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# Myasthenia gravis as a rare complication of graft-versus-host disease following allogenic bone marrow transplantation

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Graft-versus-host disease (GVHD) is an adverse immunologic reaction which occurs when a non-genetically identical donor tissue is transplanted into a recipient. GVHD following hematopoietic cell (HC) transplantation is a common complication, which can reduce the transplantation efficacy, and even increase mortality rate.[1] Many cases of GVHD following HC transplantation are diagnosed within the first year after receiving the organ. It's most common manifestations are inflammatory cutaneous lesions, which can show up over the entire body, as well as pulmonary symptoms, which may manifest as either an obstructive or a restrictive disease. Most of these symptoms can be successfully manage by using corticosteroids. However, these symptoms may relapse after discontinuation of therapy.[1,2] Myasthenia gravis (MG) is an exceedingly rare complication of GVHD, which can be life threatening if left undiagnosed and untreated.[3] We have recently encountered a case of MG in a man who had previously developed episodes of chronic GVHD after receiving bone marrow transplantation.

The patient was a 42-year-old man who had been previously diagnosed with acute lymphoblastic leukemia (ALL) 5 years prior to admission in neurology ward. The patient had received an allogenic graft a year after being diagnosed, and since the week after, had developed scaling skin rashes over his entire body as well as dysuria and frequency. With the impression of GVHD, the patient received methylprednisolone, and the symptoms diminished. The patient also had a history of treated pseudomembranous colitis 8 months after transplantation.

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Within the second year after transplantation, the patient was admitted because of dyspnea and cough. The chest high-resolution computed tomography (HRCT) scan revealed patchy ground glass as well as mosaic attenuation, which resembled bronchitis in the settings of chronic GVHD. The patient was successfully treated with 50 mg of daily oral prednisolone.

Due to severe fluctuating muscle weakness, as well as ptosis and dysphagia, he was admitted in neurology department. Neurological examination revealed normal cranial nerves except for mild nasal speech and ptosis, mild neck as well as proximal limb weakness and diminished deep tendon reflexes. The brain magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) analysis, and electrodiagnostic studies. [i.e. electromyography (EMG) and nerve conduction studies (NCS)] were normal.

The mediastinal CT scan was performed because of gradual dyspnea developed during the admission time, but the result was unremarkable. Afterwards however, dyspnea exacerbated, and so the patient was intubated and transferred to intensive care unit. At this point, he was suspected to be a case of myasthenic syndrome. Accordingly, low-frequency repetitive nerve stimulation (RNS) was conducted, and the results showed a significant decrementing pattern (i.e. positive RNS study). He was then sent for the serologic assay of acetylcholine receptor antibody, the result of which showed greater than 100 nmol/l (normal: 0-0.24 nmol/l). Based on these findings, the diagnosis of myasthenia gravis was established. He was started on 150 grams of intravenous immunoglobulins (IVIG) in conjunction with 50 mg prednisolone per day. The symptoms gradually relieved, and so prednisolone was tapered to 20 mg over a course of three months, after which he become almost symptom free.

According to the latest review by Tsutsumi et al., our patient is the second case of MG as presentation of GVHD in ALL patients who have received allogenic transplantation; most of the similar cases in the literature had aplastic anemia or chronic myeloid leukemia (CML).[4] While the exact mechanism behind development of MG following chronic GVHD is not clear, some studies have reported that the presence of autoantibodies and B lymphocytes dysfunction seems to be related to development of MG in chronic GVHD.[5] It has been reported that MG may develop in less than 1% of patients receiving allogenic hematopoietic cell transplantation, and mostly develop following discontinuation of immunosuppressive drugs after 24 months.[4] Immunosuppressive therapy and pyridostigmine bromide are considered as 2 effective drugs in treating such patients, although IVIG and plasmapheresis can also be used as more effective therapeutic approaches.[4] Our experience from the present report confirms that treatment with IVIG and corticosteroids in critical settings can be a successful treatment approach for management of MG secondary to chronic GVHD. Moreover, our report highlights the importance of conducting neurologic exam in patients who have received allogenic transplants. This method allows the clinician to better detect life-threatening diseases including MG. Our patient was first diagnosed on the basis of neurologic findings including proximal weakness along with bulbar manifestations, which was further confirmed by RNS study and positive serologic study for acetylcholine receptor antibody.

## Conflict of Interests

The authors declare no conflict of interest in this study.

## Acknowledgments

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