A Case of Wegener's Granulomatosis Treated with Mycophenolate Mofetil

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Dear Sir,

A 56-year-old male patient, 3 years before the admission, had ocular pain, photophobia and dacryorrhea without inducement, was diagnosed as scleritis and treated with prednisone 30 mg/day for 2 months. The therapy had to be stopped because of secondary diabetes mellitus. Four months after the onset, the patient intermittently nosebleeding and hoarseness. Chest X-ray films and CT scans revealed multiple nodules in both lungs which implied inflammation by MRI, C-ANCA positive and proteinuria, the patient received nodules biopsy and was diagnosed as Wegener's granulomatosis (WG). Given the treatment with prednisone 40 mg/day and total dose of 15 g of cyclophamide for 4 months until remission (C-ANCA negative and lung nodules disappeared), the patient received maintenance therapy with low dose prednisone 15 mg/q.o.d. for 18 months. The patient was on hemodialysis because renal function became worse and eventually developed to uremia 8 months ago. After 3 months of hemodialysis, a series of symptoms appeared such as low fever, headache, nausea and vomiting, cough, extremities numbness. Chest X-ray films and CT scans revealed one nodule again and C-ANCA turned to be positive, head MRI showed abnormal signal associated with vasculitis in left basal ganglia and right maxillary sinusitis. Diagnosed as relapse of WG, the patient received a therapy of low dose prednisone 30 mg/q.o.d. and mycophenolate mofetil (MMF) 1.5 g/day. After the treatment for 3 months, the clinical symptoms described above disappeared, C-ANCA became negative and lung nodule disappeared again. The patient received successful

remission and renal function returned back to be better without drug-related adverse effects.

WG comprises the triad of systemic vasculitis associated with granulomatous inflammation in the upper and lower respiratory tracts and glomerulonephritis. The pathogenesis of WG is associated with abnormalities of both humoral and cell-mediated immunity, including immune complex-mediated mechanism, autoantibody-mediated mechanism, ANCA-induced neutrophil degranulation, T-lymphocyte-mediated mechanism. WG typically is a multisystem disease with many organs involved, including nose, eye, ear, respiratory tract, kidney, nervous system, gastrointestinal tract, heart and skin. In the present case, during the course of two and half years between onset to relapse, multisystems were involved gradually with severe renal lesion, indicating that early diagnosis of WG relies on biopsy and ANCA assays, and MRI is better than CT for the diagnosis of immunovascularitis. The treatment of WG is corticosteroids combined with cytotoxic immunosuppressive drug (cyclophosphamide, azathioprine, etc.). The prognosis of WG is expected to be bad and most patients usually die from renal failure.

Mycophenolate mofetil is a potential new immunosuppressive drug, which is the 2-morpholinoethyl ester of mycophenolic acid (MPA), MPA is a non-competitive and reversible inhibitor of inosine monophosphate dehydrogenase. This enzyme is required by lymphocytes for the synthesis of guanosine nucleotides, DNA production and cell proliferation. MMF is rapidly absorbed after oral

administration and undergoes complete hydrolysis to MPA. MMF can suppress the proliferation of T and B lymphocytes, block the glycosylation of adhesion molecules and reduce the function of lymphocyte adhesion and infiltration to the vascular endothelium, inhibit production of antibodies from lymphocytes and spleen cells.

MMF was used not only in transplant field, but also in autoimmune diseases recently. Due to relapse of WG after 2 years of maintenance therapy, the patient received low-dose prednisone and MMF for 3 months, then received successful remission without gastrointestinal tract reaction, bone marrow depression and liver lesion. It could be concluded that MMF in combination with low-dose corticosteroids could be well tolerated and effective for WG. Long-term treatment with MMF is encouraging because of its low toxicity. The mechanism was most likely that MMF suppressed ANCA production and lymphocytes proliferation and reduced the incidence of vasculitis mediated by immunocytes and inflammatory materials. The treatment of WG with MMF remains to be further studied and more clinical trials.

References

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