Slit survival

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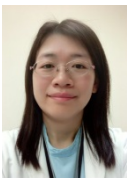

Case 1

A 65-year-old Chinese gentleman was a retired clerk with a 1 pack-year smoking history. He had history of hyperlipidemia on diet control. He was referred to our medical clinic from general out-patient clinic (GOPC) for exertional dyspnea, which had been worsened progressively over one year. He had gradual reduction of exercise tolerance from 6 flights of stairs (FOS) to 3 FOS. He had no cough, sputum, or hemoptysis. He had no chest pain, orthopnea, ankle edema or constitutional symptoms. Physical examinations of the cardiovascular, respiratory, abdominal and neurological systems were unremarkable. Blood tests including complete blood count, renal, liver and thyroid function tests were normal. Electrocardiogram (ECG) showed normal sinus rhythm. His chest X-ray was normal. Spirometry (Fig.1) showed his force expiratory volume in 1 second (FEV_1) was 2.44L (105%), functional vital capacity (FVC) was 3.37L (110%), and FEV_1/ FVC ratio was 0.73. Private computed tomography (CT) coronary angiogram showed mild coronary artery disease only. An echocardiogram was scheduled to half year later.

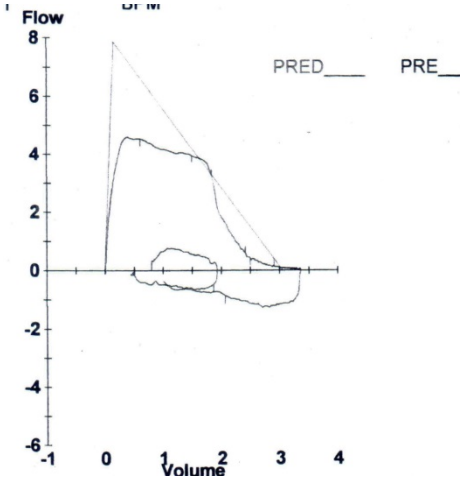

Fig. 1 Flow volume loop of baseline spirometry

He remained dyspneic, and a cardio-pulmonary exercise test (CPET) was arranged. He underwent 7.5 minutes of ramp exercise, and the test was stopped due to severe dyspnea and dizziness. Physical examination of the chest revealed bilateral wheezing with both inspiratory and expiratory rhonchi, loudest near the upper airways. Spirometry during CPET showed flattened inspiratory and expiratory limbs of the flow-volume (FV) loop, suggestive of a fixed large airway obstruction (Fig.2).

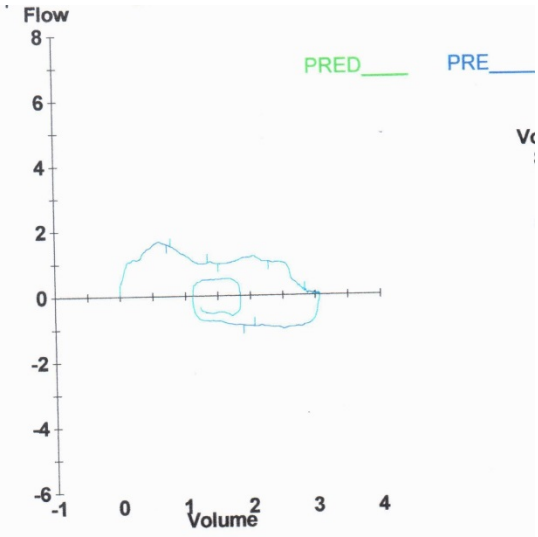

Fig.2 FV loop of spirometry during CPET

Computed tomography (CT) of the neck and thorax showed a structural lesion over upper trachea at hypopharyngeal region with air density inside, the narrowest part of the trachea was 6mm on CT (Fig.3).

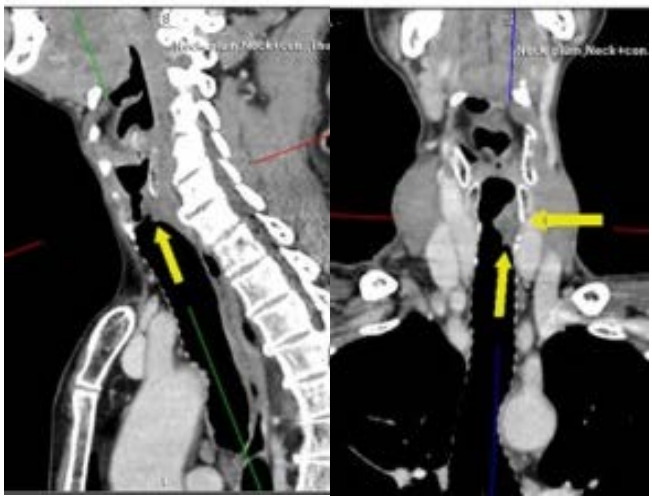

Fig. 3 CT neck and thorax showed a structural lesion over upper trachea

The patient was referred to the cardiothoracic surgeons (CTS) with flexible bronchoscopy performed which showed a diverticulum of trachea just beyond vocal cords with inflammatory and fibrotic mucosa was found. The mid and lower trachea and the rest of bronchial tree were normal. Biopsy of the diverticulum showed inflamed granulation tissue with fibrosis. Serum autoimmune markers including anti-neutrophil cytoplasmic antibody (ANCA) were negative.

A diagnosis of tracheal diverticulum causing central airway obstruction (CAO) was made. The patient was then referred to the ear, nose and throat (ENT) surgeon with resection of the tracheal granulation and Montgomery laryngeal stenting performed, followed by tracheostomy. A soft web in the upper trachea from lower border of cricoid cartilage to upper trachea, 2cm in length, was found. The symptoms were improved after surgery. The patient was scheduled for stage surgery and stent removal later.

Case 2

A 61-year-old Chinese man was a chronic smoker of 15 pack-years. He had history of rectosigmoid colon cancer with curative surgery performed in 2010, and limited stage small cell lung cancer presented with right hilar mass in 2012 with chemotherapy and radiotherapy completed in 2013. He presented to the Accident and Emergency Department (AED) with dyspnea and blood-stained sputum for 3 days. Chest examination found stridor and right lower zone crepitations. Examinations of the cardiovascular, abdominal and neurological systems were unremarkable. His oxygen saturation was 98% on 2L/min supplemental oxygen. ENT assessment with laryngoscopy at AED showed normal and mobile vocal cords. Blood-stained secretion was noted over larynx and inside trachea. There was no obvious growth over larynx, supraglottic and subglottic regions. ECG showed normal sinus rhythm. Chest X-ray revealed old scarring and fibrotic changes over right hilar region only.

He was subsequently admitted to the medical ward and was treated with empirical antibiotics for community acquired pneumonia. He remained stable until 3 days later, he developed shortness of breath suddenly with stridor impending respiratory arrest. He was intubated and then transferred to the intensive care unit (ICU) for close monitoring. Wheezing was noted which did not improve with bronchodilators and sputum suction. Bedside bronchoscopy via the endotracheal tube revealed a mass lesion, with contact bleeding, at the trachea beyond the endotracheal tube tip. Urgent CT thorax showed a 1.2 x 1.6 x 2.3cm endotracheal tumor in the lower trachea (Fig.4).

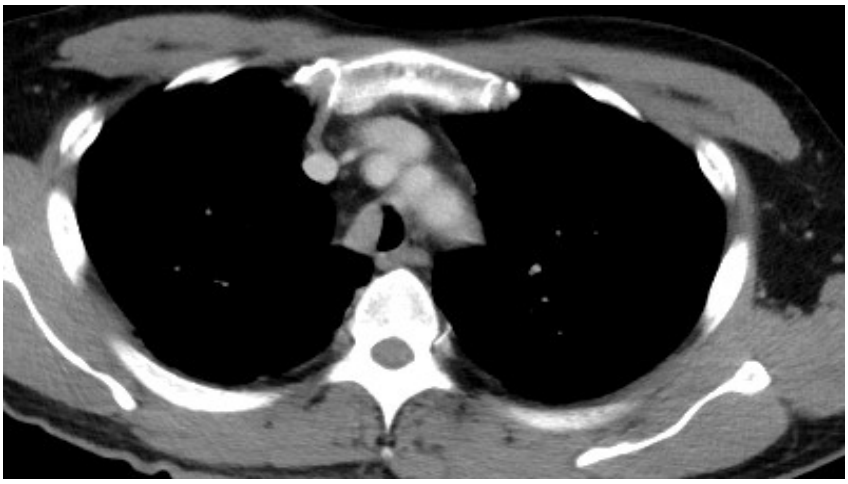

Fig. 4 CT showing a endotracheal tumor in the right lower trachea

The patient was subsequently transferred to the CTS unit for further management. Rigid bronchoscopy performed by the CTS team found a right lower tracheal mass of 3.5 cm long obscuring 50% of luminal area, with lower end at 1.5 cm above carina. Cordis balloon dilation was performed, and a Dummon stent was deployed. Biopsy of the lesion showed non-small cell carcinoma with some squamoid features. His carcinoma embryonic antigen (CEA) level was 3.0, and the plasma epidermal growth factor receptor (EGFR) mutations were negative. Positron electric tomography (PET) scan showed fludeoxyglucose (FDG) avid endotracheal lesion with dubious mediastinal lymph nodes (Fig. 5).

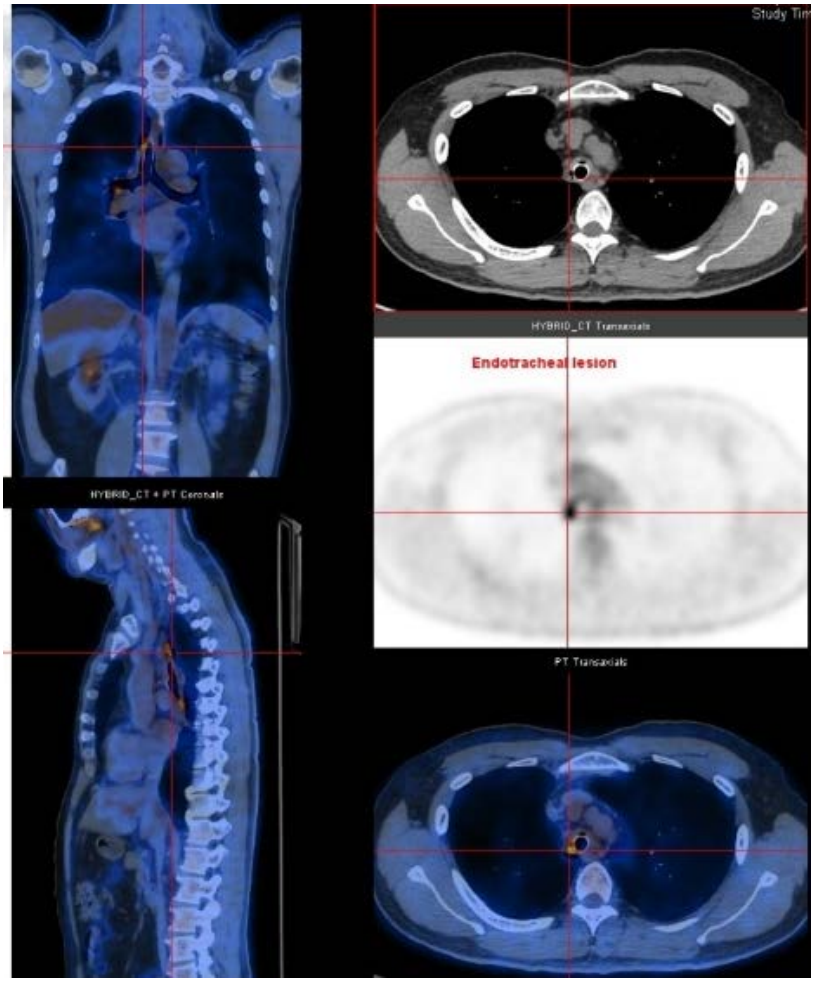

Fig. 5 PET scan showed a FDG avid endotracheal lesion

A diagnosis of tracheal non-small cell carcinoma causing CAO was made. The patient was referred to oncology unit for chemotherapy.

A summary of the two cases is provided in Table 1.

Table 1. Summary of two cases with central airway obstruction

	Age/sex	Presentation	Investigations	Diagnosis	Treatment
Case 1	65y/ Male	Chronic dyspnea	Spirometry, CT, bronchoscopy	Tracheal web	Surgical resection, stenting
Case 2	61y/ Male	Acute respiratory distress	CT, bronchoscopy (after intubation)	Tracheal non-small cell carcinoma	Stenting, systemic therapy

Discussion

The two cases above highlighted the variety of clinical presentation of CAO. The initial presentation is often non-specific, and the diagnosis may not be apparent until appropriate investigations are arranged. The morbidity and mortality are significant if left untreated. Management of these patients is difficult, but therapeutic and diagnostic tools are now available that are beneficial to most patients. With the growth of interventional pulmonology, there has been more attention and research in the treatment of complex airway pathology, and almost all airway obstruction can be relieved expeditiously.

Definition

Central airway obstruction (CAO) is generally defined as occlusion of >50% of the trachea, main stem bronchi, bronchus intermedius or a lobar bronchus[1,2]. The work of breathing in CAO depends on the pressure change along the stenotic airway and is affected mainly by the degree of obstruction and airflow velocity. In tracheal narrowing where there is <50% reduction in cross-sectional area, the airway obstruction is unlikely to cause symptoms because the pressure drop is similar to that which occurs through the normal glottic opening[3].

Epidemiology

The exact epidemiology of CAO is unknown. The incidence seems to be rising due to the epidemic of lung cancer, 20–30% of lung cancer cases are complicated by proximal airway obstruction[4]. The growing number of benign obstructive pathologies also contributes to this trend, primarily due to the use of artificial airways[5].

Etiology and pathogenesis

Central airway obstruction may be caused by non-malignant or malignant processes.

Although there are few epidemiologic data, the most commonly encountered non-malignant causes of CAO include granulation tissue resulting from prior endotracheal/ tracheostomy tubes, airway foreign bodies, and tracheobronchomalacia causing the airway wall thinning and collapse[6]. Non-malignant causes of CAO are summarized in table 2.

Table 2. Causes of non-malignant CAO

Categories	**Examples**
Lymph node	Infection (e.g. tuberculosis), sarcoidosis
Vascular	Sling, anatomical variations
Cartilage	Polychondritis
Granulation	Endotracheal/tracheostomy tube, foreign body, Wegener's granulomatosis
Pseudotumor	Harmatoma, amyloidosis, papilloma
Hyperdynamic	Tracheomalacia
Web	Idiopathic, tuberculosis, sarcoidosis
Miscellaneous	Goitre, mucus plug

The most common cause of malignant CAO is direct extension from an adjacent tumor, most commonly bronchogenic carcinoma, followed by esophageal and thyroid carcinoma. Primary tumors of the airway are less common. The majority of primary tracheal tumors are squamous cell carcinoma or adenoid cystic carcinoma. Carcinoid tumors account for the majority of primary tumors distal to the carina. Distant tumors may also metastasize to the airway, common causes including renal cell, breast, and thyroid carcinoma[7]. Malignant causes of CAO are summarized in table 3.

Table 3. Causes of malignant CAO

Categories	**Examples**
Metastatic to airway	Renal cell, breast, thyroid
Extrinsic compression	Thyroid, esopahgeal, lymphoma
Primary endoluminal	Bronchogenic, adenoid cystic, carcinoid

Clinical presentation

Signs and symptoms develop when the CAO impairs airflow to the point of increasing the work of breathing or altering cardiopulmonary interactions[8]. Although wheezing indicates airflow through a narrowed orifice, its location does not always conform to the site of airflow obstruction. Wheezing heard best over the trachea does not necessarily indicate that the source of the obstruction is the trachea[9]. Unilateral wheezing, however, often suggests airway obstruction distal to the carina and that should prompt the investigation of focal airway obstruction. Stridor is a sign of severe laryngeal or tracheal obstruction. Patients may also present with other nonspecific symptoms such

as exertional dyspnea and positional wheezing. Shortness of breath and wheezing are typically unresponsive to bronchodilators with an anatomically fixed obstruction, and failure of a patient to improve with these measures should prompt the consideration of the presence of CAO. It is important to note that the trachea is typically significantly narrowed, to less than 8 mm, before exertional dyspnea is present. Once the lumen is less than 5 mm, symptoms present at rest [9,10].

Diagnostic evaluation

The most commonly used diagnostic studies are CT, pulmonary function tests, and bronchoscopy [6].

1. Computed tomography (CT)

CT scan including neck and thorax provides good resolution of intraluminal defects and 3-dimensional reconstruction (virtual bronchoscopy) may be possible[6]. CXR is rarely diagnostic and is far less sensitive than CT[11].

2. Pulmonary function test

It is crucial to examine the shape of the FV loop in pulmonary function test in patients suspected to have CAO. The characteristic flattening of the inspiratory and expiratory limbs of the FV loop is typically seen before pulmonary function test yields abnormal results, yet may not be appreciated until the luminal diameter of the airway is already narrowed to 8-10mm[6,12-14].

3. Bronchoscopy

Bronchoscopy, either flexible or rigid, is important to diagnose and evaluate central airway obstruction, in which the lesion can be directly visualized. The location, morphology, presence of any extrinsic compression, size of lesion and intraluminal burden can be assessed, and biopsy of lesion can be obtained[6].

Management

Airway stabilization

In unstable patient, the airway must be immediately secured. Endotracheal intubation is indicated to ensure adequate ventilation and oxygenation, which can be accomplished with either a standard endotracheal tube or rigid bronchoscope. For patients with severe proximal upper airway obstruction, tracheotomy may be the stabilizing procedure of choice[5].

Determining etiology and extent of lesion

In non-life-threatening situation or when the airway is secured, the etiology and extent of the CAO should be delineated for deciding management plan. CT scan and bronchoscopy are usually performed to determine the histology, location and extent of the lesion first.

For non-malignant causes of CAO, surgical resection of the lesion is often considered. However, medical co-morbidities, high subglottic location and long vertical extent of lesion may preclude patient from surgery. In

such circumstances, bronchoscopic intervention may be an alternative.

For malignant causes of CAO, the treatment is invariably with palliative intent because it signifies advanced stage of disease. Bronchoscopic intervention combined with systemic therapy for the underlying malignancy is usually preferred.

Bronchoscopic intervention

The most commonly performed bronchoscopic interventions include mechanical debulking, airway stenting, and thermal technique.

Mechanical debulking

The rigid bronchoscope is often described as the cornerstone of therapeutic bronchoscopic management of malignant CAO. In addition to allowing the use of large instruments and high volume suction catheters which can be inserted through the rigid bronchoscope, the tip of the rigid scope itself is an effective tool for tumor debulking through the use of the beveled edge to 'core' out an endoluminal lesion. A microdebrider, which is a versatile tool for tumor debulking in the trachea and proximal mainstem bronchi, can also be used during rigid bronchoscopy[7].

Stenting

Airway stents are prosthetic devices that are used to maintain the airway patency. A stent buttresses the airway wall against tumor ingrowth or extrinsic compression once patency of the airway has been established. Airway stents can be broadly classified based on the material used as either silastic or self-expanding metallic stents. For extrinsic compression, airway stenting is the only bronchoscopic modality available which can result in prolonged airway patency. In purely endoluminal disease, stenting is usually not a primary modality. However it can be considered following debulking for treatment of residual obstruction. It must be considered that the objectives of airway stenting is either entirely palliative or for treatment and prevention of symptoms of CAO to allow systemic therapy to be performed, stenting itself does not treat the tumor. Moreover, as stents are foreign bodies, symptoms such as cough may worsen and the patient may be at risk for late complication.

Silicone stent deployment is complex and requires rigid bronchoscopy and general anesthesia. Whereas metallic stents can be placed via a flexible bronchoscope, there is higher risk of granuloma formation and airway perforation[7]. Large studies describing the use of stents in CAO show significant variability in patient population and include both non-malignant and malignant diseases, observed complications include stent migration, obstruction from secretion and granulation and

less commonly, ulcerations, perforations and infections[8,15].

Thermal technique and cold therapy

Thermal therapies utilize the biological effects of heat on cells to produce tissue degeneration, which included lasers, contact electrocautery, and argon plasma coagulation (APC). Cryotherapy is a method of tissue destruction that subject tissue to repeated cycles of extremely cold temperatures (below -40 degrees Celsius) [7].

Conclusion

In conclusion, central airway obstruction may have variable clinical presentation and a high index of suspicion should be maintained. Spirometry may provide clues to the diagnosis, typically by assessment of the flow-volume loop. CT scan provides better resolution of intra-luminal defects than other imaging techniques, and bronchoscopy is a sensitive and specific method of assessment of the airway lesion. For management, securing airway is the first priority in emergency situation. Treatments may include surgery, bronchoscopic intervention, and systemic therapy for the underlying disease.

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