Abstract

Background: The safety of thymectomy in cases of myasthenia gravis (MG) with concurrent systemic lupus erythematosus (SLE) remains unclear. There are concerns that thymectomy could lead to a loss in central tolerance and induce or exacerbate the disease. However, SLE is also associated with thymic abnormalities, which may play a role in its pathogenesis.

Case Description: We report a case of an adult female SLE patient with a previous history of Guillain-Barré syndrome (GBS) who later developed MG, in whom a thymectomy procedure was performed due to an inadequate response toward multiple attempts of conventional treatment. The effects of thymectomy in our patient were observed to be safe and beneficial (modified Osserman class IV before and class II after thymectomy), which was maintained on periodic evaluations without flare up or worsening of SLE symptoms 6 months after the procedure.

Conclusions: We postulate that thymectomy is safe to perform and may be beneficial in in patients with MG and SLE. However, further research with larger population and control groups, are needed before cementing these recommendations.

INTRODUCTION

As autoimmune conditions share similar environmental, genetic, and immunological factors in their pathogenesis, patients with one condition are susceptible to developing additional autoimmune conditions[1]. Myasthenia gravis (MG) and systemic lupus erythematosus (SLE) constitute two distinct autoimmune diseases that share common risk factors and often manifest in young women[2]. However, simultaneous occurrence in the same patient is rare. MG is characterized by generalized muscle weakness secondary to neuromuscular junction (NMJ) transmission impairment due to the presence of autoantibodies against postsynaptic acetylcholine receptors (AchRs)[3]. SLE is characterized by the presence of pathogenic autoantibodies and immune complex formation, resulting in multisystemic inflammation and dysfunction[4]. The mainstay treatment for MG is the administration of acetylcholinesterase inhibitors, with the possible addition of steroids, intravenous immunoglobulins, or plasmapheresis in cases of persistence of symptoms or myasthenic crises. A surgical option, thymectomy, can be beneficial in most patients and is recommended for all thymomatous MG patients and non-thymomatous MG patients below the age of 60 years with generalized MG with the only exception being patients with anti-muscle-specific tyrosine kinase antibody-positive MG[5]. Although evidently beneficial in MG, the role of thymectomy in coexisting MG and SLE is unclear and has not yet been explored. In the case of SLE, several concerns have been raised regarding the loss in central tolerance, which could induce or exacerbate the disease in thymectomized MG patients[6–8].

*Keywords:
Thymectomy, myasthenia gravis, systemic lupus erythematosus, autoimmune, case report

*List of Abbreviation
ANA: anti-nuclear antibody
AchRs: acetylcholine receptors
CT: computed tomography
GBS: Guillain-Barré syndrome
IV: intravenous
IVIg: intravenous immunoglobulins
NMJ: neuromuscular junction
MG: myasthenia gravis
MRC: medical research council
MRI: magnetic resonance imaging
RNS: repetitive nerve stimulation
SLE: systemic lupus erythematosus
VEP: visual evoked potential

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In this report, we present the case of an adult female SLE patient who developed MG in which a thymectomy procedure was safely performed, followed by marked improvement in myasthenic symptoms and maintenance of SLE remission.

CASE REPORT

A 48-year-old Southeast Asian woman presented with a two-week history of fluctuating weakness of the extremities that worsened during activities and improved with rest, accompanied by occasional ptosis and diplopia, resulting in difficulty accomplishing daily tasks. She was diagnosed with SLE 2 years before, for which she currently takes azathioprine. Past medical history was significant for GBS 2 years prior. Upon examination, she was alert, afebrile, with stable vitals. The neurological examination revealed presence of diplopia and generalized motor weakness. Simpson and ice-pack test was positive, and she demonstrated muscular fatigability on sustained arm abduction. Other neurological findings were non-focal. A tentative diagnosis of suspected MG was made with a differential diagnosis of GBS relapse.

Laboratory tests revealed no signs of infection or significant hematologic, metabolic, or electrolyte abnormalities. Immunology tests revealed positive anti-nuclear antibody (ANA) indirect immunofluorescence (homogenous pattern, titer 1:320) and decreased C3 levels (85.0 mg/dL). Contrast cranial, whole-spine magnetic resonance imaging (MRI), and cerebrospinal fluid analysis returned normal. Several neuro-electrophysiological tests were also conducted, including visual evoked potential (VEP), electromyography (EMG), and repetitive nerve stimulation (RNS). VEP and EMG presented with normal results, while RNS test results were consistent with a post-synaptic NMJ lesion. AchR-binding antibody test was ordered and rendered negative (<0.25 nmol/L). Anti-MUSK antibody test could not be done due to lack of availability. A contrast thoracic CT revealed presence of thymic remnant tissue (Fig. 1). No features suggestive of thymoma, mediastinal, or pulmonary masses were found. A final diagnosis of MG with remnant thymus (modified Osserman class IV) and coexistent SLE was made.

The patient was admitted and started on oral pyridostigmine and intravenous methylprednisolone for MG, as well as oral azathioprine and mycophenolate mofetil for SLE. Due to inadequate response, we administered 5% intravenous immunoglobulins (IVIg) (2 g per kilogram of body weight over 5 days) starting on the sixth day of care. The patient experienced mild improvement in diplopia and motor symptoms but continued to experience fluctuating episodes of weakness and diplopia. An elective thymectomy was planned. Preoperative plasmapheresis was done (50 mL/kg of body weight, three sessions over 5 days) starting on the fourteenth day of care, and the thymectomy procedure was performed on the fourteenth day of care. Results of the postoperative histopathological examination revealed islands of thymic tissue and several Hassall’s corpuscles surrounded by the adipose tissue, consistent with thymic involution.

Symptoms improved significantly after thymectomy (modified Osserman class II) and was discharged after 32 days of inpatient care. Upon discharge, she regained full motor strength without dyspnea, diplopia, or dysphagia. Follow-up examination a month later showed marked improvement in motor symptoms and return to daily activities, in which the patient continued to take pyridostigmine (60 mg four times daily) and mycophenolate mofetil (720 mg twice daily). In the subsequent 5 months, the dose of pyridostigmine was successfully reduced and maintained at 60 mg once daily with adequate symptomatic control. Furthermore, the patient did not experience any worsening of SLE symptoms, and disease remission was maintained.

DISCUSSION

The coexistence of multiple autoimmune diseases in an individual patient has become relatively common. Due to shared environmental, genetic, and immunological factors in the pathogenesis of autoimmune diseases, patients with one autoimmune condition are susceptible to developing additional autoimmune conditions[1]. Approximately 13% to 22% of MG patients, and 33%–45% of patients with SLE, are affected by additional autoimmune disorders. There have been few reports regarding the coexistence of MG and SLE in the same patient[9]. A study of 132 MG patients by Bekircan-Kurt et al. found that SLE was present in 3.78% of patients[10]. In another study of 1,300 SLE patients, MG was prevalent in 1.3%[11]. The nature of the relationship between these two conditions remains unclear, as either could precede, or follow the development of the other[7].

Figure 1: Imaging results from the patient. Thorax computed tomography confirms the presence of thymic remnant tissue.
Several mechanisms have been proposed explaining this association, including loss of central tolerance following thymectomy, molecular mimicry due to structural similarities between the immunogenic region of the AChR and U1 small nuclear ribonucleoprotein, functional defects involving T regulatory cells in the thymus, effects of chloroquine over the NMJ, the dysregulated expression of Fas (CD95) in both SLE and MG, and the role of chemokine CXCL13 in the pathogenesis of both SLE and MG[10,11]. Furthermore, the implications this relationship has towards treatment, in particular thymectomy, remains unclear.

The role and effects of thymectomy in patients with coexisting MG and SLE remain controversial. In MG, thymectomy is beneficial as anti-AchR autoantibody production is sourced in the thymus[3]. In SLE, there are additional concerns that thymectomy could lead to a loss of central tolerance and result in an excessive generation of autoantibodies, which may exacerbate or even induce SLE[6]. Previous studies have observed hypergammaglobulinemia, B lymphocyte hyperreactivity, and mild T cell lymphopenia in MG patients following thymectomy, and there have been several reports of the emergence of SLE following thymectomy in MG patients[7,8].

However, while previous reports suggest that in most cases, MG preceded SLE, in which this relationship is attributable to antecedent thymectomy, there are multiple mechanisms in which both conditions may be linked. In our patient, the diagnosis of SLE preceded the onset of myasthenic symptoms by approximately 2 years, suggesting an alternative mechanism, such as a shared pathogenic mechanism (molecular mimicry, non-thymomatous functional thymic defect, chemokine dysregulation), as a more likely cause of this association. Furthermore, aberrant T lymphocyte profiles and signaling has been implicated in the pathogenesis of both MG and SLE[12,13] As the thymus serves as the site of T lymphocyte differentiation, pathological changes could lead to abnormal activation of autoreactive CD4+ T lymphocytes, which, following interaction with B lymphocytes, leads to autoantibody production, subsequent immune complex formation, and organ damage. Under normal conditions, regulatory T lymphocytes can halt the autoimmune process by inhibiting CD4+ T lymphocyte activity. Thus, dysfunction or deficiency of regulatory CD4+ CD25+ T lymphocytes could predispose to MG and SLE[12,14,15]. In such situations, thymectomy may be safe to perform, and may even be beneficial in cases in which thymic abnormalities underlie both conditions.

Thymectomy was performed in our patient due to inadequate response to multiple trials of conventional treatment, namely acetylcholinesterase inhibitor, steroid, and IVIg administration. The response towards thymectomy in our patient were observed to be safe and beneficial (modified Osserman class IV pre-and class II post-thymectomy), with marked improvement in the symptomatic control of diplopia and motor strength that was maintained on periodic evaluations 6 months after the procedure without the deterioration or flare of SLE symptoms. However, it is important to note in our patient, thymectomy is likely not the sole reason for improvement. The patient has undergone both IVIg and TPE, in which clinical improvement takes effect at approximately 1 to 7 days, and time to maximal effect is 1 to 3 weeks. Furthermore, the patient was also given azathioprine and mycophenolate mofetil.[16] These agents, in addition to IVIg and TPE, could also have contributed to symptomatic improvement.

CONCLUSIONS

We present the case of an adult female SLE patient who developed MG, in which a thymectomy procedure was safely performed with substantial clinical improvement and without flare of SLE symptoms. We postulate that thymectomy is safe to perform and may be beneficial in in patients with MG and SLE. However, further research with larger population and control groups, are needed before cementing these recommendations.

INFORMED CONSENT: The patient described in this report provided written informed consent to publish this case (publication of imaging results included).

CONFLICTS OF INTEREST: None declared.

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References


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