

PDUS was significantly correlated with higher co-morbidities ($\rho = -0.48$, $P = 0.04$).

There are MSUS studies reporting early changes or baseline PDUS predicting a variety of RA outcome measures. We cite two studies that use baseline PDUS to predict other 1 year outcomes. Ellegaard *et al.* [7] demonstrated that MSUS colour fraction quantification of the wrist in 109 RA patients starting a TNF inhibitor predicted which patients would remain on therapy in 1 year ($P = 0.02$). Kamishima *et al.* [8] evaluated 29 RA patients starting i.v. tocilizumab and performed MSUS at baseline, 2 and 5 months. The authors reported that the quantitative PDUS may be predictive of structural damage progression at 1 year.

There are limitations to our study. This is a small open-label study, and we performed *post hoc* analyses to determine whether baseline PDUS can predict the 12 month response to therapy. As a result of the limited sample size, we were unable to perform multivariate regression models with more than two variables. Yet, in this small cohort, we were able to demonstrate a significant difference between patients with baseline PDUS >5 and <5 .

In conclusion, we found that those patients with severe disease activity had a wide range of baseline PDUS and that patients with high baseline PDUS had a more robust response to therapy. Perhaps high PDUS may identify patients with an RA phenotype more amenable to biologic intervention. In addition, patients with low baseline PDUS and high DAS28/CDAI may have other factors (co-morbidities, obesity, OA, fibromyalgia, etc.) besides RA disease activity that resulted in their high scores. We posit that PDUS rather than DAS28 identifies those patients with modifiable disease activity. Thus, PDUS assessment may aid in treatment decisions concerning whether escalation or switching therapy is needed in RA patients with multiple co-morbidities. Additional studies are required to validate these findings.

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Ecuzimab as rescue therapy in severe resistant lupus nephritis

Rheumatology key message

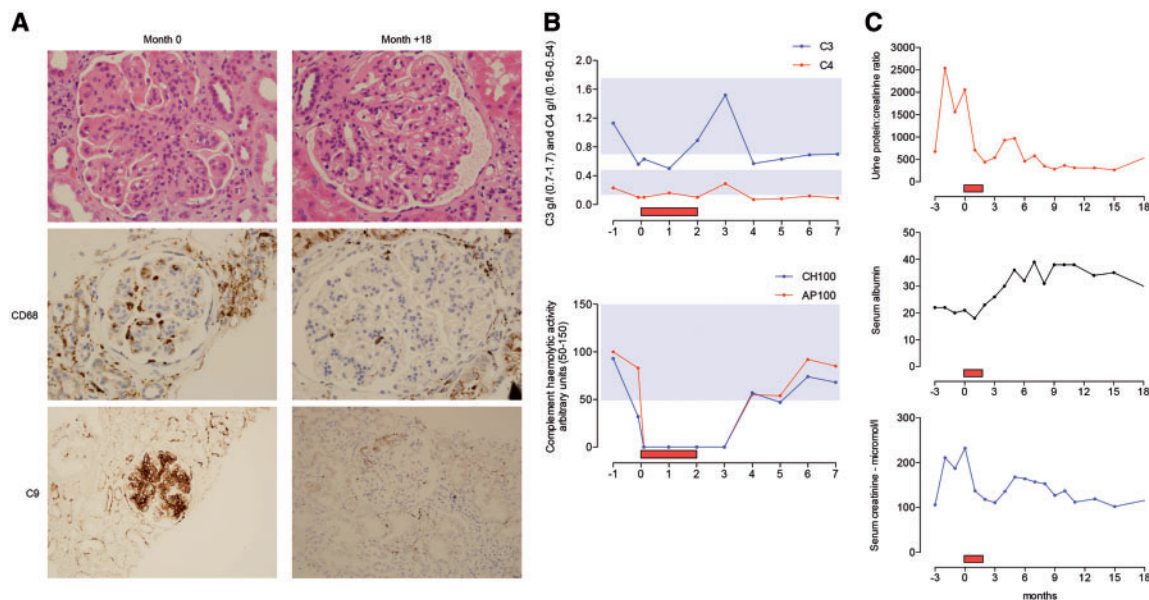
- Lupus nephritis may respond to complement C5 inhibition.

SIR, LN is a serious complication of SLE that can be refractory to existing immunosuppressive treatment. We present the clinical course of a patient with refractory LN who was treated with ecuzimab, a monoclonal anti-

complement C5 antibody therapy [1]. A Caucasian female with SLE first presented with immune thrombocytopenic purpura at the age of 14 years. Three years later she developed polyarthralgia, oral ulcerations, RP, alopecia and pleurisy. Anti-nuclear and anti-dsDNA antibodies were positive; C3 and C4 levels were reduced; antibodies to extractable nuclear antigens and cardiolipin and LA were all negative. The urine protein:creatinine ratio was 14 (normal <20 mg/mmol), serum creatinine 75 $\mu\text{mol/l}$ (normal range 60–110) and albumin 36 g/l (normal range 33–47). Disease control was achieved with prednisolone and HCQ, but 2 years later she developed proteinuria (protein:creatinine ratio 1123, albumin 27 g/l, creatinine 110 $\mu\text{mol/l}$) and renal biopsy showed florid diffuse proliferative GN, International Society of Nephrology/Renal Pathology Society class IV-G (A) LN, with active lesions in 10/10 glomeruli and crescents in 5/10 glomeruli. She was treated with six i.v. 500-mg pulses of CYC, rituximab infusions (two 1-g infusions 14 days apart) and then maintenance therapy with MMF. At 12 months she had partial improvement (protein:creatinine ratio 240, albumin 29 g/l, creatinine 92 $\mu\text{mol/l}$), but at 15 months renal function deteriorated (protein:creatinine ratio 761, albumin 26 g/l, creatinine 93 $\mu\text{mol/l}$) and repeat renal biopsy showed ongoing active class IV LN. A further cycle of CYC and rituximab was administered followed by tacrolimus monotherapy. Over the course of the next 22 months, impaired renal function persisted. A third renal biopsy, taken

due to a further deterioration in renal function (protein:creatinine ratio 1082, albumin 27 g/l, creatinine 108 $\mu\text{mol/l}$), revealed diffuse proliferative LN class IV-G (A/C). MMF was added, but renal function continued to decline (protein:creatinine ratio 2540, albumin 22 g/l, creatinine 211 $\mu\text{mol/l}$) and a fourth renal biopsy, 4 years after the first renal biopsy, showed class IV-G (A/C) LN with active lesions in 20 out of 36 glomeruli, chronic lesions in 7 out of 36 glomeruli, acute tubular damage with foci of lymphocytic tubulitis and marked chronic inflammatory interstitial infiltrate. There was granular mesangial and capillary wall staining for C9 consistent with activation of the complement terminal pathway (Fig. 1A shows a representative glomerulus with marked lobulation, mesangial proliferation, capillary wall thickening and prominent endocapillary hypercellularity with occlusion of capillary lumens. CD68 staining shows several macrophages in the glomerulus). In view of her previous poor response to CYC, rituximab, MMF and tacrolimus, together with biopsy-proven evidence of ongoing glomerular inflammation and complement C5 activation, it was decided to administer a single i.v. methylprednisolone 500-mg infusion, together with eculizumab. She received four 1200-mg weekly eculizumab infusions followed by two 1200-mg fortnightly infusions. Complement haemolytic activity remained undetectable following the first infusion and for 1 month after the sixth infusion (Fig. 1B). Antibiotic prophylaxis was instigated throughout the eculizumab treatment

Fig. 1 Renal histology, complement profile and renal function during eculizumab treatment



(A) Glomerular images from renal biopsies immediately before and 18 months after eculizumab. Immunoperoxidase staining for CD68 (middle panels) and complement C9 (lower panels) using PGM1 and NCL-CCC9 antibodies, respectively. Upper and middle panels are $\times 40$ original magnification. Lower panel is $\times 20$ original magnification. **(B)** Serum C3, C4, total (CH100) and alternative pathway (AP100) haemolytic activity are shown 1 month prior to and for 7 months following eculizumab. Shaded areas denote normal ranges. **(C)** Serum creatinine ($\mu\text{mol/l}$), serum albumin (g/l) and urine protein:creatinine ratio (mg/mmol) are shown 3 months prior to and for 18 months following eculizumab. Red box denotes the 2-month eculizumab treatment period.

period. During and following eculizumab treatment, there was a sustained and rapid improvement in her renal function (Fig. 1C). Following eculizumab therapy she was recommenced on MMF. Renal biopsy, 18 months following eculizumab treatment showed mesangial proliferation, capillary wall thickening and segmental glomerulosclerosis, but no endocapillary hypercellularity or necrosis, and C9 staining was almost undetectable. Consistent with this, staining for CD68, a macrophage marker, was markedly reduced (Fig. 1A).

The current management of LN includes corticosteroids and cytotoxic agents such as CYC, MMF and AZA, but there is increasing use of biologic therapy, most commonly rituximab [2]. Complement activation is common in lupus tissue injury [3], and blockade of complement C5 has been shown to ameliorate murine SLE [4]. Eculizumab is a recombinant fully humanized IgG2/IgG4 monoclonal antibody that binds to complement component C5 and prevents the cleavage of C5 and therefore the formation of the anaphylatoxin C5a and the membrane attack complex (C5b-9) [1]. Eculizumab has efficacy in the prevention of red cell lysis in paroxysmal nocturnal haemoglobinuria [1] and in the treatment of atypical haemolytic uraemic syndrome [5]. There have been reports of its efficacy in C3 glomerulopathy [6], but only one report of efficacy in LN [7]. However, in this case, the renal pathology was thrombotic microangiopathy (TMA), not GN. Efficacy has also been reported in TMA in the setting of IgA nephropathy [8]. To our knowledge, there are no reports of the use of eculizumab to treat non-TMA glomerular lesions in SLE. Our case indicates that, in the right setting, eculizumab may have therapeutic utility in LN. In a complex condition like LN, patient stratification will be critical for rigorously evaluating the potential benefits of eculizumab. Two criteria, which are not mutually exclusive, would include TMA and reversible GN in which there is evidence of C5 activation within the kidney.

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Adalimumab-induced remission of anterior scleritis: a very rare late manifestation of Takayasu arteritis

Rheumatology key message

- Refractory scleritis, a rare complication of Takayasu arteritis, can be controlled with anti-TNF- α therapy.

SIR, Takayasu arteritis (TA) is a rare idiopathic granulomatous vasculitis that affects the aorta, its major branches and the pulmonary arteries. Although TA is associated with Japanese ophthalmologist Mikito Takayasu, primary retinopathy is only seen in one-third of patients [1, 2]. Scleral involvement is extremely rare, reported in only three previous cases and as a presenting feature [3–5]. We report the case of a patient with a 10 year history of