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CASE REPORT

Vocal cord dysfunction diagnosed by four-dimensional dynamic volume computed tomography in patients with difficult-to-treat asthma: A case series

Wei-Tso Cheng [a], Huan-Wen Chen [a], I-Hao Su [b], Ji-Tseng Fang [a,c], Han-Pin Kuo [a,d], Chien-Da Huang [a,d,*]

[a] *Department of Medicine, Chang Gung University College of Medicine, Taoyuan, Taiwan*
[b] *Department of Medical Imaging and Intervention, Chang Gung University College of Medicine, Taoyuan, Taiwan*
[c] *Department of Nephrology, Chang Gung Memorial Hospital, Taoyuan, Taiwan*
[d] *Department of Thoracic Medicine, Chang Gung University College of Medicine, Taoyuan, Taiwan*

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Patients with asthma may also have vocal cord dysfunction (VCD), which leads to poor control of the asthma. Once patients are diagnosed with difficult-to-treat asthma with poor control, VCD should be excluded or treated accordingly. The gold standard for diagnosis of VCD is to perform a laryngoscopy. However, this procedure is invasive and may not be suitable for patients with difficult-to-treat asthma. Four-dimensional (4D) dynamic volume computed tomography (CT) is a noninvasive method for quantification of laryngeal movement, and can serve as an alternative for the diagnosis of VCD. Herein, we present a series of five cases with difficult-to-treat asthma patients who were diagnosed with VCD by 4D dynamic volume CT. Clinicians should be alert to the possibility of VCD when poor control is noted in patients with asthma. Early diagnosis by noninvasive 4D dynamic volume CT can decrease excessive doses of inhaled corticosteroids.

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* Corresponding author. Department of Thoracic Medicine, Chang Gung Memorial Hospital, 199 Tun-Hua North Road, Taipei, Taiwan.
E-mail address: cdhuang@adm.cgmh.org.tw (C.-D. Huang).

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Introduction

Asthma is defined as a chronic inflammatory disease of the airways, and the symptoms can usually be relieved with inhaled corticosteroids.[1] However, in 5–10% of asthma patients the symptoms may continue to deteriorate even with high-dose inhaled and oral corticosteroid treatment.[2] The patients with difficult-to-treat asthma may require repeated hospital admissions, which results in increased health-care costs and the patient's work performance being affected.[3] Thus, it is necessary to investigate the etiological factors for the difficulties experienced by the patients with severe asthma while treating them. Once the underlying causes of these difficulties are known, treatment can be adjusted accordingly and excessive medication can be reduced, especially inhaled corticosteroids.

Vocal cord dysfunction (VCD), also known as paradoxical vocal cord motion, is a common etiology leading to difficulty in treating asthma patients.[4,5] Because of involuntary closure of the vocal cords, which occurs most commonly during inspiration, VCD can masquerade the symptoms of asthma such as episodic and severe respiratory distress.[6] The diagnosis of VCD is traditionally based on a combination of inspiratory flow volume loops and laryngoscopy during symptom attack. However, recent studies have reported that four-dimensional (4D) dynamic computed tomography (CT) is a noninvasive method for the quantification of laryngeal movement, and can serve as an alternative for the diagnosis of VCD.[5,7] In recent years, CT has progressed from 64 slice to 320 slice, thereby providing far more detailed images of structures, making it possible to model the airflow in the respiratory system and provide more accurate imaging of laryngeal function during the phases of respiration. Therefore, 320-slice CT has the potential to become the new standard for VCD diagnosis. One study used 320-slice CT to survey upper airway dysfunction in a patient who had severe asthma,[7] and another study defined the normal parameters for laryngeal movement in the context of this new imaging modality.[5]

In the case series in this study, we used 4D dynamic volume CT to survey patients with difficult-to-treat asthma. A retrospective analysis has been performed in these patients. A 4D dynamic volume CT (Toshiba Aquilion ONE, 320-slice CT system) was performed with the following parameters: 80 kVp, 50 mAs, detector collimation, 0.5×0.5 mm^2; gantry rotation, 0.5 seconds; scanning time, 10 seconds; scanning range, 16 cm; reconstructed slice thickness/interval, 3 mm/3 mm. The radiation dose of 4D CT was in a range of approximately 3–5 mSv. The CT protocol and respiratory instructions were fully explained and given to all patients by the same radiographer. All patients were requested to breathe normally to determine their own respiratory tempo lasting for 10 seconds without a breath hold and swallowing, during the preprocedure respiratory practice and 4D-CT study.

Dynamic sagittal and coronal multiplanar images and dynamic 3D volume rendering images from approximately the hyoid level to the distal trachea including vocal cords were reconstructed using Toshiba Aquilion ONE Manufacturer's Model version V4.74ER011. We selected the mid-phase inspiration and expiration to take a steady vocal cord

Table 1 Characteristics of the study patients.

Patients	Age (y)	Sex	Smoking status	Asthma onset age	FEV1/FVC (%)	FEV1 (% of pred.)	FVC (% of pred.)	Medication	Nonpharmacologic management	Improvement time (mo)
1	52	M	No	10	55.3	17	25	Inhaled combination therapy + anticholinergics	Speech therapy + breathing control + psychological support	3
2	65	F	No	27	74.8	64	72	Inhaled combination therapy + theophylline	Speech therapy + breathing control + psychological support	2
3	64	M	Ex-smoker	60	71.5	50	51	Inhaled combination therapy + theophylline + leukotriene receptor modifier	Speech therapy + breathing control + psychological support	1
4	49	M	Ex-smoker	20	82.1	75	78	Inhaled combination therapy + theophylline + leukotriene receptor modifier + Anti-IgE	Speech therapy + breathing control + psychological support	3
5	81	M	No	71	46.1	73	63	Inhaled combination therapy + anticholinergics + leukotriene receptor modifier	Speech therapy + breathing control + psychological support	2

FEV1 = forced expiratory volume in one second; FVC = forced vital capacity; Pred. = predicted value.

luminal area and get average value, respectively, if more than one inspiration or expiration phase was recorded. We presented five patients (Table 1) who fit the VCD diagnostic criteria (vocal cord area >40% reduction and sustained >70% cycle) (Table 2) in 4D dynamic volume CT.[7]

Case series

Case 1

This 52-year-old male had asthma since the age of 10 and was prone to anxiousness. He had underlying hypertension and had suffered from an ischemic stroke when he was 50 years old. Frequent night and morning coughing were noted. His asthma symptoms and signs exacerbated when he caught a cold or suffered an allergic reaction. To better control his asthma symptoms, a leukotriene receptor inhibitor and theophylline were added along with a β2 agonist and inhaled corticosteroids. However, he still often complained of neck tightness and shortness of breath, and he frequently visited the emergency room due to dyspnea. Because of persistent progressive shortness of breath and chest tightness, he was suspected as having difficult-to-treat asthma. The 4D dynamic CT was performed. Subsequently, VCD was initially suspected. In addition to inhaled combination therapy and anticholinergics, he also received speech therapy, breathing control, and psychological support. Subjective symptomatic improvement of upper airway discomfort was noted. No emergency room or unscheduled outpatient clinic visits were noted, after such management for 3 months.

Case 2

A 65-year-old female patient had been diagnosed with asthma at 27 years of age. She also had underlying chronic rhinitis, postnasal drip, and hypertension. Frequent upper airway discomfort and a sensation of suffocation were noted despite the use of inhaled combination therapy. Her immunoglobulin E (IgE) level was 92.1 KU/L and she had received omalizumab therapy. Her symptoms improved after anti-IgE therapy; however, chest tightness and frequent upper airway infections still occurred. The 4D dynamic volume CT was performed and VCD was initially impressed. Thus, nonpharmacologic management, including speech therapy, breathing control, and psychological support were arranged. After 2 months, obvious symptomatic improvement of upper airway discomfort and a sensation of suffocation were noted. Besides, the unscheduled outpatient clinic visit was decreased.

Case 3

This 64-year-old male patient had been diagnosed with asthma at 62 years of age. He coughed more frequently after exercise or during changes in the weather. Nocturnal coughing was also noticed. He frequently suffered from persistent dyspnea and intermittent chest tightness despite receiving inhaled combination therapy. Under the impression of difficult-to-treat asthma, 4D 320-slice dynamic volume CT was arranged, which revealed paradoxical inspiratory vocal cord luminal area reduction that was diagnosed as VCD (Fig. 1). Symptomatic improvement of VCD was noted after speech therapy, breathing control, and psychological support for 1 month. No unscheduled outpatient clinic visit was noted and we downstaged the asthma severity thereafter.

Case 4

This 49-year-old male had a history of asthma and frequent dyspnea since he was 20 years of age. He had also been a heavy drinker and smoker in the past. Because of asthma attacks with chest tightness at 45 years of age, he began regular treatment with medications. He had previously suffered from a near-fatal asthma attack with acute respiratory failure, and thus an emergency intubation with mechanical ventilator support was performed. To control the asthma symptoms, a leukotriene receptor inhibitor and theophylline were added along with a β2 agonist and inhaled corticosteroids. He had also received anti-IgE therapy, which seemed to provide a good response. However, he still often complained of shortness of breath and paroxysmal nocturnal dyspnea. Under the impression of difficult-to-treat asthma, 4D dynamic volume CT was arranged and VCD was initially impressed. Thus, nonpharmacologic management, including speech therapy, breathing control, and psychological support were arranged. After 3 months, subjective symptomatic improvement of upper airway discomfort was noted. No more emergency room or unscheduled outpatient clinic visits were noted after such management for 3 months. The doses of anti-IgE therapy were also decreased thereafter.

Table 2 Vocal cord luminal area in the study patients.

Patients	Trachea luminal area (mm^2)	Maximal vocal cord/trachea luminal area (%)	Vocal cord luminal area during midphase inspiration (mm^2)	Vocal cord luminal area during midphase expiration (mm^2)	Vocal cord luminal area reduction during inspiration or expiration* (%)
1	349.5	95%	332.6	89.2	73%*
2	269.6	28%	17.1	75.9	77%
3	262.9	76%	41.9	202	79%
4	271.4	72%	113.2	195.4	42%
5	396.2	59%	40	232.4	83%

Selected trachea level: cervicothoracic junction just below the thyroid level; scan at the end of deep inspiration.
*Expiration phase.

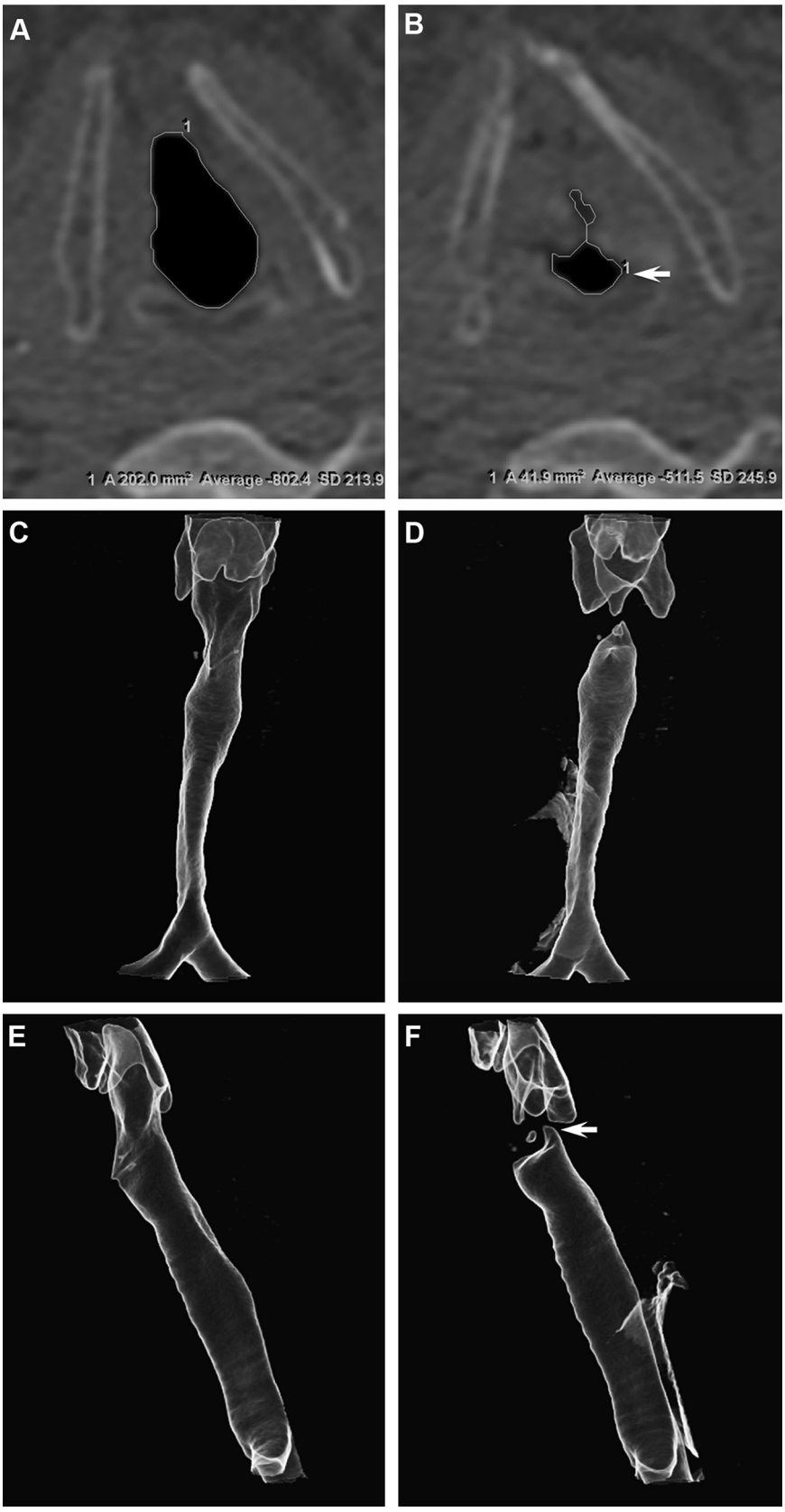

Figure 1 (A) Nonenhanced axial computed tomography images of Case 3 showing normal lumen at the vocal cord level during expiration and (B) paradoxical adduction of the vocal cords during inspiration that reduced the lumen by 79.3%, consistent with vocal cord dysfunction. A small area at the posterior part of the airway was not affected (B, arrow). Volume rendering reconstruction techniques show coronal images during (C) expiration and (D) inspiration, and sagittal images during (E) expiration and (F) inspiration, demonstrating marked luminal narrowing with a posterior chink at the vocal cord level during inspiration (F, arrow).

Case 5

This 81-year-old male patient had a history of chronic asthma for 10 years. A frequent sensation of a lump with choking was noted. He had an underlying gastroesophageal reflex disease, renal insufficiency, diabetes mellitus type II, and hypertension with irregular control. His symptoms included chest tightness and coughing with sputum. To control the asthma symptoms, a leukotriene receptor antagonist was added with a β2 agonist and inhaled corticosteroids. After a long period of outpatient department follow-up but poor improvement of his symptoms, he was considered to have difficult-to-treat asthma. Under the impression of difficult-to-treat asthma, we arranged a 4D dynamic CT for survey of VCD, and VCD was initially suspected. Thus, nonpharmacologic management, including speech therapy, breathing control, and psychological support were arranged. After 2 months, subjective symptomatic improvement of sensation of a lump with choking was noted. Besides, there was no unscheduled visit to the outpatient clinic.

Discussion

In our case series, we used a 4D dynamic CT to diagnose VCD. This technique made it possible to record the upper airway movements of suspected VCD patients during the respiratory cycle, and measure the area of the vocal cord luminal area. VCD is defined as reductions in vocal cord luminal area of >40% lasting for >70% duration of inspiration or expiration.[7] This definition is consistent with patients who abnormally adduct during inspiration or exceedingly adduct during expiration. We recorded the data from our five patients who underwent 4D dynamic CT including vocal cord luminal area during midphase inspiration (mm^2), vocal cord luminal area during midphase expiration (mm^2), and vocal cord luminal area reduction during inspiration or expiration (%) (Table 2). The most important factor was the reduction in percentage of the vocal cord luminal area during inspiration or expiration. From this, the degree of vocal cord luminal area narrowing during the respiratory cycle could be obtained. The reductions in vocal cord luminal area ranged from 42% to 83%, which all matched the imaging criteria of VCD diagnosis (reductions in vocal cord luminal area > 40%).[7] One of our patients with VCD manifested this abnormality in expiration, and four in inspiration. The VCD during expiration may mimic the expiratory wheeze of asthma, and therefore, may be more difficult to differentiate clinically.

Difficult-to-treat asthma refers to a patient with asthma who has persistent asthma symptoms and exacerbations despite high-dose asthma therapy. There is no universally accepted definite definition of difficult-to-treat asthma; however, recent work has suggested that the term "difficult-to-treat asthma" can be used when a treatment level reaches at least Step 4 of the British Thoracic Society guidelines (high-dose inhaled corticosteroid and long-acting β2 agonist treatment).[8] It has been reported that 5—10% of asthma patients suffer from difficult-to-treat asthma.[9] Once a patient with difficult-to-treat asthma is encountered, clinicians must reconsider whether or not the diagnosis is correct, and whether there are potential coexisting problems contributing to the asthma exacerbation. If coexisting conditions can be identified and managed, better symptom control may be possible. Clinicians should consider potential problems that accompany or mimic asthma including bronchiectasis, gastroesophageal reflex disease, rhinosinusitis, psychological disorders, and VCD. Among these, VCD is one of the most difficult to differentiate from asthma by clinical symptoms such as wheezing, breathlessness, and triggering through exercise.

The prevalence of VCD is uncertain, and the diagnosis requires a high index of suspicion and direct visualization of the vocal cords by laryngoscopic demonstration when symptomatic.[10] The golden standard to diagnose VCD is to use endoscopy to visualize the exact movement of the vocal cords. However, the accuracy is limited by the subjectivity of the clinician. By contrast, 4D dynamic CT provides an objective, noninvasive, alternative diagnostic tool for VCD diagnosis. In addition, it is simple and makes it easier to detect the laryngeal function in those who are suspected of having VCD. The crucial consideration regarding our case series is whether excessive narrowing of the vocal cords as demonstrated by CT may be an error in the interpretation of the CT images or alternatively, a physiological phenomenon. Thus, when this technique is used to make a diagnosis, clinicians have to consider whether the excessive narrowing we detected is the natural state or an error of CT image interpretation.

The primary treatment for VCD is laryngeal control therapy, which is typically provided by speech language pathologists and is a noninvasive treatment that has shown modest improvement in VCD.[11] Some patients benefit from speech therapy, which can emphasize breathing through the abdomen as opposed to thoracic breathing. A previous study found that 95% of female athletes treated with speech therapy were able to adequately control their symptoms.[12] However, whether it has an impact on asthma control has not yet been established. Other proposed therapies are psychotherapy, biofeedback, and inhaled anticholinergic medications.[13] It is also crucial to control the accompanying irritating factors such as allergic rhinitis with postnasal drip and gastroesophageal reflux. Patients with psychological or psychiatric illnesses may not be able to overcome VCD. When this is the case, it is important to avoid continued treatment with systemic corticosteroids unless it is demonstrated that there is both persistent asthma and VCD.[14]

Conclusion

A high index of suspicion is required to diagnose VCD.[15] Clinicians should consider VCD in any patient with a history of asthma and continued symptoms despite treatment. Early diagnosis by noninvasive 4D dynamic volume CT can decrease excessive doses of inhaled corticosteroids.

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