Misdiagnosis asthma in adult, three rare causes

Faux asthme chez l'adulte, trois causes rares

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Abstract

Introduction: All that wheezes is not asthma. Although, asthma is the most common cause of wheeze and cough in children and adults, it is often attributed inappropriately to these symptoms from other causes.

Aim: We illustrate through this manuscript three rare causes of wheeze in adults, misdiagnosis as asthma.

Observations: The three reported cases were misdiagnosed as difficult-to-treat asthma. They were found as mimicking asthma. Final diagnoses were localized tracheobronchial amyloidosis, aortic arch anomalies, and idiopathic chronic eosinophilic pneumonia.

Conclusion: Although asthma is a common cause of various respiratory symptoms, all that coughs and wheezes is not asthma. So before retaining the severe asthma diagnosis, we have to exclude various differential diagnoses, even the rarest ones. Several diagnostic tests have to be done to have the appropriate diagnosis.

Key Words: Wheezing, misdiagnosis, asthma

Résumé

Introduction : Tout ce qui siffle n'est pas de l'asthme. Bien que l'asthme soit la cause la plus fréquente de dyspnée sifflante et de toux chez les enfants et les adultes, d'autres pathologies peuvent mimer un asthme et être considérées à tord comme de l'asthme difficile à contrôler.

Objectif : Nous illustrons à travers ce manuscrit trois causes rares de dyspnée sifflante chez l'adulte, considérées à tord comme de l'asthme sévère.

Observations : Dans les trois cas rapportés, le tableau clinique mimait celui d'un asthme difficile à traiter. Les diagnostics retenus, après une panoplie d'explorations adaptée au contexte et à la suspicion clinique, étaient une amylose trachéobronchique localisée, des anomalies de la crosse aortique et une pneumonie éosinophile chronique idiopathique.

Conclusion : Bien que l'asthme soit une cause fréquente de divers symptômes respiratoires, tout ce qui siffles et tousse n'est pas de l'asthme. Ainsi, avant de retenir le diagnostic d'asthme sévère, il faut exclure divers diagnostics différentiels, même les plus rares. Plusieurs explorations à visée diagnostiques devraient être effectuées afin de redresser le diagnostic.

Mots clés : Dyspnée, sifflement, diagnostic différentiel, asthme.

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INTRODUCTION

Not all that wheezes is asthma (1). Although, Chronic Obstructive Pulmonary Disease (COPD) heads the list of diagnosis most likely to be confused with asthma in everyday practice, many other diagnoses, even more rare, must be kept in mind. Therefore, before retaining the severe asthma diagnosis, we have to exclude various differential diagnoses, even the rarest ones. Thus, different diagnostic tests, including spirometry, chest CT scan, flexible bronchoscopy and bronchoalveolar lavage, with cardiopulmonary monitoring can generally result in the appropriate diagnosis and more specific treatment (2).

Aim: We illustrate through this manuscript three rare causes of wheeze in adults, misdiagnosis as difficult-to-treat asthma.

OBSERVATIONS

Observation 1

A 47 year-old no smoker woman was admitted for dyspnoea of exertion associated to wheezing, reported since 2 years. Physical examination found diffuse sibilance. Chest X ray was normal. Pulmonary function test showed a reversible obstructive ventilator disorder. When symptomatic, she had a forced vital capacity (FVC) at 78%, forced expiratory volume (FEV) at 43% and FEV/FVC at 48%. She had a normal respiratory function when asymptomatic. Diagnosis of asthma was initially retained. Inhaled beta adrenergic agonist and corticosteroid were established without amelioration of symptoms or pulmonary function test. Chest computed tomographic scan (CT scan), practiced in the balance sheet of severe asthma, revealed irregular thickening of the tracheal wall, with nodules protruding into the lumen of the right main bronchi and lower lobe bronchiectasis (figure 1). Fibroptic bronchoscopy showed infiltration and nodular lesions protruding into the lumen of the lower third portion of trachea and main bronchi (figure 2). Diagnosis of AA amyloidosis was confirmed by endo-bronchial biopsy. The characteristic findings of amyloidosis were obtained in tissue specimens stained by congo red and these specimens exhibited green birefringence under polarized microscopy. Extensive investigations, including renal and hepatic ultrasonography, liver function, creatinine clearance rate, serum and urine protein electrophoreses, electro and echocardiography, were normal leading to rule out systemic amyloidosis. Diagnosis of localized broncho-pulmonary amyloidosis was retained.

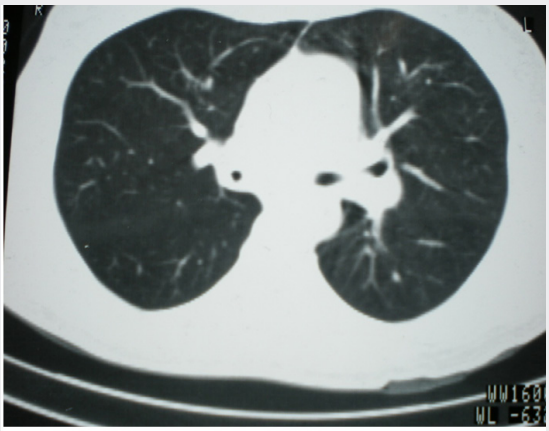

Figure 1. Chest CT scan: Irregular thickening of wall of the right main bronchi

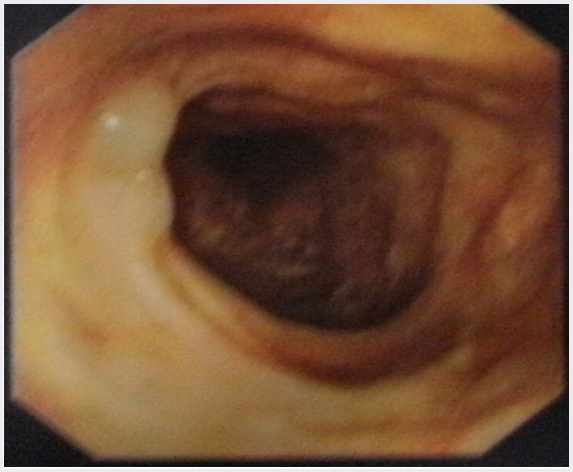

Figure 2. Bronchoscopic view: nodular lesions distributed along the cartilaginous rings of lower portion of trachea and the main bronchi

Observation 2

A 56-year-old no smoker woman, with past medical history of diabetes and arterial hypertension, was referred to our department with the diagnosis of difficult-to-treat asthma. She had 20-years-past history of dry cough and wheezing dyspnoea diagnosed as uncontrolled asthma, despite her adherence to her asthma treatment witch was optimal.

Here physical examination was normal. Pulmonary function test was normal. Chest X ray revealed right side aortic arch.

Chest CT Scan has done, confirmed right-sided aortic arch with an aberrant retro-oesophageal left subclavian artery arising from a Kommerell's diverticulum, inducing tracheal compression (figure 3). The diverticulum was considered as the cause of chronic cough and wheezing dyspnoea, in our case, as it was causing tracheal compression and also there were no other obvious causes which could explain symptoms.

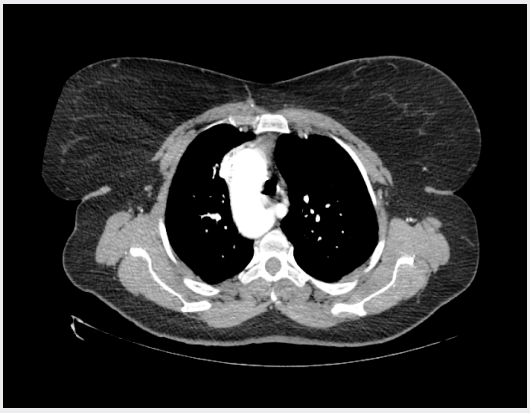

Figure 3. Chest Angio-CT scan: right-sided aortic arch and Kommerell's diverticulum at the origin of an aberrant left subclavian artery, with tracheal compression.

Observation 3

She was a 53-year-old no smoker women, with past medical history of arterial hypertension. She was admitted in our department for cough and wheezing dyspnoea, reported since 2 years, without extra-pulmonary signs. Physical examination found sibilance. Chest X ray was normal. Diagnosis of asthma was initially considered. But, to no improvement in optimal treatment chest CT scan was practiced revealing bilateral and scattered alveolar infiltrates, with a peripheral predominance (figure 4).

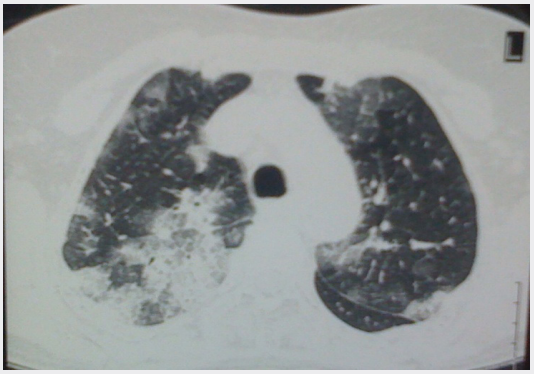

Figure 4. Bilateral and scattered alveolar infiltrates, with a peripheral predominance

Pulmonary function tests showed a restrictive pattern. Laboratory examinations obtained at presentation revealed a total WBC count of 6300 cells/µL with 54% eosinophils. Serologic tests for autoantibodies including antinuclear antibody, rheumatoid factor, and P-anti-neutrophil cytoplasmic antibodies, were negative. Aspergillus serology and acid-fast-bacilli smear were negative. Stool examination revealed no ova or parasites. Biological tests found peripheral blood eosinophilia at 3400 cells per microliter (54%). Bronchoalveolar lavage fluid revealed alveolar eosinophilia at 43%. Cardiac and abdominal sonographies were normal. All known causes of eosinophilic pneumonia have been removed. Diagnosis of Carriongton disease or idiopathic chronic eosinophilic pneumonia was suspected. Oral corticotherapy was started. Outcome was favourable with spectacular improvement (figure 5).

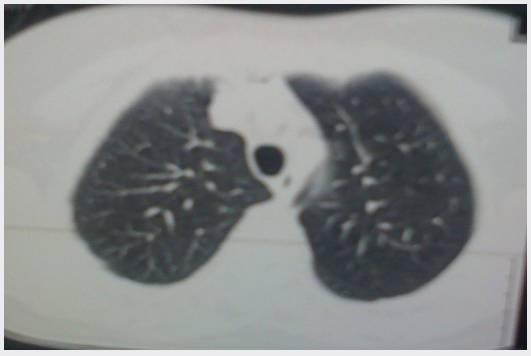

Figure 5. Spectacular improvement after corticotherapy

So, diagnosis of Carriongton disease was retained; diagnosis was based on respiratory symptoms of more than 2 weeks duration without extra-pulmonary manifestations, pulmonary infiltrates with peripheral predominance on chest imaging, blood and alveolar eosinophilia, exclusion of other known cause of eosinophilic lung disease and favourable response to corticotherapy.

DISCUSSION

Asthma is a serious disease with high social and economic costs that affect approximately 300 million individuals worldwide. Its incidence varies by country between 1% and 18% (3). The prevalence of physician-diagnosed-asthma has risen over the past three decades and misdiagnosis of

asthma is potentially common (4).

Proper treatment (i.e. Corticosteroids), usually, results in a good control; however, some patients remain symptomatic despite optimal treatment and systematic assessment of these patients must begin with confirmation of the diagnosis (3).

Although asthma is the most common cause of cough, wheeze, and dyspnoea in children and adults, asthma is often attributed inappropriately to symptoms from other causes (2).

Here we report three rare causes, which were misdiagnosed as asthma: primary tracheobronchial amyloidosis, aortic arch anomalies, and Carrington's disease.

Amyloidosis is defined by a deposition of an amorphous, extracellular and fibrillar protein material with characteristic physicochemical properties (5). Tracheobronchial amyloidosis, an uncommon localized form of amyloidosis, is one of the rarest differential diagnoses of asthma. It produces tumour-like lesions in the tracheobronchial tree. The patients present with a variety of symptoms such as dyspnoea, cough haemoptysis, stridor, rhonchi and crepitations. These nodular lesions produce progressive airway obstruction resulting in symptoms suggestive of bronchial asthma, atelectasis and obstructive pneumonia (6). The diagnosis of amyloidosis is rarely evoked before bronchoscopy has been done. It usually requires histological confirmation. Congo red staining that produces green birefringence under crossed light remains the gold standard (7). The treatment of choice is actually based on the bronchoscopic resection (7).

Our first case highlights the importance of routinely carrying out an endoscopy in any patient complaining of atypical bronchial symptoms or with uncontrolled asthma.

Aortic arch anomalies are congenital malformations of vessels derived from gill arches (especially 4th and 6th). The prevalence of aortic arch anomalies clinically symptomatic is low, representing less than 1% of congenital heart disease (8). The right aortic arch is a rare anatomic variant occurring in only 0.1% of population (9). Left aortic arch with an aberrant right subclavian artery being the most common anomaly with prevalence of 0.5 à 2%, other rare anomalies can be seen, including right aortic arch with an aberrant left subclavian artery with a diverticulum at its origin, known as Kommerell's diverticulum with prevalence of 0.05 to 0.1% (10). This anomaly, usually asymptomatic, may present as dyspnoea, wheezing or chronic cough, mimicking asthma. These symptoms are induced by tracheal compression, in our case caused by Kommerell's diverticulum. Several mechanisms could explain that. In fact, the enlargement of the Kommerell's diverticulum by itself, and the sling-like effect of the left subclavian artery, which pulls the right aortic arch towards left side, may be responsible for that. Age-related atherosclerotic changes occurring in the diverticulum could be another mechanism that may contribute to compression of the surrounding structures (10). In our case, Kommerell's diverticulum did not produce any symptoms until the age of 56 years, and this latter mechanism could explain the late onset of symptoms.

Carrington's disease or Idiopathic Chronic Eosinophilic Pneumonia (ICEP) is an idiopathic process characterized by a marked eosinophilia infiltration of the lungs. ICEP most commonly affects women of middle age. Our patient was 53-year-old women. Although many patients are healthy without any symptoms prior to the disease onset, about a half of patients present with respiratory symptoms such as wheezing dyspnoea or chronic cough usually misdiagnosed as asthma, especially to the frequent coexistence of atopic dermatitis (11). There are no strict diagnostic criteria for ICEP. Diagnosis is usually based on the association of (12):

- Respiratory symptoms of usually more than 2 weeks duration
- Blood and/or alveolar eosinophilia (blood eosinophilia ≥ 1000/mm3; alveolar eosinophilia ≥ 40% at bronchoalveolar lavage)
- Pulmonary infiltrates with usually a peripheral predominance on chest imaging (chest x ray and CT scan)
- Exclusion of any known cause of eosinophilic lung disease.

All previous criteria were found in our case.

Treatment of ICEP is based on oral corticosteroids. After initiation of treatment, the symptoms as well as the peripheral blood eosinophilia regress within a few hours and resolution of the chest radiographic findings is seen within a few days (11). In our patient, improvement was dramatic with corticosteroid treatment.

CONCLUSION

Although asthma is a common cause of various respiratory symptoms, all that coughs, wheezes, and dyspnoea is not asthma. Before retaining the diagnosis of severe asthma, we have to exclude various differential diagnoses, even the rarest ones. Thus, several diagnostic tests have to be done to have the appropriate diagnosis, such as spirométrie, chest CT scan, flexible bronchoscopy and bronchoalveolar lavage.

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