Case Report

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TANAFFOS

Systemic AL Amyloidosis of the Tracheobronchial Tract and Lungs: a Rare Finding

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A 67- year old man presented with cough, weight loss and night sweats. Fiberoptic bronchoscopy did not show any abnormality. Chest computed tomography scan revealed peribronchovascular thickening, sheathing and narrowing of some bronchi. There were also mediastinal and interbronchial Lymphadenopathies. The patient became lost to follow-up. He presented 5 years later with pneumonia. Flexible bronchoscopy showed diffuse infiltration of the bronchi suggesting lung cancer. Histopathological study with histochemical staining revealed tracheobronchial tract AL amyloidosis. Chest CT-scan revealed extension of the broncho-vascular thickening and superimposed pulmonary calcified nodules and lymphadenopathies. Labial biopsy revealed AL amyloidosis. No specific treatment of amyloidosis was thought to be necessary for the patient. At 6 years follow-up the disease had not progressed. This case report highlights the fact that even very rarely, systemic AL amyloidosis can involve the tracheobronchial tract. Moreover, the lungs and the tracheobronchial tract can, although rarely, be affected in the same patient.

Key words: Amysloidosis, Tracheobronchial tract, Lung

INTRODUCTION

Amyloidosis is the deposition of an amorphous, extracellular and fibrillar protein material. This protein binds with Congo red and reveals green birefringence under polarized light. Amyloidosis can be classified either based on the type of the deposited protein or its location in the body. Concerning the former, the two more frequent types of amyloidosis are: AL amyloidosis due to the deposition of light chain immunoglobulins and AA amyloidosis due to the deposition of AA proteins. As for the latter, amyloidosis can involve either many organs, and is therefore called systemic amyloidosis or one organ and therefore called localized amyloidosis. AL amyloidosis is the more frequent type of amyloidosis and is mostly systemic. Respiratory involvement in amyloidosis is very rare and involves almost exclusively the tracheobronchial tract (TBT). Conversely, when the disease is systemic, the TBT is generally spared. We report a rare case of systemic AL amyloidosis with involvement of the TBT and the lungs (1-3).

CASE SUMMARIES

A 67 year-old man, smoking 94 pack/year presented to our department in 2004 complaining of a 3–month history of cough and weight loss associated with night sweats. His

physical examination was normal. Chest X ray showed thickened airway walls associated with a middle lobe collapse. Blood cell count, C-reactive protein and liver function test results were within the normal range. Blood creatinine level was slightly elevated at 125µmol/l. Arterial blood gas analysis was normal. The fiberoptic bronchoscopy did not show any abnormality. Acid fast bacilli were negative in the sputum and in the bronchial fluid. No malignant cells were observed in the bronchial fluid. The patient was given 3 g of penicillin per day for 10 days after which he showed a favorable clinical outcome. Chest computed tomography (CT) scan revealed peribronchovascular thickening, sheathing and narrowing of the right upper bronchus and the middle one which was collapsed. There were also bilateral mediastinal and interbronchial lymphadenopathies. The patient became lost to follow-up. He presented 5 years later with persistent chest pain, fever and worsening of the cough with abundant green sputum. On examination his temperature was high at 39.7°C. The respiratory rate was 28 per minute. Chest auscultation revealed bilateral rhonchi. Blood gas analysis on ambient air showed: PH: 7.43; PaO_2: 72.3 mm Hg; Pa CO_2:33 mm Hg; and HCO_3^-: 22.4 mmol/l. Chest x-ray was unchanged. White blood cells were 1.5×10^9 L^{-1}. C-reactive protein was 111.1 mg/L and ESR 69 mm at the first hour. Polymorphous bacteria were isolated from sputum smear. The patient took amoxicillin/ clavulanic acid 3 g per day for 10 days and showed good clinical and biological outcome. Flexible bronchoscopy revealed infiltration of the lingula, the right upper bronchus and the middle bronchus suggesting lung cancer. Brain CT-scan was normal. Biopsy of the bronchial infiltration was examined with Hematoxylin-Eosin staining and showed amorphous eosinophilic deposition in the mucosa (Figure 1). Specimen examination under polarized light with Congo Red staining revealed green- yellowish amyloid deposition predominating in the vessel walls (Fig.2). Histochemical study revealed lambda light chains (Fig.3). Neither kappa nor serum amyloid A (SAA) test were present. Based on these findings, the diagnosis of AL amyloidosis of the bronchial tract was made. Chest CT scan revealed bilateral broncho-vascular thickening narrowing the proximal bronchi diameter, collapsed middle lobe, numerous pulmonary nodules with many calcified ones, collapsed left lower lobe, septal thickening of both lower lobes and lymphadenopathies of the interbronchial, hilar and mediastinal chains with central and peripheral calcifications (Fig.4). Immunoelectrophoresis of the serum and the urine did not reveal monoclonal immunoglobulins. No light immunoglobulin chain was detected in the serum or in the urine. Bence Jones proteinuria was absent. Functional lung testing showed irreversible obstructive syndrome. Electrocardiogram and echocardiography were normal. No pericardial effusion was present. Labial biopsy revealed AL amyloidosis associated with chronic sialadenitis type 3 of the Chisholm's classification (Figure 5). The creatinine blood level was normal: 113 µ mol/l. Renal sonography did not reveal any feature of amyloidosis.

No specific treatment for his amyloidosis was thought to be necessary. At 6 years follow-up the patient did not present any worsening of the dyspnea which was of moderate intensity.

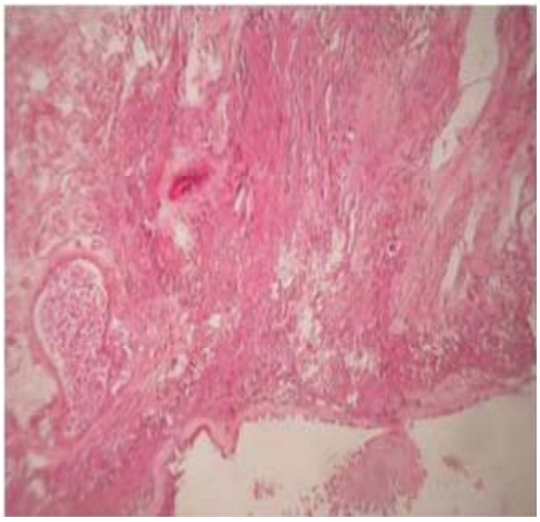

Figure1. Histological examination of the infiltrated bronchial mucosa with Haematoxylin-Eosin staining: amorphous eosinophilic deposition

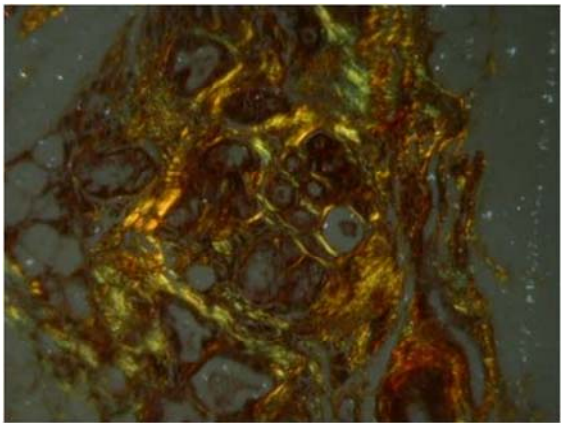

Figure 2. Histological examination of the infiltrated bronchial mucosa under polarized light with Congo Red staining: green- yellowish amyloid deposition.

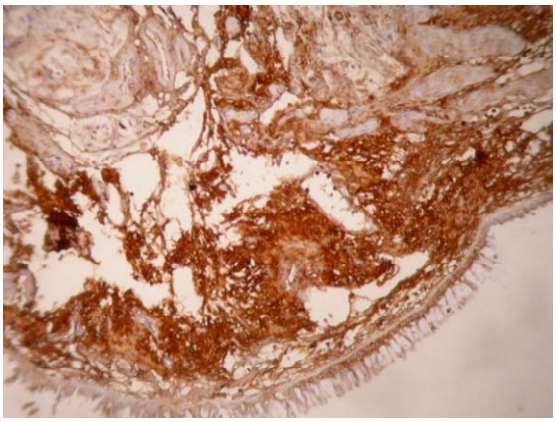

Figure 3. Histological examination of the infiltrated bronchial mucosa with immunochemical study: positive amyloid deposition by the anti-lambda antibody.

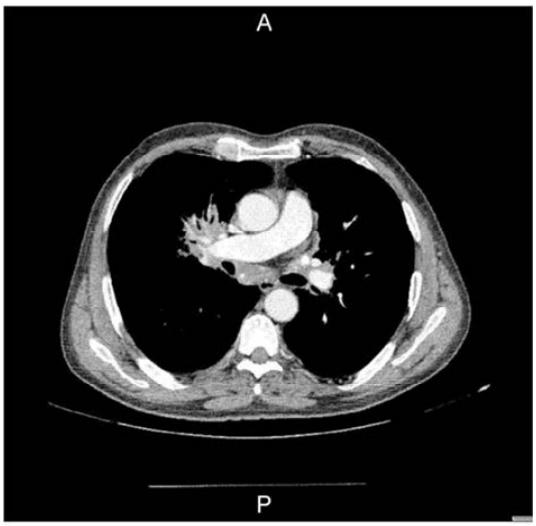

Figure 4. Chest CT scan: bilateral broncho-vascular thickening, narrowing the proximal bronchi diameter, calcified mediastinal lymphadenopathies and pulmonary nodules.

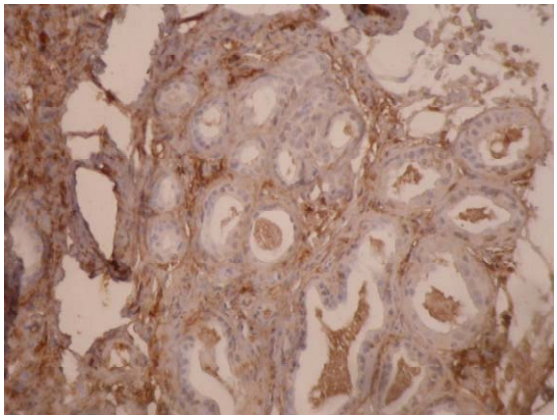

Figure 5. Histological examination of salivary glands with immunohistochemical study: positive amyloid deposition by the anti-lambda antibody.

DISCUSSION

We report a case of a primary amyloidosis involving the TBT and the lungs. Two immunologic types of amylodosis are described:

- AA amyloidosis which is a reactive or secondary disease. It is characterized by the deposition of an AA protein deriving from a serum precursor (SAA), synthesized by the liver which increases in inflammatory events (1). Nowadays, this type of disease is encountered mainly in rheumatoid arthritis and in familial Mediterranean fever.
- AL amyloidosis which is most of the time a primary disorder. It is characterized by the deposition of monoclonal light chains of immunoglobulins.

AL amyloidosis may be either localized or systemic (1,2). It represents the major type of the systemic form of amyloidosis (3,4). In 80% of the cases, AL amyloidosis is primary and due to a monoclonal dysfunction of plasmocytes without any malignancy.

AL amyloidosis generally affects many organs because pathologic immunoglobulins are produced by the bone marrow and are deposited in different tissues. Respiratory involvement of the disease is very rare and affects almost exclusively the TBT. Since the first case reported by Lesser (1) in 1877, only 150 cases of TBT amyloidosis have been reported (2,3). Conversely, in systemic AL amyloidosis the TBT is almost always spared (4,5). In a study carried out by the University of Boston, 685 cases of AL systemic

amyloidosis were noted over 15 years. No patient presented TBT amyloidosis (6). Among the respiratory locations of amyloidosis, the tracheobronchial site is the most common. The lungs are less frequently involved (6,7,8). We report an original case since our patient presented a respiratory location of AL amyloidosis, and in spite of the systemic character of the disease, the TBT was involved.

As in our patient, systemic amyloidosis occurs mostly in the fifth and seventh decades of life (9) and men are more frequently involved than women (10). Symptoms revealing systemic AL amyloidosis are usually related to cardiac involvement (11). Respiratory symptoms occur in less than 10% of the cases (12). They are numerous and non specific, consisting of cough, wheezing, dyspnea mimicking asthma, hemoptysis and repetitive episodes of pneumonia (12). Our patient presented all these symptoms apart from hemoptysis. Symptoms are explained by the fibrillar material deposition in either the proximal, middle or distal respiratory tract. Therefore, patients with proximal involvement can show different degrees of dyspnea related to the obstruction severity and may even present respiratory failure. Those with middle or distal respiratory tract involvement are more prone to develop repetitive infections which result over time in the destruction of the bronchial walls and bronchiectasis (13).

Fiberoptic bronchoscopy with bronchial biopsy is the cornerstone of the diagnosis. Different endoscopic lesions may be seen. Pseudo-tumoral localized nodules manifesting as airway polyps represent the principle endoscopic finding (14,15). Diffuse infiltration of the sub mucosal multifocal plaques that present a major bleeding tendency or diffuse airway calcification or ossification are less frequent (14,15). Intermediary lesions are possible between the unique lesion and the diffuse bilateral massive infiltrations (15). Our patient presented these intermediary aspects as he showed bilateral infiltration narrowing the bronchial lumen of the right upper lobe and left basal segments.

Chest x-ray is of poor interest because it is usually normal. It sometimes shows a collapse related to bronchial obstruction (2). Chest CT-scan is very helpful for the diagnosis of respiratory amyloidosis. Three findings are described in the respiratory tract: tracheobronchial amyloidosis sometimes associated with irregular calcifications which may protrude in the lumen, parenchymal nodular amyloidosis or diffuse parenchymal amyloidosis (5). Hilar and/or mediastinal lymphadenopathies have also been reported (14). Our patient presented both tracheobronchial lesions manifesting as bilateral bronchial thickening and narrowing the proximal bronchi diameter and nodular parenchymal lesions. He also presented mediastinal and hilar lymphadenopathies. The third unique characteristic of the present case report is that amyloidosis affected not only the TBT but also the lungs.

To prove the systemic character of AL amyloidosis, it is necessary to find out if the fibrillar material has been deposited elsewhere other than in the diagnosed organ. This can be achieved through rectal, abdominal fat or salivary glands biopsy. In our patient, salivary glands biopsy determined the systemic character of the disease.

Tracheobronchial and lung amyloidosis may present complications over time including progressive airway narrowing, fatal airway obstruction and obstructive pneumonia (15). After 6 years of follow-up, our patient represented with a progressive airway narrowing but without significant dyspnea and 2 episodes of pneumonia. The amyloidosis complications may be treated by endoscopic methods consisting of debridement, ablation by the CO_2 or the Nd Yag laser (6), dilatation with a stent (4), repeated resections which are highly associated with bleeding (16,17) and external radiotherapy (5). These therapies allow a significant improvement in the respiratory symptoms. However, they remain insufficient for treatment of systemic amyloidosis. Moreover, various medical treatment modalities have been used with agents like corticosteroids, melphalan, and colchicine, but have had limited success. When symptoms are not very

important and the tracheal and bronchial narrowing is not life threatening, patients may be followed by simple observation as it was the case for our patient (16,17).

CONCLUSION

AL amyloidosis can affect the respiratory tract and involves either the TBT which is the more frequent location, or the lungs with a nodular or diffuse pattern. TBT amyloidosis is a rare disease that almost never occurs in the systemic form. We report a case of systemic AL amyloidosis manifesting with a tracheobronchial involvement and a coexisting nodular parenchymal form of disease. Endoscopic features evoked lung cancer. The diagnosis was made based on bronchial biopsy and immunohistochemistry study and labial biopsy revealed the systemic character of the disease despite the absence of extrarespiratory complaints. No treatment was necessary for our patient who presented moderate symptoms over 6-years of follow-up.

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