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CASE OF THE WEEK-4

CLINICAL HISTORY:

A 39 year old lady, received live related renal transplantation (basic disease SLE -nephritis) 18 months back. Presented with acute deterioration of renal functions and pedal edema; serum creatinine rose from 106 u mol/l (1.2 mg%) to 185.6 u mol/l (2.1 mg%), over one week. There was no history of skin rashes, joint pains,fever, dirrhoea or drug non-compliance . She was on triple immunosuppression (Tacrolimus, MMF and steroids) with satisfactory calcineurin inhibitor levels throughout post-transplant period.

EXAMINATION:

Pallor + , pedal edema +,BP: 140/88 mmHg (at presentation)

INVESTIGATIONS:

Urine Albumin 3+,RBC: 8-10/hpf, Pus cells 8-10/hpf, Casts: Granular casts and occasional RBC casts +.

Urea: 74 mg% (26.4 ¤ mol/L), Creatinine: 2.1 mg% (185.6 ¤ mol/L)

HIV/HBsAg/HCV- negative, ANA- positive

Total protein/Albumin/Glob: 5.0/2.8/2.2 g/L

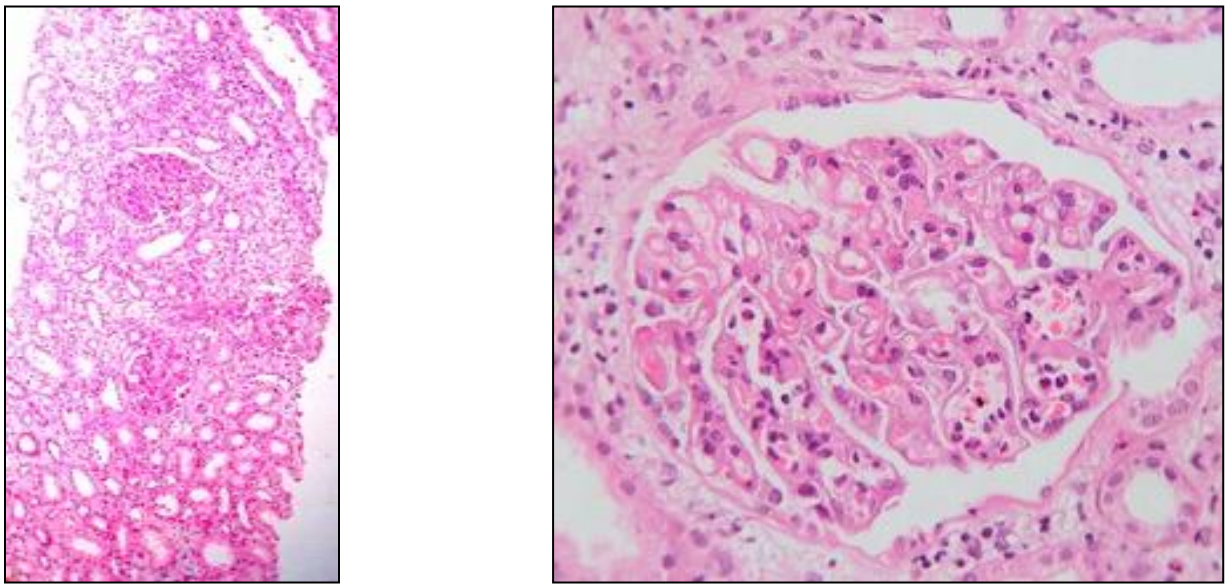
Complement: C3: 62 mg% (0.62g/L), C4: 19 mg% (0.19 g/L)

USG abdomen: Normal sized graft with raised cortical echogenicity. Doppler studies- normal

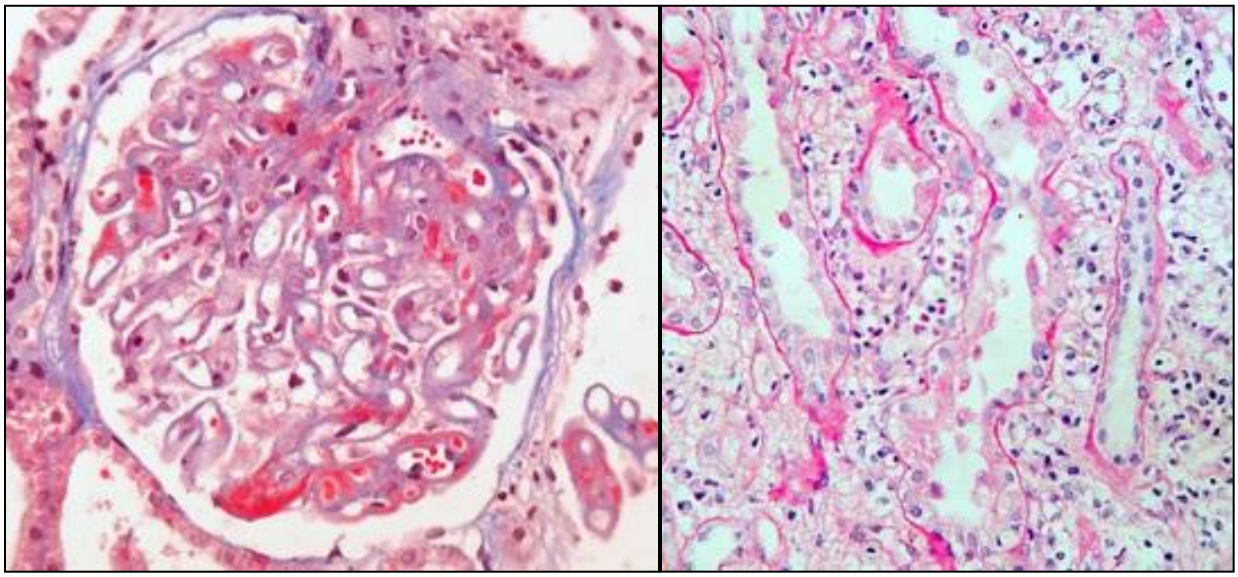
Hemoglobin: 8.2 g% , TLC:16,000/mm3, DLC: P75 L22 E1 M2, Platelets:300 X 10 3/mm3 (300 x 10 9/L)

A renal allograft biopsy suspecting recurrence of native renal disease (lupus nephritis) was performed.

MICROSCOPY:



Low power image (left) shows cellular glomerular tufts and evidence of focal acute tubular injury, interstitial inflammation and edema . Higher magnification image (right panel)shows a glomerulus with thickened capillary basment membranes and endocapillary cellularity involving almost 50% of the tuft.



Masson's trichrome stain reveals few subendothelial fuchsinophilic capillary wall deposits. PAS stained section (right image) shows evidence of peritubular capillaritis with margination of polymorphs and few mononuclear cells.

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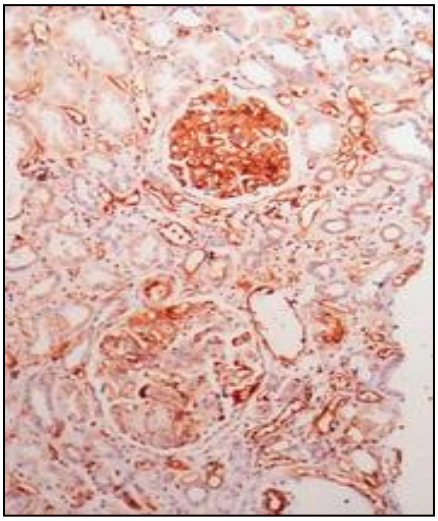
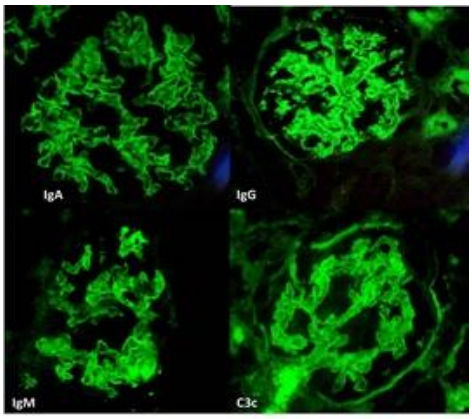
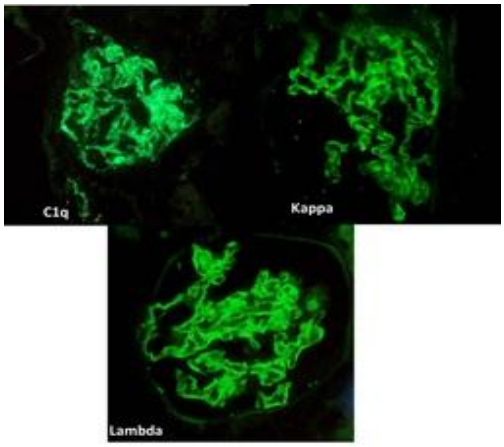


Stain for C4d (by immunohistochemistry) shows diffuse positivity (C4d3) along the peritubular (and glomerular) capillaries





Direct Immunofluoroscence studies show “full house” capillary wall granular and mesangial staining (IgA,IgG,IgM,C3c,C1q, and kappa & lambda light chains)

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KEY FINDINGS

- Diffuse proliferative glomerulonephritis with Membranous thickening of capillaries
- "Full house" glomerular immunopositivity in DIF studies (immunoglobulins, complement components and light chains).
- Features of peritubular capillaritis, glomerulitis and diffuse staining for C4d along the glomerular capillaries (by IHC technique)

DIAGNOSTIC CONSIDERATIONS:

- Recurrence of lupus nephritis in the renal allograft (Class V and Class IV lesions)
- ? co-existing acute antibody mediated (humoral) rejection

FOLLOW UP:

As C4d staining and glomerulitis can be a feature of proliferative lupus nephritis per se (see discussion), evaluation of circulating Donor specific antibody (DSA) was performed which revealed high titers, confirming the presence of a coexisting AMR.

FINAL DIAGNOSIS:

Recurrent lupus nephritis (ISN/RPS class IV G-A and Class V lesions) and co existing acute antibody mediated rejection (AMR).

TREATMENT

After initial treatment with intravenous pulse steroids, patient was offered plasmapheresis, and achieved partial remission of proteinuria (24 hour urinary protein 1.1 gms) and serum creatinine settled to 1.3 mg% (114.9 ¤ mol/L), three months after the onset of current episode.

DISCUSSION:

The reported incidence of ESRD in patients with SLE ranges from 5-22% in various series [1-2]. The incidence of recurrent lupus nephritis (RLN) after transplantation has ranged from 0 to 44% [3-11]. Predictably, the use of light microscopy alone in the examination of allograft biopsy specimens would yield a low rate of RLN diagnosis. Various studies on outcome of patients with RLN have reported conflicting outcomes, perhaps reflecting the demographic and study population characteristics. [6,8,9-11].Goral et. al [6] reported that while RLN was not uncommon, it had a milder clinical course and graft loss was rare. Burgos et. al [11] suggested that RLN was relatively infrequent and recurrent lesions tended to be predominantly mesangial compared to proliferative and Membranous lesions in the native

kidneys. On the other hand, Contreras et. al. [9] found that recipients with RLN had a significantly higher RR for allograft failure compared with control subjects and only 17% of the recipients had WHO class II lesions, whereas most of the recipients had aggressive histologic forms of lupus nephritis(58% demonstrating WHO class IV and 25% demonstrating WHO class V).

C4d staining along the peritubular capillaries in renal allografts has been considered a hallmark of antibody mediated rejection (AMR) [13-14]. In recent years however use of C4d as a biomarker of disease activity in patients with SLE has been investigated. [15-17]. Staining of glomerular and peritubular capillaries in biopsies has been described [18-19], and may confound with detection of a co-existing AMR in cases with RLN. Though differences in staining pattern of C4d deposition associated with AMR and lupus nephritis have been emphasized [18], this distinction may not be easy, particularly in biopsies stained for C4d by immunohistochemistry technique, where interpretation of granular versus linear pattern of deposition may be difficult to distinguish.

Learning Points:

- **Peritubular capillary C4d staining can be seen in biopsies with lupus nephritis.**
- **In renal allograft biopsies from patients with ESRD secondary to SLE, a careful interpretation is warranted as lesions of recurrent proliferative Lupus nephritis and C4d staining along peritubular capillaries overlap with AMR.**
- **A careful differentiation of these entities is essential from treatment point of view.**
- **Evaluation of Donor Specific antibodies should be performed in such cases to reliably diagnose a co-existing AMR.**

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