Successful use of cyclosporin A in progressive anti-glomerular basement membrane nephritis

Sir,

Goodpasture syndrome or anti-glomerular basement membrane (GBM) nephritis is mediated by anti-basement membrane autoantibodies with poor prognosis regarding kidney function [1,2]. Nonetheless, autoreactive T-cells seem to play an important pathogenetic role [3]. They are able to orchestrate the inflammatory response and to stimulate B-cell antibody production against the NC1 domain of α3 type IV collagen. Thus, it seems rational to use a T-cell directed immunosuppressive drug to obviate deterioration of kidney function. We report the successful use of cyclosporin A in a female patient with rapidly progressive glomerulonephritis (RPGN) caused by anti-GBM antibodies who failed to respond to conventional therapy.

Case. A 63-year-old female presented with a 3-week history of weight loss, weakness, anaemia, proteinuria and haematuria. She was admitted with a serum creatinine of 2.1 mg/dl and a haemoglobin of 10.4 mg/dl. Her past medical history included hypertension for at least 10 years and coronary heart disease with myocardial infarction in 1983. Kidney biopsy showed a diffuse nephritis with focal necrosis of glomerular tufts in 1/3 and segmental cellular crescents in 2 of 11 glomeruli. Along the GBM deposits of linear IgG were detected. Anti-α 3(IV) NC1 antibodies were demonstrated by ELISA and immunoblot. Treatment was initiated with daily plasmapheresis, pulse methylprednisolone (3 × 250 mg) followed by an oral dose of 1 mg/kg per body weight, and cyclophosphamide 2.0 mg/kg daily. Despite conventional therapy, kidney function rapidly declined, so cyclosporin A was added at a dose of 4 mg/kg per day. After the initiation of cyclosporin A therapy, the patient’s renal function improved as shown in Figure 1. The anti-GBM antibody titre fell and serum creatinine was 2.1 mg/dl when she was discharged from hospital. One month later the patient developed a severe systemic infection related to neutropenia (0.5/nl) and immunosuppressive therapy was stopped. The patient improved under broad-spectrum antibiotics. Since antibodies could still be detected immunosuppressive therapy was restarted with low dose steroids in combination with cyclosporin A. The patient improved clinically with acceptable renal function (serum creatinine 1.8 mg/dl).

Fig. 1. Course of disease with respect to serum creatinine (s-creatinine) level, anti-GBM antibody titre, white blood cells (WBC) and therapy.

<table>
<thead>
<tr>
<th>Creatinine mg/dl</th>
<th>2.0</th>
<th>3.0</th>
<th>4.0</th>
<th>5.0</th>
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<tr>
<td>WBC cells/ml</td>
<td>9.0×10^3</td>
<td>4.5×10^3</td>
<td>1.8×10^4</td>
<td>1.8×10^4</td>
</tr>
<tr>
<td>anti GBM-antibody-titer</td>
<td>18×10^3</td>
<td>1×10^4</td>
<td>1×10^3</td>
<td>1×10^4</td>
</tr>
</tbody>
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Course of disease (days)
Comment. In Goodpasture syndrome or anti-GBM nephritis, advanced renal impairment is not generally prevented by current treatments when the patient presents initially with progressive renal insufficiency. Here we used cyclosporin A, which is commonly used in organ transplantation, because of its selective inhibition of immune response. The immunosuppressive effect is mediated by the inhibition of calcineurin, which impairs the expression of several T-cell activation genes including interleukin-2 and its receptor. This drug has been used in humans with anti-GBM antibody mediated nephritis, but experiences are limited [4,5]. The growing knowledge of immune pathogenesis has led to the concept that cellular immunity also plays a key role in this disease and thus it seems plausible to use a T-cell directed immunosuppressive therapy. This case illustrates the beneficial use of cyclosporin A in a patient whose kidney function worsened after the initiation of conventional immunosuppressive therapy. Furthermore, cyclosporin A seems to be an alternative treatment option in cytotoxic drug induced leukopenia.

We conclude that cyclosporin A may be helpful to both achieve and maintain remission in rapidly progressive anti-GBM glomerulonephritis and might be considered as an alternative approach to conventional immunosuppression. The clinical results support the idea that T-cells are of major importance in Goodpasture syndrome.

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