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# Post-kidney transplant Lupus Nephritis associated with chronic antibody-mediated and acute cellular rejection- a case report and review of the literature

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**Abstract**

*The risk of recurrent lupus nephritis (RLN) in renal transplant recipients with systemic lupus erythematosus (SLE) used to be rare (1-4%). The interval from transplantation to recurrence of LN has been reported to vary from five days to eight years. Although RLN significantly increases the risk for graft failure, it contributes far less than rejection to its overall incidence. We report rare case of a 32-year-old female with a history of lupus nephritis who underwent a kidney transplantation 2016 from LURD in China. She has stable graft function, during her regular follow up. She developed severe gastroenteritis. At that time her immunosuppression therapy doses were decreased (both MMF and TAC) and she developed acute graft dysfunction and graft biopsy revealed lupus nephritis Class 4, chronic active AMR and ACR Banff2A, which is successfully treated, as it is a very rare case in the literature review a unique treatment challenge. The main concern in these patients is management of post- transplant RLN associated with c ABMR and ACR. Several questions remain for these patients' following transplantation, including fear of LN recurrence when holding immunosuppression, and how to manage the disease, although additional studies are needed to establish the standard regiment of treatment for such cases.*

**Keywords:** Recurrent Lupus Nephritis (RLN), Systemic Lupus Erythematosus (SLE),kidney transplant, Graft Failure, Immunosuppression Therapy, Chronic Active Antibody-Mediated Rejection (AMR), Acute Cellular Rejection (ACR), and Banff Classification (A2).

## INTRODUCTION:

The reported rates of clinically evident recurrent lupus nephritis (LN) following kidney transplantation range between ( 2 - 11%). Patients who experience recurrent LN after transplantation typically show elevated serum creatinine levels beyond their normal baseline, variable levels of new or worsening proteinuria, and new-onset hematuria during routine screenings. These low rates of recurrent LNare believed to be due to reduced immunologic activity due to ongoing immunosuppression (1,2). Serologic markers such as low complement levels and elevated anti-double-stranded DNA (anti-dsDNA) antibody titers are unreliable in predicting recurrence (1). Additionally, serologic parameters and infrequent extrarenal SLE symptoms may not provide accurate insight into disease activity, and do not assist in forecasting recurrence in the transplanted kidney (3,4). The risk of graft loss due to recurrent LN remains low,

typically less than 2 to 4 percent throughout 5 to 10 years, according to most studies (5,6). Long-term outcomes for both the patient and graft remain poor. It has been reported that kidney transplant recipients (KTR) with chronic active antibody-mediated rejection (cAMR) have a graft half-life of just 12 months if left untreated (7). When treated with pulse steroids and intravenous immunoglobulins (IVIGs), the graft half-life improved to 24 months. Adding a single dose of rituximab to this regimen further enhanced graft survival, with 70% survival at 4 years (7,9). Acute rejection, when it occurs, can significantly impact graft survival (4,5), and should be considered a key possibility in cases of unexplained graft dysfunction in transplant recipients. The diagnostic criteria for T cell- mediated rejection have not changed significantly in recent years. These include lymphocytic infiltration of the tubules (tubulitis) and larger vessels (vasculitis), with the severity determined by the density of the lymphocytic infiltrate under high- powered microscopy. Treatment strategies differ between T cell-mediated rejection and antibody-mediated rejection, and the intensity of treatment generally corresponds to the severity of the diagnosed lesions. The prognosis for graft survival after treated acute rejection is dependent on the type and severity of the rejection (10). The co-occurrence of recurrent class IV lupus nephritis, chronic antibody-mediated rejection (cABMR), and acute cellular rejection (ACR) in this case raises the question of which condition occurs first, and whether one triggers the other. The purpose of this case report is to highlight the challenges in diagnosing and managing ofr recurrent lupus nephritis complicated by concurrent chronic antibody-mediated rejection (c AMR) and acute cellular rejection (ACR) after kidney transplantation, providing insights into treatment strategies and outcomes.

## METHODS:

## A CASE REPORT

### Case history:

**A** 32-year-old Saudi single female was diagnosed with SLE at the age of 13 years and she was on regular follow-up. Two years later when her kidney function started to deteriorate she was diagnosed with LN biopsy-proven class 4 and at that time she received immunosuppression treatment for lupus nephritis 5 years later from diagnosis of lupus nephritis, kidney function worsened approaching the dialysis she continued on RRT for four years with No history of Blood transfusion. She underwent a LURD (first ) kidney transplant in China in 2016, regarding pre-transplant data unavailable such as donor and pre and post-kidney transplant courses operation, but when She was on regular follow-up in the post- kidney transplant clinic in KSMC had stable graft function with baseline serum creatinine 120 She is on triple immunosuppression therapy include tacrolimus 1mg /0.5 mg MMF 1g twice/day, prednisone 5 mg once per day. On 1st October/23, She developed severe non-infectious gastroenteritis and was admitted to the ICU (hypovolemic shock) in another hospital for 3 days at that time MMF was held for 3 days and then resumed mycophenolate sodium with a dose of 360 mg twice/day. and tacrolimus doses decreased to 0.5 mg twice/day and prednisone dose 5 mg once/day and a few days later discharged. Admitted ON 30/October from the kidney transplant clinic in KSMC as creatinine trended up (255) and she developed nephrotic range proteinuria in the urine at tacrolimus level Below therapeutic target was 3ug/L (reference 5---10 ug/L). Upon admission vitals signs were stable and clinical examination was unremarkable, Laboratory investigation included the urinary

sediment analysis revealed the presence of proteins (3þ) and red blood cells (3þ), with 25-- 50 leukocytes and red blood cells per field. Urine culture was negative for bacteria, lupus activity marker including anti-DsDNA was negative but complement completely depletedC4 was 0.132 (reference 015 ----0.57 gm/dl), and C3 was 0,69 (reference range was0.82--- 1.93 g/L). Albumin /creatine ratio of more than 400 mg/mmol (severe proteinuria), virology screening was negative(BKV and CMV PCR were negative), as the patient donor had unknown data so HLA antibodies reveal multiple antibodies.
Types see table 1.

US and Doppler kidney transplants were unremarkable, on day 3 from admission kidney biopsy was performed that revealed lupus nephritis class 4 and immunofluorescence, regarding the glomeruli revealed granular mesangial and capillary wall staining with antisera- specific for IgA(1+), IgG (1+), IgM (1+), C3 (1+), C1q (1+), and Kappa (1+) and Lambda (1+) light chains and electron- microscopic examination revealed multiple subendothelial and mesangial electron- showed dense deposits. This finding is typical of those found in lupus nephritis class 4, confirming the findings of immunofluorescence. kidney biopsy also reveals c ABMR as microscopic examination of elven glomeruli shows severe glomerulitis, moderate neutrophil infiltration, and, associated with diffuse thickening of the capillary walls with segmental double contour. There is mild interstitial fibrosis and tubular atrophy (5% of the cortical tissue). Mild to moderate peritubular capillaries contain neutrophils. Confirming of immunofluorescence Present of the component of complement C4d diffusely positive in peritubular capillaries and SV40 Is negative in tubular epithelium cells excluding BKV nephritis In addition to Acute cellular rejection Banff2A is evidenced by the presence of interstitial edema and severe interstitial mononuclear inflammatory cell infiltrate admixed with abundant plasma cell and few eosinophils associated with foci of mild to moderate tubulitis and Arteries show mild intimal arteritis and mild intimal fibroelastosis. (see Table 1 and Figures 1-5).

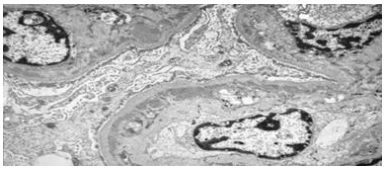

**Figure 1: Electron Microscopic examination: showed multiple subendothelial and Mesangial dense deposits.**

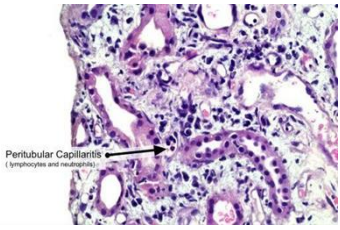


**Figure 2: EM examination: peritubular capillaritis.**

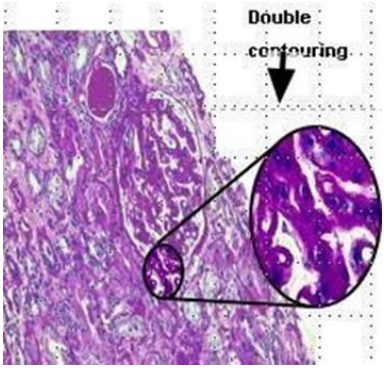


**Figure 3: Microscopic examination used Trichrome, and Jones Silver stains: examination**: **Diffuse thickening of the glomerular capillary walls**


**Figure 4: immunofluorescence shows the complement component C4d is diffusely positive in peritubular capillaries**

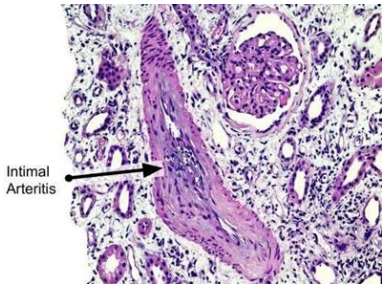


**Figure 5: Microscopic examination examined with H&E, PAS, Trichrome, and Jones: intimal Arteritis.**

On the second day from admission, immunosuppressive induction therapy for LN and the possible presence of acute rejection was instituted with methylprednisolone (.5 g for 5 d)) then prednisolone taper to 5 mg once/day. The immunosuppressive maintenance treatment for LN was the same as that used for the KTX. On the rd, 5th day after the biopsy report, one dose of Rituximab 375 mg/m2 and r ATG1.5mg/kg three doses And IVIg 2 doses every two weeks, after a few days later discharge and has close regular follow up in Kidney transplant clinic, creatinine improved from 255 to 180 umol/L and A/Creatinine ratio from 400 to 207mmol/L. Current immunosuppression therapy is augmented as tacrolimus (trough level 6ng/dl)mycophenolate sodium 720 mg PO twice/day and prednisolone 5 mg once/day in addition to valganciclovir 450mg dialy and sulphamethoxazole 480mg dialy for3 months .hower was challenge case as in the literature few cases report combined recurrent lupus nephritis, ACRbanff2A, and c

ABMR , presence of Lower chronicity index and timing of treatment leading to favorable outcome.

## DISCUSSION:

Recurrent lupus nephritis after kidney transplantation is a significant challenge in the presence of c ABMR, and acute cellular rejection Banff 2A, with implications for graft survival and patient outcomes.

**Table 1:HLA Antibody tests using Luminex single bead antigen HLA Antibody screening test.**

| HLA antibody Identification | |
|---|---|
| Investigatio n | Result |
| HLA PRA1SA Luminex ID | *A1,A3 -* A11,24,A25,A26,A29,A30, A31,A32,A33,A34,A36,A43,A66,A68, A69,A74,A80,B46,B57,B58,B73,Cw1,Cw1 4 |
| HLA PRA11SA Luminex ID | DQ2,DQ4,DQ5,DQ6,DQ7,DQ8,DQ9,DR1 ,DR9,DR12,DR15,DR16,DR51,DR52,DR10 3 |
| HLA antibody screen | |
| Investigatio n | Result |
| HLA PRA 1 screen- Luminex | Positive |
| HLA PRA 11 screen-Luminex | Positive |

We discuss a patient who developed recurrent lupus nephritis post-transplant, characterized by both antibody-mediated rejection (ABMR) and acute cellular rejection. The patient presented with elevated serum creatinine levels and nephrotic range proteinuria. A kidney biopsy revealed features consistent with recurrent lupus nephritis, along with signs of cABMR and acute cellular rejection Banff 2A. The presence of histological findings in the kidney biopsy coped class 4 and LN further corroborated the diagnosis of lupus nephritis. Lupus nephritis is characterized by the deposition of immune complexes and subsequent inflammation in the renal interstitial. Post-transplant, the risk of recurrence is influenced by several factors, including the underlying disease, immunosuppressive regimen, and genetic predisposition. In this case, the presence of both cABMR and acute cellular rejection indicates a complex interplay between all immunity and autoimmunity.

Chronic Antibody-Mediated Rejection (ABMR) occurs when donor-specific antibodies (DSA) mediate damage to the graft, leading to chronic endothelial injuryand inflammation. In our case, the presence of multiple antibodies against donor HLA antigens was confirmed through serological tests. Presence of pericapillaritis and IF examination showed diffuse complement C4d in PT. Acute Cellular Rejection This type of rejection is T-cell mediated, characterized by infiltrates of lymphocytesin the graft. The biopsy findings revealed asignificant lymphocytic infiltrate, supporting the diagnosis of acute cellular rejection The management of recurrent lupus nephritis post-transplant involves balancing immunosuppressive therapy to control both autoimmune activity and rejection. In this case, the patient was treated with high-dose corticosteroids ATG, Rituximab, and IV immunoglobulin.

Additional immunosuppressive agents, such as mycophenolate sodium and tacrolimus, were utilized in therapy as maintains to control cellular rejection and lupus activity after initiating aggressive immunosuppressive therapy, the patient's renal

function gradually improved, with a significant decrease in proteinuria and stabilization of creatinine levels. Long- term follow-up will be necessary to monitor for further recurrence of lupus nephritis and potential graft dysfunction. This case highlights the complexities of managing recurrent lupus nephritis in the context of kidney transplantation, especially when both chronic ABMR and acute cellular rejection are present. A tailored immunosuppressive strategy is crucial to optimize outcomes in such patients.

## CONCLUSION & RECOMMENDATION

Severe RLN is uncommon in recipients of a kidney allograft, but black recipients, female recipients, and younger recipients are at increased risk. Although RLN significantly increases the risk for graft failure, the presence of acute cellular rejection, and c ABMR it contributes far more to the overall incidence of graft loss. No definite recommendation exists regarding optimal treatment of recurrent LN combined with ACR and cABMR post- renal transplantation. Additional studies are needed to evaluate the relation of holding MMF and RLN, and for treatment RLN, c ABMR and ACR.

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