The Diagnosis and Management of Laryngeal Myasthenia Gravis: A Systematic Review

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Abstract

- Isolated laryngeal myasthenia gravis (LGMG) is a rare manifestation of a usually systemic disease process.
- As such, LGMG is not widely studied and lack of awareness may preclude diagnosis[1].
- We aim to provide a systematic review of the existing literature on isolated LGMG.

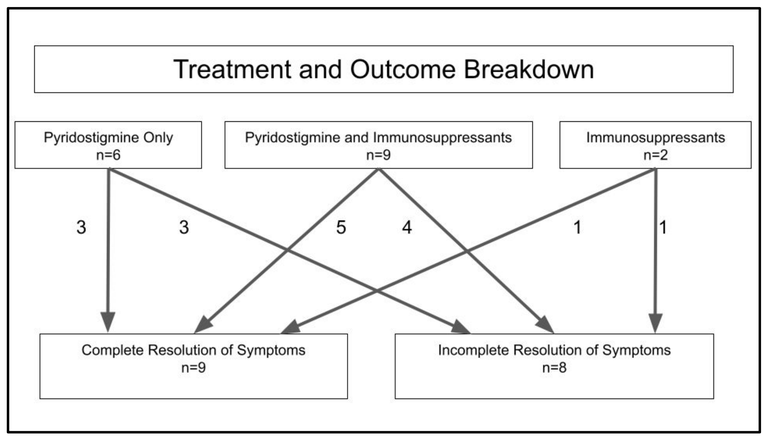
Introduction

- Laryngeal myasthenia gravis (LGMG) is a rare manifestation of myasthenia gravis (MG), a systemic autoimmune neuromuscular disorder characterized by weakness of skeletal muscles from impaired neuromuscular transmission[1]. In cases of LGMG, weakness is isolated to the intrinsic laryngeal musculature.
- Current diagnostic tools include laryngeal electromyography (LEMG), anticholinesterase trial, and serologic testing for acetylcholine receptor antibodies. However, no formal guidelines exist for LGMG diagnosis.
- Management of LGMG typically mirrors that of systemic MG and may include acetylcholinesterase inhibitors, immunosuppressants or corticosteroids. This review aims to synthesize existing literature on isolated LGMG, with a focus on clinical presentation, diagnostic approaches, common laryngoscopic findings, and therapeutic response.

Materials and Methods

- A systematic review of the literature pertaining to LGMG was conducted using Pubmed, Cochrane Library, Scopus, Web of Science, and CINAHL. Papers with unique data regarding LGMG were included. Isolated abstract screening followed by full-text review was performed to determine eligibility. The data extracted includes patient demographics, presentation, diagnoses, treatment, and outcomes.

Figure 1: Treatment and Outcome Breakdown



Results

Patient Demographics and Chronicity	n (%) or mean ± σ
Demographics	
Total Patients	26 (100%)
Female Sex	14 (56%)
Age at Presentation (Overall)	49.4 ± 19.0 years
Age at Presentation (Male)	54.5 ± 17.5 years
Age at Presentation (Female)	45.0 ± 19.8 years
Gender of patients in 3rd Decade or Less	4 (15.4%) females + 1 (3.8%) male
Gender of Patients in 8th Decade	3 (11.5%) male
Ethnicity	Asian, 2 (100% of those reported)
Chronicity	
Time from Symptom Onset → Presentation	1.9 ± 3.5 months
Time from Presentation → Diagnosis	Median - 5.5 months Range: 4 days – 26 years
Clinical Presentation and Findings	**n (%)**
Symptoms	
Dysphagia	16 (61.5%)
Dysphonia	16 (61.5%)
Dyspnea	6 (32.1%)
Stridor	3 (11.5%)
Weight Loss	2 (7.7%)
Cough	2 (7.7%)
Laryngoscopy Findings	
Vocal Fold Paralysis	6 (30.0%)
Pooling of Secretions in Piriform Recess	4 (20.0%)
Vocal Fold Paresis	2 (10.0%)
Respiratory Status and Intervention	
Respiratory Failure	4 (22.2%)
Oxygen Supplementation Only	1 (5.6%)
Intubation	2 (11.1%)
Surgical Airway	2 (11.1%)
Symptom Patterns	
Fluctuating Symptoms	11 (42.3%)
Worsened by End of Day	5 (19.2%)
Common Differential Diagnoses	
Parkinson's Disease	2 (7.7%)
Shy-Drager Syndrome	1 (3.8%)
GI Disorders	2 (7.7%)
Misdiagnoses	
GERD	1 (3.8%)
Laryngeal Spasm	1 (3.8%)
Anxiety	1 (3.8%)
Associated Conditions	
Thymoma	3 (11.5%)
Hypertension	4 (15.4%)
Diagnostic Methods and Antibody Findings	**n (%) or nmol/L**
Diagnostic Methods	
Anticholinesterase	9 (50.0%)
Serology	7 (38.9%)
Anticholinesterase and Serology	2 (11.1%)
Anticholinesterase Agents Used	
Edrophonium	3 (27.3%)
Neostigmime	3 (27.3%)
Pyridostigmine	3 (27.3%)
Edrophonium and Pyridostigmine	1 (9.1%)
Serology Results	
Seronegative	4 (26.7%)
Anti-AChR Antibodies	10 (66.7%)
Anti-LRP4 Antibodies	1 (6.7%)
Antibody Titer Levels	
Mean	29.4 nmol/L
Range	0.67 – 124 nmol/L
Treatments	**n (%) or mg/day**
Common Treatment Approaches	
Pyridostigmine + Immunosuppressants	9 (50.0%)
Pyridostigmine alone	6 (33.3%)
Immunosuppressants alone	2 (11.1%)
Pyridostigmine Dosage	
Mean starting dose	240 mg/day
Median starting dose	210 mg/day
Range	60 – 480 mg/day
Outcomes	**n (%)**
Overall	
Complete Resolution of Symptoms	10 (52.6%)
Improvement of Symptoms	9 (47.4%)

Age at Presentation - Outcomes Association	Resolution of Symptoms (mean ± σ)	Improvement of Symptoms (mean ± σ)	p value
Age at Presentation**	54.2 ± 20.0 years	53.88 ± 14.1 years	0.97
Treatment - Outcome Associations	**Resolution of Symptoms (n (%))**	**Improvement of Symptoms (n (%))**	**p value**
Anticholinesterase and Immunosuppressant*	5 (55.6%)	4 (44.4%)	0.6
Anticholinesterase*	3 (50.0%)	3 (50.0%)	0.63
Immunosuppressant*	1 (50.0%)	1 (50.0%)	0.74

Positive Antibody Detection Associations		Positive antibody n (%) or (mean ± σ)	Negative antibody n (%) or (mean ± σ)	p value
Time to diagnosis***		0.4 ± 0.7 years	14.0 ± 17 years	0.06
Age at Presentation**		57.8 ± 14.4 years	53.25 ± 19.1 years	0.68
Symptoms		**(n (%))**	**(n (%))**	
	Dysphonia*	8 (53.3%)	4 (26.7%)	0.52
	Dyspnea*	3 (20.0%)	0 (0.0%)	0.52
	Dysphagia*	9 (60.0%)	2 (13.3%)	0.52
	Stridor*	2 (13.3%)	0 (0.0%)	1.0
	Weight Loss*	2 (13.3%)	0 (0.0%)	1.0
Laryngoscopy		**(n (%))**	**(n (%))**	
	Vocal paralysis*	2 (13.3%)	0 (0.0%)	0.48
	Vocal paresis*	1 (6.7%)	1 (6.7%)	1
	Vocal paralysis or Paresis*	3 (20.0%)	1 (6.7%)	1
Need for respiratory support		**(n (%))**	**(n (%))**	
	Oxygen Supplementation*	1 (6.7%)	0 (0.0%)	1
	Intubation*	2 (13.3%)	0 (0.0%)	1
	Surgical Airway*	1 (6.7%)	0 (0.0%)	1
Outcome				
	Complete Resolution*	5 (33.3%)	3 (20.0%)	0.58

*Fisher's Exact Test
** Independent Samples T-Test
*** Mann-Whitney U Test

Discussion

- Dysphagia, dysphonia, and dyspnea were the most common symptoms.
- Fluctuating symptoms are present in 42.3% of LGMG patients compared to 96% of systemic MG patients[2]. Also, only 19.2% of LGMG reported worse symptoms at the end of the day. These differences in symptoms could contribute to diagnostic difficulties in LGMG and under diagnosis.
- Similarly, LGMG patients have higher seronegative rates compared to systemic MG, which may lead to under diagnosis.
- Notably, we did not find that age of onset was a prognostic factor. This differs from systemic MG where patients with an older age of onset tend to have more severe disease[3].
- No treatment modality was found to be most effective which is in contrast to other subtypes of MG (ocular or thymomatous MG) which have specific treatment recommendations[4].
- Symptom resolution is thankfully improved in LGMG compared to systemic MG as 100% of LGMG patients experienced at least partial symptom improvement and over half of experienced complete resolution. This is in comparison to systemic MG, in which approximately 15% of patients are refractory to treatment[6].

Conclusion

- LGMG is a rare and potentially fatal disease that is difficult to diagnose due to the lack of specific symptoms. However, it is treatable with conventional therapies.

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