

Case Report

Tracheobronchial amyloidosis*

LUCIANO MÜLLER CORRÊA DA SILVA^(TE SBPT), JAMILA BELLICANTA,
RENATA DINIZ MARQUES, LUIZ CARLOS CORRÊA DA SILVA^(TE SBPT)

Amyloidosis is a disease characterized by extracellular deposition of pathologic fibrillar protein in organs and tissues. Diffuse primary tracheobronchial amyloidosis is rare. Herein, we report a case of a male patient with diffuse tracheobronchial amyloidosis, initially diagnosed as bronchial asthma.

J Bras Pneumol 2004; 30(6) 581-4.

Key words: Asthma/pathology. Amyloidosis/diagnosis. Trachea/pathology.

INTRODUCTION

Amyloidosis is a disease characterized by extracellular deposition of pathologic fibrillar protein in organs and tissues⁽¹⁾. Respiratory amyloidosis was first described in 1877 by Lesser and innumerable classification systems, based on radiographic and bronchoscopic findings, have since been suggested⁽²⁾. Respiratory impairment is uncommon and presents in one of four forms: two tracheobronchial forms (local and diffuse) and two parenchymal forms (nodular and diffuse). Of these four forms, diffuse tracheobronchial amyloidosis is the least common⁽³⁾.

Tracheobronchial amyloidosis is an idiopathic disease that has been associated with tracheobronchopatia osteoplastica, characterized by the deposition of fibrillar proteins in the submucosa of the trachea and bronchi⁽⁴⁾. Due to the rarity of amyloidosis in this presentation⁽⁴⁾, we

report herein the case of a patient suffering from diffuse tracheobronchial amyloidosis.

CASE REPORT

A 34-year-old, previously healthy, married white male was admitted to the Pereira Filho ward of the Santa Catarina Hospital Complex in the city of Porto Alegre, in the state of Rio Grande do Sul (RS). He was originally from the city of Canoas (RS) and was working as a scaffold builder at the petrochemical complex in the city of Triunfo (RS). He complained of dyspnea upon minimal exertion, productive cough and episodes of hemoptysis for approximately one year. The patient also reported many episodes of respiratory infection, requiring antibiotic treatment, during this period. In addition, he had been receiving treatment for difficult-to-manage bronchial asthma (the inhaled corticosteroid used was a β_2 -adrenergic agonist,

*Study carried out at the Pavilhão Pereira Filho, Porto Alegre, RS. Keywords: Diffuse Tracheobronchial Amyloidosis. Bronchial asthma. Correspondence to - Luciano Müller Corrêa da Silva. Rua Dr. Barcelos 741 casa 2, Bairro Tristeza, Porto Alegre, RS. Tel: 55-51-3221 8522. E-mail: lmcsm@terra.com.br.
Submitted: 4 November 2003. Accepted, after review: 30 April 2004.

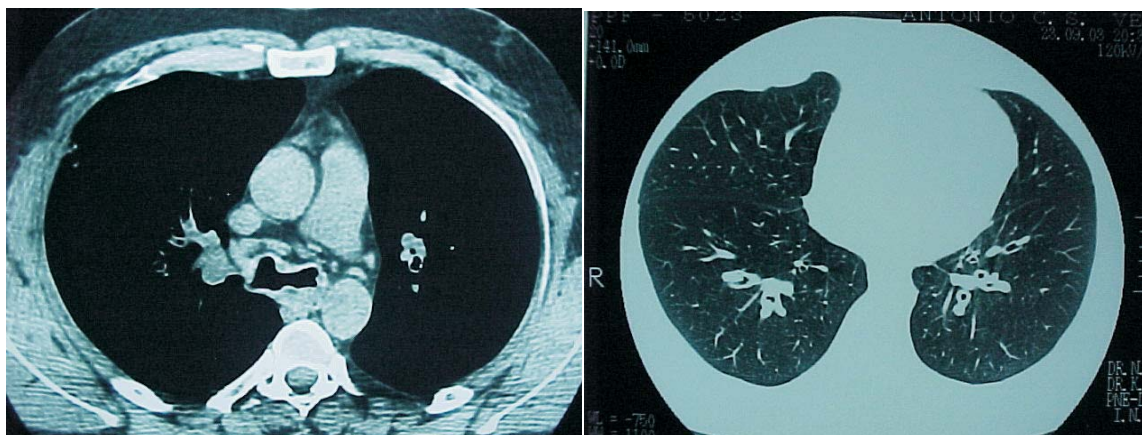


Figure 1 – Computed tomography of the chest showing significant tracheobronchial wall thickening (white arrow)

combined with frequent courses of oral corticosteroids) with little therapeutic response. At the time of admission, the patient also presented hypertensive peaks, having started anti-hypertensive treatment with enalapril and hydrochlorothiazide. Upon physical examination, the patient presented tachypnea (respiratory rate: 26 breaths/min), and pulmonary auscultation revealed diffuse rales upon expiration.

The radiogram of the thorax revealed bronchial wall thickening. A computed tomography scan of the chest (26 February 2003) showed significant tracheal wall thickening, as well as thickening of

the larger bronchi. There was no evidence of relevant alterations in the pulmonary parenchyma (Figure 1). In the forced-expiration slices, air trapping was predominantly seen in the right lung (Figure 2). Total abdominal echography and transthoracic Doppler echocardiography were normal. Serum proteinogram and bone marrow biopsy showed no alterations. A control computed tomography scan of the chest, carried out on 19 March 2004, presented no significant changes in the degree of tracheobronchial wall infiltration and thickening when compared with that of 26 February 2003.

Pulmonary function testing revealed a moderate obstructive pattern that was nonresponsive to the bronchodilator. Lung volumes, as determined through plethysmography (total lung capacity and residual volume), were high. Pulmonary function testing conducted on 26 September 2003 revealed worsening when compared with the previous control (17 March 2003). However, the most recent test (22 March 2004), in comparison to that of 23 September 2003, showed relatively stable pulmonary function (Table 1).

Fiberoptic bronchoscopy revealed ill-defined infiltrative lesions in the respiratory mucosa adjacent to the tracheal carina and diffuse infiltrative lesions in the tracheobronchial tree. There were no nodular lesions. A biopsy of the bronchial mucosa was conducted, and the

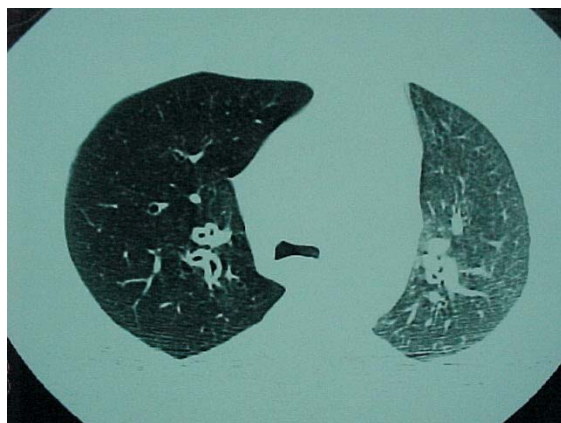


Figure 2 – Forced-expiration tomographic slices showing air trapping, predominantly in the right lung

TABELA 1
Evolução da espirometria desde a avaliação inicial até o último controle

| Variáveis | Valores de referência | 17/03/2003 | | 26/09/2003 | | 22/03/2004 | |
|-----------------------------|-----------------------|------------|--------|------------|--------|------------|--------|
| | | Pré-BD | Pós-BD | Pré-BD | Pós-BD | Pré-BD | Pós-BD |
| CVF (L) | > 3,84 (L) | 3,95 | 3,70 | 3,93 | 3,73 | 3,21 | 3,57 |
| VEF ₁ (L) | >3,15 (L) | 2,33 | 2,20 | 1,73 | 1,58 | 1,73 | 1,70 |
| VEF ₁ /CVF | 75,6 (L) | 59% | 59% | 44% | 42% | 54% | 48% |
| FEF _{25-75%} (L/s) | 2,67 (L/s) | 1,50 | 1,50 | 0,93 | 0,84 | 1,14 | 1,0 |
| PEF (L/s) | 9,5 (L/s) | 3,88 | 3,86 | 3,02 | 3,10 | 3,42 | 3,12 |
| CPT (L) | 5,74-7,92 (L) | 7,21 | 6,70 | 6,40 | -* | 6,41 | 6,52 |
| VR (L) | 1,14-2,36 (L) | 3,26 | 2,68 | 2,47 | -* | 2,79 | 2,78 |
| Difusão (mmol/Kpa.min) | | 11,1 | 105% | - | - | 10,2 | (95%) |

* Paciente não conseguiu realizar o exame, interrompido por dispnéia e hemoptise.

BD: broncodilatador; CVF: capacidade vital forçada; VEF₁: volume expiratório forçado no primeiro segundo; FEF_{25-75%}: fluxo expiratório forçado médio entre 25% e 75% da CVF; PEF: pico de fluxo expiratório; CPT: capacidade pulmonar total; VR: volume residual.

histological slices, stained with Congo red, revealed amyloidosis.

Between September 2003 and March 2004, we also observed relative stability in the symptoms, consistent with the radiological and functional profile.

DISCUSSION

Amyloidosis is a generic term for a heterogeneous group of diseases associated with the deposition of abnormal fibrillar proteins. There are several different forms of amyloidosis⁽¹³⁾.

Reactive amyloidosis⁽²⁾, also known as amyloid A (AA) amyloidosis (related to serum levels of amyloid A protein), is correlated with heredity and chronic infectious processes, and has also been associated with familial Mediterranean fever and tuberculosis. This form of amyloidosis rarely presents as a respiratory disease. Reactive amyloidosis includes some subtypes that are considered hereditary and frequently involves the nervous system. The b2 subtype has been correlated with prolonged dialysis⁽¹⁾.

Primary idiopathic⁽²⁾, or amyloid light-chain (AL), amyloidosis is the most common type. It is considered a systemic process, characterizes by widespread deposition of products of immunoglobulin cleaving and manifesting as heart failure, kidney failure or neuropathy. This idiopathic

amyloidosis deposition is also seen in a nonsystemic form, presenting isolated involvement of organs in the nervous system, respiratory tract or elsewhere⁽¹⁾.

Familial transthyretin amyloidosis (ATTR) is associated with senile systemic amyloidosis, with a predominant cardiac involvement, polyneuropathy or impaired renal function⁽¹⁾.

The pulmonary manifestation of amyloidosis may be accompanied by both systemic and secondary familial amyloidosis, and the parenchyma or pleura may be affected⁽¹¹⁾. Tracheobronchial amyloidosis and lung parenchyma amyloidosis rarely appear concomitantly. Patients suffering from the local form of pulmonary amyloidosis present no systemic lesions, and the presentation may be either parenchymal or tracheobronchial⁽⁴⁾.

Tracheobronchial amyloidosis is distinct from the pulmonary forms because of the primary or secondary systemic involvement, in which serum levels of monoclonal proteins are typically evident. It is considered a type of localized amyloidosis, presenting fibrillar protein deposition in a specific organ. However, there has been at least one reported case of localized tracheobronchial amyloidosis in which a monoclonal protein was detected in the serum⁽⁹⁾. Amyloid deposition in the tracheobronchial tree is usually of the light-chain

type and is considered a local phenomenon, which suggests it is an abnormal immune response of the lymphoid tissue and is associated with the bronchi, rather than being a systemic response⁽⁶⁾.

Tracheobronchial amyloidosis produces both plaque in the mucosa and endobronchial masses that simulate neoplasia. It typically affects individuals over the age of 50⁽²⁾.

The most common presentation in plaque is the diffuse type, which manifests as cough and dyspnea, as well as, occasionally, hemoptysis. When endobronchial masses are present (localized form), there is a higher probability of obstruction, evidenced by areas of atelectasis, air trapping and recurrent pneumonia⁽⁶⁾. In the present case, albeit a case of the diffuse form, these manifestations were observed. Pronounced tracheobronchial thickening constitutes a significant radiographic finding.

Diagnosis requires histological confirmation through biopsy, in which sections stained with Congo red reveal greenish birefringence under polarized-light microscopy^(1,2).

Unfortunately, there is no known effective treatment. Treatment options range from observation and clinical-radiological follow up to local aggressive radiotherapy. Laser ablation therapy was initially described as efficient in the control of local tracheobronchial amyloidosis^(6,12,14). However, in a recent study⁽⁴⁾, it had no apparent effect on outcome in the diffuse form of the disease and was therefore only palliative. In diffuse tracheobronchial amyloidosis, there have been no studies demonstrating the efficacy of the prednisone-melphalan combination, which is commonly used in systemic amyloidosis⁽⁸⁾. Kurrus *et al.*⁽⁹⁾ reported the use of external radiotherapy in a case of local tracheobronchial amyloidosis, which presented a good therapeutic response. Kalra *et al.*⁽¹⁰⁾ proposed external beam radiotherapy with 20 Gy. In a patient with diffuse tracheobronchial amyloidosis, the authors observed a significant improvement of symptoms over a two-year period. Therefore, radiotherapy seems to be the only treatment that provides a chance of a long-term response in patients with diffuse tracheobronchial amyloidosis. The prognosis varies, which means that, in some patients, the disease may remain stable for long periods⁽⁷⁾, whereas in others it may progress and lead to death. In this

sense, the deterioration of pulmonary function seems to be an important marker⁽⁴⁾.

Although spontaneous resolution has been reported, most cases present recurrence and require multiple therapeutic interventions in order to control progressive respiratory symptoms.

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