Adult idiopathic subglottic stenosis: a diagnostic and therapeutic challenge

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A 22-year-old woman presented with effort dyspnea unresponsive to bronchodilators. Harsh respiratory sounds were audible at the neck. Thoracic and cardiac evaluation was normal. Spirometry revealed an obstructive ventilatory defect, and the flow-volume loop indicated upper airway obstruction. Bronchoscopy and tracheal computed tomography revealed a stenosis of the subglottic larynx. A biopsy specimen of the stenotic area of the trachea showed a normal mucosa and non-specific chronic inflammation. The tracheal stenosis was managed by means of endobronchial laser therapy, which led to the resolution of the patient’s symptoms. As we could not identify any specific pathogenetic process, our final diagnosis was idiopathic subglottic tracheal stenosis.

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Key words: Asthma; Bronchoscopy; Effort dyspnea; Endobronchial laser therapy; Subglottic stenosis.

Introduction

Adult idiopathic subglottic stenosis (ISS) is a rare and slowly progressive inflammatory disorder of unknown cause, which is limited to the subglottic larynx and usually occurs in women. Its rarity and variable presentation make it difficult to formulate an accurate early diagnosis and may lead to inappropriate treatment.

We here describe the case of a patient with ISS, misdiagnosed as asthma, and summarize the guidelines for the diagnosis and management of this intriguing disease.

Case report

A 22-year-old woman was admitted to our Department in September 1999 because of a 2-year history of effort dyspnea. One year before, she had been diagnosed as having asthma at another institution, and had been unsuccessfully treated with steroids and bronchodilators. She had never smoked, and had no personal or family history of allergic diseases. The environmental/occupational history was unremarkable.

Harsh respiratory sounds originating in the throat were audible through the neck. No other pathological findings were disclosed by physical examination. Chest and cardiac evaluation (chest radiography, electrocardiography and echocardiography) was normal, as were all the laboratory tests, which included arterial blood gas analysis, the erythrocyte sedimentation rate, C-reactive protein levels, the complement profile, the levels of rheumatoid factor, and antinuclear and antineutrophil cytoplasmic antibodies (ANCA). Spirometry revealed an obstructive ventilatory defect: the forced vital capacity (FVC) was 3.7 L (104% of the predicted value), the forced expiratory volume in 1 second (FEV₁) was 2.1 L (68% of the predicted value), and the FEV₁/FVC ratio was 57% (32% less than the predicted value); the flow-volume loop was suggestive of upper airway obstruction (Fig. 1A). A computed tomography scan of the tracheobronchial tree showed a hypo-dense formation (24 Hounsfield units) 15 mm distal to the vocal cords, which descended for 2 cm and narrowed the subglottic larynx (Fig. 2). There was no surrounding mass or inflammation, and the cricoid cartilage was normal. Optic fiber bronchoscopy revealed a diaphragm-shaped, subglottic, soft tracheal stenosis obstructing two thirds of the lumen (Fig. 3). A biopsy of the stenotic tracheal area revealed a normal mucosa and non-specific chronic inflammation, with no evidence of neoplasm or granulomas. The results of Congo red staining for amyloid were negative. There were no signs of acid-fast bacilli or fungi. The tracheal stenosis was treated by means of endobronchial laser therapy, which led to the resolution of the patient’s symptoms. Post-treatment follow-up confirmed normal spirometric values (FVC 4.3 L, FEV₁ 3.7 L, FEV₁/FVC 87%), and a normal flow-volume loop (Fig. 1B).

No apparent cause for the subglottic stenosis was found. The patient did not have a history of previous laryngeal trauma, endotracheal intubation or upper respiratory tract infection such as diphtheria or tuberculosis. There was no clinical or pathological evidence of amyloidosis, benign or malignant tumors, vasculitis (e.g. Wegener’s granulo-

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matosis) or connective tissue disorders (e.g. relapsing polychondritis). Laryngopharyngeal reflux, a potential contributing or causative factor of subglottic stenosis, was excluded on the basis of the results of 24-hour pharyngeal pH monitoring (the pH at the level of the pharyngeal probe was never < 4). As no pathogenetic process was identified, we formulated a diagnosis of ISS. One year later, high-resolution computed tomography and bronchoscopy documented airway patency without any evidence of restenosis.

**Discussion**

The patient presented with effort dyspnea, a symptom that is usually associated with heart or lung disease. Cardiac dyspnea was excluded on the basis of her history (no previous heart diseases), clinical examination (no evidence of ventricular enlargement, jugular neck vein distension or peripheral edema), and other noninvasive examinations (chest radiography, echocardiography). Effort dyspnea may occur in asthma, but this type of airway obstruction is typically reversible. In our patient, the dyspnea was unresponsive to steroids and bronchodilators; fur-
thermore, chest examination failed to reveal any signs of wheezing in either lung. Severe expiratory flow limitations and lung hyperinflation are characteristic of chronic bronchitis and emphysema, but she had no history of chronic cough or sputum production. Upper airway obstruction was suspected on the basis of the tracheal localization of the harsh respiratory sounds, the reduction in the peak expiratory flow and the flattening of the expiratory limbs at flow-volume loop measurement. The diagnosis of subglottic stenosis was established by means of tracheal tomography and bronchoscopy.

Patients with subglottic stenosis experience varying degrees of effort dyspnea, sometimes voice changes, and occasionally life-threatening airway obstruction. Stridor or harsh respiratory sounds may typically be heard in the area of the trachea, but it is not usual to find widespread lung wheezing. The clinical features of tracheal stenosis may occasionally lead to a misdiagnosis of asthma, but the pronounced upper airway component of the dyspnea and its immediate onset on exertion (together with the unresponsiveness of the expiratory wheeze to bronchodilators) should help in terms of the differential diagnosis. A flattened inspiratory and expiratory flow-volume loop measurement curve may suggest the presence of upper airway obstruction, but endoscopic examinations (i.e. bronchoscopy or direct laryngoscopy) and tracheal tomography are required in order to establish a diagnosis of glottic dysfunction. A biopsy should be performed to exclude tumors, granulomas, vasculitis and other systemic connective tissue disorders. Once a diagnosis of subglottic stenosis has been established, the patient should be closely monitored for signs of airway impairment.

The most common cause of adult subglottic stenosis is trauma due to endotracheal intubation or tracheotomy; other causes include external airway injury, laryngopharyngeal reflex, benign and malignant tumors, tuberculosis, histoplasmosis, and systemic disorders such as Wegener’s granulomatosis, sarcoidosis, amyloidosis and relapsing polychondritis. Wegener's granulomatosis-related subglottic stenosis may occur without any symptoms of systemic inflammatory disease and without any clinical signs of systemic vasculitis. In this localized form of Wegener’s granulomatosis, the diagnosis may be established on the basis of the clinical features, positive cytoplasmic(c)-ANCA testing and histological findings (necrotizing granulomatous vasculitis, epithelioid granulomas with varying degrees of chronic inflammatory cells). In patients with relapsing polychondritis, tracheal dysfunction is associated with hearing loss, vestibular imbalance, ocular inflammation and arthritis. The patients with a stenosis that cannot be attributed to any one of the aforementioned causes are considered as having ISS, a condition that seems to occur mainly in females (although the significance of this prevalence has not yet been explained). It is not certain whether this group of patients represents a distinctly separate group or a collection of different systemic illnesses that have not yet been identified.

Any hypothesis concerning the pathogenesis of ISS is purely speculative: a still unproven autoimmune mechanism has been suggested in some cases, and there has been a recent report describing an association between laryngopharyngeal reflex and ISS but not all ISS patients have reflux. Two types of subglottic stenosis have been identified on the basis of their endoscopic and histopathological characteristics: “soft” stenoses (most frequently characterized by the presence of granulation tissue or submucosal mucous gland hyperplasia) and “hard” stenoses whose fibrous tissue and disorganized scars are probably related to some form of laryngeal injury. The condition is apparently comparable with other inflammatory processes of unknown cause, such as abdominal or extra-abdominal fibromatosis, collagenous colitis, and idiopathic retroperitoneal fibrosis.

The clinical course of ISS is unpredictable and, given that it has no defined cause, its treatment raises a number of difficulties. Endoscopic methods (such as dilation, with or without resection) by means of diathermy, cryotherapy or laser therapy may be helpful in patients with mild symptoms and thin, soft stenotic lesions. In case of patients with hard, fibrous unresponsive scars and recurrent subglottic stenoses, laryngotraheal resection and reconstruction is considered the treatment of choice and offers promising long-term results.

Riassunto

Viene riportato il caso di una donna di 22 anni, ricoverata per dispnea durante l’esercizio o sotto sforzo, attribuita ad asma bronchiale e risultata resistente al trattamento steroideo e broncodilatatore. L’esame clinico ha evidenziato normali reperti cardiaci e polmonari ed un respiro aspro, prevalentemente inspiratorio, in corrispondenza dell’ipofaringe e della trachea. La spirometria ha rivelato un disordine funzionale di tipo ostruttivo e la curva volume-flusso un’ ostruzione delle vie aeree superiori di tipo fisso. La broncoscopia e la tomografia computerizzata tracheale hanno mostrato una stenosi della laringe subglottica e la biopsia dell’area stenotica una mucosa normale con segni di flogosi cronica aspecifica. La stenosi tracheale è stata trattata mediante lasserterapia endobronchiale con risoluzione della dispnea e normalizzazione degli indici di funzione polmonare. Non essendo stata individuata alcuna causa responsabile della stenosi, è stata formulata diagnosi di stenosi subglottica idiopatica.
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References


