Clinical Analysis of 2 Cases of Late-onset Myasthenia Gravis

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Abstract: Objective: Improve the recognition ability of late-onset myasthenia gravis, reduce misdiagnosis and improve prognosis. Methods: The data of 2 patients with late-onset myasthenia gravis were collected, including basic information, clinical features, auxiliary examinations, treatment and effects. Results: Both male patients were elderly. The clinical manifestations were bulbar palsy with diplopia or limb weakness. Symptoms were mild in the morning and severe in the evening, and the neostigmine test was positive. According to the criteria, myasthenia gravis was diagnosed, and pyridostigmine treatment was effective. The severity of the condition was different. Tests for myasthenia gravis antibodies, thyroid function, autoimmune antibodies, and tumor markers were also different. Follow-up of treatment effect was required for prognosis. Conclusion: Late-onset myasthenia gravis is easily misdiagnosed. Neurological examination can help to detect skeletal muscle involvement, and medical history can help to detect clinical features. The auxiliary examinations of myasthenia gravis have clinical significance for the diagnosis, treatment and prognosis.

Keywords: Late-onset; Myasthenia Gravis.

1. Foreword

Myasthenia gravis (MG) is an autoimmune disease with acquired neuromuscular junction (NMJ) transmission disorder mediated by autoantibodies. In recent years, studies have found that MG gradually increases in the elderly. Some neurological symptoms and signs have also been misdiagnosed as clinical manifestations of other systemic diseases. By analyzing the case data of late-onset MG, it is hoped to improve the identification ability, reduce misdiagnosis and improve prognosis.

2. Clinical Data and Methods

2.1. Basic Information and Neurological Examinations

Basic information included gender, age, and past medical history. Neurological examinations included eye movement, gag reflex, limb muscle strength and so on.

2.2. Medical History and Auxiliary Examinations

According to the diagnostic criteria of MG, take medical history, complete auxiliary examinations which included neostigmine test, repeated nerve stimulation (RNS), MG antibodies, thyroid function, autoimmune antibodies, tumor marker tests, etc.

2.3. Treatment and Effects

<p>| Table 1. Basic information and clinical features |</p>
<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Other systems</th>
<th>Bulbar palsy</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>74 years old</td>
<td>High blood pressure</td>
<td>Mild</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>78 years old</td>
<td>Severe lung infection</td>
<td>Severe</td>
</tr>
</tbody>
</table>

In the course of treatment, pyridostigmine, gamma globulin, and mycophenolate mofetil were used. The patient's condition improved.

<p>| Table 2. Diagnostic tests for MG |</p>
<table>
<thead>
<tr>
<th>Neostigmine test</th>
<th>RNS</th>
<th>MG antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Positive</td>
<td>Decreased volatility</td>
<td>MuSKAb Positive</td>
</tr>
<tr>
<td>2 Positive</td>
<td>Not done</td>
<td>Negative</td>
</tr>
</tbody>
</table>

<p>| Table 3. Immune-related tests |</p>
<table>
<thead>
<tr>
<th>Thyroid function</th>
<th>Autoimmune antibodies</th>
<th>Tumor markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 None</td>
<td>Negative</td>
<td>CEA Increased</td>
</tr>
<tr>
<td>2 Subclinical hypothyroidism</td>
<td>Anti-SSA Increased Anti-Ro-52 Increased</td>
<td>CEA Increased CA125 Increased</td>
</tr>
</tbody>
</table>

3. Results

3.1. Clinical Features

Two male patients had late onset. Both patients suffered from choking after drinking water, slurred speech, and weakened gag reflex. The first patient had hypertension, mild bulbar palsy, diplopia, and limited binocular abduction. The second patient had severe pulmonary infection, severe bulbar palsy, dysphagia, hoarseness, limb weakness, positive pyramidal tract sign and confusion. See Table 1.

3.2. The Diagnosis of MG

The clinical features of 2 patients were mild in the morning and severe in the evening, the neostigmine test was positive. According to the criteria, MG was diagnosed, and pyridostigmine treatment was effective. The first patient was mildly ill, with decreased amplitude during RNS, positive
MuSKAb, no thyroid disease, negative autoimmune antibody, and increased CEA. The second patient was severely ill and failed to cooperate with RNS, MG antibody was negative, thyroid function showed subclinical hypothyroidism, anti-SSA antibody and anti-Ro-52 antibody increased, CEA and CA125 increased. See Table 2, Table 3.

3.3. Treatment and Prognosis
Both patients were treated with pyridostigmine, and their symptoms improved. Fecal occult blood was positive in 2 patients, and glucocorticoids were not used in the acute phase. The first patient's MUSK antibody was positive, mycophenolate mofetil was administered during the remission period, and the condition was stable within a short period. The second patient had obvious limb weakness and dyspnea which were gradually relieved by combined use of gamma globulin, immunosuppressants were not used due to possibility of pulmonary tuberculosis, and there was no recurrence within a short period. The CEA of 2 patients was increased, and further follow-up was needed.

4. Conclusion
4.1. Pay Attention to Late-onset Myasthenia Gravis
In contrast to early-onset MG, late-onset myasthenia gravis was defined as myasthenia gravis with onset of age over 50 years, including non-elderly LOMG (onset age: 50-64 years) and elderly LOMG (onset age: 65 years or older). The incidence of LOMG is increasing, and the male is dominant [1]. The data of 2 cases showed that the age of onset was over 65 years old and both were male.
People with late-onset myasthenia gravis usually have cardiovascular disease and other systemic conditions [2]. The first patient was accompanied by hypertension, and the second patient was accompanied by severe pulmonary infection. Treatment for the primary disease could not improve the symptoms of myasthenia gravis. Diagnosis of myasthenia gravis was based on the characteristics of the disease, neostigmine test, repetitive nerve stimulation, and myasthenia gravis antibody testing.

Studies have found that RNS abnormalities and myasthenia gravis antibody positivity significantly increase the systemic risk of ocular myasthenia gravis [3]. In the first patient with OMG, it was necessary to test for RNS and myasthenia gravis antibodies to prevent conversion to systemic form. In addition, it should not be overlooked that myasthenia gravis patients with dyspnea may have asthma [4]. The second patient was complicated with pulmonary infection. It was necessary to improve the pulmonary function test, identify the multiple causes of dyspnea in the early stage, and give comprehensive treatment.

4.2. Neurological Examination and Medical History
The first patient was referred to the ophthalmology department because of blurred vision, and was later transferred to the neurology department because of diplopia. The second patient was admitted to the Department of Respiratory Medicine due to limb weakness, dyspnea, and pulmonary infection [5][6], and was then transferred to the neurology department due to significant dysphagia.

Two patients were old and had acute onset. They were misdiagnosed as cerebral infarction [7] in the early stage which were later ruled out by head MRI.
The first patient drank water naturally and had clear vision in the morning, however, he choked after drinking water and had diplopia in the afternoon. The second patient could get up in the morning and walk with the help of family members, but felt weak in the afternoon and could not get up.
The clinical features of 2 patients were mild in the morning and severe in the evening, the neostigmine test was positive. According to the criteria, MG was diagnosed, and pyridostigmine treatment was effective [8].

Neurological examination can help identify abnormal signs of skeletal muscle involvement, including diplopia, bulbar palsy, and decreased limb muscle strength. The medical history helps to distinguish whether the clinical features are mild in the morning and severe in the evening. The combination of the 2 methods helps to select the appropriate auxiliary examination to assist the diagnosis of MG.

4.3. Auxiliary Examination and Significance
For MuSKAb-positive MG, the guidelines recommend the early use of glucocorticoids and immunosuppressants to improve the symptoms of ocular muscle weakness and prevent secondary systemicization [8]. The first patient's MuSKAb was positive. Glucocorticoids were not used because the patient had positive fecal occult blood, mycophenolate mofetil was administered during the remission period.

MG and Lambert-eaton syndrome (LES) are both autoimmune diseases. Clinical manifestations are similar and include ophthalmoplegia, bulbar palsy, and limb weakness. MG mainly involves acetylcholine receptors on the postsynaptic membrane of the neuromuscular junction. LES is a syndrome of impaired acetylcholine release of the presynaptic membrane.

In the examination of motor nerve conduction, the action potential amplitudes of MG and LES are different. MG is normal, LES is lower than normal. After low-frequency RNS, the amplitude of action potentials in MG decrease. After high-frequency RNS, the amplitude of action potentials in LES increase significantly.

Both MG and LES are accompanied by other autoimmune diseases [9][10], such as thyroid diseases, rheumatic immune diseases, etc. Some patients also have small cell lung cancer [11][12].
The second patient with late onset was severely ill and failed to cooperate with RNS. The patient's MG antibody was negative, other autoimmune antibodies and tumor markers were elevated. The patient's condition was complex, with positive fecal occult blood and possible pulmonary tuberculosis. Glucocorticoids and other immunosuppressants were not selected [13].

5. Closing Remarks
Late-onset myasthenia gravis is easily misdiagnosed. Neurological examination and medical history can help detect skeletal muscle involvement and clinical features. For diagnosis, treatment and prognosis, it is necessary to complete auxiliary examinations, including neostigmine test, RNS, MG antibodies, thyroid function, autoimmune antibodies, tumor marker tests, etc.

In addition, the need for attention is late-onset myasthenia gravis and other neurological disorder occur in the same patient. Some studies have found that myasthenia gravis is associated with Parkinson's disease and Parkinson's syndrome.
Impaired cholinergic transmission may be responsible for peripheral and central nervous system involvement. Amyotrophic lateral sclerosis has also been found in patients with myasthenia gravis, the pathogenesis of which may be related to anti-LRP4 antibodies at neuromuscular junctions.

References


