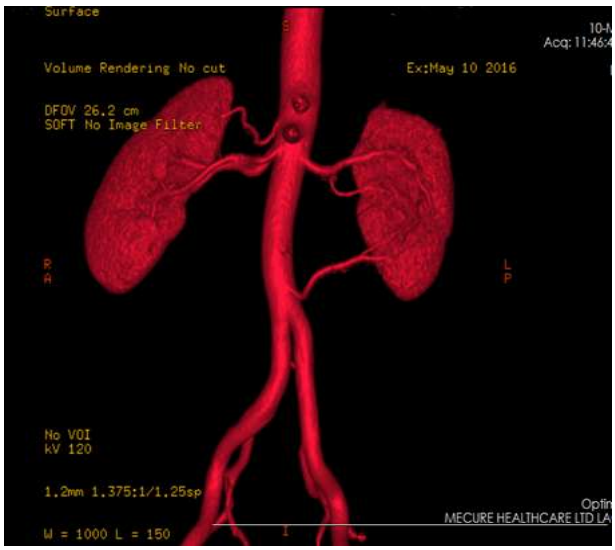

Figure 1: *showing donor CT angiogram with multiple vessels in both kidneys*

He had renal transplant done with living related donor (elder brother) 4 years after the diagnosis of end stage renal disease. He had induction therapy intra-operative and 4th day post-op with I.V basiliximab (20mg) and other immunosuppressant medications are mycophenolatemofetil (myfortic) 720mg night before surgery and oral cyclosporine (neoral) 5mg/kg PO stat and was continued on both as maintenance therapy.

Intra-operative note revealed that there were 3 vessels on the transplanted kidney (left kidney), and 2 of them (middle and lower pole artery) were anastomosed and joined to the right external iliac artery, with cold ischemic time of about 45minutes.

However, he did not achieve adequate renal function post-op. Urinary output immediate post op was 60mls per hour, but gradually reduced to 45mls per hour from 3rd day post op and remained at that level until discharge. His serum creatinine ranged between 2.83 - 4.2mg/dl and urea ranged 106 – 120mg/dl, PCV ranged between 22.7 – 24.4%, no evidence of sepsis WBC count ranged from 6.7 – 10.1 × 10^9/l. Cyclosporin assay (C_2) done 3rd day post op was 1144ng/ml (with reference range post-transplant at 11-month1700ng/ml).

Furthermore, post-transplant renal ultrasound scan revealed anechoic area surrounding the upper pole of the kidney, with a depth of 1.37cm, and no segmental blood flow to the upper pole of the transplant kidney on colour Doppler scan, but no evidence of thrombosis within the arterial and venous system, peak systolic velocity (PSV) was 27.54cm/s and end-diastolic velocity (EDV) was 11.39cm/s, with resistivity index (RI) of 0.59, images is as shown in figure 2. Diagnosis of early graft loss secondary to post renal transplant segmental infarction and possibility of acute allograft rejection was made.

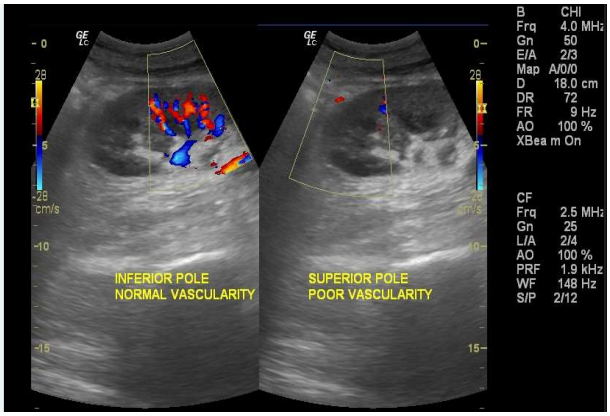

Figure 2: *showing Doppler ultrasound scan with reduce perfusion of the superior pole.*

Patient was discharged 20th day post-op, on oral cyclosporine 200mg 12hourly, mycophenolatemofetil (myfortic) 720mg 12hourly,

ranitidine 150mg bd, isoniazid 300mg daily, pyridoxine 25mg daily, labetalol 200mg tds, methyldopa 500mg tds, nifedipine 40mg bd, nystatin drops 2mls tds, valganiclovir 450mg twice weekly, cotrimoxazole 960mg thrice weekly, I.V iron sucrose 100mg weekly, s/c erythropoietin 4000 i.u thrice weekly.

There was no improvement in patient's renal function 3 months after discharge with creatinine range from 3.8 – 7mg/dl, and K^+ 5.8 – 6, and he became anuric. Repeat abdomino-pelvic scan 10 weeks post renal transplant was still in keeping with upper pole infarct, and lymphocele, with PSV = 97.05cm/s and EDV = 10.4cm/s and RI = 0.89. He was thereafter recommenced on thrice weekly maintenance haemodialysis 3 months after discharge. He developed depression after recommencement of dialysis and died about 1 year after transplant.

Table 1: HLA cross-match of both recipient and donor

NAMES	A	B	DRB1	DRB3/DRB4/ DRB5
Patient	30, 66	15, 51	03, 12	DRB3
Donor	30, 66	15, 51	03, 12	DRB3

DISCUSSION

Segmental infarction can result in delayed graft function and acute allograft rejection. Graft tubular damage [5,6] and prolonged ischemic time and multiple vessel anastomosis [6 – 8] have been identified as the risk factors for total graft thrombosis. Ischemia induces endothelial thrombogenicity, and graft oedema and diminished perfusion were postulated as the underlying mechanism [7,8]. The index patient had multiple renal arteries with the one pole artery severed, and lower pole arteries anastomosed, which were implanted into the external iliac artery. In addition, high renovascular resistance and a reduction in renal blood flow have been demonstrated in grafts with tubular damage [9], which was the case in this patient with a resistivity index of 0.89, and reduced blood flow to the upper pole. Other risk factors for graft infarcts include cyclosporine toxicity which presents with late onset infarct in an optimal functioning graft, high levels of donor specific antibodies, hypercoagulable state from Factor V leiden mutation, protein C or S deficiency and lupus anticoagulants which all increase the risk of thrombosis. However, this was not evident in this patient, since C_2 assay was below target and ultrasound scan ruled out presences of vascular thrombosis.

However, studies have shown that C_2 level assay above 1500ng/ml in the first 2-month post op among transplant patients who had basiliximab, prednisolone and cyclosporine was associated with lowest risk of rejection [10,11]. Therefore, low C_2 level in this patient could have predisposed him to the development of acute graft rejection. Although, acute graft rejection in this patient, should have been confirmed from renal biopsy if it was done. Renal biopsy was not done due to lack of facility and expertise to analyze the kidney specimen. Furthermore, this patient developed lymphocele and early graft loss, which are features that support acute graft rejection. However, lack of strong evidence for pre-sensitization (i.e no previous blood transfusion or transplant, no HLA mismatch or ABO incompatibility, and absences of donor specific antibody in pre-op evaluation, except for African race) did not support acute rejection. However as stated previously, absence of renal biopsy was a strong challenge in making the diagnosis of acute allograft rejection.

Where segmental infarction has occurred, conservative treatment is indicated in most patients, particularly if the area involved is small, or diagnosis has been delayed. Contributory aetiological factors should be sought for and treatment optimized in order to prevent more extensive thrombosis. Appropriate intervention should include maintenance of adequate renal perfusion and effective immunosuppression. Cyclosporin should be avoided where possible, especially in the setting of delayed graft function, due to the vasoconstrictive effect of afferent arterioles by cyclosporine, which will further impair renal perfusion.

Indications for operative intervention should consider the interval since onset, infarct size, and arterial anatomy. For successful thrombectomy, early diagnosis is crucial, but in practice, this is rarely obtained. Infarction of a single segment should be well tolerated, and the surgery should be reserved for the graft with extensive lesions, where unacceptable loss of graft function is expected. The potential benefit must also be weighed against the associated risks. Re-exploration of a solitary renal artery may jeopardize the remaining viable area,

risking total loss of the kidney. The index patient already had extended infarct in the upper half of the transplanted kidney following multiple vessel anastomosis. Therefore, only conservative management could be done to preserve the remaining functioning segment of the kidney. However, this did not last for more than 3 months before the patient had to recommence haemodialysis. Onset of depression after recommencement of dialysis also contributed to the early demise of this patient.

In conclusion, post renal transplant segmental infarction is a risk factor for early graft loss. Also, multiple vessel anastomosis increases the risk for its development, furthermore, segmental infarction typically occurs in the early postoperative and prompt diagnosis may be difficult. Therefore, avoidance of multiple vascular anastomosis may reduce the occurrence of this condition.

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