A Perplexing Presentation of New Onset Wheezing

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Can you guess the underlying condition causing this patient's episodic wheezing and difficulty breathing?

A 17-year-old girl presented to the emergency department (ED) reporting difficulty breathing and wheezing, which had begun the previous day. The patient had no history of asthma or other breathing difficulties. During the physician-patient interview, the patient was having such significant difficulty breathing that she was unable to provide a medical history apart from head-nod responses to yes or no questions.

According to her father, the patient was at school when she experienced 4 to 5 episodes of wheezing with shortness of breath—each episode lasting approximately 20 minutes—followed by asymptomatic periods with no wheezing or difficulty breathing. She was treated with nebulized albuterol by the school nurse, which did not result in any significant improvement. The wheezing episodes recurred throughout the evening at home and, when the symptoms persisted the following day, she was taken to see her primary care provider.

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At the primary care provider's office, the patient received multiple albuterol nebulizer treatments for the wheezing and difficulty breathing. When the patient showed no appreciable response to the treatments, she was transferred via ambulance to the ED for further evaluation and treatment. During the transfer, she again received additional albuterol nebulizer treatments.

In the ED, the patient received multiple 2.5 mg and 5.0 mg albuterol nebulizer treatments, intravenous methylprednisolone 125 mg, nebulized racemic epinephrine 2.25% (.75 ml), and heliox (helium/oxygen mixture) treatments. While the patient did not seem to respond to the repeated albuterol treatments, the heliox and racemic epinephrine appeared to provide a fair amount of symptom relief.

The patient's medical history was significant for an anxiety disorder, which manifested a year ago, after surviving a motor vehicle accident in which her friend's father died. Otherwise, she had no history of asthma, allergic rhinitis, cardiac disease, exposure to any airway irritants (such as paint products, allergens, or tobacco), gastroesophageal reflux disease (GERD), posttraumatic stress disorder, drug allergies, prior surgeries, involvement in sports, or regular exercise. She denied using tobacco, alcohol, illicit drugs, over-the-counter medications, herbal remedies, or other supplements; she also denied any inhalation exposures or sexual activity. Her prescribed medications at the time included escitalopram 10 mg/day, for her anxiety disorder, and the birth control pill, for regulating her menses.

Upon physical examination, the patient's vital signs included heart rate, 123 beats per minute; respiratory rate, 24 breaths per minute; blood pressure, 139/77 mm Hg; temperature, 99.7°F; and weight, 126 lbs. Examinations of her abdomen, all 4 extremities, head, ears, eyes, nose, and throat were unremarkable. Cardiac auscultation revealed tachycardia with a regular rhythm, and no evidence of murmurs, rubs, gallops, or jugular venous distension.

Examination of her pulmonary functions revealed moderate respiratory distress with tachypnea, increased work of breathing with the use of accessory muscles of respiration, and pronounced head bobbing back and forth, particularly with inspiration. Breath sounds were minimal throughout the lung fields, and there was intermittent stridor and inspiratory wheezing, but no rhonchi or rales were auscultated.

Results of laboratory studies included a normal complete blood count, a normal electrolyte panel, a normal urinalysis, and urine negative for beta human chorionic gonadotropin. A chest roentgenogram showed no evidence of hyperinflation, infiltrate, pneumotho-

rax, foreign body, or any other abnormality. Analysis of arterial blood gas (ABG) on supplemental oxygen revealed a normal pH level of 7.42, a normal carbon dioxide (PCO2) level of 38.3 mm Hg, an elevated oxygen (PO2) level of 450 mm Hg (reference range, 80 mm Hg to 100 mm Hg), a normal serum bicarbonate level of 23.8 mEq/L, and a normal base deficit of +1 mEq/L.

The patient's initial presentation of marked stridor and wheezing resolved after approximately 8 minutes. Then, she was calm and able to speak in complete sentences, without any difficulty. With the clinical picture suggesting an upper airway component, she was evaluated further with a computerized tomography scan of the upper airway, which noted a normal epiglottis, normal aryepiglottic folds, normal paratracheal soft tissues, and no evidence of retropharyngeal abscess or other soft-tissue abnormality.

With the continued episodic stridor and wheezing, the patient was prepared for transfer to the intensive care unit, and aggressive treatments were ordered, including intravenous methylprednisolone 125 mg every 6 hours, oral zileuton 600 mg every 6 hours, nebulized racemic epinephrine 2.25% (.75 ml) every hour, and continued heliox treatments.

What's your diagnosis?

OUR DIAGNOSIS

An otolaryngologist was consulted in the ED and a nasopharyngeal endoscopic examination was performed at bedside. The examination revealed that the oropharynx (including the base of the tongue and the epiglottis), nasopharynx, hypopharynx, and larynx were unremarkable in appearance, with no evidence of erythema or edema. The patient exhibited obvious evidence of paradoxical vocal cord motion (PVCM), however, with the vocal folds adducting upon inspiration.

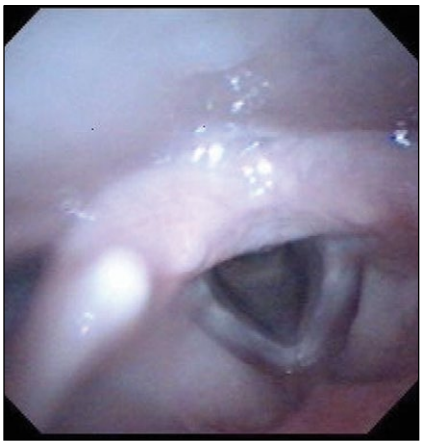

Figure 1. Normal vocal cord abduction during inspiration.

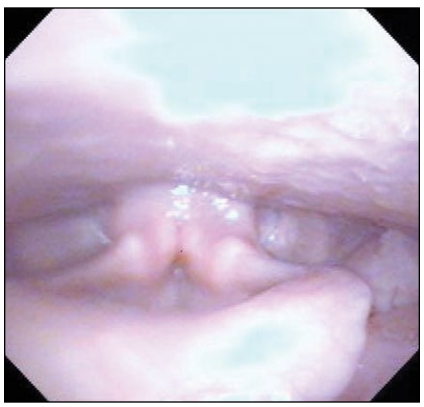

Figure 2. Paradoxical vocal cord movement, with vocal cord adduction during inspiration.

With the diagnosis of PVCM confirmed on endoscopic evaluation, the patient was admitted to the hospital for overnight observation, largely to allay patient and parental anxiety, and to provide them with further education on this condition. Once the diagnosis was confirmed, the methylprednisolone, zileuton, racemic epinephrine, and heliox treatments were discontinued.

Treatment

The patient proceeded to have several additional episodes of acute respiratory distress during the initial 2 hours of hospitalization. For symptom relief, she was given a brief trial of bilevel positive airway pressure, which was discontinued after approximately 5 minutes because of patient discomfort. A trial of continuous positive airway pressure was provided for several hours, which did result in some relief and was well tolerated by the patient.

A speech therapist was consulted and provided the patient with interventions to ameliorate the PVCM symptoms, including breathing pattern exercises, tactile feedback, and visualization; these techniques resulted in significant relief of the patient's symptoms. A psychiatrist also was consulted, who concurred with the speech therapist and recommended continuing the escitalopram for generalized anxiety disorder.

Outpatient follow-up included evaluation by a psychologist, with a biofeedback trial of respiration pacing. Additionally, videostroboscopic evaluation was performed by the speech therapist, which noted the complete abduction of her vocal cords with sniff breathing as well as "S" breathing. When asked to imitate an episode of respiratory distress, vocal cord adduction was noted on the videostroboscope. Outpatient follow-up with the otolaryngologist concurred with the assessment and treatment recommendations of the psychologist and speech therapist.

ABOUT THE CONDITION

Located in the larynx, the vocal cords are comprised of a muscular component (the 2 thyroarytenoid muscles, forming the "body") and a nonmuscular component (the inner and outer layers and lamina propria, forming the "cover").[1] At rest, the vocal cords form a v-shaped space, known as the glottis, and during normal inspiration, they abduct (Figure 1). PVCM

occurs when the vocal cords inappropriately adduct during inspiration and abduct on expiration (Figure 2).

The resultant airway obstruction can manifest as stridor and often is mistaken for asthmatic wheezing, with a diagnosis of asthma or "refractory asthma" being made, and patients receiving bronchodilator treatments, intubation, and even tracheostomy.[2-4] While other such conditions as croup, epiglottitis, laryngospasm, and angioedema may mimic the symptoms of PVCM, lack of awareness of the condition, combined with misdiagnosis, are reasons PVCM is thought to be an underdiagnosed condition.[4]

Published description of laryngeal muscle disorders dates back to 1842, when a medical textbook termed a condition known as "hysterical croup," as it was postulated that the disorder was brought on by hysteria.[5] With the advent of laryngoscopy in 1854,[6] the following decade noted the first visualization of PVCM in patients symptomatic with stridor.[7] Since then, various names have been ascribed to the condition, including "irritable larynx syndrome," "Munchausen's stridor," and "pseudoasthma."[8,9] Medical literature review is noteworthy for over 70 terms used to describe this disorder, such as paradoxical vocal fold motion, paradoxical vocal fold movement disorder, paradoxical vocal cord movement, episodic paroxysmal laryngospasm, and vocal cord dysfunction.[10]

Although the precise pathogenesis of PVCM is not entirely understood, it has been hypothesized that the underlying mechanisms for the condition may include laryngeal hyperresponsiveness, altered autonomic balance, direct stimulation of the sensory nerve endings in the upper and lower respiratory tract, and hyperventilation.[8] With PVCM frequently associated with underlying psychiatric diagnoses, social stresses, and sexual abuse,[4] a psychogenic component also is thought to play a key role in the condition.

Additional patient demographic descriptions and epidemiologic associations include a 2:1 female-to-male ratio,[10] with 63.6% of PVCM cases reported in females and 36.4% reported in males.[8] While the reported age range of the affected population is broad (from < 1 year to 82 years), PVCM is more prevalent in children and young adults, with a median pediatric age of 14 years and a median adult age of 36.5 years.[10]

Even though psychosocial factors may play a role in PVCM, there are a number of other etiologies and associations that the evaluating clinician should consider in the differential diagnosis. While some patients may report dyspnea and exercise-induced asthma-like symptoms, [4] such conditions as GERD,[11] irritant-induced PVCM (caused by inhaling smoke, gases, vapors, dust, airborne pollutants, or odors),[4] and even extubation following general anesthesia have been linked to PVCM. Also included in the differential diagnosis are neurologic diseases, such as Parkinson disease, Arnold-Chiari malformation, cerebral aqueduct stenosis, and amyotrophic lateral sclerosis.[12]

Although the gold standard for diagnosis is direct laryngoscopy,[8] with a broad differential, patients often will have additional diagnostic evaluations. Pulmonary function testing often is used to support the diagnosis of PVCM and typically reveals a highly variable pattern of inspiratory flow configurations, as well as a ratio between the forced expiratory flow (FEF) at 50% of the exhaled vital capacity and the forced inspiratory flow (FIF) at 50% (FEF_{50}/FIF_{50}) that often is > 1.[10] Additionally, these patients frequently have a decrease of > 25% in the maximum inspiratory flow during histamine inhalation challenge.[13]

Methacholine challenge testing typically induces PVCM during laryngoscopic evaluation.[14] Despite overt respiratory distress, ABG analysis typically is normal; however, patient breath-holding can result in a decreased PO2, while hyperventilation can result in a decreased PCO2.[10] Chest roentgenograms are not helpful in the diagnosis of PVCM.[4]

With various possible mechanisms of disease, treatment of PVCM is multifactorial and multidisciplinary in nature. In the acute setting, reassurance, benzodiazepines, heliox treatments, and even botulinum toxin injections and sedation have been utilized.[8,10] Long-term management involves speech therapy, biofeedback, psychotherapy, and hypnosis, all of which have been shown to relieve symptoms.[4] Speech therapy, which teaches proper breathing techniques, with a focus on laryngeal-area control, plays a vital role in the treatment of PVCM, and is considered to be the cornerstone of long-term management.[8,10] Although the medical literature demonstrates inconclusive results regarding the long-term prognosis of patients with PVCM, there are some data that suggest spontaneous resolution of symptoms may be common.[15] Additionally, for patients with GERD-associated PVCM, acid-suppression therapy potentially may provide relief of PVCM symptoms.[16]

IN CONCLUSION

The patient was seen by her primary care provider 2 weeks after the initial presentation and noted almost complete resolution of her PVCM symptoms after utilizing the speech and biofeedback techniques. She did report that she had some increasing

anxiety symptoms related to her previous motor vehicle accident, as the 1-year anniversary of the accident was less than 2 weeks away. As such, she was referred to a pediatric psychologist for outpatient evaluation and further treatment of her anxiety disorder.

On follow-up assessment 2 years following her initial presentation, the patient reported experiencing only mild, brief (few seconds duration), sporadic episodes of respiratory symptoms, typically coinciding with excessively stressful situations. The episodes occurred 2 to 4 times a year and were easily resolved with the breathing techniques the patient had learned previously.

Author disclosures

The authors report no actual or potential conflicts of interest with regard to this article.

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