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Paroxysmal Laryngospasm Secondary to Gastroesophageal Reflux

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Over a 2-year period (1992 to 1994), 12 consecutive adult patients with paroxysmal laryngospasm were prospectively studied. All had had other symptoms of gastroesophageal reflux (GER); however, only 4 (33%) experienced symptoms of heartburn. Each patient underwent fiberoptic laryngeal examination, barium swallow/esophagography, and ambulatory, 24-hour, double-probe pH monitoring (pH-metry).

Eleven (92%) of the 12 patients had evidence of GER on examination, and 10 (83%) had abnormal pH-metry, including 3 who demonstrated pharyngeal reflux while having normal total acid exposure times in the esophageal probe. All the patients responded to antireflux treatment, using dietary and lifestyle modifications and omeprazole, with complete cessation of the laryngospastic episodes.

This study documents the role of GER in the etiology of paroxysmal laryngospasm, it highlights the advantages of double-probe pH-metry in diagnosing this extraesophageal manifestation of GER, and it demonstrates that antireflux therapy with omeprazole is effective in controlling GER-induced laryngospasm.

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INTRODUCTION

Patients with gastroesophageal reflux (GER) are commonly encountered in otolaryngology (ORL); however, most ORL patients do not have complaints of heartburn.[1] Instead, ORL patients complain of symptoms related to the reflux of gastric contents into the upper aerodigestive tract. Therefore this type of GER appears to be different from that seen by gastroenterologists, and it may be more precisely termed *gastropharyngeal reflux.*

GER is believed to be an important contributing etiologic factor in many inflammatory and neoplastic laryngopharyngeal disorders.[1–6] Its most common symptoms are hoarseness, globus pharyngeus, dysphagia, aspiration, chronic cough, and throat clearing.[1] Laryngospasm is uncommon but is a highly significant and distressing symptom in patients with GER.[6–8]

Laryngospasm is defined as a sudden, prolonged, forceful apposition of the vocal cords, and it is believed to be the result of a laryngeal reflex response to noxious stimuli. The reflex arc, as described by Suzuki and Sasaki,[9] consists of an afferent limb carried by the stimulated superior laryngeal nerve (SLN) and an efferent limb carried by the recurrent laryngeal nerve (RLN). The authors showed that electrical stimulation of the SLN produces repetitive, excitatory "after discharges" of the RLN, which in turn cause prolonged adduction of the vocal folds by stimulation of the thyroarytenoid and lateral cricoarytenoid muscles and inhibition of the posterior cricoarytenoid muscle.

In humans, GER-induced laryngospasm was first described by Chodosh[7] in 1977. It has since been reported by others,[1,6–14] and studies using animal models have implicated acid contact with the endolaryngeal mucosa as a cause of both laryngospasm and reflex central apnea.[15–17] In addition, it has been postulated that GER may be a cause of sudden infant death syndrome in children.[8,15–19]

Bortolotti[6] reported two adult patients with recurrent episodes of sudden upper airway obstruction followed by choking. Twenty four–hour, double-probe pH monitoring (pH-metry) confirmed a diagnosis of GER, and antireflux treatment with famotidine, metoclopramide hydrochloride, antacids, and dietary and lifestyle modifications resulted in the cessation of the laryngospastic episodes in both patients over a period of 6 months. Campbell et al.[10] reported six patients with laryngospasm. On the basis of history and barium esophagography, the authors considered GER to be contributory in two of the patients and "nonspecific laryngeal irritation" to be contributory in the other four.

At the Center for Voice Disorders of Wake Forest University we have seen an increasing number of patients whose chief complaint was episodic, sudden upper airway obstruction associated with stridor and "choking spells" (laryngospasm). In some patients the

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episodes were related to eating, and in some they awoke the patient from sound sleep. For diagnostic purposes most of the patients could mimic their stridor, and in most cases it was consistent with that of acute laryngospasm.

Upon further inquiry, these patients also complained of many of the other ORL symptoms of GER. Therefore, beginning in 1992, we began to prospectively study a group of such patients using 24-hour, double-probe pH-metry and barium swallow/esophagography as routine parts of each patient's diagnostic evaluation. We hypothesized that GER was the cause of the laryngospasm in these patients, that pH-metry would assist in making this diagnosis, and that antireflux therapy aimed at preventing GER would result in resolution of the distressing symptoms in these patients. This report presents a prospective study of 12 patients with laryngospasm, and it appears to validate our hypothesis.

MATERIALS AND METHODS

From 1992 to 1994 a prospective study was carried out on 12 consecutive, adult, nonsmoking patients (age range, 24 to 79 years) who presented to the Center For Voice Disorders of Wake Forest University with laryngospasm. All patients suffered from recurring episodes of sudden-onset airway obstruction with loud inspiratory stridor, dyspnea, and coughing. These episodes lasted from 30 seconds to 5 minutes. In most cases no predisposing events could be recalled by the patient.

Most of the episodes of laryngospasm occurred during wakefulness, but every patient reported at least one episode that had awakened him or her from sound sleep. One patient had required intubation for an episode that had occurred postprandially and worsened over a 20-minute period.

The initial diagnostic evaluation consisted of the following: *1.* a history obtained by the physician and a "reflux data sheet" filled out by the nursing staff during the initial office visit,[1] *2.* a complete head and neck examination, and *3.* transnasal fiberoptic laryngoscopy (TFL) with laryngeal photography.

None of the 12 patients had a history of cardiovascular, neurologic, or pulmonary abnormalities. The most common symptoms other than laryngospasm were hoarseness (9/12), dry cough (6/12), and globus pharyngeus (6/12); but only 33% (4/12) of the patients experienced heartburn and/or regurgitation.

Laryngeal examination revealed signs of GER in 11 patients, including laryngeal erythema, Reinke's edema, edematous and erythematous arytenoids and interarytenoid region ("posterior laryngitis"), thick endolaryngeal mucus, and/or vocal process granulomas. One patient had a laryngospastic episode documented on TFL after an episode of regurgitation during examination.

All of the study patients underwent barium swallow/esophagography with videofluoroscopy and 24-hour, double-probe pH-metry. The technique of double-probe pH-metry has been reported previously in detail.[1,21,22] The distal probe is placed 4 cm above the lower esophageal sphincter (LES), and the second probe is placed 1 cm above the upper esophageal sphincter (UES) behind the laryngeal inlet. Manometry is performed prior to positioning of the probes to accurately locate the UES and LES. Normal values for esophageal acid exposure times detected by the distal probe (percentage of time that pH < 4) in our laboratory are as follows: <8.1, upright; <2.9, supine; and <5.5, total.[22] These values are similar to other reported norms.[1] Even a single reflux episode detected by the pharyngeal probe is considered indicative of GER.[1]

In some cases thyroid function testing and electrolyte measurements, including calcium and magnesium, were obtained to exclude hypothyroidism, hypomagnesemia, and hypocalcemia as contributing factors to laryngeal edema and/or spasm. In none of our study patients were abnormalities of thyroid function or electrolytes found. In addition, none of the patients had neurologic disorders or spasmodic dysphonia predisposing them to laryngospasm.

Once a presumptive diagnosis of laryngospasm due to GER was made, patients were placed on an antireflux treatment regimen consisting of dietary and lifestyle modifications,[1] plus oral omeprazole 20 mg two times daily. Three patients who had been taking cimetidine (1200 mg per day) without benefit were converted to omeprazole treatment.

Study patients were followed on a monthly basis for at least 1 year (mean, 16 months; range, 1.0 to 2.5 years), and the medical therapy was considered to be successful if the patients reported a complete cessation of their laryngospastic episodes.

RESULTS

Ten (83%) of the 12 patients had abnormal pH-metry (Table I). Of those 10, 7 had abnormal esophageal acid exposures and 5 had pharyngeal acid exposures (range, 1 to 7 exposures; median, 3) in a 24-hour period. Three patients with abnormal pharyngeal reflux had normal esophageal acid exposure times. In other words, in 30% of patients with abnormal studies, the diagnosis of GER was made with no abnormality in esophageal exposure to refluxed gastric acid.

Ten patients had abnormalities on barium esophagography, including nonspecific dysmotility, a cricopharyngeal bar, diverticula, esophagitis ring, and hiatal hernia.[20] Only 3 patients had evidence of esophagitis on barium swallow/esophagography.

Patients were followed monthly after the initiation of antireflux therapy. Within 1 to 4 months of the start of omeprazole, laryngospasm in all 12 of the patients ceased completely. Other symptoms related to GER also declined; hoarseness and throat clearing were the most persistent symptoms. In addition, repeat laryngeal examination revealed that all patients had shown improvement of laryngeal findings within 4 months of the initiation of therapy.

Once patients reported a cessation of laryngospastic episodes, they were followed up at less frequent intervals, varying from every 2 to every 4 months. After a mean follow-up of 14 months, 8 patients had normal findings on laryngeal examinations;

TABLE I.
Results of Double-Probe pH-Metry and Barium Esophagography.

Patient No.	Age/Sex	Esophageal: Upright (mean±2 SD)	Esophageal: Supine (mean±2 SD)	Esophageal: Total (mean±2 SD)	Pharyngeal Episodes (mean±2 SD)	Barium Swallow
1	60/F	1.3	0.4	1.1	0	Esophagitis
2	59/F	[9.1]	0.0	[7.2]	[1]	HH
3	24/M	6.6	[24.8]	[13.4]	0	HH, ED
4	73/M	[8.8]	0	[6.3]	0	HH, esophagitis, diverticula
5	41/F	7.2	0.1	3.5	[2]	Normal
6	67/M	[13.0]	[25.6]	[16.7]	[3]	HH, ED, cricopharyngeal bar, ring
7	70/M	2.6	[23.9]	[14.4]	0	ED
8	71/M	4.7	2.1	4.4	0	HH, esophagitis
9	53/M	3.2	[5.4]	4.4	0	HH
10	45/F	3.0	0	1.9	[3]	Normal
11	75/M	[9.1]	1.1	[6.0]	0	HH, ED, ring
12	55/F	4.5	0.3	3.2	[7]	HH

[] = abnormal value; HH = hiatal hernia; ED = esophageal dysmotility.

the other 4 had persistence of Reinke's edema.

Within 1 year of starting omeprazole therapy, 10 patients were switched to therapy with the histamine (H_2) blocker ranitidine, 150 mg orally, twice daily, and 2 patients to cimetidine, 400 mg orally, three times a day. Interestingly, two of the patients taking ranitidine experienced recrudescence of paroxysmal laryngospasm within 6 weeks and were then restarted on a regimen of omeprazole, 20 mg orally, two times daily (again, with eradication of the laryngospasm). Both patients were subsequently referred for Nissen fundoplication, and neither has experienced any laryngospastic episodes since antireflux surgery.

DISCUSSION

The preceding data suggest that GER may be the most common cause of laryngospasm; however, it is important to note that only one third of the patients had symptoms of heartburn or regurgitation. This finding is consistent with the findings of others that the manifestations (and possibly the pathogenesis) of "gastropharyngeal reflux" are different from those of reflux esophagitis.[1] Heartburn is associated with impaired mucosal protective mechanisms and esophageal mucosal injury (i.e., esophagitis). Since only three of our patients had esophagitis on barium esophagography, it is not surprising that most of our patients did not report heartburn.

In the event that double-probe pH-metry is not available or affordable, a presumptive diagnosis of GER-induced laryngospasm can be made based on a history suggestive of laryngospasm and GER symptoms and findings suggestive of GER on laryngeal fiberoptic examination. As shown by our results, treatment for GER could be expected to resolve symptoms of laryngospasm within approximately 4 months. If laryngospasm persists, the diagnosis may need to be rethought, or pH-metry then performed to exclude continued GER.

Even a single GER event may set off a severe laryngospastic episode in susceptible patients. We chose the proton pump inhibitor omeprazole as the primary therapy over the H_2 blockers because of its effectiveness in arresting gastric acid production when administered in a twice-daily dose. At the time this study was initially performed, omeprazole was the only proton pump inhibitor available for use. Newer proton pump inhibitors currently available may be predicted to have similar efficacy. Once the laryngospasm and GER are controlled with a proton pump inhibitor, we will switch our patients to H_2-blocker therapy as a cost-saving measure. If such therapy subsequently fails, we recommend either restarting therapy with the proton pump inhibitor or referring for antireflux surgery.

CONCLUSIONS

1. This study presents the largest series to date of patients with GER-induced laryngospasm, their diagnostic workup, and results of treatment for GER.

2. Double-probe pH-metry appears to be useful in confirming the diagnosis of GER in patients with laryngospasm; all but 2 of our 12 patients had abnormal pH studies. (Conversely, barium swallow/esophagography appears to be the less sensitive diagnostic test for gastropharyngeal reflux.)

3. The second (pharyngeal) probe is especially helpful in detecting gastropharyngeal reflux: three patients with normal esophageal acid exposure times in the esophageal probe had reflux documented by the pharyngeal probe.

4. Initial therapy with twice-daily omeprazole appears to be a highly successful treatment for patients with GER-related laryngospasm.

5. Nissen fundoplication appears to be an effective treatment alternative in selected patients—those who fail maintenance medical therapy.

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