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Asthmatic extrathoracic upper airway obstruction: Laryngeal dyskinesis

Jeffrey Nahmias, MD
Michael Tansey, PhD
Monroe S. Karetzky, MD

Laryngeal dyskinesis is a functional asthma-like disorder refractory to bronchodilator regimens. Patients treated with electroencephalographic neurofeedback training demonstrate clinical improvement with reversal of their variable extrathoracic upper airway obstruction.

Laryngeal dyskinesis (LD) often is misdiagnosed as asthma, since patients present in significant respiratory distress with dyspnea, cough, wheezing, and/or stridor. Laryngoscopy reveals abnormal adduction of the vocal cords during inspiration for LD patients.1-14 LD is notable in being resistant to standard asthma therapy. Since asthma and a wide variety of muscle spasm activity have responded positively to electroencephalographic (EEG) neurofeedback, it was decided to test its efficacy on LD.

The eponym of Munchausen's stridor was given to LD when it first was described in 1974.15 Since then, more than 31 of these patients with functional upper airway obstruction, along with a characteristic variety of psychogenic disorders, have been described.1-14, 16-27 These reports have consisted of anecdotal case histories with systematic assessments performed on a small number of patients.1,4 This investigation consists of a relatively large (n=15) group of patients with LD that were studied prospectively for the purpose of evaluating clinical and physiological responses to treatment that included the application of EEG neurofeedback training.

Table 1.	*Abbreviations.*
ANX	Anxiety neurosis
CZ	Central scalp surface electrode placement along the midline of the top of the head
DEP	Depression
EEG	Electroencephalographic
EMG	Electromyographic
FEF_{50}	Expiratory flow rate at 50 percent of forced expiratory vital capacity
FEV_1	Volume expired in first second of forced vital capacity
FIF_{50}	Inspiratory flow rate at 50 percent of forced inspiratory vital capacity
FVC	Total volume forcefully expired-starting at full inspiration
LD	Laryngeal dyskinesis
MMFRR	Mid-maximal flow rate ratio (FEF_{50} / FIF_{50}
PTSS	Post-traumatic stress syndrome
ROAD	Reversible obstructive airway disease
SEM	Standard error of the mean
VEO	Variable extrathoracic upper airway obstruction
WC	Spirometric tracing of maximal inspiratory and expiratory efforts starting at full expiration (residual volume) and full inspiration (total lung capacity), respectively.

SUBJECTS AND METHODS

Fifteen patients seen between January 1986 and December 1990 for evaluation of resistant (persistent) asthma were found to have LD. Inclusion criteria for patients consisted of the demonstration of normal expiratory flow rates in conjunction with reduced inspiratory flow rates during an acute episode of dyspnea. This is detected in the symptomatic acute phase as a flattening of the inspiratory limb of the flow volume loop with a normal contour to the expiratory limb previously defined as variable extrathoracic upper airway obstruction (VEO)28 In addition, while breathing room air, arterial blood samples (n = 14) were drawn (one patient refused) for the determination of pHa, PaCO2, and PaO2. Patients social histories and their response to standard asthma therapy, including duration and adverse effects, were tabulated. In addition, each patient underwent an independent psychiatric assessment.

Fiberoptic laryngoscopy, not routinely done initially, was performed in the last 11 patients to confirm the diagnosis of LD by demonstrating paradoxical adduction of the vocal cords during inspiration. In the performance of this examination, no anesthesia was administered to the oropharynx. Bronchoprovocation testing utilizing methacholine, delivered via a Rosenthal dosimeter, was performed starting in 1988 on all patients (n = 8) during their chronic stable state.29

EEG neurofeedback training was offered to all patients. Five patients elected to participate in this treatment regimen: the EEG neurofeedback training was oriented about the neuroregulation of the brain via trained increases in the amplitude of a 14 Hz brainwave band.30 Three saline sensors were used (impedance in saline of 1K ohm). The active sensor was positioned so that its 6.5 x l.3 cm contact surface lay lengthwise along the midline of the top of the skull (overlaying the cerebral longitudinal fissure), centering about Cz (10/20 system). It was held in place with two elasticized headbands with velcro on the ends. One band was placed about the head, parallel to the eyebrows, across the middle of the forehead. A second band was placed across the top of the head and the

active sensor, attaching at either end on the other headband, near each ear. In this position, the active sensor was kept in place over the Rolandic cortex (pre- and post-central gyri) of the right and left cerebral hemispheres. For a 40-minute duration per each session, 14 Hz EEG neurofeedback was performed weekly. Treatment duration varied from 7 to 14 sessions. Following a course of EEG neurofeedback, the patients were re-evaluated clinically and with repeat generation of maximal effort flow volume curves. Statistical comparisons between preand post-flow volume curves were made, with a *P* value of less than 0.05 considered significant.

CLINICAL SYMPTOMOLOGY

All 15 patients were female, ranging in age from 25 to 67 years. Presenting symptoms consisted of hoarseness, cough, and dyspnea with a duration ranging from two weeks to 9 years with a mean (± SEM) of 36.0 ± 9.6 months. On auscultation, 8 patients had an inspiratory wheeze heard above the sternal notch but none audible in the chest. Asthma therapy was reported to be uniformly unsuccessful with the adverse effects of corticosteroid usage present in 7 patients: Cushingoid facies (4), steroid myopathy (1), carpal tunnel syndrome (1), and hallucinations (1).

PULMONARY FUNCTION TESTS

Spirometric measurements revealed the FEV1 and FVC to be less than 70 percent predicted in only one patient and FEV1/FVC greater than 70 percent in all patients (Table 2). Flattening of the inspiratory limb was evident in all patients, during acute episodes of dysnea; the mid-maximal flow rate ratio (MMFRR=FEF50/FIF50) being greater than or equal to 1.

Arterial blood gases revealed a mean pH of 7.42, PaCO2, of 36.7 mmHg, and PaO2 of 91.3 mmHg. While three patients had a PaCO2 less than 80 mmHg, no patients had a PaO2, less than 70 mmHg or hypercapnia.

Methacholine provocation testing was positive in four of the nine patients tested, but with a 20 percent or greater decrease in FEV1 being observed only at the highest concentration of methacholine in three of these patients. One patient reacted at the third concentration of inhaled methacholine.

Table 2. ***Spirometric and psychological profile.***

FEV_1 (L)	(%PRED)	FVC (L)	(%PRED)	FEV_1%	MMFRR	VEO	PSYCH
2.38	(87%)	2.50	(79%)	89%	1.2	+	PTSS
2.34	(70%)	3.27	(80%)	72%	1.1	+	DEP
2.88	(95%)	3.27	(96%)	84%	1.5	+	PTSS
2.19	(85%)	3.87	(96%)	74%	1.0	+	ANX
2.28	(88%)	3.04	(101%)	75%	1.1	+	ANX
3.27	(84%)	3.87	(98%)	84%	1.3	+	ANX
2.68	(97%)	3.20	(97%)	84%	1.6	+	ANX
3.34	(104%)	3.70	(96%)	90%	1.7	+	DEP
1.95	(87%)	2.24	(81%)	87%	2.8	+	ANX
2.52	(76%)	2.88	(71%)	87%	1.3	+	PTSS
1.98	(64%)	2.27	(63%)	85%	1.3	+	ANX
2.09	(81%)	2.66	(89%)	78%	1.1	+	ANX
1.60	(86%)	1.99	(90%)	84%	3.0	+	ANX
2.22	(79%)	2.63	(83%)	89%	1.7	+	ANX
2.04	(75%)	2.63	(83%)	89%	1.7	+	ANX
1.98	(64%)	2.26	(73%)	85%	2.2	+	ANX
mean							
2.38	(84%)	2.89	(88%)	83%	1.56		

Spirometric values initially obtained during acute episodes of dyspnea in the 15 patients.
FEV_1% = FEV_1/FVC MMFRR = mid-maximal flow rate ratio (FEF_{50}/FIF_{50}) VEO = variable extrathoracic upper airway obstruction as suggested by flattening of inspiratory limb of flow-volume loop
ANX = anxiety neurosis DEP = depression PTSS = post-traumatic stress syndrome

LARYNGOSCOPY

Direct fiberoptic laryngoscopic examination revealed paradoxical adduction of the vocal cords at full inspiration in 10 of the 11 patients evaluated. This effect was enhanced by deep and rapid breathing. In all cases, glottal hyper-reactivity was readily elicited by gently touching the cords with the laryngoscope.

EEG NEUROFEEDBACK

The baseline brain wave signatures of the patients who underwent 14 Hz EEG neurofeedback training are shown in Figure 1. It is interesting to note that each patient at baseline demonstrated a pathologically significant signature generally reflective of diminished voluntary motor control.30 This is evidenced in the significantly greater EEG energy as exhibited in the 7 Hz brain wave band as compared with the energy levels found in the rest of the signature.

The progressive normalization of these brain wave signatures occurred in a similar fashion for all patients who underwent 14 Hz EEG neurofeedback training. The normalization of the brain wave signature across their neurofeedback sessions are shown for two patients in Figure 2. The neuroregulation and shifting of the EEG brain wave signature for these two patients is representative of the other three patients as well.

All five patients reported significant improvement in their symptoms after 7 to 14 sessions with repeat VVC demonstrating restoration of convexity of the inspiratory limb

and significant decrease in mean mid-maximum flow rate ratio (MMFRR) from 1.58 - 0.30 to 0.94 - 0.13 ($P<0.05$) (Figure 3) with no changes in expiratory flow rates. One patient reported continued remission one-year post-EEG neurofeedback.

DISCUSSION

Clinical characteristics. LD, often misdiagnosed as asthma, is refractory to the usual medical regimens employed in alleviating bronchospasm. These patients typically present with side effects of prolonged corticosteroid treatment, suffering from iatrogenic Cushing's syndrome.4,20 All of the patients were female and a 3:1 female to male ratio exists in the published case reports, but a similar spasmodic entity of largyngeal dysfunction has been observed to predominate in male patients.31 Routine polysomnography has been suggested because of the frequent association of obstructive sleep apnea. In the present series, two of three patients studied were found to have significant sleep disordered breathing.

Laryngoscopy has revealed exaggeration of normal vocal cord adduction during inspiration or expiration with almost complete closure.20,32 During asymptomatic periods between attacks, normal vocal cord function is observed with normal degrees of closure with expiration and widening during inspiration.4,20 Variability exists in the primary site of airway obstruction even in "true" asthmatics with evidence of upper airway obstruction demonstrated by a greater resistance to flow during early inspiration and improvement with HeO2 mixtures.32 Thus, narrowing of the glottis or larger extrathoracic upper airways is an important pathophysiological mechanism in some asthmatics. In addition, in patients with LD, hyper-reactivity of the vocal cords can be readily demonstrated by touching them with the laryngoscope.

Another feature of LD is that arterial oxygenation usually is in the normal range with normocapnia. Review of the literature revealed that of the 21 patients with LD who have had blood gas determinations, only 3 patients had a PaO2 less than 80 mmHg and no patient had a blood gas determination below 70 mmHg.4,5,12,15,16,19,22,24,26,31 Thus, the normal PaO2, as well as expiratory flow ratio, has been suggested as valuable tools to use in differentiating an episode of LD from "true asthma" where arterial hypoxemia frequently is present.

AIRWAY HYPERREACTIVITY

Bronchoprovocation testing utilizing either methacholine or histamine4,19,20,22,23 has shown bronchial hyper-reactivity in 1 of 13 patients, 22 with histamine-induced upper airway stridor in another patient.5 In the present study, 4 of 9 patients had a positive methacholine challenge test; 3 patients had a positive methacholine delivered at the highest concentration. These patients may have a combination of upper and lower airway dysfunction with minimal reversible obstructive airway disease (ROAD).8

PSYCHOGENESIS

Bronchial asthma can be precipitated by psychogenic stimuli.33 Such an apparent predisposition to emotional lability with psychiatric diagnoses is emphasized in the numerous reports of LD.1,5,6,10,15,17,20-22,26 The physiologic and psychiatric findings in five patients with LD have been reported in comparison to three patients with expiratory laryngeal stridor with asthma and five patients with asthma alone.1 Psychiatric disorders have been portrayed as playing a pivotal role in the LD patients as compared to those patients with asthma.1

A variety of psychiatric diagnoses have been associated with LD including depression,1,6,9,10 anxiety,2,6,13,19,20,27,29 hysterical conversion,5,11,15,18,21,22,24,26,31 and obsessive-compulsive1,4 and dependent personality disorders.2,6,7,13,17

Treatment has been attempted with psychotherapy,9,17,21 speech therapy,4,10,18,27 and neurofeed back,13,27 while medical treatment has been found to be uniformly unsuccessful. Each of our patients was diagnosed with a concurrent emotional disorder. In addition, four patients were diagnosed to have irritable bowel syndrome, and 2 patients were diagnosed with hysterical conversion disorders (pseudoseizures and syncope). Three patients developed LD as part of a previously diagnosed post-traumatic stress syndrome: one patient was mugged, one patient experienced prolonged sexual harassment, and another patient following the sudden death of her spouse at age 36.

THERAPEUTIC

Helium-oxygen mixtures have been used for upper airway obstruction. Its benefit attributed to the reduction in density resulting from substituting helium for nitrogen-reducing turbulence and, therefore, resistance to gas flow. For patients with severe or life-threatening episodes, physical therapies advocated include tracheostomy3 and arytenoidopexy, and, for those with the laryngeal features of what has been tenned Gerhardt's syndrome, the injection of botulinum toxin into the thyroarytenoid muscle.34 Sedatives and anxiolytics also have been employed as primary or ancillary modes of therapy.1,17,18,22 it is of importance when considering such therapy to be aware of the deaths due to LD that followed the administration of neuroleptics.35 It now is clearly understood that the behavior of the laryngeal vocal folds are a function of laryngeal striated muscle whose motor neurone pool is in the nucleus ambiguous.36,37

This can be influenced by associated neurone activity to serve a normal autoregulatory function during expiration or, as suggested in this entity, be the basic pathophysiologic mechanism for upper airway dysfunction (laryngeal dystonia) during the respiratory cycle.

A review of the literature revealed that 11 patients were successfully treated with speech therapy,4,10,18,23,27 6 patients treated with relaxation therapy,1,13,17,21 and 3 patients treated with biofeedback (2 patients treated in combination with speech therapy).14 Each report discussed the clinical response but none followed up the flow/volume studies to objectively measure the treatment outcome. Utilizing EEG neurofeedback training, we

were able to demonstrate objective improvement in the inspiratory limb of the flow volume curve with significant decreases in MMFRR (3 of the 5 patients had a normal MMFRR after treatment).

- Figure 1. Comparison of baseline EEG amplitudes.
- Figure 2. Changes in brainwave signature in two patients undergoing EEG neurofeedback training.
- Figure 3. MMFRR (FEF50 / FIF50) values in five patients before and after EEG neurofeedback training. Mean values indicated by inverted solid triangles.
- Note: These three figures are being prepared in 'GIF' format for internet use and will be included here as soon as they have been completed.

The authors are affiliated with Newark Beth Israel Medical Center. *The paper was submitted on April 1994 and accepted on June 1994.* *Address reprint requests to Dr. Karetzky, Newark Beth Israel Medical Center, 201 Lyons Avenue, Newark, NJ 07112.*

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