THE USA JOURNALS
THE AMERICAN JOURNAL OF MEDICAL SCIENCES AND PHARMACEUTICAL RESEARCH
(ISSN – 2689-1026)
VOLUME 06 ISSUE08

PUBLISHED DATE: - 21-08-2024
DOI: - https://doi.org/10.37547/TAJMSPR/Volume06Issue08-03 **PAGE NO.: - 13-20**

RESEARCH ARTICLE **Open Access**

MYASTHENIA GRAVIS PRESENTS AS BULBAR PALSY WITHOUT THYMOMA

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Abstract
Myasthenia gravis is the most common neuromuscular junction disorder associated with autoimmune diseases, although around 10-15% of patients have no detectable antibodies, and 85% of patients have antibodies. Bulbar symptoms are not commonly present in the early stages, although they often occur as the disease advances. We report 2 unique cases of myasthenia gravis manifesting as isolated bulbar palsy. The first case involves a 56-year-old male patient with a history of diabetes mellitus presenting with the early onset of bulbar palsy in the course of myasthenia gravis. The second case features a patient diagnosed with rheumatoid arthritis, presenting symptoms of speech and swallowing difficulties alongside joint pain, without the usual muscle weakness associated with myasthenia gravis. Prompt assessment is emphasized in this case study, even when faced with challenges in diagnosing MG due to the lack of general weakness with ocular symptoms, which ultimately increases the patient's chances of survival.

Keywords Neuromuscular Symptoms, Myasthenia Gravis, Bulbar Palsy, Electroneuromyography, MuSK Antibody, Acetylcholine receptors, Pyridostigmine.

INTRODUCTION

When the body's immune system mistakenly targets its own postsynaptic acetylcholine receptors (AChR) and leads to fatigue that improves with rest goes by the name of myasthenia gravis (MG) [1]. Thymoma and thymic hyperplasia are associated with MG [2]. The clinical classification system established by the Myasthenia Gravis Foundation of America (MGFA) divides MG into 5 primary classes, depending on the severity and specific clinical features. Although the most common form of MG is ocular (50%), manifested with ptosis, class IIb is characterized by a predominant involvement of the oropharyngeal and respiratory muscles [3]. There is a strong connection between the existence of AChR antibodies and the severity of MG, suggesting that individuals who test positive for these antibodies may have a more difficult clinical experience, as occurred in a patient who was wrongly diagnosed with motor neuron disease (MND), demonstrating the challenges of identifying bulbar palsy. The patient's experience, marked by worsening bulbar symptoms and puzzling upper motor neuron signs, emphasizes the importance of conducting thorough clinical assessments, especially in older individuals [4-6].

Our case report details the clinical progression of MG and the importance of emphasizing the significance of timely and accurate diagnosis.

Case presentation:

Case 1

A 56-year-old male presented with difficulty swallowing and feeling of a lump in the throat, choking, hoarseness, dyspnea, and dizziness, which persisted for a month. Initially, the patient had hoarseness and nasal voice; the general practitioner (GP) treated it as a common cold. Following 10 days, his condition got worse, and new symptoms such as choking, inability to swallow, and shortness of breath started to appear. GP referred this patient to the neurologist, where he was diagnosed with motor neuron disease (MND) in Surkhandarya, a region of Uzbekistan. The treatment plan with 15mg of corticosteroids showed no improvement. Due to the deficiency of nutrients, he experienced a general weakness, which eventually led him to AKFA Medline University Hospital.

He has no allergy history. Type 2 Diabetes Mellitus, managed with insulin twice daily, was notable in his medical history. The patient's general condition during the examination was satisfactory, with clear consciousness and orientation in time and place. Neurological examination revealed regular and round pupils with full eyeball movement, no nystagmus or diplopia, normal convergence and accommodation, and sufficient photoreactions. Prominently, the patient exhibited dysphagia and dysphonia. The absence of tremor with no change in muscle tone was considered. Deep tendon reflexes (Biceps, Radial brachialis, Triceps, Distal finger flexors, Quadriceps knee jerk, Ankle jerk) are intact with the negative plantar reflex (Babinski sign). Sensory loss and meningeal signs are not detected. Romberg test and further coordination tests were performed confidently. He was referred to undergo a comprehensive analysis consisting of blood tests, electroneuromyography (ENMG), nerve conduction test (NCT), and chest Computed Tomography (CT).

Prior to the patient's arrival at our hospital for the comprehensive assessment, he was unable to undergo a blood test for antibody detection because it was not accessible in his previous healthcare setting. Upon arrival, he underwent serological testing, where blood test results showed normal anti-skeletal muscle antibodies (IgG), elevated (0.78 units/ml) muscle-specific tyrosine kinase antibody (MuSK, IgG), and significantly elevated level (2.34 nmol/l) of acetylcholine receptor antibody (Table 1).

Test	Results	Norma	Units
Striated Muscle Antibody, IgG	16	up to 20	
Muscle-specific tyrosine kinase antibody (MuSK), IgG	0.78	up to 0.40	U/mL

Acetylcholine Receptor (ACHR) Antibody	2.34	less than 0.45	nmol/L

Table 1. Antibody testing results in Case 1.

ENMG demonstrated a weakly positive decrement test following pyridostigmine administration, with normal muscle unit (MU) action potentials and no spontaneous activity in needle EMG of the deltoid and general extensor muscles of the hand. Post-administration of 2 ml of neostigmine showed no clinical changes and a negative decrement in ENMG. No signs of motor neuronal processes or neuromuscular conduction disorders were expressed, indicating compensated myasthenic syndrome. Obtained results ultimately exclude the initial diagnosis he arrived with and allow us to come to a more accurate treatment strategy.

In a clinical evaluation, a chest CT scan (Figure 1) was performed as part of the standard diagnostic procedure for a patient with MG to check for thymoma. The absence of any abnormalities in the thymus allows us to focus more on addressing the autoimmune aspect of MG without having to manage complications related to a thymic tumor. Moreover, a comprehensive chest CT scan effectively eliminated the possibility of small-cell lung carcinoma.

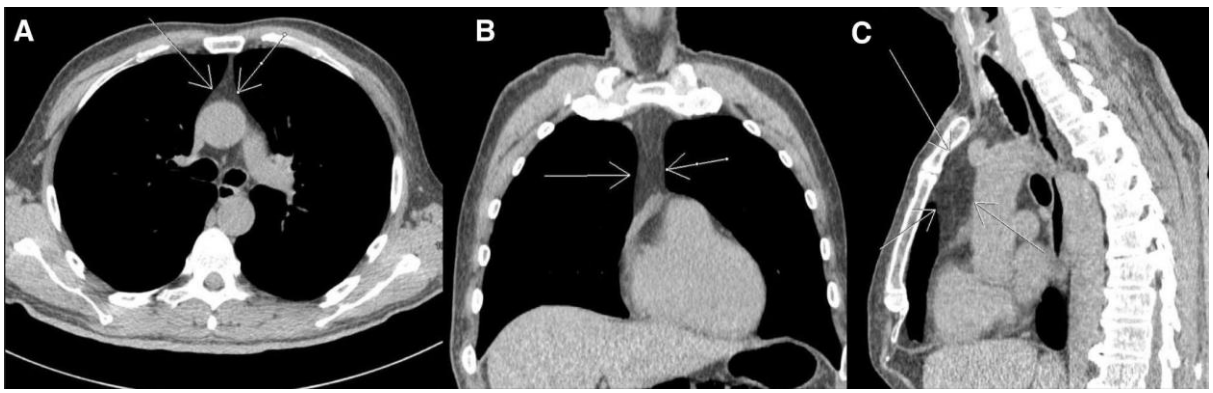

Figure 1: Chest CT in Case 1

Arrows show a normal appearance of the thymus in the anterior mediastinum. (A) Axial CT, (B) Coronal CT, (C) Sagittal CT.

A treatment plan focuses on managing neurological symptoms and addressing his diabetes. Pyridostigmine 60 mg was initiated every 8 hours. The doses are scheduled precisely at 8 AM, 4 PM, and midnight to ensure optimal concentration in the bloodstream and effectiveness in managing muscle weakness and jaw movements. Additionally, the patient's diabetes is being managed with insulin, which is administered at 12 AM and 8 PM.

The coexistence of diabetes may have influenced the progression of neuromuscular symptoms. Long-term follow-up and management focusing on both neuromuscular and diabetic control enhances results for the patient.

Case 2

A 66-year-old female experienced worsening speech and swallowing issues, as well as severe joint pain that had been developing for the past 9 months. Her medical background included

confirmed rheumatoid arthritis (RA) through high levels of anti-cyclic citrullinated peptide (A-CCP) antibodies, characteristic of this autoimmune condition. Although there was no widespread muscle weakness usually seen in myasthenia gravis, the ongoing presence and particular nature of her bulbar symptoms raised concerns about MG as a possible alternative diagnosis.

Therapeutic interventions aimed at managing RA did not help with her bulbar symptoms, and using pyridostigmine, a common treatment for MG, did not lead to any notable improvement. This lack of response required a thorough diagnostic assessment to rule out other potential causes and issues.

Ultrasonography (USG) Doppler examination of the brachiocephalic arteries showed no major abnormalities except for kinking of the internal carotid artery, indicating that vascular factors were unlikely contributors to her symptoms.

Blood tests showed normal levels in a complete blood count (CBC), but C-reactive protein (CRP) was three times higher (15.05 mg/l) than normal, pointing to ongoing inflammation. Rheumatoid factor (RF) level was seven times above (97.48 U/ml) the normal range (Table 2), confirming the RA diagnosis and hinting at heightened autoimmune activity that could potentially overlap with other conditions like MG.

Test	Results	Normal range	Units
C-reactive protein (CRP)	15.05	0-5	mg/l
Rheumatoid Factor	97.48	0-14	U/ml

Table 2. Acute Phase Proteins in Case 2.

MRI of submandibular soft tissues (Figure 2) and CT (Figure 3) scans were conducted to rule out thymoma and squamous cell carcinoma (SCC), only showing signs of chronic bronchitis without any significant issues or masses.

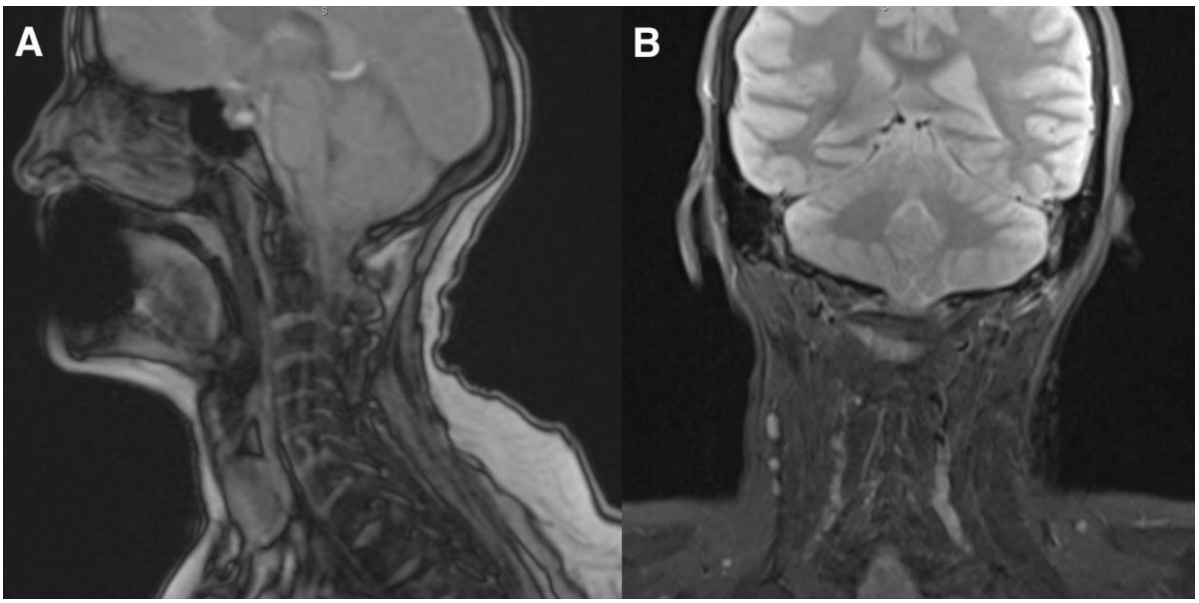

Figure 2. Neck MRI in Case 2.

No structural alterations in the soft tissues of the neck were identified through imaging.

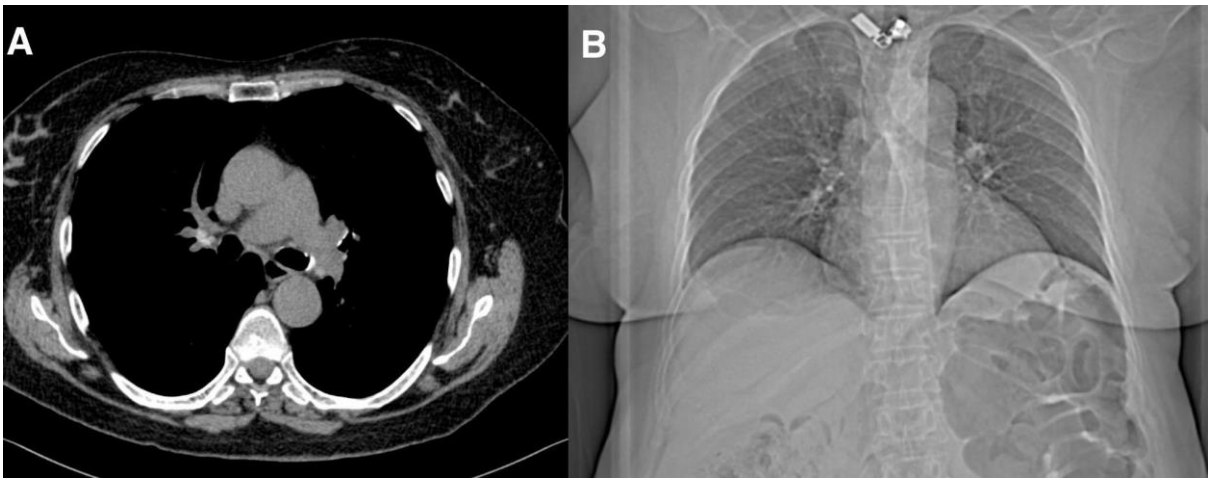

Figure 3. Chest CT in Case 2.

Imaging confirms the absence of thymoma and small cell carcinoma within the examined region.

Patient also went through blood testing to examine the possible autoimmune origin of her symptoms, focusing specifically on certain indicators that could confirm a diagnosis of myasthenia gravis. The test results indicated MuSK antibody level of 0.97 U/mL (increased) and antibodies targeting AChR at a level of 3.2 nmol/L (increased). Identifying these antibodies provided crucial evidence confirming the myasthenia gravis diagnosis alongside her existing rheumatoid arthritis, underscoring the challenges involved in managing patients with overlapping autoimmune conditions.

Test	Results	Norma	Units
Striated Muscle Antibody, IgG	18	up to 20	
Muscle-specific tyrosine kinase antibody (MuSK), IgG	0.97	up to 0.40	U/mL
Acetylcholine Receptor (ACHR) Antibody	3.2	less than 0.45	nmol/L

Table 3. Antibody testing results in Case 2.

Management plan of neurological symptoms with Pyridostigmine 60 mg was commenced at intervals of every 8 hours. The doses are scheduled precisely at 8 AM, 4 PM, and midnight to ensure optimal concentration. Additionally, the patient's rheuemotological symptoms is being managed with Leflunomide 20 mg once a day.

This kind of approach may result in an overall enhancement in the quality of life for patients dealing with overlapping autoimmune and neuromuscular conditions.

DISCUSSION

The occurrence of MG in Asia is increasingly seen among older patients who have other health conditions such as high blood pressure, diabetes, and cancer [7]. There is a connection between MG and thymoma [2], which is extensively recorded, but our case did not have this typical association, making the diagnosis more complicated. When thymoma is not present in MG patients, especially those with bulbar symptoms, it is important to highlight the importance of comprehensive serological and neurophysiological testing for unusual presentations of MG. A considerable portion of individuals with MG possess autoantibodies that attack the AChRs, although a small number exhibit antibodies targeting different proteins like MuSK [8-11]. The different clinical presentations of MG, such as those with antibodies against AChRs or MuSK, present unique challenges in managing respiratory dysfunction during a myasthenic crisis [4,12].

As was mentioned above, our patient was initially misdiagnosed with MND, which could subsequently lead to bad consequences, so comprehensive and detailed diagnostic approaches are emphasized in cases where there are overlapping symptoms of MND due to the role of immune mechanisms in their development [13]. It is important to be more careful and thorough when diagnosing MG, especially in patients with unexplained bulbar symptoms, regardless of their deep tendon reflexes [6].

The majority of patients with bulbar palsy in MG are recommended to start taking acetylcholinesterase inhibitors, like pyridostigmine, which enhances the communication between nerves at the neuro-muscular junction by preventing the acetylcholinesterase enzyme from breaking down acetylcholine [14,15].

CONCLUSION

MG with the early onset of bulbar palsy may frequently be undetected or misdiagnosed, particularly in these two unique instances, in light of concurrent conditions - diabetes mellitus in the first case and rheumatoid arthritis in the second. Highlighting connection between autoimmune neuromuscular disorders and systemic autoimmune or metabolic illnesses. Moreover, patients are unable to obtain proper diagnostic tools due to shortages and financial limitations in underdeveloped areas. In these circumstances, government assistance in healthcare becomes important for medical diagnosis and treatment.

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