What lies behind this late-onset wheeze?

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Case history

A 67-year-old male retired police officer presented to the casualty department in May 2005 with worsening dyspnoea on exertion and cough productive of yellowish sputum. He was being treated for hypertension and had been diagnosed with asthma by his general practitioner in March 2005. He had a 15 pack-year smoking history, until the age of 35 years. On examination, pulse rate was 110 beats per min, temperature 37.5°C and blood pressure 130/80 mmHg. A diffuse wheeze across both lung fields was noted on chest examination. Chest radiography was unremarkable (figure 1).

The patient was diagnosed with an infective exacerbation of asthma and received: co-amoxiclav 1.2 g *i.v.* 8-hourly; hydrocortisone 100 mg *i.v.* 8-hourly; and salbutamol and ipratropium by nebuliser 6-hourly with good effect. He was discharged in good condition and given a follow-up appointment at the asthma clinic.

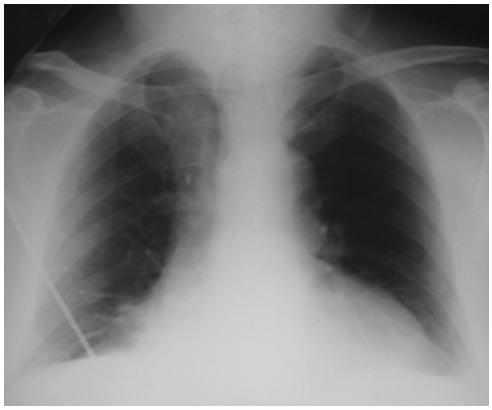

Figure 1.
Chest radiograph taken during admission.

Investigations

Lung function tests revealed a forced expiratory volume in one second (FEV_1) of 33% predicted and a forced vital capacity (FVC) of 72% pred. The FEV_1/FVC ratio was 46%. There was 15% reversibility in FEV_1 post-bronchodilator therapy. The patient was unable to produce a flow–volume loop suitable for interpretation.

Task 1
Interpret the spirometry data.

Answer 1
The FEV_1/FVC ratio of 46% is suggestive of obstructive lung disease. The 15% reversibility post-bronchodilator treatment is consistent with a diagnosis of asthma.

During follow-up visits, repeat pulmonary function tests showed a steady decline in FEV_1 and FVC, despite increasing asthma treatment. By November 2005, the patient was on fluticasone inhaler 250 µg 12-hourly, salmeterol inhaler 50 µg 12-hourly and salbutamol inhaler on a *pro re nata* basis. He was given a tailing-down dose of prednisolone 60 mg in an attempt to control his asthma.

Despite being prescribed oral steroids, the patient required hospital admission in November and December owing to worsening dyspnoea, cough and difficulty in expectorating thick sputum. During the December admission, inspiratory stridor was suspected on clinical examination and an urgent computed tomography (CT) scan of the neck and chest was requested (figures 2 and 3).

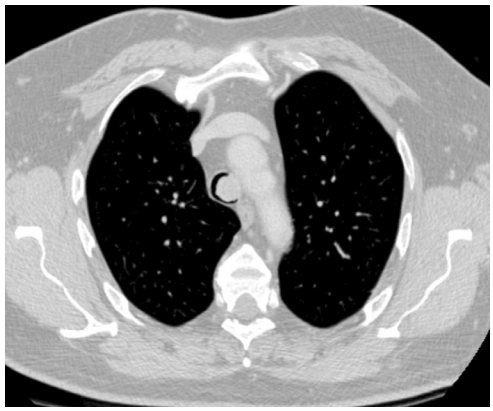

Figure 2
Spiral thoracic CT scan.

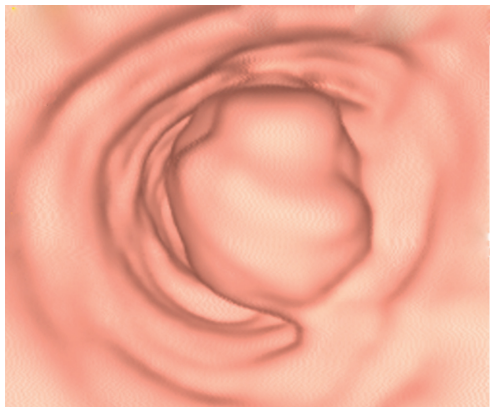

Figure 3
Virtual reconstruction of the trachea using the CT images.

Task 2
Interpret the CT scan and virtual reconstruction.

Task 3
How would you manage this patient?

Answer 2
A polypoid intrathoracic tracheal mass is obstructing 90% of the trachea.

Answer 3
Urgent debulking of the tumour through a rigid bronchoscope.

A polypoid mass occluding 90% of the trachea was noted. Since the patient had respiratory compromise, he was booked for urgent debulking of the tumour through a rigid bronchoscope. Rigid bronchoscopy has the advantages of superior suctioning capacity of blood and clots, excellent visualisation and better airway control when compared with flexible bronchoscopy [1]. After the procedure, there was an immediate improvement in the patient's respiratory symptoms. All inhalers were stopped and prednisolone was rapidly tailed off.

Following debulking, FVC normalised but FEV_1 did not; an important obstructive component remained, caused by the residual tumour (figure 4). The histological results of the tumour were reported as mucoepidermoid carcinoma of the trachea (figure 5). The patient was subsequently referred to a specialist centre in the UK for complete resection of the tumour and tracheal reconstruction, to provide a definitive cure.

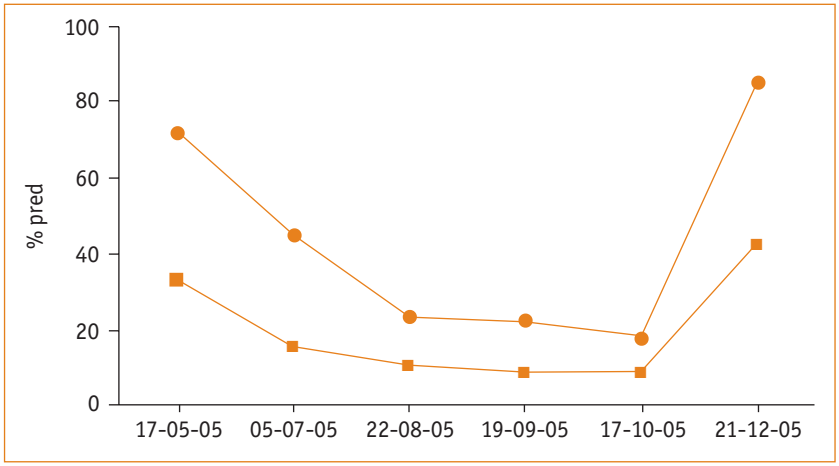

Figure 4
The steady decline in FEV_1 (bottom line) and FVC (top line) noted during the outpatient visits, followed by a sudden improvement after debulking.

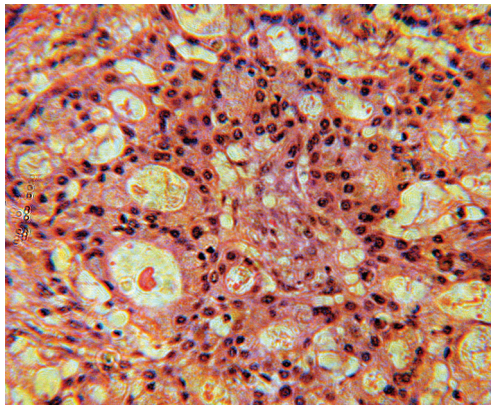

Figure 5
Histology of the trachea showing malignant proliferation of tubular and epithelial cells compatible with mucoepidermoid carcinoma.

Discussion

Tracheal tumours are extremely rare, with a prevalence of 0.1–0.2 per 100,000 population [2–4]. Peak incidence occurs in the fifth and sixth decades of life. These tumours are 140 times less common than lung tumours. They are slightly more predominant in the lower part of the trachea (57%). As in bronchial carcinoma, there is a strong association with smoking. The two main histological types of primary tracheal malignancy are squamous and adenoid cystic carcinoma. Undifferentiated and small cell carcinomas are uncommon. Bronchial carcinoid, mucoepidermoid and primary lymphomas are rare. Mucoepidermoid and adenoid cystic carcinomas are locally invasive but tend to metastasise late and are associated with a better prognosis [3].

Extrathoracic tracheal tumours generally present with stridor and hoarseness and a prompt diagnosis is often made. Intrathoracic tracheal tumours typically present the most diagnostic difficulty, with the condition masquerading as adult-onset asthma. WU *et al*. [2], in a retrospective study of 40 patients with tracheal tumours, reported a median delay in diagnosis of 10 months from the initial presentation. In a series of 67 patients from Taiwan, YANG *et al*. [3] also reported a delay in diagnosis, in particular for slow-growing mucoepidermoid and adenoid cystic carcinomas. This delay is usually attributed to the nonspecific presentation of this condition, usually with dyspnoea, cough, hoarseness and wheeze. Recurrent attacks of respiratory obstruction due to secretions and recurrent infections are common and are often mistaken for infective exacerbations of asthma. Haemoptysis is reported in less than one-third of cases. Weight loss and general malaise are uncommon in the early stages. There are usually no significant abnormalities on chest radiography. Spirometry is of limited value in distinguishing between asthma and a tracheal tumour, as both conditions produce an obstructive picture. How, then, can the two conditions be distinguished?

Failure to respond to standard anti-asthmatic treatment and recurrent admissions while on oral steroids should be regarded with suspicion and an alternative diagnosis sought [5]. In the present patient, there was no objective response to inhaler therapy despite assurances about compliance and good inhaler technique.

The wheeze heard in large airway obstruction is classically described as monophonic, whereas that heard in asthma is described as polyphonic. The apparent location of the wheeze is also important. Wheezing secondary to large airway obstruction is best heard unilaterally, or over the trachea or larynx, whilst that of asthma is heard all over the chest wall. However, even the most localised lesions can produce diffuse sounds. In the case presented, a monophonic expiratory wheeze was heard diffusely across both lung fields.

During an infective exacerbation, the patient sometimes spoke about a choking sensation from thick sputum, which was difficult to expectorate. In retrospect, this can be explained by pooling of secretions at the level of the tumour. In practice, however, it is usually attributed to the bronchitis or pneumonia.

The flow–volume loop can be used to distinguish extrathoracic or intrathoracic large airway obstruction from small airway obstruction. Extrathoracic tracheal tumours predominantly affect the inspiratory part of the loop, making stridor a prominent feature. In cases of intrathoracic tracheal tumour, as presented here, there is markedly diminished expiratory flow but inspiration is largely preserved. During forced expiration, the intrathoracic pressure is higher than the intratracheal pressure, worsening the obstruction and decreasing expiratory flow. During inspiration, airway diameter is improved and the degree of obstruction reduced. Inspiratory stridor is therefore not a prominent feature of intrathoracic airway obstruction until very late in the disease. Fixed tracheal stenosis will produce flattening of both the inspiratory and expiratory flow–volume curves. This is often secondary to benign tracheal stenosis, although fixed invasive tracheal tumours can sometimes produce a similar picture.

Care must be exercised when attributing abnormal flow–volume loops to poor technique, and in interpreting flow–volume loops in the presence of concurrent lung disease. Poor technique does not produce reproducible loops.

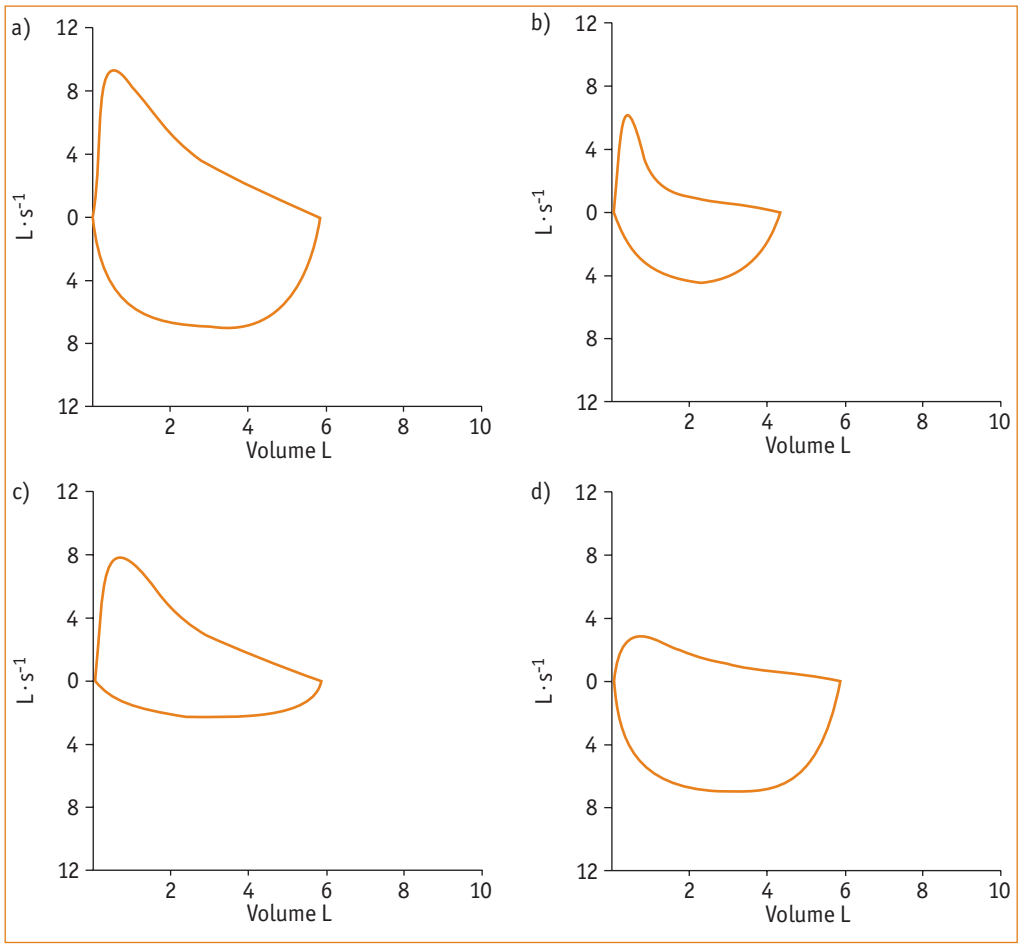

Figure 6
Examples of flow–volume loops.

Task 4
Interpret the flow–volume loops

Answer 4

a) Normal.
b) Small airway obstruction.
c) Extrathoracic tracheal tumour (variable extrathoracic obstruction).
d) Intrathoracic tracheal tumour (variable intrathoracic obstruction).

Surgical resection is potentially curative. Surgical mortality for resection with primary reconstruction is quoted at 5% in specialist centres, with the highest mortality associated with infiltration of the carina [3]. Laser therapy and radiotherapy are both performed as palliative measures and offer no hope for cure. Extensive local infiltration and the presence of distant metastases or multiple primary tumours are both contraindications to surgery. Post-surgery, 5-year survival rates have been reported as 25–50% with squamous cell carcinoma, and up to 80% for adenoid cystic carcinoma [6, 7].

In conclusion, tracheal tumours carry a relatively good prognosis if diagnosed early. For this reason, all patients with asthma resistant to treatment or evident monophonic wheezing on physical examination should be investigated fully. In such cases, the possibility of intrathoracic tracheal obstruction should be kept in mind in order to offer the patient the best hope for cure.

Acknowledgements

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Further reading

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