Myasthenia Gravis Mimicking Acute Cerebrovascular Events

Lakshmi P Digala MBBS[1], Emily Bailey BS[1], and Raghav Govindarajan MD[1]
[1] Department of Neurology, University of Missouri, Columbia – 62502

ABSTRACT

Background and Objective: Myasthenia gravis (MG) is an immune-mediated disorder that can sometimes present acutely with a focal neurological deficit and thus mimic a cerebrovascular event. The objective of this study was to describe the clinical characteristics in a large cohort of patients who were initially misdiagnosed with an acute vascular event and later diagnosed with MG.

Methods: This is a retrospective chart review of patients who were initially diagnosed with an acute cerebrovascular event but subsequently found to have MG. The chart review was done for the period from January 2013 to December 2017, and patients with at least one-year follow-up included. Data are reported as means ± SEM, and the results reported using prevalence rates.

Results: Twenty-one patients met our inclusion criteria. Among them, 13 (61.9%) were female with a mean age of 56.7 ± 4.07 years. Ten were MGFA class 3a; seven were MGFA class 2b, 3 were MGFA 3b and one was MGFA class 2a. Eighteen patients were acetylcholine receptor antibody positive; one was MuSK positive, and the rest two seronegative. Slurred speech (8 patients, 38.1%) was the most common symptom that resulted in misdiagnosis, followed by hemibody weakness (7 patients, 33.3%) and dysphagia (3 patients, 14.3%). Smoking (12 patients, 57.1%) and hypertension (11 patients, 52.4%) were common risk factors for cerebrovascular disease. Small vessel disease was suspected the most common etiology (15 patients, 71.4%) of the vascular event. Ten patients had received thrombolytic therapy, and sixteen patients were on antiplatelets. Four patients who presented recurrent symptoms placed on anticoagulants.

Conclusion: Acute presentation of bulbar symptoms and hemibody weakness resulted in the misdiagnosis of MG.

Keywords: *Myasthenia Gravis, Stroke mimics, acute cerebrovascular event.*

Introduction

Myasthenia Gravis (MG) is the most common primary disorder of neuromuscular junction (NMJ) transmission. Myasthenia gravis is an autoimmune disease in which antibodies bind to receptors at the post-synaptic membrane of the neuromuscular junction, inducing various degrees of muscle weakness. The annual incidence of MG is 8 to 10 cases per 1 million persons, and prevalence is 150 to 250 cases per 1 million making it one of the rare diseases.[1] The hallmark of the disease is a fluctuating weakness.[1-2] In some cases, MG can present acutely with focal neurological deficits, thus mimicking an acute cerebrovascular event.[3] Previous studies have included case reports/case series that have described acute bulbar weakness in older patients as being misdiagnosed as stroke.[3,7-8] The objective of this study was to describe the clinical characteristics in a large cohort of patients who were initially misdiagnosed with an acute vascular event and later diagnosed with MG.

Methods

This is a retrospective chart review of patients diagnosed with myasthenia gravis from January 2013 to December 2017. The inclusion criteria were: 1) Patient's age > 18 years. 2) Patients initially diagnosed with an acute cerebrovascular event, but the subsequent diagnosis was Myasthenia Gravis. 3) Patients who have had at least one year follow up.

Patient demographics, clinical presentation, vascular risk factors, type of vascular event, treatment given for the vascular event, patient MGFA class at diagnosis, antibody status were recorded. Data are reported as means ± SEM, and the results reported using prevalence rates. This study was approved by the Institutional Review Board (IRB) at the University of Missouri, Columbia, MO.

Results

During the study period, 33 patients were identified with 21 patients included in the study as they had at least a one year follow up. 13 (61.9%) were female, and 8 (38.1%) were male. 19 (90.5%) patients were Caucasians with a mean age of 56.7 ± 4.07 years. Slurred speech (8 patients, 38.1%) was the most common symptom that resulted in misdiagnosis, followed by hemi body weakness (7 patients, 33.3%) and dysphagia (3 patients, 14.28%). 18 (85.71%) patients were acetylcholine receptor antibody positive, and 1 (4.76%) was MuSK positive, and two were seronegative diagnosed based on a repetitive nerve stimulation confirmed by single-fiber EMG. These patient demographics and characteristics are described below in table 1.

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Table 1. Demographics and Clinical Characteristics of the Patients (n=21)

Age (years)	56.7 +/- 4.07 yrs
Sex (male : female ratio)	8 (38.1%): 13 (61.9%)
Race (Caucasian: African-American)	19 (90.5%): 2 (9.5%)
Initial clinical symptoms- n (%)	Slurred speech - 8 (38.1%) Hemibody weakness - 7 (33.3%) Dysphagia - 3 (14.3%) Ptosis - 2 (9.5%) Double vision - 2 (9.5%) Blurred vision - 2 (9.5%) Dizziness - 1 (4.8%) Headache - 2 (9.5%) Wrist drop - 1 (4.8%)
Antibody Status - n (%)	Acetylcholine - 18 (85.7%) Musk -1 (4.8%) Seronegative - 2 (9.5%)

18 (85.7%) presented to the Emergency room, while 1 (4.8%) presented to the Primary care practitioner (PCP) clinic and 2 (9.5%) to the Neurology clinic. Smoking (12 patients, 57.1%) and hypertension (11 patients, 52.4%) were common vascular risk factors.

All patients underwent emergent CT-head to rule out bleeding. 10 (47.61%) patients acutely treated with intravenous tPA. Follow up MRI brain showed no evidence of infarct in any of these ten patients. In 10 patients who received tPA the duration of symptoms was within 3.5 hours. In 11 other patients the duration ranged from 2 to 6 hours (median=4 hours).

At the time of follow up in our clinic, 10 (47.61%) patients were on dual antiplatelets, and 4 (19.04%) patients who presented recurrent symptoms were placed on anticoagulation due to suspicion of cardioembolic etiology while seven were on single antiplatelet therapy. CT Angiogram (CTA) was subsequently done in all the patients. CTA was normal in 15 (71.42%) patients, while 2 (9.1%) each had unilateral chronic carotid artery dissection and extracranial vertebral artery stenosis (40% occlusion) and 1 (4.8%) had incidental basilar artery aneurysm (20mm in diameter).

Caucasian. Follow-up visits of these patients led to the diagnosis of Myasthenia Gravis, in which 10 (47.61%) patients were MGFA class 3a, 7 (33.33%) were MGFA class 2b, 3 (14.28%) were MGFA class 3b and 1 (4.8%) was MGFA class 2a. The characteristics like risk factors, image findings, and other variables of the misdiagnosed patients shown in table 2.

The titers of AchR binding antibody ranged from 8nmol/L to 50nmol/L (mean 20.8nmol/L, normal values< or= 0.02nmol/L).[4] RNS decrement ranged from 15% to 55% (mean=25%) with spinal accessory nerve stimulation and trapezius recording.

Mean concentric density with concentric needle electrode and voluntary contraction of extensor digitorum communis ranged from 38 micros in patient 1 and 50 micros in patient 2.

Discussion

Myasthenia Gravis (MG) is most commonly underdiagnosed in the elderly (5). The presenting features, especially bulbar symptoms in the elderly, pose a significant diagnostic challenge to the neurologists, as they have a broad differential diagnosis. It is also intriguing to note that bulbar symptoms can be predominantly seen as an initial presentation in the elderly, thus posing a diagnostic challenge.[5-6]

Acute and focal presentations are uncommon in myasthenia and have been reported in a few cases in the literature.[7-8] Ocular presentations (diplopia, ptosis) are the most common focal presentations seen in almost 53% of myasthenia gravis patients. The next common is the focal bulbar symptoms presenting as either dysphagia or dysarthria is seen around 28% of myasthenia patients, but isolated dysphagia as presenting complaint is seen only in 6%.[9]

Our study reported two patients with ptosis misdiagnosed as stroke. Ptosis, although commonly seen in myasthenia, when presented atypically, could give rise to a diagnostic dilemma. In a 58-year-old acute presentation of ptosis with facial droop gave rise to the suspicion of stroke.[2]

In our study, the most common symptom in misdiagnosed patients is slurred speech. Fatigability, the characteristic finding of myasthenia, is not always seen in such bulbar symptoms, increasing the chance of misdiagnosis.[7-8,12]

The focal weakness of extremities as an initial complaint, although rare, occurs in 14% to 27% of myasthenia cases[8] and can lead to misdiagnosis. In our study 7 patients presented with hemibody weakness and one presented with wrist drop. Cerebrovascular events are on the rise in young-

Table 2. Characteristics of the Misdiagnosed Population

Variables	Patients n=21	
CT Angiography findings	Normal	15 (71.4%)
	Vertebral dissection	1 (4.8%)
	Basilar aneurysm	1 (4.8%)
	Carotid dissection	2 (9.5%)
	Vertebral occlusion	2 (9.5%)
Treatment for Stroke n (%)		
	Anti-platelets	16 (76.2%)
	Anticoagulant	4 (19%)
	Endovascular Treatment	1 (4.8%)
	None	3 (14.3%)
Place of presentation n (%)		
	Emergency Room	18 (85.7%)
	Primary care physician	1 (4.8%)
	Neurology Clinic	2 (9.5%)
Stroke risk factors n (%)		
	Hyperlipidemia	2 (9.5%)
	Smoking	12 (57.1%)
	Hypertension	11 (52.4%)
	Diabetes Mellitus	4 (19%)
How MG was subsequently diagnosed n (%)		
	Positive antibody titers: 8nmol/L to 50nmol/L (mean 20.8nmol/L)	19 (90.5%)
	Repetitive nerve stimulus	18 (85.7%)
	Single fiber electromyography	2 (99.5%)
MGFA Class n(%)		
	2a	1 (4.8%)
	2b	7 (33.3%)
	3a	10 (47.6%)
	3b	3 (14.3%)

er patients,[10] thus posing diagnostic challenge when patients present with acute symptoms to the emergency room.

An isolated symptom of diplopia is seen in 50% and dysphagia in 15% of myasthenia patients. In our study cohort, two patients presented with diplopia and two with dysphagia. In one previous case report, myasthenia presented with diplopia secondary to unilateral abducens nerve palsy.[11] Dysphagia with dysarthria reported in an elderly patient with myasthenia got misdiagnosed as a stroke due to the high index of suspicion.[12]

Symptoms like dizziness though uncommon, was reported in addition to other constellation of symptoms like facial palsy and leg weakness in a patient misdiagnosed as Stroke.[13]

Headache, though occasionally reported as an initial complaint in myasthenia patients, could be secondary form the concomitant ocular complaints like diplopia. In a retrospective study of 184 Myasthenia patients, tension-type headache is reported in 38.6% and migraine headache in 4.9%.[14]

The limitations of our study are, the cohort is only from our emergency department, and we are unaware of the true extent of the misdiagnosis. Also, we cannot entirely rule out the overlapping vascular events at the time of presentation, which makes the diagnosis complicated.

Conclusion

Acute presentation of bulbar symptoms and focal weakness in patients with vascular risk factors resulted in the misdiagnosis of myasthenia gravis as a cerebrovascular event.

Correspondence: Raghav Govindarajan MD.
govindarajanr@health.missouri.edu

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