Myasthenia gravis associated with nephrotic syndrome

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Myasthenia gravis (MG) is an autoimmune disease that is characterized by the development of IgG autoantibodies against postsynaptic nicotinic acetylcholine receptors at the neuromuscular junctions. The disease is seen predominantly in women, while it increases in males over 50 years of age. Glomerulonephritis rarely occurs during the course of MG. Reports on the co-existence of idiopathic or thymoma associated MG with glomerulonephritis are rare in the literature.

A 55-year-old male patient was admitted to our hospital with complaints of malaise, dyspnea, and edema of the legs. Myasthenia gravis had been diagnosed 5 years before his admittance, based on the development of ptosis on the left eyelid, diplopia and dysphagia, good response to anti-cholinesterase test, typical decremental response in repetitive nerve stimulation, and presence of anti-acetylcholine receptor antibodies in his serum. The patient used pyridostigmine 6 tablets/day, as a reversible acetylcholinesterase inhibitor, and did not have any complaints during the follow-up. He developed edema of both legs and dyspnea, and proteinuria was found in the laboratory investigations. The patient was admitted to the Department of Internal Medicine when he developed dyspnea. On his physical examination, blood pressure was 125/70 mm Hg, pulse rate was 70/minute. He had pitting edema of both legs. The respiratory system examination disclosed crepitant rales at the end of inspirium on the lower zones of bilateral lungs. The other system and neurologic system examinations were found normal. His hematological laboratory findings and clotting tests were normal. Erythrocyte sedimentation rate was 66 mm/h. Serum biochemistry findings were as follows: glucose 70 mg/dl, blood, urea and nitrogen 22 mg/dl, creatinine 0.6 mg/dl, sodium 139 mmol/L, potassium 4.5 mmol/L, chloride 107 mmol/L, calcium 6.8 mg/dl, phosphorus 1.5 mg/dl, lactate dehydrogenase 612 U/l (normal <480 U/l), total protein 3.2 gr/dl, albumin 1.3 gr/dl, gamma globulin 0.4 gr/dl, iron 65 µg/dl, total iron binding capacity 134 µg/dl (normal 250-410 mg/dl), ferritin 1017 ng/ml (normal 25-320 ng/ml). Thyroid hormone profile was normal, parathormone level was 94 pg/ml (normal 15-65 pg/ml). Protein in urine was 8 g/day. Viral serology, antinuclear antibody, anti-neutrophil autoantibodies, anti-streptolysin O titer and anti-DNA serology were found negative and complement 3 and 4 levels were normal.

The patient was diagnosed as nephrotic syndrome due to focal segmental glomerulosclerosis on renal biopsy. His nutrition was supported by essential amino acids, and candesartan was started for its antiproteinuric effect. The serum albumin level increased, and calcium and phosphorus supplements were given. In order to decrease proteinuria, ramipril was added to his therapy. Cyclosporine, which was started for focal segmental glomerulosclerosis, was stopped later because sufficient serum levels of cyclosporine could not be achieved. It was replaced by mycophenolate mofetil therapy. The edema and malaise regressed, and proteinuria dropped to 3 g/day level. Chest radiography was normal. Spiral CT showed a lesion with dimensions of 6 x 2.5 cms at the thymus region. Magnetic resonance imaging of the lesion was characterized by a hypodense signal with intense contrast enhancement, which further supported the presence of thymoma. He was not eligible for thymectomy due to his general condition. He is still being followed up in our outpatient clinic.

Thymoma is found in approximately 15% of patients with MG. Its co-existence with other autoimmune conditions, such as Hashimoto thyroiditis, Graves disease, polymyositis, and pernicious anemia are well-known. However, the development of glomerulonephritis during the course of MG, particularly in thymoma associated MG, is rarely reported. However, glomerulonephritis is also reported to develop in patients with thymoma that is not associated with MG. The association of thymoma associated MG with glomerulonephritis is thought to be on an immunological based pathogenesis. Thus, it is hypothesized that the T cell dysfunction associated with thymoma might play a role in the etiopathogenesis of nephrotic syndrome. Thymus may play a crucial role in the pathogenesis, since the severity of glomerulonephritis decreases by thymectomy.

Glomerulonephritis may develop during MG. It may be severe and require therapy in some patients, as in our case. Immunosuppressive drugs play a crucial role in the treatment of MG. Since myopathy developed due to steroid treatment, cyclosporine therapy was instituted in the present case. However, a sufficient serum level of cyclosporine could not be achieved, possibly due to decreased gastrointestinal absorption. Therefore, mycophenolate mofetil was added to the treatment and a significant decrease in proteinuria was achieved. The use of mycophenolate mofetil has been reported in several case reports, and...

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it should be kept in mind as an alternative therapeutic agent to decrease proteinuria in cases of MG and thymoma associated with nephrotic syndrome.\(^5\)

In conclusion, glomerulonephritis may occur during immunologic disorders, such as MG. More research should be carried out to clarify the pathogenetic association between glomerulonephritis and MG, although autoimmunity is supported by the benefits following thymectomy.

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