CHAPTER 18

MYASTHENIA GRAVIS

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Myasthenia gravis (MG) is an autoimmune disease blocking the transmission at the neuromuscular junction, leading to neuromuscular transmission impairment and fatigable muscle weakness. The first description of MG in the medical literature was made by Thomas Willis, an English physician, in the book "De anima brutorum" in 1672. The term 'myasthenia gravis' was first used by Friedrich Jolly in 1895, whereby 'myasthenia' comes from Greek, meaning muscle weakness, and 'gravis' comes from Latin, meaning severe [1].

EPIDEMIOLOGY

The incidence and prevalence of MG, which were calculated based on 55 studies published between 1950 and 2007, were found to be 5.3 and 77.7 per million people worldwide. Moreover, it was also revealed that the prevalence of MG increased starting from the half of the last century. The reasons for this increase could be related to several factors such as the increasing knowledge about the disease and the increasing rate of diagnosis, the growing number of treatment options, the advancements in intensive care technology, and the increasing survival rates among the patients [2]. Although MG mostly affects young individuals, recent epidemiological studies have revealed that the incidence of MG has increased in individuals aged over 50 years. MG has a bimodal age pattern of incidence in females, with two peak ages including 20-30 years and older than 50 years, whereas it mostly occurs in males aged older than 50 years. Clearly then, MG has a female preponderance in young ages and has no gender preponderance in old ages. However, MG is unlikely to occur in children aged below 1 year [3].

PATHOGENESIS

Myasthenia gravis (MG) was the first neurological disease to be identified as antibody-mediated. The pathogenesis of MG involves an autoimmune attack on the postsynaptic acetylcholine receptor (AChR) on the neuromuscular junction. AChR antibodies, which impair neuromuscular transmission, are present in patients with generalized MG (GMG) and ocular MG (OMG). A muscle-specific receptor tyrosine kinase (MuSK) has been described as another antigenic target in AChR-negative MG. Recently, another autoantibody has been detected in AChR-negative and MuSK-negative MG, targeting the low-density lipoprotein receptor-related protein 4 (LRP4) [1].

Antibodies to AChR are detected in most MG patients, which are complement-activating and

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tomy and reported that 84.6% of the patients showed symptomatic improvement after an average follow-up of 33.5 months. However, the authors suggested that thymectomy is not advisable as the first-step treatment in OMG patients but should be considered in patients unresponsive to drug therapy (good practice point) [22]. Similarly, the available evidence does not recommend the use of thymectomy in MG patients with MuSK and LRP4 antibodies. Additionally, thymectomy is also unadvisable in patients negative for all antibodies. On the other hand, some MG patients may be present with AChR antibodies that cannot be detected by routine tests; therefore, it is suggested that thymectomy should be considered only in GMG patients with similar biomarkers to those of early-onset MG patients who are negative for antibodies and remain unresponsive to immunosuppressive therapies [7]. Nevertheless, the clinical value of thymectomy remains unclear and its clinical practice varies among physicians due to the scarcity of randomized controlled studies. Therefore, future randomized controlled studies are needed to investigate the effectivity of thymectomy in GMG patients [1].

MYASTHENIC CRISIS

Myasthenic crisis is a life-threatening complication of MG characterized by worsening of muscle weakness, bulbar dysfunction, and respiratory failure. Myasthenic crisis usually occurs once in two years, with a prevalence of 15-20%. Patients experiencing myasthenic crisis should be followed up in an intensive care unit. The crisis can be triggered by infections, surgical interventions, perimenstrual period, pregnancy, sleep deprivation, exposure to extreme heat changes, sudden drug cessation, and the use of drugs aggravating myasthenia (aminoglycosides, calcium channel blockers, quinolones, quinidine, magnesium, and contrast agents). Mainstay treatment of the crisis includes IVIG, high-dose steroids, and plasmapheresis [3].

DURING PREGNANCY

Oral pyridostigmine, prednisone, or prednisolone can be safely used during pregnancy [7,23,24]. The available evidence suggests that the use of azathioprine and cyclosporine is also safe. However, mycophenolate mofetil and methotrexate are contraindicated in pregnancy due to teratogenic risks. Women are advised to avoid pregnancy until 1 year after the completion of rituximab therapy. IVIG and PLEX can be useful for coping with fatigue during pregnancy. Breastfeeding is recommendable. Transient neonatal MG can be seen in 15% of neonates of MG mothers as a result of transplacental transfer of antibodies against AChR, MuSK, and LRP4 [7,24,25]. Normal delivery is advisable; if anesthesia is needed, epidural anesthesia is recommended [10].

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