CLINICAL VIGNETTE

Mycophenolate Mofetil Therapy in Frequently Relapsing Steroid-dependent Minimal Change Disease

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Case Report

A 23-year-old Caucasian male was referred to renal for evaluation of proteinuria and elevated creatinine. Reportedly the patient was diagnosed with nephrotic syndrome (NS) at age three. He was treated with different medications including cyclosporine (CSA), steroids and Mycophenolate mofetil (MMF). He had been treated with chronic steroid therapy for relapse of steroid-dependent (SD) nephrotic syndrome, three to four relapses per year. The patient stated that he had been on CSA since age three and later during his adolescence been instructed to self-titrate and receive prednisolone for his proteinuria relapse based on dipstick urine test monitoring for proteinuria at home. The patient underwent kidney biopsy a few years ago. Per patient, the biopsy was not completely conclusive and a pathologic diagnosis of minimal change disease (MCD) or focal segmental glomerulosclerosis (FSGS) was considered as the cause of his NS.

The patient had been off of prednisone for three months prior to his renal visit and had recently restarted prednisone 30 mg/day for relapse of proteinuria (per dipstick urine test at home) while already on CSA 100 mg two times a day and MMF 500 mg two times a day. The patient's physical examination was unremarkable, and there was no sign of fluid overload. A blood test and urine test on the day of visit showed a serum creatinine of 1.3 mg/dl; and a urine protein to creatinine ration of 0.10. The patient's prednisone was tapered off and discontinued over 10 days and his CSA and MMF were also discontinued.

The repeat blood test and urine test three weeks later showed a serum creatinine of 1.7 mg/dl and urine protein to creatinine ratio of 4.7. The patient noted foamy urine, increased weight, and edema in the face and lower extremities. He was admitted to the hospital with diagnosis of acute kidney injury and NS relapse. He was started on prednisone 40 mg/day, CSA 100 mg two times a day. A kidney biopsy was performed during hospitalization, which showed complete glomerular foot process effacement, consistent with longstanding minimal change disease - Mild chronic changes.

Considering the side effects of prolonged steroids use and also CSA associated nephrotoxicity, it was decided to treat the patient with MMF for his SD nephrotic syndrome and to discontinue steroids and CSA. The patient was started on MMF 1000 mg two times a day; his CSA was discontinued and his steroid was tapered and eventually discontinued over a few months. The patient has been maintaining a serum creatinine of 1.3-1.5 mg/dl; a urine protein of <4 mg/dl; and a urine protein to creatinine ratio of 0.03 over the past 10 months while just on MMF with no symptoms.

Discussion

Minimal change disease is the most commonly seen histopathology in children with idiopathic nephrotic syndrome (INS), 77% of cases in one study report.[1] Most children with MCD nephrotic syndrome will respond to steroid therapy with complete resolution of proteinuria. There is a 30% rate of relapse of NS in children with steroid- responsive MCD.[2] Prednisone is the preferred therapy in case of relapse. Given the serious side effects of prolonged steroids therapy in patients with SD nephrotic syndrome, steroid-sparing agents have been considered for patients with frequent relapses.[3] These drugs include alkylating agents (cyclophosphamide and chlorambucil), levamisole, CSA, MMF, and Rituximab. Among the above agents, MMF has a better safety profile in terms of side effects and toxicity. In one study, MMF was found to be therapeutically effective in 59.5% of cases of both steroid-and cyclophosphamide-resistant INS.[4] In a different study in a group of 36 patients, MMF was found to be 91.6% effective in children with SD nephrotic syndrome and frequent relapses versus 8.3% effective in those children with steroid-resistant NS ($P < .001$), concluding MMF as an ineffective drug in children with steroid-resistant NS.[5] MMF compare to other alternatives such as CSA and steroids has more favorable safety profiles and is increasingly used as the first line of therapy in other primary glomerulonephritis including membranous glomerulonephritis and IgA glomerulonephritis, or an addition to reduce the dosage for other more toxic medication.[6] MMF has been found to be an effective therapy in some patients who had primary glomerulonephritis and who failed to respond to CSA and corticosteroid.[7]

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Submitted August 27, 2015