

mib was added to thalidomide and dexamethasone because of worsening renal insufficiency. Serial SUPCR demonstrated that the proteinuria decreased after each cycle of bortezomib followed by a rebound during each 10-day rest period. The changes in the SUPCR grossly paralleled changes in SFLC levels. A bone marrow examination showed extensive replacement by multiple myeloma, confirming treatment resistance.

Patient 4 had three consecutive SFLCA in which the free kappa light-chain levels were mildly increased, ranging from 14.2 to 15.3 mg/dL (nl <1.94 mg/dL). During this same interval, two SUPCR samples were dramatically elevated at 5.2 and 6.0 mg/mg (nl <0.3 mg/mg). UPEP of the spot urine sample showed that 79% of the proteinuria was monoclonal. As the monoclonal proteinuria was disproportionately higher than the mildly abnormal SFLCA results, the SFLCA was repeated utilizing higher dilutions, and the correct SFLC concentration was found to be ~10-fold higher. The falsely low results were attributed to 'antigen excess' [10].

Patient 5 was referred with lambda light-chain myeloma and deteriorating performance status. At her first visit, the free lambda light chain was 90 mg/dL (nl <2.63 mg/dL), but the SUPCR was markedly increased at 5.7 mg/mg. UPEP of the spot urine showed that most of the protein was albumin indicative of a glomerular lesion. A skin biopsy showed amyloid.

These preliminary results suggest that the SUPCR can be used to monitor response in patients with light-chain proteinuria and, in contrast to SFLCA, may detect other causes of proteinuria that can be further evaluated by electrophoresis. The SUPCR can also identify patients in whom the SFLCA is falsely low due to antigen excess.

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### Additional antibody suppression from rituximab added to conventional therapy in severe, refractory anti-GBM nephritis

Sir,

Anti-glomerular basement membrane (GBM) nephritis is an autoimmune disease characterized by IgG antibody-formation against the  $\alpha 3$  (IV)NCI non-collagenous region of type IV collagen resulting in rapid progressive glomerulonephritis and, ultimately, renal failure when left untreated [1]. Several novel agents have been used when conventional therapy fails to suppress antibody formation. We describe the case of a young woman with severe anti-GBM disease who had persistently high antibody titres despite conventional therapy, experiencing successful antibody suppression after rituximab was added to her therapeutic regimen.

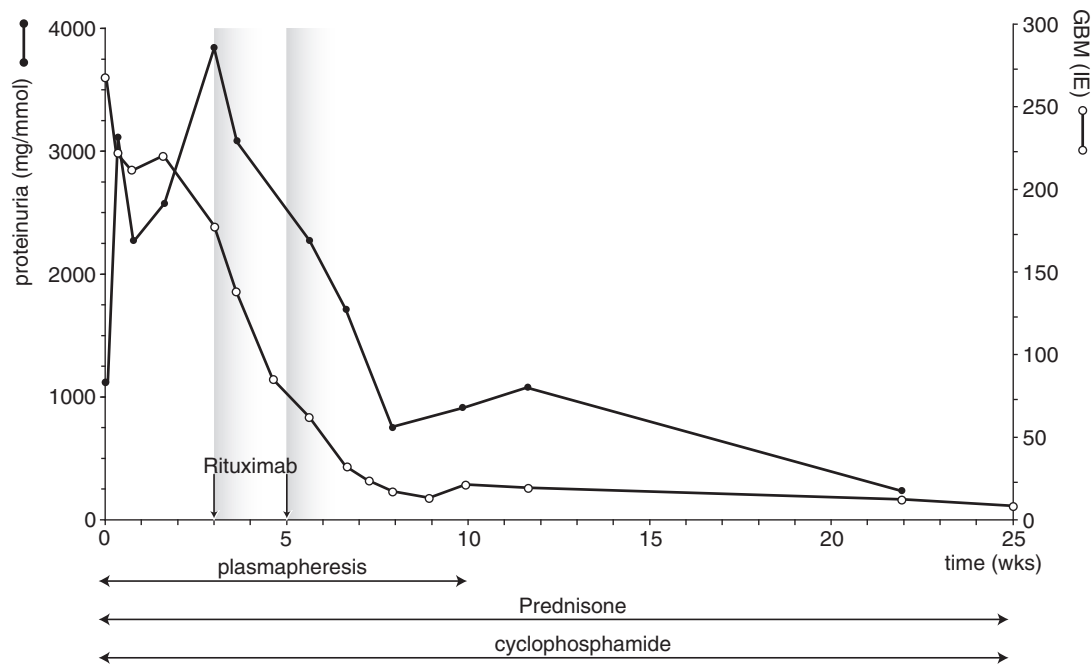
A 20-year-old woman presented at the emergency department with acute, oliguric renal failure due to glomerulonephritis. Creatinine level was 624 mmol/L, urea level was 16 mmol/L, and 24-h protein excretion was 6.2 g. Anti-GBM titre was positive with 270 units, while ANCA-P3/MPO and ANA were negative.

The diagnosis of anti-GBM glomerulonephritis was made, and plasmapheresis was initiated while the patient was started on methylprednisolone 1 g i.v. for 3 days followed by 1 mg/kg and cyclophosphamide 2 mg/kg, both orally.

At Day 21, after 17 sessions of plasmapheresis with 3 L plasma volumes, the anti-GBM titre remained elevated at 180 units, and proteinuria worsened to 40 g/day.

Rituximab was initiated at a dose of 375 mg/m<sup>2</sup> with a 2-week interval. Four days after first rituximab treatment, the anti-GBM titre dropped to 130 units, and 11 days later the titre had further decreased to 85 units. Four weeks after the first dose of rituximab and 2 months after the diagnosis was made, the anti-GBM titre had dropped to below reference level, while proteinuria declined to 2 g/24 h and creatinine clearance rose to 32 (Modification of Diet in Renal Disease formula). Phenotyping of peripheral lymphocytes showed B cells to be almost completely absent.

The use of rituximab in anti-GBM nephritis has only been described in case studies, with mixed outcome, but its use has been successfully studied as adjuvant or salvage



therapy in antibody-mediated autoimmune diseases such as autoimmune thrombocytopenic purpura, autoimmune haemolytic anaemia, systemic lupus erythematosus and rheumatoid arthritis. [2–4] The production of antibody depends on the antigenically driven clonal expansion of B cells into antibody-producing effector plasma cells. Plasma cells are short-lived cells, and survival of the populations depends on differentiation from their progenitor B cells [5]. B-cell ablation with rituximab could prevent further plasma cell and subsequent antibody formation, extinguishing the inflammatory anti-GBM response.

In our case, the anti-GBM titre did not decrease below reference level even though 51 L of plasma volume had been exchanged, suggesting a high rate of antibody formation. The rapid decline of antibody titre and proteinuria could very well have been due to a late effect of simultaneous earlier therapy, but the theory behind the use of rituximab does not rule out that the rituximab might have had beneficial effect on antibody formation.

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### Interaction between tacrolimus and clindamycin

Sir,

Tacrolimus is widely used in organ transplantation to prevent allograft rejection. Its hepatic metabolism via cytochrome P450 (CYP) 3A4 represents the major eliminating process. In addition, its bioavailability depends on intestinal P-glycoproteins (PGP) and CYP3A5 activities. Due to its potential toxicity, tacrolimus usage requires a close drug monitoring, as well as the early identification of any pharmacological interaction. Here, we report on a novel interaction between tacrolimus and clindamycin in a renal transplant recipient with *Pneumocystis jirovecii* pneumonia (PJP).

A 61-year-old woman underwent kidney transplantation from a deceased donor for end-stage renal disease secondary to chronic glomerulonephritis with IgA deposits. Two months later, she presented with grade IV dyspnoea. Maintenance immunosuppression included modified-release (MR) tacrolimus 15 mg/day, mycophenolate mofetil (MMF) 720 mg/day and prednisolone 4 mg/day. Thorax computed tomography showed bilateral ground-glass opacities compatible with PJP, as confirmed by bronchoalveolar lavage analyses. MMF was interrupted, and sulpha-