Efficiency of mycophenolate-mofetil in resistant nephrotic syndrome – case reports

B. Milic, T. Ilic, I. Mitic, I. Budosan and S. Curic

Clinic of Nephrology, Institute of Internal Diseases, Clinical Centre, Novi Sad, Serbia and Montenegro

Abstract

Patients with nephrotic syndrome (NS) in the primary glomerulonephritis are usually treated with standard immunosuppressive treatment including steroids and cyclophosphamide. This is a case report of two patients resistant to standard therapy who showed remarkable improvement in their NS when using mycophenolate-mofetil (MMF). First patient, (male, 54-year old) was admitted to our hospital with a 1-month clinical and laboratory history of NS. He was diagnosed with membranoproliferative glomerulonephritis after renal biopsy. After three months of standard steroid therapy (methylprednisolone 1-2 mg/kg BW) he did not achieve remission. Because of that we continued the treatment with pulse doses of methylprednisolone, followed with cyclophosphamide pulses. During the following two years of therapy patient continued to have frequent relapses. Proven to be steroid and cyclophosphamide resistant he was shifted to MMF therapy (dose of 2g/day). One month after starting therapy patient achieved complete remission with no side effects. The other patient (male, aged 62) was diagnosed with NS (membranous nephropathy) two months before admitting in our hospital. Standard therapeutic procedure included pulse doses of methylprednisolone during one month and then cyclophosphamide per os (2 mg/kg BW) for one year but with no respond in decreasing of proteinuria. In order to achieve remission, Cyclosporin A (2-5 mg/kg BW) was given. Finally, after one month of no response, we administered mycophenolate-mofetil when patient promptly entered partial remission of nephrotic syndrome. We concluded that MMF was found to be effective and beneficial drug in cases of resistant primary nephrotic syndrome.

Key words: resistant nephrotic syndrome, mycophenolate-mofetil

Introduction

Patients with nephrotic syndrome (NS) in the primary glomerulonephritis are usually treated with standard immunosuppressive treatment including steroids and cyclophosphamide. However, a small proportion of patients run a multiply relapsing course despite treatment. Some go into remission with cyclosporine but are dependent on this drug, with which prolonged usage can lead to nephrotoxicity. Mycophenolate-mofetil (MMF) is a specific inhibitor of inosine monophosphate dehydrogenase which is involved in de novo purine synthesis. MMF, an immunosuppressive agent that preferentially inhibits stimulated lymphocytes and down regulates the expression of cell-surface adhesion molecules, has been used successfully for the prevention of acute rejection of renal allografts (1,2). Preliminary studies suggest that it may also be effective in treatment of the resistant NS in the primary glomerulonephritis.

Patients and methods

We report data on two patients with NS who were diagnosed with primary glomerulonephritis. First patient, (male, 54-year old) was admitted to our hospital with a 1-month clinical and laboratory history of NS. He had nephrotic range proteinuria (mean proteinuria 8,5 g/24h) and stable serum creatinine level and creatinine clearance. Biopsy documented membranoproliferative glomerulonephritis by light microscopy and immunofluorescence was showed. After three months of standard steroid therapy (methylprednisolone 1-2 mg/kg BW) he did not achieve remission. Because of that we continued the treatment with pulse doses of methylprednisolone, followed with cyclophosphamide pulses. During the following two years of therapy patient continued to have frequent relapses (proteinuria range 0,4-15 g/ 24h). Proven to be steroid and cyclophosphamide resistant he was shifted to MMF therapy (dose of 2g/day). The other patient (male, aged 62) was diagnosed with NS (membranous nephropathy) two months before admitting in our hospital (mean proteinuria of 10 g/24h) with stable serum creatinine level and halved creatinine clearance. Standard therapeutic procedure included pulse doses of methylprednisolone during one month and then cyclophosphamide per os (2 mg/kg BW) for one year but with no respond in decreasing of proteinuria. In order to achieve remission, Cyclosporin A (2-5 mg/kg BW) was given but with no response. Finally MMF was administered in standard dose of 2g/day along with Cyclosporine A. Both patients received steroids along with MMF (median dose was 20 mg/kg/day). Baseline evaluations on enrolment consisted of physical examination; serum albumin, serum cholesterol, and serum creatinine levels; and a 24-hour urine collection for protein and creatinine clearance. Patients were followed up for 6 months, and evaluated at 1- to 2-month intervals for these parameters. A partial remission was defined as at least a 50% reduction of proteinuria with a stable serum creatinine level (3). A complete remission was defined as proteinuria less than 0,3 g/24 h with a stable serum creatinine level. Side effects of MMF were also observed.

Correspodence to: B. Milic, Clinic of Nephrology, Institute of Internal Diseases, Clinical Centre, Novi Sad, Serbia and Montenegro

Results

Both patients experienced remissions following MMF therapy. First patient, only one month after starting therapy, achieved complete remission (mean proteinuria 0,07 g/24h), with stable serum creatinine and increased serum albumin level, while the serum cholesterol levels were reduced significantly. Other patient promptly entered partial remission of NS (mean proteinuria 4 g/24 h), with stable serum creatinine and increased serum albumin level while serum cholesterol level decreased. There was no improvement in creatinine clearance level. In both cases, there was no side effect of MMF.

Conclusions

MMF is a relatively new immunosuppressive drug now being used in the prevention of allograft rejection. Preliminary studies have shown that MMF is effective in treatment in several types of primary glomerular diseases when conventional therapy has failed (4,5). In the majority of patients it was well tolerated and achieve the goals of improvement of nephrotic syndrome and stabilisation of renal function. Although being usually given with variable doses of steroid, results demonstrate that MMF has major steroid-sparing effects and can be even effective as monotherapy. We concluded that MMF was found to be effective and beneficial drug in cases of resistant primary nephrotic syndrome.

References

1. Eugui EM, Mirkovitch A, Allison AC. Lymphocyte-selective antiproliferative and immunosuppressive effects of mycophenolic acid in mice. *Scand J Immunol* 1991; 33: 175-183
2. Sintchak M, Fleming MA, Futer O *et al*. Structure and mechanisms of inosine monophosphate dehydrogenase in complex with the immunosuppressant mycophenolic acid. *Cell* 1996; 85: 921-930
3. Cattran DC, Greenwood C, Ritchie S, Bernstein K, Churchill DN, Clark WF, Morrin PA, Lavoie S. A controlled trial of cyclosporine in patients with progressive membranous nephropathy. Canadian Glomerulonephritis Study Group. *Kidney Int* 1995; 47:1130-1135
4. Choi MJ, Eustace JA, Gimenez LF *et al*. Mycophenolate mofetil treatment for primary glomerular diseases. *Kidney Int* 2002; 61: 1098-1114
5. Badid C, Desmouliere A, Laville M. Mycophenolate implications for the treatment of glomerular disease. *Nephrol Dial Transplant* 2001; 16: 1752-1756