CASE REPORT

Rare causes of persistent wheeze that mimic poorly controlled asthma

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SUMMARY

Upper airway obstruction can present with stridor or expiratory or inspiratory wheeze and is commonly misdiagnosed as asthma. As asthma is common, such cases can remain hidden among patients with lower airway obstruction who attend primary care or respiratory clinics. We describe four causes of upper airway obstruction (paradoxical vocal cord movement, subglottic stenosis, retrosternal goitre and double aortic arch) which were misdiagnosed as 'poorly controlled asthma'.

BACKGROUND

Wheeze is a continuous sound, lasting longer than 0.25 s that is produced by oscillation of opposing airway walls.^{1 2} Wheeze can be inspiratory or expiratory, and can result from narrowing of any airway, including larger extrathoracic upper airways. Stridor is a high-pitched wheeze, typically arising from air flow turbulence in the upper airway. Clinicians often mistake stridor for wheeze. We describe four cases of different causes of upper airway obstruction, highlighting the importance of careful history taking and examination, as well as a comprehensive workup (imaging, laryngobronchoscopy and interpretation of spirometric flow-volume curves) in assessing a patient who presents with wheeze.

CASE PRESENTATION**Case 1**

A 15-year-old girl was referred with a 2-year history of 'poorly controlled asthma', manifest with dyspnoea on exertion and wheeze. Her symptoms started after she was pushed over while playing football. She had been treated with inhaled corticosteroids, short-acting and long-acting β_2 -agonists and a leukotriene receptor antagonist without improvement.

Inspiratory stridor was noted on clinical examination. The spirometric flow-volume loop showed blunting of the inspiratory loop, consistent with variable extrathoracic airway obstruction (figure 1A). Laryngobronchoscopy revealed apposition of the vocal cords during inspiration with a classical 'posterior chink' (figure 1B) consistent with paroxysmal vocal cord dysfunction (PVCD). Speech and language therapy, combined with videostroboscopy led to complete resolution of symptoms and discontinuation of all medications.

Case 2

A 58-year-old woman was referred with 'poorly controlled asthma'. She reported prolonged wheeze and chronic cough, was unresponsive to a range of

Figure 1 (A) Showing flattening of inspiratory flow-volume loop and (B) showing apposition of the vocal cords during inspiration with a classical 'posterior chink'.

inhaled therapies prescribed by her general practitioner. She worked as a hairdresser and was a non-smoker. She had no history of atopy. She had been treated for asthma for 4 years and had never been intubated.

Inspiratory stridor was noted on clinical examination. The spirometric flow-volume loop showed truncation of inspiratory as well as expiratory flow-volume loops consistent with fixed upper airway obstruction (Figure 2A). Laryngobronchoscopy revealed fixed subglottic stenosis (SS; figure 2B). She was referred to an otorhinolaryngologist for endoscopic repair.

Case 3

A 75-year-old man with a 20 smoking pack-years was referred with a 6-week history of worsening wheeze, cough, green sputum and dyspnoea on exertion.

Inspiratory stridor and expiratory wheeze were noted on clinical examination. CT of the thorax showed a large retrosternal goitre extending to the lower trachea causing 70% stenosis of the midtrachea (figure 3A). Bronchoscopy revealed extrinsic

Figure 2 (A) Showing flattening of expiratory as well as inspiratory flow-volume loops and (B) showing subglottic stenosis.

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tracheal compression (figure 3B). Thyroidectomy led to resolution of symptoms without postoperative complications of tracheomalacia.

Case 4

A 56-year-old man non-smoker was referred with poorly controlled asthma. He reported wheeze and fatigue and his wife described intermittent apnoea while sleeping on his left side.

Inspiratory stridor was noted on clinical examination. The spirometric flow-volume loop showed fixed upper airway obstruction (figure 4A). Polysomnography showed an apnoea-hypopnoea index of 7.8/h. CT of the thorax revealed a congenital double aortic arch, causing tracheal compression (figure 4B). He was referred for vascular and cardiothoracic surgery opinion and the consensus was for conservative management with CT follow-up at 1 year. All inhaled therapies were discontinued without a significant change in symptoms.

DISCUSSION

We present a series of cases that presented with symptoms consistent with asthma but who in fact had upper airway obstruction.

Upper airway obstruction can present with expiratory or inspiratory wheeze as well as stridor and is therefore commonly misdiagnosed as asthma. Our first case is an example of PVCD in a patient who was on asthma therapy without a clinical response. Our second case illustrates a cause of wheeze due to idiopathic subglottic stenosis (ISS) and the third case is of a patient who presented with a wheeze due to retrosternal goitre. Our fourth case illustrates a case of a patient who presented with wheeze that was misdiagnosed as asthma, as well as intermittent sleep apnoea, with positive polysomnography mimicking obstructive sleep apnoea.

PVCD is a rare entity characterised by adduction of the vocal cords during inspiration, which causes airway obstruction and stridor. The exact prevalence of PVCD is unknown but it is believed to be relatively uncommon but women are more frequently affected (female-to-male ratio 3:1).³ The pathophysiology of PVCD is unclear but it has been associated with psychological disorders, exercise, stress, gastro-oesophageal reflux and inhalational exposures.³⁻⁵

Diagnosis is based on clinical symptoms, spirometric flow-volume curve showing variable extrathoracic airway obstruction (flattening of the inspiratory loop) as well as direct inspection of the vocal cords during respiration. Laryngoscopy shows paradoxical adduction of the cords during inspiration with a diamond-shaped 'posterior chink', particularly if the patient is

symptomatic at the time.³⁻⁵ Closure of vocal cords of greater than 50% during inspiration is consistent with the diagnosis.

Management involves the detection of contributing factors. Relaxation techniques such as pursing lips, panting and relaxing shoulders may provide short-term control. Management of asthma and other comorbid conditions such as gastro-oesophageal reflux disease (GORD) is critical. Long-term therapy includes speech and behavioural treatment, counselling and psychopharmacological treatment.³⁻⁵

ISS is an uncommon inflammatory and fibrotic disease involving the subglottic region and proximal tracheal rings. GORD may play a role as chronic aspiration of acidic material may cause inflammation in the subglottic region. One paediatric study suggested improvement with antireflux treatment; however, this result was not replicated in an adult study.^{6,7} There is a female preponderance in ISS, but no familial cases have been reported in the literature. ISS is a diagnosis of exclusion after acquired causes of SS such as prolonged endotracheal intubation, autoimmune and inflammatory disorders, toxic inhalation, gastro-oesophageal reflux and SS associated with granulomatosis with polyangiitis are excluded.

In our case, all of these causes were excluded, including prolonged intubation. Without treatment, the airway may progressively narrow, ultimately requiring tracheotomy. Potential therapeutic interventions include laser resection, corticosteroid therapy, dilation, local resection, tracheal stenting and grafting. Many of these interventions result in improvement, but do not provide cure, with some patients progressing to require tracheotomy. In a study of 52 patients, 21 achieved long-term disease control.⁸

Intrathoracic goitres are usually benign (incidence of malignancy is approximately 2-3%). Retrosternal goitres are most commonly observed in the anterolateral mediastinum and thus can cause tracheal compression. Although retrosternal goitres may rapidly grow and cause obstructive symptoms, most grow insidiously over many years and may be found incidentally on imaging studies. Evaluation of retrosternal goitre includes checking serum thyroid-stimulating hormone to evaluate for subclinical or overt hyperthyroidism, performing CT or MRI to evaluate the extent of the goitre and any local compression, and spirometric flow-volume loop in patients with obstructive symptoms or in those with tracheal narrowing (<1 cm) on cross-sectional imaging.

Ultrasound is important in assessing the features of the goitre and characterising thyroid nodules. Fine needle aspiration biopsy is indicated if malignancy is suspected. Patients with obstructive symptoms require treatment with either

Figure 3 (A) Showing a retrosternal goitre causing tracheal compression with 70% stenosis of midtrachea and (B) showing extrinsic tracheal compression during bronchoscopy.

Figure 4 (A) Showing flattening of the expiratory as well as inspiratory flow-volume loops and (B) showing double aortic arch splitting to come around trachea causing tracheal compression.

thyroidectomy or ablation (Radioiodine, RAI) of the thyroid. Surgery is preferred over ablation because reduction in thyroid volume with RAI is only moderate, and there are theoretical concerns that RAI could acutely worsen obstruction or a missed malignancy and hence RAI is only indicated in patients who are poor surgical candidate.

Indications for thyroidectomy include the presence of compressive symptoms, malignancy, tracheo-oesophageal compression and cosmetic reasons. Our third case report illustrates upper airway obstruction due to retrosternal goitre and thyroidectomy lead to complete resolution of symptoms with no post-operative complications.

A double aortic arch is a congenital anomaly that occurs because the paired aortic arch arteries fail to remodel appropriately, which results in two aortic arches connecting the ascending and descending aorta. The ascending aorta bifurcates anterior to the trachea and oesophagus, and encases the trachea and the oesophagus. The arches rejoin into a single descending aorta posterior to the trachea and oesophagus, thereby completely encircling the two structures. In 70% of cases, the right arch is dominant.

Patients develop dysphagia due to compression of the oesophagus or wheeze, apnoea, dyspnoea, stridor due to compression of trachea and in rare occasions dysphonia due to vocal cord paralysis if there is involvement of the laryngeal nerve. Most anomalies of the aortic arch present in childhood, but when presentation is in adulthood, a double aortic arch can mimic exercise-induced asthma or other obstructive disease.^{9 10}

A thoracic CT scan or MRI and aortography can confirm the diagnosis and assist with preoperative planning. Bronchoscopy can exclude other causes of airway obstruction.¹¹ The spirometric flow-volume curve may be normal or may show fixed or variable large airway obstruction. Surgical correction is indicated for symptomatic younger patients. In those with persistent symptoms despite surgery, tracheal resection or intraluminal stenting may be necessary.¹²

These four cases highlight the need for careful assessment of the patient with poorly controlled asthma. While each case had a relatively uncommon diagnosis, such cases can remain hidden amid the large numbers of patients with poorly controlled asthma who attend a primary care or respiratory service.

Learning points

- ▶ These four cases of upper airway obstruction highlight rare conditions that can present with persistent wheeze.
- ▶ Assessing for stridor during physical examination and evaluating the flow-volume loop is useful in detecting misdiagnosed upper airway obstruction.
- ▶ In evaluating patients with asthma, remember that 'all that wheezes is not asthma; all that wheezes is obstruction' and hence a comprehensive workup for patients presenting with uncontrolled asthma is indicated to detect misdiagnosed upper airway obstruction.

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Competing interests None.

Patient consent Obtained.

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