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Case report

Co-existence of vocal cord dysfunction with pulmonary conditions other than asthma: A case series

Merritt L. Fajt[a,*], Kevin M. Birnie[b], Humberto E. Trejo Bittar[c], Andrej A. Petrov[a]

[a] Division of Pulmonary, Allergy, and Critical Care Medicine; Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
[b] Greater Washington Radiology, Washington, PA, USA
[c] Division of Anatomic Pathology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

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ABSTRACT

Background: Vocal cord dysfunction (VCD) is defined as inappropriate movement of the vocal cords resulting in functional airway obstruction and symptoms including cough, wheezing, and dyspnea. VCD is often misdiagnosed with asthma but can also co-exist with asthma. The association of VCD with other serious pulmonary conditions has not been described to date.

Case reports: We describe the first case series of two adult patients evaluated at a university asthma clinic who in addition to having VCD also had significant pulmonary pathology other than asthma. Patient 1 had VCD and pulmonary veno-occulsive disease which necessitated a lung transplant. Patient 2 had VCD and a patent ductus arteriosis who necessitated surgical closure.

Conclusion: It is important to recognize that VCD can exist with pulmonary conditions other than asthma. Lack of improvement in respiratory symptoms after appropriate treatment for VCD should alert the clinician to evaluate for additional conditions.

1. Introduction

In 1902, Sir William Osler defined vocal cord dysfunction (VCD) as spasms of laryngeal muscles occurring during inspiration and in times of great distress [1]. Currently, VCD is described as exaggerated adduction of vocal cords during inspiration and/or expiration causing respiratory and laryngeal symptoms [2]. Laryngoscopy, the gold standard for diagnosis, involves direct visualization of abnormal vocal cord motion during an acute attack or provocation with known triggers. Classic laryngoscopic findings include inspiratory vocal cord adduction of the anterior two thirds with a posterior diamond-shaped chink [3]. Additionally, abnormal spirometric findings may include flattening of the inspiratory flow-volume loop and increased FEF-50/FIF-50 (ratio of forced flow at 50% of expiration to forced flow at 50% of inspiration) [3–5]. The common respiratory symptoms observed in VCD include cough, dyspnea, wheezing and chest tightness. Because of the overlapping symptoms, the relationship between VCD and respiratory diseases is of particular interest for physicians specializing in pulmonary conditions.

The association between VCD and asthma has been well documented [6–8]. VCD can exist in isolation, can coexist with asthma, or can mimic asthma. Our group has shown that VCD and asthma co-existed in 32.6% of patients seen in a university asthma practice [6]. Comorbid VCD and asthma resulted in increased frequency of long-acting β-agonist use and worse quality of life [6,9]. In our cohort of VCD patients, 42.4% had been previously misdiagnosed as having asthma for an average of 9.0 years, contributing to more ED visits and systemic steroid use [6,10]. To date VCD has not been described in association with pulmonary diseases other than asthma. We describe a case series of two patients with co-existing VCD and non-asthma pulmonary conditions.

1.1. Case 1

A 21-year-old woman, diagnosed with exercise induced asthma at age 14 by exercise spirometry, presented with worsening exertional dyspnea over the past six months. She reported shortness of breath after walking 160 m (2 blocks) that would last 1–3 hours. Despite previous asthma treatment with inhaled corticosteroids, long-acting muscarinic agents, short acting beta agonists and nedocromil, she experienced minimal symptom improvement. Due to lack of improvement in her symptoms, she underwent a methacholine challenge test which was interpreted as positive. Interestingly, there was a parallel decrease in both the FEV1 and FVC without significant change in the FEV1/FVC

* Corresponding author. 3459 Fifth Ave, UPMC Montefiore Hospital – NW628, Pittsburgh, PA, 15213, USA.
E-mail address: fajtml@upmc.edu (M.L. Fajt).

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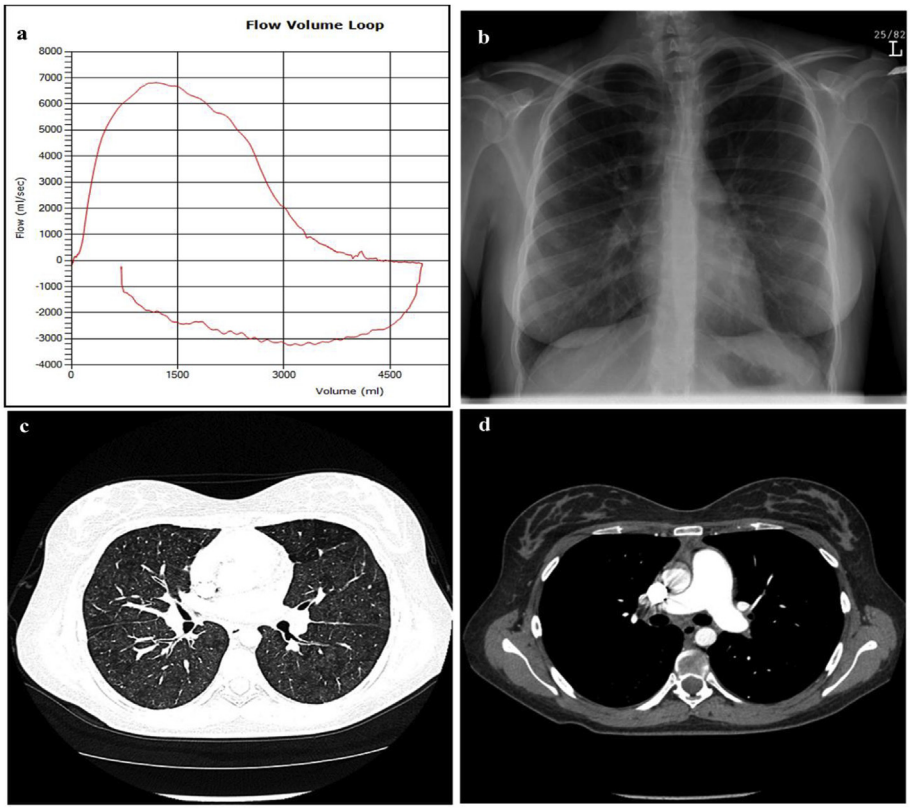

Fig. 1. a. Flattening of inspiratory flow volume loop; b. CXR with interstitial changes in lung bases; c,d. CT Chest with ground-glass opacities (c) and air-trapping and enlarged pulmonary artery (d).

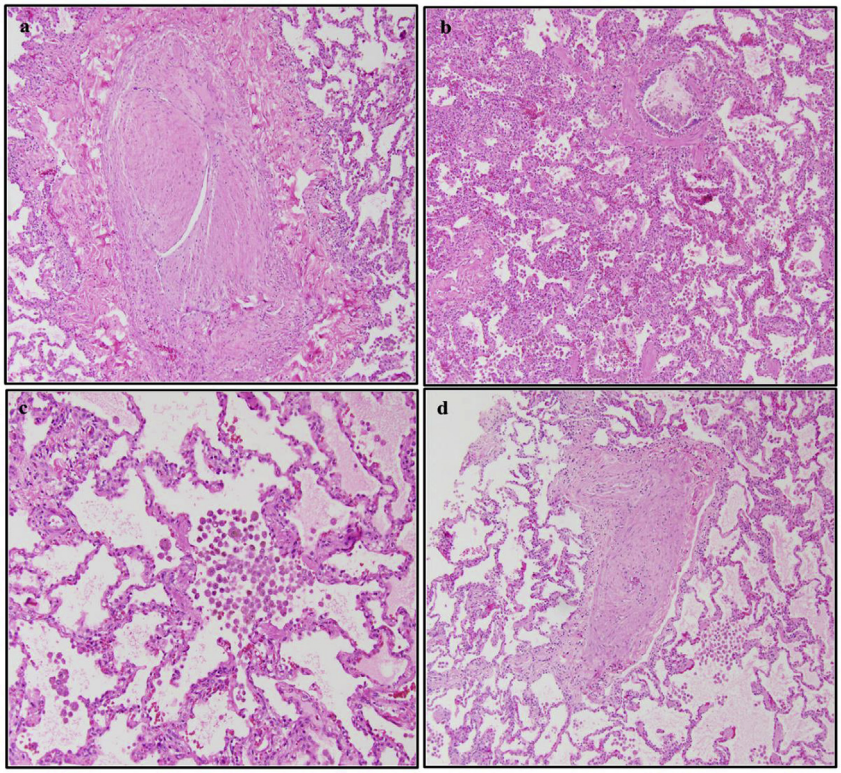

Fig. 2. a–d. Explanted lungs showing intimal fibrosis of veins and venules, diffuse alveolar septal thickening, alveolar hemosiderosis and intimal fibrosis of pulmonary arteries and hypertensive arterial changes.

ratio. Previous CXR showed increased interstitial and peribronchial markings felt to be most consistent with air trapping and asthma. Her dyspnea was also associated with episodic throat and chest tightness triggered by strong perfume scents and tobacco smoke. Due to persistence of symptoms, she was prescribed sertraline and lorazepam for presumptive diagnosis of vocal cord dysfunction, both of which provided no relief of her symptoms.

At initial evaluation in our office, physical exam was unremarkable and pulse oximetry was 97% at rest. Baseline spirometry was normal with normal diffusion capacity of carbon monoxide (DLCO) of 105% predicted and flattening of the inspiratory flow volume loops, which was consistent with upper airway obstruction seen in VCD (Fig. 1A). Flexible laryngoscopy demonstrated adduction of the vocal cords with inspiration consistent with VCD.

However, due to persistence of exertional dyspnea, the patient underwent a treadmill exercise desaturation study. The patient was able to reach 80% of her maximal heart rate (155 beats per minute) after 6 minutes. However, her oxygen saturation dropped to 86% on room air and she was markedly short of breath. Therefore, a stress echocardiogram was ordered. Prior to having this testing, she presented with an episode of gross hemoptysis, soaking 15 tissues over a 30 minute period. CXR showed mild interstitial changes within the lung bases (Fig. 1B).

Computed tomography (CT) of the chest, while negative for pulmonary embolism, demonstrated diffuse nodular ground-glass opacities and soft centrilobular nodules bilaterally (Fig. 1C). Additionally, there were areas of air trapping and the main pulmonary artery was enlarged (Fig. 1D). The initial differential included hypersensitivity pneumonitis, pulmonary hemorrhage and pulmonary hypertension.

Echocardiogram showed normal ejection fraction of 60–65% and a normal pulmonary artery systolic pressure of 24 mmHg. Therefore, as the diagnosis remained uncertain and she continued to be symptomatic, the patient underwent open lung biopsy. The explanted lungs demonstrated veins and venules with marked intimal fibrosis (Fig. 2A) and diffuse alveolar septal thickening (Fig. 2B). Additionally, there was congestion and edema noted with the presence of alveolar hemosiderosis indicating with chronic congestion. (Fig. 2C). Furthermore, the pulmonary arteries showed intimal fibrosis and hypertensive arterial changes (Fig. 2D). These pathologic findings were diagnostic for pulmonary veno-occlusive disease (PVOD).

Subsequent right heart catheterization demonstrated pulmonary arterial hypertension of 65/31 mmHg (Mean of 47 mmHg) and pulmonary wedge pressure of 7 mmHg. The patient was referred for a lung transplant evaluation and started on home oxygen therapy. Following a syncopal episode, she was started on warfarin and sildenafil. Ultimately, she underwent a double lung transplant nine months after initial presentation with no major complications and significant improvement in her dyspnea. Eleven years later, she remains improved and has no evidence of chronic lung allograft dysfunction.

1.2. Case 2

A 55-year-old female with a previous diagnosis of asthma presented with progressive exertional dyspnea over the preceding four years. Prior echocardiogram at the start of her dyspnea showed an estimated ejection fraction of 56–60%, a thickened aortic valve with mild aortic regurgitation and normal pulmonary artery pressure. Her asthma was diagnosed based on symptoms of wheezing and chest tightness, which were partially relieved with albuterol. She had been treated with inhaled corticosteroids and montelukast which provided no relief. Prior pulmonary function testing showed a mild restrictive pattern with an FVC of 61% predicted, FEV1 of 67% predicted and a normal FEV1/FVC ratio of 82. Total lung capacity was 72% predicted and the DLCO was decreased at 74% predicted. Chest x-ray was normal with the exception of mild mid-thoracic scoliosis (Fig. 3A).

The patient presented to our office for further evaluation. Repeat spirometry showed flattening of the inspiratory limb of the flow-volume loop and restrictive pattern that were not consistent with asthma (Fig. 3B). She also complained of throat tightness triggered by exposure to smoke and perfume. Therefore, flexible laryngoscopy was performed and showed adduction of the vocal cords during inspiration consistent with VCD. Her dyspnea triggered by strong odors improved with respiratory retraining and breathing exercises. However, as her exertional dyspnea persisted, it was further evaluated with a high resolution chest CT scan which showed a focal area of bronchiectasis in the right upper lobe and otherwise normal lung parenchyma (Fig. 3C). There was mild aneurysmal dilatation of the ascending aorta at 3.7cm and mild enlargement of the main pulmonary artery at 3.4cm (Fig. 3D).

To further evaluate this mild aneurysm, a chest CT with contrast in conjunction with 3D volume rendered images was obtained. These were remarkable for a large patent ductus arteriosus (PDA) with a diameter of 5mm (Fig. 4A &B). The resting echocardiogram was repeated, showing a preserved ejection fraction of 60% with a normal pulmonary artery systolic pressure of 10 mmHg. Subsequent stress echocardiogram showed an elevated pulmonary artery pressure during exercise of 59 mmHg with concomitant shortness of breath. Color doppler of the proximal pulmonary artery demonstrated a late systolic flow reversal and a continuous flow in the suprasternal notch view, caused by the PDA.

During cardiology evaluation, the exam revealed an S2 with a loud P2 component and a 1/6 early peaking crescendo/decrescendo murmur in the left upper sternal border. One month later the patient underwent left and right heart catheterization that showed no significant disease of the left main, left anterior descending, and left circumflex arteries with normal cardiac output and index. A restrictive PDA was identified, measuring 2 mm in diameter in the pulmonary artery and 4 mm in the ampulla. Hemodynamics showed a small left-to-right shunt with an elevated pulmonary to systemic blood flow ratio (PQ-QS) of 1.25. She had normal resting pulmonary artery pressures (18 mm Hg) and normal pulmonary wedge pressure (10 mm Hg). She underwent successful coil closure of the PDA at the time of catheterization. At two weeks post-procedure, her exertional dyspnea had resolved. She remains improved 10 years later.

2. Discussion

Our group found that 42.4% of VCD patients had been previously misdiagnosed with asthma for an average of 9 years [6]. Therefore, in patients who have not responded to traditional asthma treatments and whose diagnostic studies are not suggestive of asthma, VCD should be one of the top considerations in the differential diagnosis. In this case series, both patients were initially misdiagnosed and treated for asthma with subsequent evaluation revealing the presence of VCD. The patient in Case 1 had a likely false positive methacholine challenge test secondary to VCD, while the patient in Case 2 had spirometry that was inconsistent with asthma. Once the VCD diagnosis is made, therapy for VCD includes treatment of co-morbidities such as post nasal drainage and gastroesophageal reflux disease (GERD), relaxation techniques, respiratory re-training exercises and speech therapy which lead to symptom improvement in the majority of patients [2]. In our VCD population, we found that 76.4% of VCD patients reported improvement in symptoms when implementing the breathing exercises alone without any additional training, and the remaining patients were referred to speech therapy [10]. Importantly, ours and other groups have reported that VCD coexists with asthma in up to one third of patients [6,7,11]. Failure of symptom improvement despite treatment of VCD and asthma (if it co-exists) should lead to further evaluation which may reveal additional pulmonary diagnoses as presented in our case series.

A Pub Med literature search from 1980 to 2018 using the terms vocal cord dysfunction and/or paradoxical vocal fold motion disorder with pulmonary veno-occlusive disease yielded no results. A Pub Med search from the same time-frame using the terms vocal cord

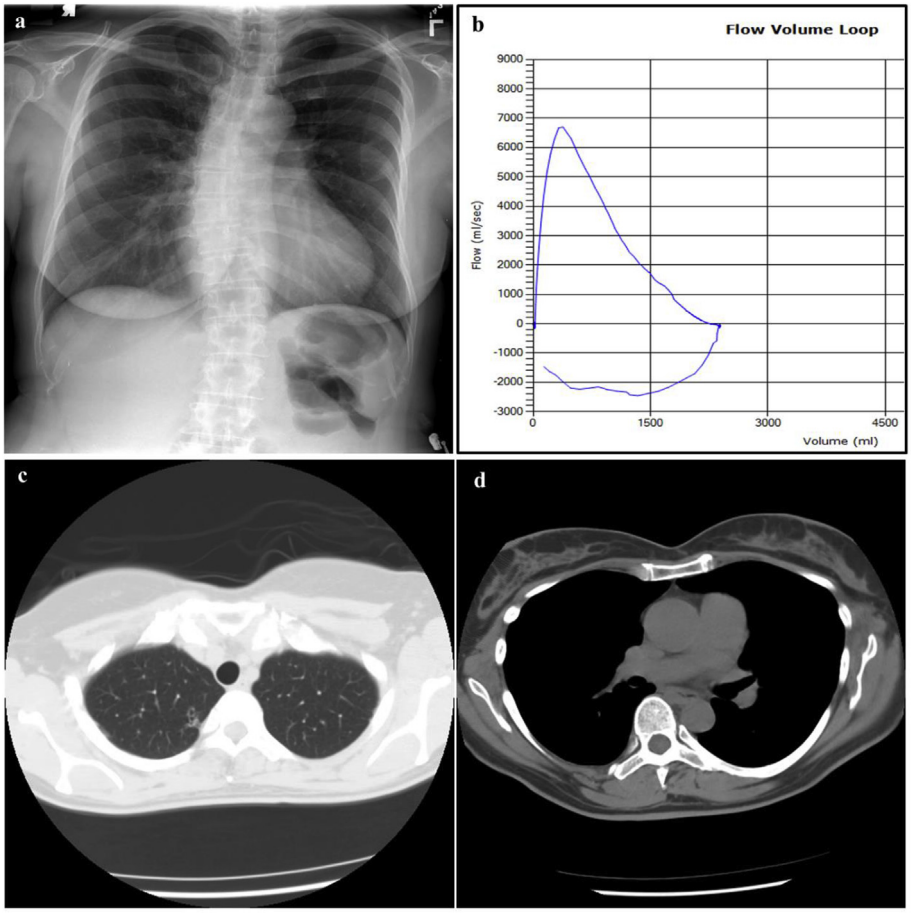

Fig. 3. a. Normal CXR; b. Flow volume loop with flattening of inspiratory limb; c-d. CT chest showing bronchiectasis, ascending aorta aneurysm and mild pulmonary artery enlargement.

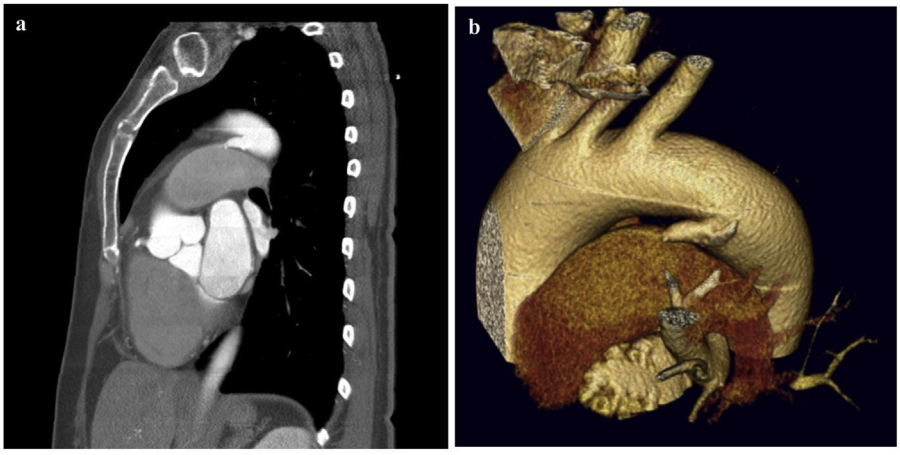

Fig. 4. a–b. Chest CT with volume rendered images showing a large patent ductus arteriosis.

dysfunction and/or paradoxical vocal fold motion disorder with patent ductus arteriosus yielded 3 studies that reported post-operative complications of PDA closure [12–14]. While 2 articles discussed vocal cord paralysis following surgery to close a PDA [12,13], in the 3rd article, 1.7% of 2255 children who underwent cardiovascular surgery (including PDA closure) had postoperative VCD confirmed by laryngoscopy [14]. None of these studies reported the presence of VCD prior to PDA repair.

To our knowledge, this is the first case series that reports the co-existence of VCD with pulmonary disorders other than asthma, specifically pulmonary veno-occlusive disease and patent ductus arteriosus (preceding surgery). Common symptoms seen in VCD such as shortness of breath, chest tightness, and cough, can also be due to other conditions [2,6]. In this case series, once asthma was ruled out, it was necessary to consider additional pulmonary conditions besides VCD as symptoms persisted despite treatment. In complex cases such as these, a detailed history, physical exam, and appropriate interpretation of diagnostic tests may facilitate the development of broad differential diagnoses. This case series highlights that VCD can not only mimic or co-exist with asthma, but can also co-exist with other pulmonary

conditions. Each of these pulmonary diseases identified in our case series required additional therapies (lung transplant for PVOD and coil closure of PDA) to prevent further morbidity and mortality. Failure to respond to common treatment modalities should alert the clinician to search for alternative diagnoses.

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Appendix A. Supplementary data

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