

Ciclosporin-Induced Partial and Transient Improvement of Nephrotic Syndrome in Recurrent Focal Segmental Glomerulosclerosis

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Dear Sir,

Recently, it has been reported that ciclosporin (CsA) may be effective in the treatment of corticosteroid-resistant nephrotic syndrome, mainly in minimal change disease [1–3]. The usefulness of CsA in controlling nephrotic syndrome due to focal segmental glomerulosclerosis (FSGS) is controversial [1–3]. At the moment the clinical experience of CsA therapy in FSGS is scarce, especially in recurrent FSGS.

We present herein the clinical data of a renal transplant patient with nephrotic syndrome due to recurrent FSGS. When CsA was started, a partial and transient clinical improvement maintained during 8 months was observed.

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Case Report

A 20-year-old woman was started on hemodialysis in 1983 because of FSGS. In May 1985 a cadaveric renal transplant was performed under prednisone and azathioprine treatment. The patient developed proteinuria following renal function recovery after a very prolonged period of acute tubular necrosis with evidence of acute rejection superimposed on it. In the 11th posttransplant month recurrent FSGS was clearly documented. The clinical and histological sequence of this recurrent FSGS was published before [4]. The last biopsy, performed because of renal function worsening and persistent nephrotic syndrome, showed focal segmental hyaline sclerosis with IgM and C3 deposition in immunofluorescence. In addition, an important tubulointerstitial affection was evident [4]. Because of persistent clinical and biochemical nephrotic syndrome, 2 months later CsA (Sandimmune) was started. The initial dose was 12 mg/kg/day orally, and then the dose was decreased. CsA blood trough levels were determined by radioimmunoassay. At that moment a moderate renal failure (serum creatinine 2.2 mg/dl) was evident. Coincidental

with CsA therapy clinical and biochemical improvements were observed. Proteinuria diminished and total proteins and serum albumin increased and edema disappeared. Additionally, cholesterol and triglycerides diminished in parallel with the in-

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Fig. 1.
CsA.

Clinical evolution of nephrotic syndrome treated with crease in total proteins and serum albumin (see fig. 1). This response was maintained without complications of CsA therapy such as acute renal failure with low fractional excretion of sodium [5–7] or CsA-related neurotoxicity. In the 9th month after CsA was started, a reappearance of the complete nephrotic syndrome with edema and a worsening of the renal function were observed. For these reasons

284

Morales/Andres/Prieto/Praga/GutierrezMillet/Rodicio

CsA was stopped. Following this, the disease progressed and 4 months later the patient returned to hemodialysis.

This patient who had persistent clinical and biochemical nephrotic syndrome due to recurrent FSGS was treated with CsA. Coincidental with the start of CsA, proteinuria slowly diminished and edema disappeared. Therefore, it seems reasonable to think that the partial response of nephrotic syndrome was due to CsA treatment. Also, 8 months after the start of treatment a relapse of the complete nephrotic syndrome with a worsening of the renal function was observed, in spite of the maintenance of CsA therapy.

This case has several points of interest. First, we have shown that CsA treatment was partially effective in controlling nephrotic syndrome due to recurrent FSGS. After 40 days of CsA treatment a clinical and biochemical improvement of the nephrotic syndrome was evident: proteinuria diminished, serum albumin and total protein concentration rose and edema disappeared. Additionally, cholesterol and triglyceride levels diminished. Although this development could be spontaneous, the slow and the partial diminution of proteinuria, without changes of renal function, with appreciable rise of serum albumin strongly supports the hypothesis that it is an effect of CsA treatment. This clinical sequence is similar to the of some idiopathic FSGS patients treated with CsA [1]. In renal allograft the problem could probably be similar to adult idiopathic FSGS in whom a failure or a partial remission are the most frequent responses to CsA [1, 2]. It has recently been reported that CsA induced complete remission of idiopathic FSGS in children, but in these cases there was always evidence of normal renal function [3]. On the other hand, our patient presented with moderate renal failure and well-established lesions of FSGS. Therefore, it could be speculated that if the improvement was not complete, perhaps this was due to the presence of advanced FSGS lesions with tubuloin-terstitial affection. In this way we agree with Meyrier et al. [1] that in FSGS CsA may suppress only the functional part of proteinuria, but may have no effect on its organic component when the glomerular lesion is well established, as in our case.

Second, interestingly, in this nephrotic patient CsA was well tolerated during 8 months. Acute worsening of renal function [5], and diminution of urinary sodium or fractional excretion of sodium [6,7] as expression of CsA nephrotoxicity were not seen. Renal function and fractional excretion of sodium were unaltered in spite of severe nephrotic syndrome, moderate renal failure and high CsA blood levels.

Third, in the study of Meyrier et al. [1] at 1 year of treatment partial remission depended on the maintenance of CsA. Additionally, in all patients renal function improved after treatment. By contrast in our patient in spite of CsA maintenance relapsed clinical and biochemical nephrotic syndrome and a worsening of the renal function were seen. For these reasons CsA was stopped, but renal function did not improve. Although theoretically the renal function impairment could be explained by chronic CsA nephrotoxicity, the relapse of nephrotic syndrome and the clinical evolution after CsA was stopped strongly support that it was due to FSGS progression.

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