

# Hemi-laryngopharyngeal Spasm (HeLPS): Defining a New Clinical Entity

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## Abstract

**Objective:** Hemi-laryngopharyngeal spasm (HeLPS) has recently been described in the neurosurgical literature as a cause of intermittent laryngopharyngeal spasm and cough due to vascular compression of the vagus nerve at the cerebellopontine angle. We present the diagnostic criteria for this syndrome.

**Methods:** A retrospective chart review of six patients with HeLPS and three patients misdiagnosed with this condition are presented. All patients were diagnosed and treated at a tertiary care academic centre from July 2013 to July 2017.

**Results:** Patients with HeLPS had five defining characteristics: 1) All patients had symptoms of episodic laryngopharyngeal spasm and coughing. Patients were asymptomatic between episodes and were refractory to speech therapy and reflux management. 2) Laryngoscopy showed hyperactive twitching of the ipsilateral vocal fold in two of the six patients. No other inter-episodic abnormalities were seen. 3) Botulinum toxin A injections into the thyroarytenoid muscle on the affected ipsilateral side reduced laryngopharyngeal spasms. Botulinum toxin injection in the contralateral thyroarytenoid muscle did not improve laryngopharyngeal spasm. 4) Magnetic resonance imaging revealed ipsilateral neurovascular compression of the vagus nerve rootlets by the posterior inferior cerebellar artery. 5) Microvascular decompression (MVD) surgery of the ipsilateral vagus nerve resolved all symptoms (follow-up 2–4 years).

**Conclusion:** The diagnostic criteria for hemi-laryngopharyngeal spasm (HeLPS) are proposed. Otolaryngology recognition of this new clinical entity may lead to a surgical cure and avoid the unnecessary therapies associated with misdiagnosis.

**Level of Evidence:** 4

## Keywords

hemi-laryngopharyngeal spasm, laryngospasm, vagus nerve, neurovascular conflict, microvascular decompression, inducible laryngeal obstruction

## Introduction

Hemi-laryngopharyngeal spasm (HeLPS) has recently been described in the neurosurgical literature.<sup>1,2</sup> Patients present with progressively severe episodes of laryngopharyngeal spasm and cough. These episodes can occur while sleeping and can be severe enough to prompt intubation or tracheostomy. Patients do not respond to speech, anti-reflux, or psychological therapy. Our review of six patients successfully cured of HeLPS following microvascular decompression of their vagus nerve revealed that all had been initially misdiagnosed with a psychiatric condition. The responsibility of correctly diagnosing patients with HeLPS will fall to the otolaryngology community. Our initial experience with this condition also resulted in three patients being misdiagnosed with HeLPS and undergoing neurosurgery without benefit. We now present a summary of our experience with the diagnosis of hemi-laryngopharyngeal spasm and highlight the clinical features, laryngoscopy, imaging, and response to Botox that are unique to this condition. This work presents

the largest cohort of patients diagnosed with HeLPS and introduces a unique laryngoscopy feature of this condition.

## Methods

Approval for this study was obtained from the Clinical Research Ethics Board at the University of British Columbia (H17-03320). A retrospective chart review was conducted for all patients correctly (n = 6) and incorrectly (n = 3)

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diagnosed with hemi-laryngopharyngeal spasm (HeLPS) by the Otolaryngology and Neurosurgery Divisions at a single tertiary care academic centre between July 2013 and July 2017. The medical records and laryngoscopic examinations for these patients were reviewed. A final confirmatory diagnosis of HeLPS was made if a patient had complete resolution of their symptoms for more than 1 year following microvascular decompression (MVD) surgery of the affected vagus nerve. A misdiagnosis was assumed if there was no improvement following MVD.

The presumptive diagnosis of HeLPS and ultimate recommendation for MVD was made after a multidisciplinary evaluation. All nine patients were seen by a laryngologist, speech language pathologist, and a neurosurgeon. Six were also seen by a psychiatrist and four by a gastroenterologist.

All patients had pre- and post-operative laryngoscopy/stroboscopy by a laryngologist (MM) and the videos were reviewed for this publication by a second laryngologist (AH) not involved in the initial decision-making process for neurosurgery. All patients worked with an experienced speech language pathologist. This included clinic sessions and home exercises with voice therapy and breathing exercises.

All patients were investigated and empirically treated for acid reflux. Investigations for reflux included 24-hour pH impedance studies ( $n = 3$ ), barium or modified barium swallow ( $n = 6$ ), and upper GI endoscopy ( $n = 4$ ).

All patients except one received unilateral botulinum toxin A injections into the thyroarytenoid muscle. The one patient who did not receive botulinum toxin had a concurrent diagnosis of glossopharyngeal neuralgia and the decision to proceed with neurosurgical microvascular decompression surgery was made without a trial of botulinum toxin A injection. The response to botulinum toxin A injection was evaluated for each of the individual patient's symptoms (ie, the motor symptoms of choking and stridor, and the sensory symptoms of retrosternal tickle causing cough). A positive response was recorded if there was more than a 50% subjective reduction in symptoms. One patient (number 6 in Table 1) was deliberately given botulinum toxin A injection into the contralateral thyroarytenoid muscle.

All patients had magnetic resonance imaging of the head using a CISS sequence to assess for neurovascular conflict between the vagus nerve rootlets and the posterior inferior cerebellar artery on the ipsilateral side of the symptoms (Figure 1).<sup>3</sup> All patients were followed for at least 2 years post-operatively.

## Results

Six patients were correctly diagnosed with hemi-laryngopharyngeal spasm (HeLPS) and had complete and sustained resolution of their symptoms following unilateral

microvascular decompression of their vagus nerve. These patients' demographics are presented in Table 1. The five women and one man had a mean age of 50 years (range 33-60 years). Follow-up for this cohort ranged from 30 to 58 months.

All patients reported episodic symptoms of laryngopharyngeal spasm and coughing. These symptoms universally progressed in severity over the years and eventually occurred even while sleeping. Four patients developed intermittent stridor (not wheezing), most had multiple presentations to the emergency department, one was intubated on two occasions, and one received a tracheostomy for "laryngospasm NYD."

Some patients also reported episodic hoarseness. These vocal symptoms could be triggered by loud or prolonged speech. They would typically resolve spontaneously but could magnify into an episode of laryngopharyngeal spasm.

All patients also had episodic severe coughing triggered by a "tickling" sensation deep to the suprasternal notch. The cough was a response to the "tickling" and could be temporarily suppressed. The coughing progressed in severity, frequency and duration and could be severe enough to cause visual phosphenes, post-tussive headache, urinary incontinence, vomiting, and tussive syncope with unconsciousness.

All patients were completely asymptomatic between episodes. The episodic nature of these severe symptoms along with their complete resolution between episodes prompted psychiatric evaluation in almost all patients. Four were diagnosed with an anxiety disorder. None of these patients were diagnosed with a conversion disorder and each had dramatic improvement of their anxiety following surgical resolution of their condition.

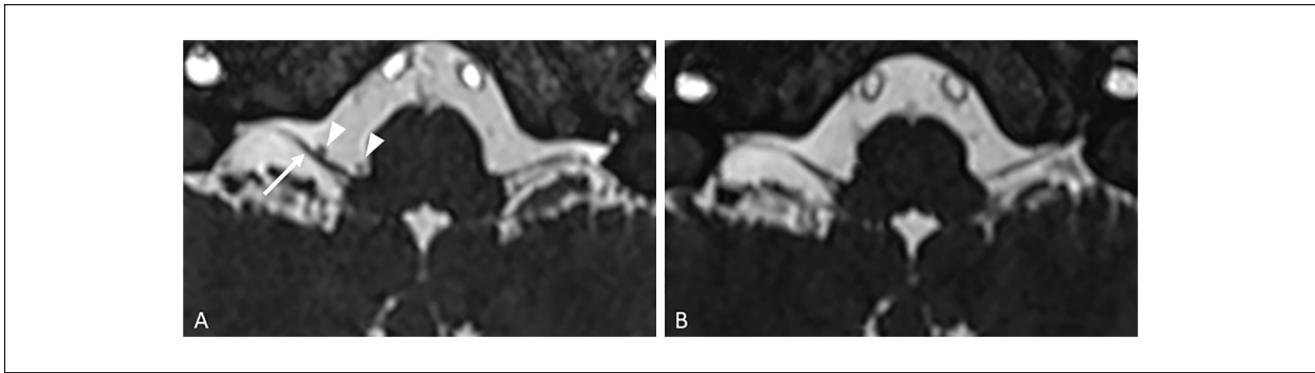
All patients were evaluated by multiple specialists (eg, pulmonologists, gastroenterologists, allergists, neurologists, psychiatrists, otolaryngologists, emergency physicians, and intensivists). Table 1 shows the characteristics of these patients including: their age and gender at surgery; presenting symptoms; co-morbidities; history of emergency room or intensive care unit admission, intubation, or tracheotomy; laryngoscopy/stroboscopy findings; MRI findings; response to botulinum toxin injection; and date of surgery. All patients received a course of proton pump blockers with no benefit and all tests for gastroesophageal reflux were negative.

All patients (6 out of 6) had complete resolution of their HeLPS symptoms with unilateral microvascular decompression of their vagus nerve. Resolution of symptoms were immediate in most but delayed in a few. One patient reported an 80% reduction in symptoms at the 1-year mark followed by complete resolution at the one-and-a-half-year follow up. After surgery, two of the six successful patients developed an ipsilateral vocal fold paralysis and one developed an ipsilateral vocal fold paresis. These three patients have

**Table 1.** Characteristics of Patients with HeLPS Who Were Treated Successfully with Unilateral Microvascular Decompression Surgery.

Patient	Gender, age at surgery	Episodic Laryngo-spasm	Episodic coughing	Co-morbidities	Aggressive treatment	Laryngoscopy	MRI vascular conflict	Response to botulinum toxin	Surgery
1	F, 50	Y, stridor	Y	anxiety	ER, ICU, intubation	Pre-op: normal Post-op: normal	R - Y L - N	R - Y L - N/A	R. MVD 1/2015
2	M, 66	Y, stridor	Y	anxiety, asthma, COPD	ER, ICU, tracheostomy	Pre-op: normal Post-op: L VF paresis	R - N L - Y	R - N/A Y - L	L. MVD 7/2016
3	F, 33	Y	Y	anxiety, depression, CFS	ER	Pre-op: L VF hyperactive Post-op: L VF paralysis	R - N L - Y	R - N/A L - N/A	L. MVD 1/2017
4	F, 44	Y, stridor	Y	asthma, sleep apnea	ER	Pre-op: Normal Post-op: R VF paralysis	R - Y L - N	R - Y L - N/A	R. MVD 1/2017
5	F, 48	Y, stridor	Y	asthma, anxiety, CFS, IBS, Ehlers-Danlos, GPN	N	Pre-op: normal Post-op: normal	R - N L - Y	R - N/A L - Y	L. MVD 4/2017
6	F, 60	Y	Y	hypo-thyroidism	N	Pre-op: L VF hyperactive Post-op: normal	R - N L - Y	R - N L - Y	L. MVD 5/2017

CFS, chronic fatigue syndrome; COPD, chronic obstructive pulmonary disease; ER, Emergency Room visit; F, female; GPN, glossopharyngeal neuralgia; IBS, irritable bowel syndrome; ICU, Intensive Care Unit admission; L, left; M, male; MRI, magnetic resonance imaging; MVD, microvascular decompression; N, no; R, right; VF, vocal fold; Y, yes.



**Figure 1.** Pre- and Post-operative MRI of vagus nerve and posterior inferior cerebellar artery (PICA). The pre-operative (A) axial CISS image shows the PICA (arrow heads) compressing the right vagus nerve (arrow). The vessel is looping against the nerve, hence two arrow heads. The post-operative (B) image shows vagus has been decompressed. The PICA's rostral loop has been moved caudally below the level of this image.

complete glottic closure and deny dysphonia, dysphagia, and aspiration. Formal pre- and post-operative self-reported measures were not available to report. These patients have normal voices on perceptual analysis as judged by the laryngologist, GOR0B0A0S0.

Three additional patients were initially thought to have HeLPS and received unilateral MVD surgery. Unfortunately, their symptoms did not resolve with surgery and they were therefore ultimately determined not to have HeLPS. Table 2 shows the characteristics of these patients. Patient 7 had glossopharyngeal neuralgia and would have had MVD surgery to treat this condition regardless of the possible diagnosis of HeLPS. Her glossopharyngeal neuralgia was resolved with surgery. She developed an ipsilateral vocal fold paralysis with a large glottic gap and symptomatic dysphonia, but no dysphagia or aspiration. Patient 8 received botulinum toxin A injections (at different times) in both the right and left thyroarytenoid muscles and her symptoms responded to both injections. She was determined to have paradoxical vocal fold dysfunction. Patient 9 was believed to have a functional disorder after subsequent psychiatric evaluation.

## Discussion

Hemi-laryngopharyngeal spasm (HeLPS) has recently been recognized by us as a rare cranial neuropathy caused by a unilateral vascular compression (posterior inferior cerebellar artery) of the vagus nerve rootlets.<sup>1,2</sup> This neurovascular compression triggers symptoms related to the vagus nerve with both a motor (episodic laryngospasm, choking, or dysphonia) and a sensory (a tickling sensation triggering severe cough) component. These patients typically do not report any pain. Rarely, however, the glossopharyngeal and vagus nerve can be concurrently compressed by the same vessel causing both glossopharyngeal neuralgia and HeLPS (eg, patient 5).

A neurovascular compression syndrome refers to the clinical symptoms caused by compression of a cranial nerve by a blood vessel.<sup>4</sup> Jannetta proposed the neurovascular compression theory in 1967 as a cause of trigeminal neuralgia and a rationale for microvascular decompression of the trigeminal nerve in these patients.<sup>5</sup> Since then, it has become widely accepted that hemifacial spasm can be due to a neurovascular compression of the facial nerve and glossopharyngeal neuralgia can be due to a neurovascular compression of the glossopharyngeal nerve. All three conditions are routinely cured with unilateral microvascular decompression surgery.<sup>6</sup> Several pathophysiologies have been proposed but most believe that the compression of the cranial nerve causes a focal demyelination with ephaptic transmission and ectopic excitation.<sup>7</sup> Others have suggested a more central cause with hyperexcitability of the trigeminal nucleus.<sup>8</sup>

The diagnosis of HeLPS requires a thoughtful review by a multidisciplinary team ideally composed of a laryngologist, a speech language pathologist, a psychiatrist, and a neurosurgeon. Patients present with episodic laryngopharyngeal spasm, stridor and coughing, but are asymptomatic between episodes. Those with pharyngeal contractions can feel which side is affected, similar to patients with hemifacial spasm. Those with laryngeal contractions, however, cannot lateralize the sensation and report a circumferential “choking.” Also, in similarity with hemifacial spasm, the motor contractions can occur while sleeping. The tickling sensation triggering cough may respond to anti-neuralgia medications.

Patients do not respond to speech therapy, anti-reflux management, or psychiatric therapy. Laryngoscopy or stroboscopy can be normal because the symptoms are episodic. Two (out of six) of our patients with HeLPS had a unique movement disorder of the affected vocal fold: brief, speech-induced, unilateral twitches (Video 1). This unique, unilateral vocal fold movement disorder may be

**Table 2.** Patient Characteristics of Those Who Had Surgery and Did Not Respond.

Patient	Gender, Age at Surgery	Episodic Laryngo-spasm	Episodic Coughing	Co-morbidities	Aggressive Treatment	Laryngoscopy	MRI vascular Conflict	Response to Botulinum Toxin	Surgery
7	F, 54	Y	Y	glossopharyngeal neuralgia, irritable bowel syndrome	N	Pre-op: normal Post-op: Left VF paralysis	L - Y R - N	L - N/A R - N/A	L. MVD 9/2017
8	F, 52	Y	Y	depression, asthma, paradoxical vocal fold dysfunction	ER	Pre-op: normal Post-op: normal	L - N R - Y	L - Y R - Y	R. MVD 7/2016
9	F, 57	Y	Y, stridor	Conversion aphonia,	N	Pre op: normal Post op: functional splinting open of VF	L - N R - Y	L - N/A R - Y	R. MVD 3/2017

ER, Emergency Room visit; F, Female; L, Left; MRI, Magnetic resonance imaging; MVD, microvascular decompression; N, No; N/A, not done; R, Right; VF, Vocal Fold; Y, Yes.

pathognomonic for this condition. Unfortunately, it was present in the minority of patients. Additional laryngoscopic features may be discovered when more patients are examined in the future.

Magnetic resonance imaging of the brain showed a neurovascular conflict between the vagus nerve and the posterior inferior cerebellar artery in all patients (Figure 1). By definition, patients without this finding were excluded from the diagnosis. Our group has shown that the presence of a vascular conflict with the lower cranial nerves is common in the population.<sup>3</sup> This MRI finding is thus necessary but not sufficient for the diagnosis of HeLPS. Patients without a vascular conflict can be excluded from the diagnosis, but patients with this finding need further confirmatory tests. We propose that patients refractory to all the standard therapies for laryngospasm and cough be offered an MRI to evaluate for a potential neurovascular compression of their vagus nerve.

We propose that the definitive test for HeLPS may be the reduction of the motor symptoms following unilateral but not contralateral injections of botulinum toxin A in the affected thyroarytenoid muscle. These injections must be appropriately spaced in time to avoid bilateral vocal fold paralysis. The results should parallel the expected benefits of botulinum toxin A on the affected side of hemifacial spasm.

Differentiating HeLPS from paradoxical vocal fold dysfunction or adductor respiratory dystonia may be challenging. Both these other conditions, however, would be expected to benefit from botulinum toxin A injections regardless of the laterality of injection into the thyroarytenoid muscle.<sup>9,10</sup> A solely unilateral response, on the side of neurovascular compression determined by the MRI, may be the definitive diagnostic test for HeLPS.

All patients with HeLPS who received pre-operative botulinum toxin A injections reported a dramatic reduction in the severity of their choking (but no change in cough) following unilateral botulinum toxin A injection on side ipsilateral to their MRI documented neurovascular conflict. As our understanding of HeLPS evolved, we started deliberately injecting potential HeLPS patients sequentially on both sides as a diagnostic test. Patient 6 passed this test (ie, a reduction in symptoms following ipsilateral but not contralateral botulinum injection) and subsequently had complete resolution of symptoms following MVD surgery. In retrospect, the misdiagnosis of Patient 8 could have been avoided because they responded to botulinum toxin A injection on both sides and therefore did not have HeLPS. She was ultimately diagnosed with paradoxical vocal fold dysfunction.

Laryngeal electromyography (LEMG) was not utilized because it was felt that it would not be helpful. Patients with HeLPS are asymptomatic in-between episodes and the LEMG would therefore be normal. During an episode, these patients would not likely tolerate LEMG (similar to patients with PVFD).

It is a big step to offer microvascular decompression surgery to a patient and we do not make this decision lightly. Operating near the vagus nerve is technically more challenging than similar surgery near the trigeminal or facial nerves. Six of the patients had complete resolution of their symptoms and Patient 2 had his tracheostomy removed three months later. Two of the six successful patients had an ipsilateral vocal fold paralysis and one had an ipsilateral vocal fold paresis. Initially, we were concerned that the surgery was curing the symptoms by causing an iatrogenic vocal fold paralysis, similar to how a vestibular neurectomy cures vertigo.<sup>11</sup> The other three patients, however, had normal vocal fold mobility after surgery and complete cure of symptoms. We surmise that there was a stretch injury to one or more of the vagus nerve rootlets during surgery in those three patients. Although 1 year is the classic time frame for recovery of the vocal fold paralysis, recent publications have alluded that this deadline is more a convention than based on rigorous scientific evidence.<sup>12</sup> We continue to follow these patients.

There were three patients who had MVD surgery and did not respond. Patient 7 had glossopharyngeal neuralgia and would therefore have been offered surgery regardless of whether she had HeLPS or not. Her left glossopharyngeal neuralgia resolved but she still reported laryngospasm and episodic coughing. She had a left vocal fold paralysis post-operatively. We presume that pre-operative botulinum toxin A injection in the left vocal fold would not have improved her HeLPS-like symptoms (since her post-operative paralyzed left vocal fold did not resolve her symptoms). In retrospect, sequential botulinum toxin A injections could have ruled out HeLPS syndrome but she would still have had MVD surgery for her glossopharyngeal neuralgia. Patient 8 responded to botulinum toxin A injections on both sides. If we had applied our new rule of sequential botulinum toxin injections, this patient would not have been offered MVD. She most likely had PVFD. Patient 9 was ultimately diagnosed with a functional disorder after further psychiatric evaluation. She had some personal stressors in her life after surgery that brought out her psychiatric condition. This patient also had a past episode of conversion aphonia. This last case stresses the importance of a multidisciplinary team for diagnosis.

The true incidence of HeLPS is difficult to determine, but it is likely rare. Other conditions, like PVFM, irritable larynx syndrome, muscle tension dysphonia, and reflux induced laryngospasm are more common. This condition is likely underreported, with patients being misdiagnosed as having a psychiatric disorder.<sup>1,2</sup> The correct diagnosis will lead to appropriate and timely curative management. Misdiagnosis, however, could lead to unnecessary surgery.

The purpose of publishing this series in an otolaryngology journal is to promote awareness of this new clinical entity. Otolaryngologists will see many patients with symptoms of laryngospasm, choking, and coughing. We invite

the otolaryngology community to start a dialog, to refine the diagnostic criteria for HeLPS, and to give us constructive feedback. There is already an active discussion on HeLPS in the neurosurgery literature<sup>1,2,13</sup> and we hope to have a multidisciplinary approach to serving these patients. When selecting MVD or repeated botulinum toxin A injections to treat HeLPS, patients will need to be educated by their otolaryngologist and neurosurgeon about the potential benefits and risks of each therapy. MVD offers the advantage of a permanent cure and complete resolution of both laryngospasm and cough (none of our patients had significant improvement in their cough following botulinum toxin injections). Botulinum toxin injections has less chance of a permanent vocal fold paralysis.

This is the largest case series of HeLPS to date. We have openly compared our successful patients with our (previously unpublished) unsuccessful patients to further refine the diagnostic criteria.

## Conclusion

The diagnostic criteria for hemi-laryngopharyngeal spasm (HeLPS) are proposed. The five defining characteristics are as follows: 1) Clinically, patients present with episodic laryngopharyngeal spasm and coughing and are asymptomatic between episodes. These symptoms are refractory to speech and psychiatric therapy and reflux management. 2) In-office laryngoscopy between episodes is normal in the majority of patients but vocalization-induced hyperactive twitching of the ipsilateral vocal fold was seen in two of six patients (this may be a pathognomonic sign). 3) Patients given pre-operative botulinum toxin A injections into the thyroarytenoid muscle on the ipsilateral side have reduced motor symptoms (laryngopharyngeal spasm). Sequential botulinum toxin injection in the contralateral thyroarytenoid muscle should not result in any reduction in motor symptoms. Cough is typically unaffected. 4) Magnetic resonance imaging reveals an ipsilateral neurovascular conflict between the vagus nerve rootlets and posterior inferior cerebellar artery (this finding is a *sine qua non* but does not by itself confirm the diagnosis). 5) Finally, ipsilateral microvascular decompression (MVD) of their affected vagus nerve will permanently resolve all symptoms. Recognition of this new clinical entity will avoid misdiagnosis, lead to accurate evaluation, and timely curative management.

## Authors' Note

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## Supplemental Material

Supplemental material for this article is available online.

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