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Case Report

Late Onset Myasthenia Gravis Masquerading As Stroke

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Abstract

Myasthenia gravis is the most common disease of neuromuscular transmission; however, it may be difficult to diagnose in the elderly patient with comorbid illnesses and vague symptoms. We report two elderly cases of MG, with a critical clinical course, in whom the diagnosis was missed by neurologists. A diagnosis of stroke was made in each of them, because of presence of abnormal cranial imaging findings. In one patient, the neurophysiological tests yielded negative findings at the initial examination. Clinicians should consider the diagnosis of MG, when faced with patients with new-onset weakness, especially of the cranial musculature and not be misled by the incidental neuroradiologic abnormalities. Confirmatory neurophysiologic tests are important, but should be repeated if the initial tests prove to be negative.

Keywords: Magnetic resonance imaging; muscle weakness; myasthenia gravis; single fiber EMG; repetitive nerve stimulation test; stroke

İnmeyi Taklit Eden Geç Başlangıçlı Myastenia Gravis

Özet

Myastenia Gravis nöromuskuler bileşkenin en sık rastlanılan hastalığıdır. Birlikte başka hastalıklar ve belirsiz semptomları olan yaşlı hastalarda tanı konulması güç olabilir. Bu yazıda MG olan ve nörolog tarafından yanlış tanı konulan iki yaşlı hasta verildi. Anormal kranial görüntüleme bulguları olup, başlangıçta yapılan elektrofizyolojik testleri negatif olan herbir hastaya inme tanısı konmuştur. Özellikle yüz kaslarında ortaya çıkan yeni başlangıçlı kas güçsüzlüğü ile gelen hastalarda klinisyen rastlantısal nöroradyolojik anormalliklere aldanmayarak MG tanısını mutlaka düşünmelidir.Başlangıçta yapılan nörofizyolojik testler negatif olsa bile tekrarlayan testlerin yapılması önemlidir.

Anahtar Kelimeler: Manyetik Rezonans Görüntüleme, kas güçsüzlüğü, Myastenia Gravis, tek lif EMG, repetetif sinir stimülasyonu; inme

INTRODUCTION

Myasthenia gravis is the most common disease of neuromuscular transmission[10]. Although it is a well-described entity with classic features including ptosis, dysphagia, dysarthria, and extremity and respiratory weakness, this disease may be difficult to diagnose in elderly patients. In the elderly population, this constellation of symptoms can be easily mistaken for the

considerably more common entity of stroke[5,6]. Between 6-20 % of myasthenia gravis (MG) cases are observed among individuals over 60 years of age[11]. One of the reasons for misdiagnosis is confusion with the significantly more common entity of stroke in the elderly patients[7]. Despite the fact that the differentiation from stroke had been discussed in previous reports, the poor outcome of late onset myasthenia gravis in case of wrong diagnosis was not stressed. In this report we describe two elderly men with MG whose initial diagnoses were ischemic stroke, an error compounded by false-positive results on imaging studies.

CASE PRESENTATION

Case 1

A 76-year old man sought medical attention because of a 4-week history of dizziness and difficulty in speech and swallowing in first examination. Past medical history was notable for atherosclerotic heart disease and hypertension. He was admitted to the Neurology service with a left sided hemiparesis 6 years ago. A diagnosis of stroke was made and the patient was put on antiaggregants. Physical therapy was started. He was relatively stable until 2 years before this hospital admission, when he developed a speech disorder and difficulty swallowing, which improved within a few days. Neurological examination revealed dysarthric speech, left sided hemiparesis with increased deep tendon reflexes and bilateral Babinski signs. A computed tomogram (CT) of the brain revealed findings consistent with a left parietal infarct in the cerebral white matter. Antiaggregants were continued and the patient was discharged. Three months later, he developed right sided ptosis, followed a couple of months later by a left sided ptosis and diplopia, which became worse towards the evening. On admission, examination revealed bilateral ptosis, most marked on the right side. Vertical gaze, as well as adduction of the right eye was limited. Nerve conduction study was normal except for the slightly prolonged F-wave latencies of the right peroneal and posterior tibial nerves. Giant motor unit potentials (>3 mV) were present on concentric needle EMG of the right vastus lateralis, peroneus longus, tibialis anterior and medial gastrocnemius muscles. A single fiber EMG performed by voluntary activation of the right extensor digitorum communis and frontalis muscles revealed no definite jitter abnormalities (Figure 1a). Magnetic resonance imaging of the brain revealed bilateral small multiple cerebral and brainstem infarcts. The patient was discharged. Ten days later the patient was readmitted and switched to warfarin because of detection of a possible cardioembolic source due to left ventricular dysfunction. Control visit 6 months later revealed moderate malaise and bilateral severe ptosis. Twelve days before final admission, he had an attack of vertigo and unsteady gait.

On examination, he was found to have bilateral ptosis. Eyes were totally immobile. Dysarthria was present and spastic crying at intervals was noted. Motor examination was notable for a left spastic hemiparesis. An ice pack test on the right eye neither improved the ptosis, nor the eye movement abnormalities. Repetitive nerve stimulation on the right abductor digiti quinti muscle showed a borderline decremental response. No decrement was observed on the orbicularis oculi muscle (Table 1). Extramuscular axonal microstimulation on the left orbicularis oculi muscle showed increased jitter in all investigated potentials, with a mean jitter of 156 µs. Block phenomenon was noted in 64% of examined potentials (Figure 1b). Acetylcholine receptor antibody (AChRAb) was positive. Pyridostigmine was started and eye movement abnormalities definitely improved. However, soon after the patient developed chest pain and succumbed to a sudden cardiac arrest.

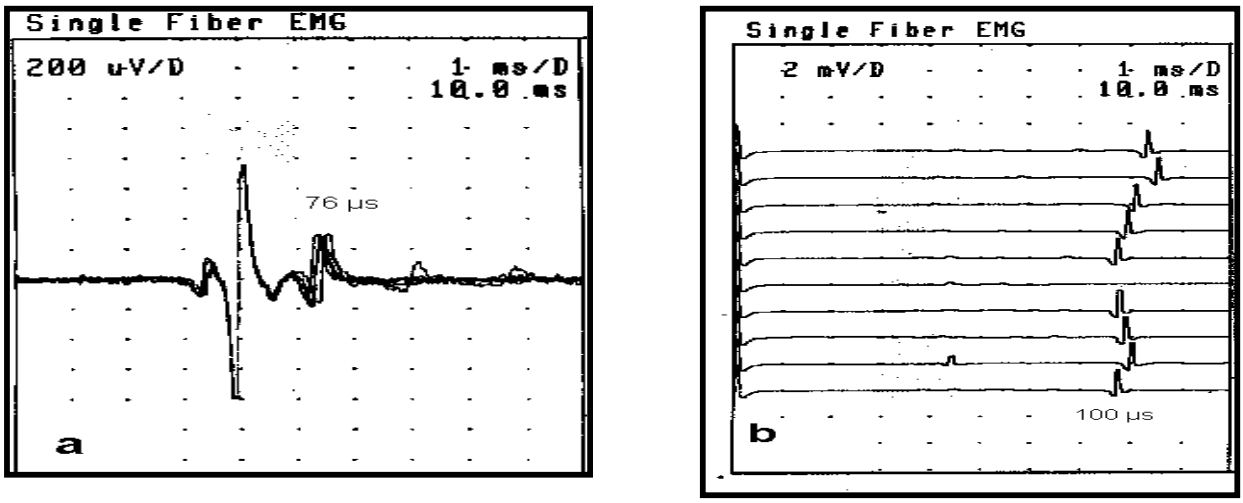

Figure 1: *(a) Borderline jitter in a single fiber action potential pair on voluntary activation of the right frontalis muscle. The mean jitter was borderline prolonged at 47 µs (normal<46.2 µs) (2) (b) One year later, markedly abnormal jitter was discovered on extramuscular axonal microstimulation of the orbicularis oculi muscle, with blocking (6 th tracing from the top).*

Case 2:

A 71-year-old man with no remarkable medical history sought medical attention a month before admission due to left sided ptosis and slurred speech. Symptoms worsened gradually and a left facial droop developed, as well as difficulty swallowing. Speech deteriorated. A cranial computerized tomography was normal. Magnetic resonance imaging of the brain revealed bilateral periventricular multiple millimetric signal abnormalities. A diagnosis of cerebrovascular disease was made and the patient put on antiaggregant therapy. Despite these measures, patient's condition progressed and he was transferred to our hospital.

Physical examination revealed a mild respiratory distress. Both eyes were ptotic. Bilateral facial weakness and dysphonic speech were noted. There was a moderate weakness on tongue protrusion, along with weakness of the shoulder and hip girdle muscles, more prominent in the upper extremities. Although repetitive nerve stimulation test on the right abductor digiti minimi yielded negative findings, the investigation on the orbicularis oculi muscle revealed a decremental response (Table 2, Figure 2). AChRAb titers were strongly positive. Plasma exchange was started the next day, but the patient developed respiratory failure and put on mechanical ventilation and transferred to the intensive care unit. Because no benefit was obtained from this therapy, intravenous immuglobulin was instituted to no avail. Prednisone was started, but the patient developed renal failure and expired a month later.

Table 1: Repetitive nerve stimulation test findings in the abductor digiti quinti and orbicularis oculi muscles in patient 1.

Test	Abductor Digiti Quinti		Orbicularis Oculi	
	FINDING	NORMAL LIMIT	FINDING	NORMAL LIMIT
CMAP Amplitude (mV)				
Rest	14	4	1.2	0.5
Post exercise	15			
Increment (%)	7	25		
Repetitive nerve stimulation				
2 /sec (%)	-8	-7.5	-7	-10
3 /sec (%)	-11	-7.5	-3	-10
5 /sec (%)	-13	-10.5	-4	-13
50 /sec (%)	+30	+34		
5 /sec 4 minutes PT (%)	-11	-9		

CMAP: compound muscle action potential, PT: post-tetanic, (-): decrement, (+): increment

Table 2: Repetitive nerve stimulation test findings in the abductor digiti quinti and orbicularis oculi muscles in patient 2.

Test	Abductor Digiti Quinti		Orbicularis Oculi	
	FINDING	NORMAL LIMIT	FINDING	NORMAL LIMIT
CMAP Amplitude (mV)				
Rest	11	4	1.3	0.5
Post exercise	13			
Increment (%)	18	25		
Repetitive nerve stimulation (Decrement)				
2 /sec (%)	-7	-7.5	-26	-10
3 /sec (%)	-8	-7.5	-30	-10
5 /sec (%)	-5	-10.5	-27	-13
50 /sec (%)	-21	+34		
5 /sec 4 minutes PT (%)	-7	-9		

CMAP: compound muscle action potential, PT: post-tetanic, (-): decrement, (+): increment

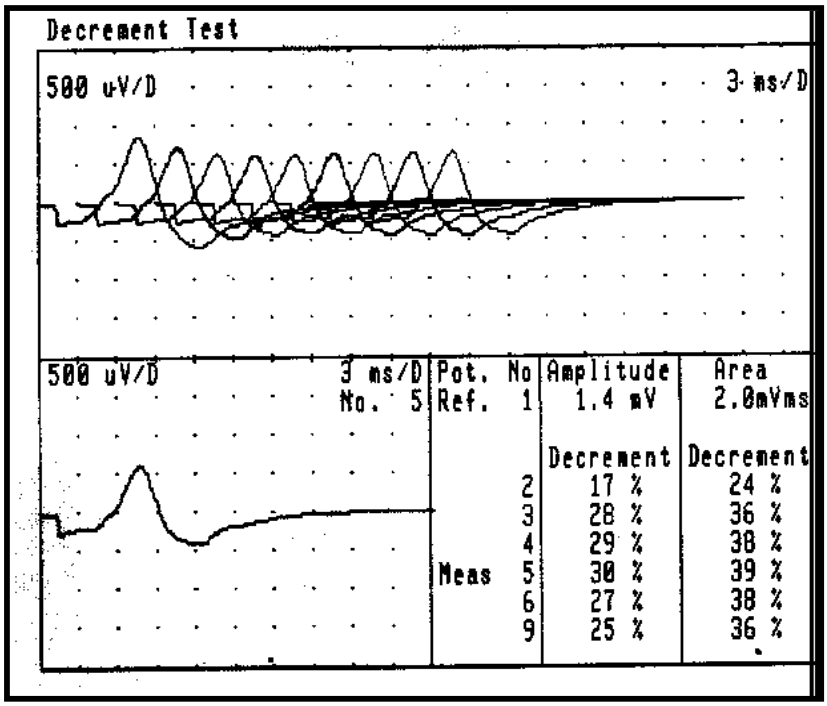

Figure 2: *Three cycle per second stimulation of the zygomatic branch of the right facial nerve recorded from the orbicularis oculi muscle. A 30% decrement is observed in the fifth response*

DISCUSSION

Both patients were elderly men with late onset myasthenia gravis, whose diagnoses were misled because of confusion with cerebrovascular disease, despite the fact that they had been previously evaluated by competent neurologists. The first patient was started on anticholinesterase agents, but succumbed to myocardial infarction, before the treatment took effect. He may have fared better off, had the diagnosis been confirmed earlier and had sufficient time for follow-up to evaluate the need for immune modulating therapy. The second patient was on the verge of myasthenic crisis, due to delay in the diagnosis. Although he was started immediately on appropriate treatment, he did not respond well and died from the complications of myathenic crisis in the intensive care unit. An increased mortality and morbidity in elderly patients had also been previously reported[6], but others failed to confirm such findings[4]. However, complications due to steroid therapy are reportedly encountered more frequently over the age of 50[4].

Imaging studies in such patients can be misleading, because symptomatic or silent cerebrovascular lesions is commonplace in the elderly and do not confer immunity against myasthenia gravis as observed in our first patient. Both patients had positive AChRAb titers, but a few weeks are needed before the results are available, therefore other pharmacological and neurophysiological tests are needed in the interim. Especially the use of long acting anticholinesterase agents for pharmacological testing can cause unwanted side effects, especially in patients with a history of cardiac disease. We tried the ice pack test on our patient but obtained a negative result, showing that this procedure is not always s reliable. Neurophysiological tests such as repetitive nerve stimulation can sometimes be negative in around 30% of the cases[8], although the diagnostic yield rises in more severe cases[9]. The single fiber EMG, although sensitive, requires expertise and

not performed in many EMG laboratories. Another problem is that it can be normal in distal muscles, in which case it should be repeated in a second, more proximally situated muscle[9]. In our first patient this test was negative in both the proximal and distally situated muscles (frontalis and extensor digitorum communis), but abnormal jitter was found in the third tested muscle, orbicularis oculi, although this test was carried out later in the course of the disease. Another confounding factor is that upper motor neuron lesions can cause jitter abnormalities due to transsynaptic degeneration. It has been demonstrated that marked abnormalities occur on axonal microstimulation, in the weak muscles of stroke patients, the jitter becoming more abnormal in patients with longer disease duration[3]. In patient 1, this possibility is ruled out by the finding of abnormally positive AChRAb titers. Because jitter abnormalities are reported in other neuromuscular disorders, the diagnosis must be made in the context of the clinical findings. The majority of patients with MG, whether it be early or late onset, have circulating antibodies to the acetylcholine receptor, but the concentration is often lower in those with late onset disease[1].

In conclusion, when new onset weakness, especially of the cranial musculature is encountered in an elderly patient, MG should be ruled out by appropriate studies. Failure to diagnose MG can, prove fatal as demonstrated by our cases. It is imperative to bear in mind that even the most sensitive neurophysiologic tests can be negative, in which case the test should be repeated later to confirm the diagnosis.

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REFERENCES

1. *Aarli J.A. Late-onset myasthenia gravis. A changing scene. Arch Neurol. 1999;56:26-27.*
2. *Ad hoc committee of the AAEM special interest group on single fiber EMG, Gilchrist JM, Coordinator. Single fiber EMG reference values: a collaborative effort. Muscle Nerve. 1992;15:151-161.*
3. *Chang CW. Evident trans-synaptic degeneration of motor neurons after stroke: a study of neuromuscular jitter by axonal microstimulation. Electroenceph Clin Neurophysiol. 1998;109:199-202.*
4. *Donaldson DH, Ansher M, Horan S, Rutherford RB, Ringel SP. The relationship of age to outcome in myasthenia gravis. Neurology 1990;40:786-90.*
5. *Drachman DB. Myasthenia gravis. N Engl J Med 1994;330:1797-1810*
6. *Herishanu Y, Abramisky O, Feldman S. Myasthenia gravis in the elderly. J Am Geriatr Soc 1976,24:228-31.*
7. *Kleiner–Fisman G, Kott H.S. Myasthenia Gravis mimicking stroke in elderly patients. Mayo Clin Proc. 1998;73:1077-1078.*
8. *Oh SJ. Electromyography: Neuromuscular transmission studies. Baltimore: Williams Wilkins, 1988:255*
9. *Oh SJ. Kim DE, Kuruoglu R, Bradley RJ, Dwyer D. Diagnostic sensitivity of the laboratory tests in myasthenia gravis. Muscle Nerve. 1992;15:720-724.*
10. *Sanders DB, Howard JF Jr. Disorders of neuromuscular transmission. In: Bradley WG, Daroff RB, Fenichel GM, Marsden CD, editors. Neurology in Clinical Practice: The Neurological Disorders. Vol 2. Boston: Butterworth-Heinemann; 2000. pp 2167- 2185.*
11. *Schon F, Drayson M, Thompson R.A. Myasthenia gravis and elderly people. Age Ageing.1996; 25:56-58..*