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Case Report

Perilymphatic micronodular pattern as a manifestation of pulmonary amyloidosis on high-resolution computed tomography [☆]

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ABSTRACT

The term amyloidosis describes a group of diseases caused by the fibrillar deposit of poorly folded proteins in tissues with a secondary alteration of their function. Diffuse parenchymal lung disease associated with amyloidosis is rare and is most often diagnosed in autopsy. A 45-year-old male patient presented an acute episode of cough with mucoid expectoration. He had also dyspnea, dry cough, chest pain, and constitutional symptoms of 6 months of evolution. Initially the case was treated as acute pneumonia. After taking radiological images of the thorax, a diagnostic suspicion of lymphangitic spread of neoplasia was assumed. Histopathological findings of an open pulmonary biopsy demonstrated interstitial thickening with perivascular eosinophilic invasion. Congo Red staining and immunohistochemistry studies were done and turned out to be positive for amyloid. The perilymphatic micronodular pattern as a radiological manifestation of parenchymal pulmonary amyloidosis has been very rarely described in the literature, therefore it must be considered as a differential diagnosis in patients with this pattern in CT scan and should be an incentive for its histopathological study once a neoplasm is ruled out.

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Introduction

The lung disease associated with amyloidosis is described in its primary and secondary forms [1]. Classically, 2 presentations of pulmonary amyloidosis are considered: nodular and diffuse parenchymal or diffuse alveolar septal. The diffuse parenchymal presentation is uncommon, and its radiological alterations are not specific, making it difficult to diagnose [2,3]. Among the manifestations of diffuse parenchymal pulmonary amyloidosis in High-Resolution Computed Tomography scan (HRCT), perilymphatic micronodularity is described. This finding is associated in most cases with disorders such as lymphatic carcinomatosis, leukemia/lymphoma and sarcoidosis [4]. We present the case of a patient with diffuse parenchymal pulmonary amyloidosis who had a perilymphatic micronodularity as revealed on the HRCT.

Case Report

This 45-year-old male patient presented to our hospital with a 5-day history of cough and mucoid expectoration. He also had a 6-month history of progressive dyspnea, dry cough, precordial pain, and constitutional symptoms. The Chest X-ray showed interstitial and alveolar infiltrates in both lungs, and a thickening of the minor fissure (Fig. 1). He was initially diagnosed with community-acquired pneumonia which was managed with antibiotics but showed no improvement.

On HRCT, lymphangitic spread of neoplasia was considered in the initial differential diagnosis (Fig. 2). A transbronchial lung biopsy suggested an amyloid deposition, however, negative Congo Red staining ruled out the diagnosis initially.



Fig. 1 – Chest X-ray. Interstitial and alveolar infiltrates in the middle and lower zones of both lungs, greater to the right side. Thickening of the minor fissure is displayed.

The open pulmonary biopsy showed lung parenchyma with a thickened interstitium at the expense of eosinophilic material with significant perivascular predominance. Congo Red staining and immunohistochemistry studies were done and turned out to be positive for amyloid (Fig. 3). Gastric and duodenal biopsies, performed in the context of a disease with systemic manifestations, showed eosinophilic material in lamina propria, compatible with an amyloid deposition and confirmed by an immunohistochemistry study.

Additional studies reported elevated serum kappa light chains with an increased kappa/lambda ratio and a rise in beta 2 microglobulin levels, findings suggestive of monoclonal gammopathy. A persistent elevation of the Brain Natriuretic Peptide and troponins with alterations in the heart MRI, suggested heart disease secondary to amyloidosis.

Thus, the diagnosis of primary amyloidosis associated with monoclonal gammopathy with lung, gastrointestinal, and cardiac disease was confirmed. During the hospitalization, the patient presented acute cholecystitis managed with cholecystectomy, with posterior multisystemic failure secondary to sepsis and then died.

Discussion

The amyloidosis is a heterogeneous group of diseases, in which normally soluble protein are deposited in the extracellular space, becoming insoluble. The deposition of amyloid material can occur in the presence of abnormally synthesized proteins, in association with excessive production of normal proteins or associated with the natural aging process [5–7]. Due to extracellular accumulation, atrophy, necrosis and loss of normal tissue structure occur. The incidence of amyloidosis is variable. In the United Kingdom, there is a general incidence of approximately 1 per 100,000 inhabitants. The peak incidence of amyloidosis occurs at age 65 and two thirds of the patients are male [5]. The 4 main types of amyloidosis are systemic light chain amyloidosis (AL), secondary amyloidosis - associated with Amyloid A protein- (AA), transthyretin amyloidosis (ATTR) and amyloidosis related to Beta-2-microglobulin (A β 2M) [5,8,9]. Amyloidosis can be classified into two types based on the extent of the disease: systemic amyloidosis and localized amyloidosis [6]. To confirm a diagnosis of amyloidosis, the gold standard test is birefringence under a polarized light microscope using Congo Red staining [5,6].

Amyloidosis in the chest can occur with lung, tracheo-bronchial, cardiac, and lymph node diseases [10,11]. The main clinical manifestations of pulmonary amyloidosis are coughing (74%), wheezing (70%), dyspnea (60%), hemoptysis (50%), and stridor (30%) [12]. Patients with Pulmonary Amyloidosis (PA) may experience repeated pneumonia, bronchiectasis, and lobar atelectasis (50%). Two basic patterns in amyloidosis lung disease are nodular pattern and the diffuse parenchymal or diffuse alveolar septal patterns [12]. Nodular amyloidosis is characterized by variable number of nodules, with peripheral or bilateral subpleural location, well-defined contours, variable size, slow growth, and occasionally cavitation that can end up in the formation of thin-walled, cystic-like lesions [13]. The subpleural location is the most frequent. In morphology,



Fig. 2 – (A, B, and C). CT of chest (A) Lung window (B) Mediastinum window (C) Coronal CT image. Perilymphatic micronodularity (subpleural and periarteriolar). Nodular thickening of interlobular septa and thickening of the peribronchovascular interstitium (A and B). Mediastinal adenomegalias (C).

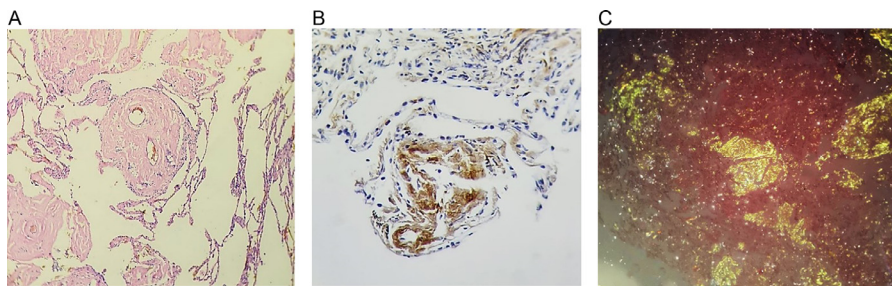


Fig. 3 – (A, B, and C). Lung, thoroscopic biopsy. Amorphous perivascular material corresponding to amyloid. (A) Hematoxylin-Eosine (40X) (B) Amyloid A immunohistochemistry (40X) (C) Congo Red Apple green coloring (40X).

it is round or ovoid with variable contours, which are determined by the presence of adjacent vessels or partitions. Their size varies from 0.5 cm to 5 cm and they can become calcified [13]. If several nodules converge, they can give the appearance of an irregular consolidation [14]. The nodular form is accompanied by high cellularity of plasmocytes, lymphocytes, and multinucleated giant cells [3,12,15]. On the other hand, diffuse presentation is less frequent and is characterized by amyloid deposits between the alveolar septum and vessel walls. The radiological manifestations include well-defined micronodules (2–4 mm), reticulation, thickening of the interlobular septa and peribronchovascular interstitium, ground-glass opacity, reticulonodular opacities or fine linear subpleurals that may converge, and consolidations [16,17].

Clinically, patients present hypoxemia, and the prognosis is poor (survival is between 13 months and 2 years). In a significant percentage of cases, it is found by autopsy [18]. The differential diagnosis is variable and depends on the finding that predominates in the HRCT. In patients with micronodularity and thickening of interlobular septa, the following should be considered among the first possibilities: lymphangitic carcinomatosis and lymphoproliferative disorders [16–18].

There are 2 additional types of pulmonary amyloidosis: the tracheobronchial and the mediastinal. In the first, the presentation in HRCT is varied and includes nodule(s), plaque, and concentric thickening with or without airway stenosis. Does not compromise the posterior tracheal membrane. It can generate endoluminal masses with small or large caliber airway obstruction [19]. The mediastinal type include adenomegalias, may be variable in size and can be found associated with the

radiological pattern of alveolar septal amyloidosis, they can calcify in the long term, and their prognosis depends on the infiltration of other organs [20,21].

In the literature, there are several case reports about pulmonary amyloidosis, especially of the tracheobronchial type. Recently, Peng et al. published a case of tracheobronchial amyloidosis, in which HRCT showed atelectasis in the middle lobe with diffuse calcification and thick-walled in the bilateral bronchi [22]. On the other hand, Tilve et al. described three case reports of thoracic amyloidosis, including tracheobronchial, nodular and lymph node amyloidosis. In the first case, chest CT revealed 2 masses in the trachea, a stenosis of the intermediate bronchus and an opacity in the apical segment of the right lower lobe. In the second case, a solitary nodule was found in the lower lobe of the right lung on both chest X-ray and CT. Finally, in the case of lymph node amyloidosis, a contrast CT showed numerous mediastinal masses in the prevascular and right and left paratracheal regions, in the subcarinal, hilar, and pulmonary areas [23].

Feldman et al. published another series of cases, all of them being nodular pulmonary amyloidosis; all three cases demonstrated pulmonary nodules with a calcified center on chest CT scan. Interestingly, these patients underwent PET-CT, in which there was no metabolic activity [24].

Pulmonary alveolar septal amyloidosis is the rarest variant of the disease, and there are few case reports in the literature. Liu et al. recently published a case of alveolar septal amyloidosis, in which the chest CT scan revealed ground glass opacities with thickening of the interlobular septum in both lungs. Subsequently, a video-assisted thoracoscopic lung

biopsy was performed, which gave the definitive diagnosis of the disease [16]. Tret'yakov et al. published another case report in this regard, in which chest CT found free fluid in both pleural cavities, visualizing a delimited accumulation of fluid along the oblique fissure of the right lung, with thickening of the interlobular septa and the intralobular interstitium, the vascular pattern was enhanced, and the pulmonary hilum were prominent [25]. Tomita et al. described another unusual radiological pattern of alveolar septal amyloidosis, since the chest CT scan of the patient found an encapsulated mass in the lower lobe of the right lung. Subsequent histopathological studies defined the diagnosis of ATTR amyloidosis [26]. Kevorkof et al., Zanelli et al., and Sato et al. published different cases of alveolar septal amyloidosis in patients with an initial diagnosis of multiple myeloma [27–29].

Only Shin et al. has published a case like ours. In his report, he describes a patient with similar symptoms, whose chest CT showed a prominent interlobular septal thickening, especially in the lower lung fields bilaterally, simulating lymphangitic carcinomatosis [18]. In this way, to date, there are only 2 cases in the literature that reported a typical tomographic pattern of a neoplastic spread of the chest, in which the clinical picture and the paraclinical studies pointed to an initial diagnosis of carcinomatosis.

Although the number of case reports associated with pulmonary amyloidosis is wide in the literature, our case reflects an interesting radiological manifestation of the less frequent variety of this disease. Therefore, knowledge of the different imaging manifestations is necessary in the diagnostic approach to amyloidosis, especially in pulmonary involvement. The diagnosis of pulmonary amyloidosis, and especially the alveolar septal type, is a challenge for any medical team, since there are various differential diagnoses such as interstitial lung diseases, including interstitial fibrosis, rheumatoid lung and scleroderma, and other neoplastic diseases such as lymphangitic carcinomatosis. Therefore, the finding of the perilymphatic micronodular pattern in the computed tomography should be an incentive to consider conducting histopathology and immunohistochemical studies when necessary and the clinical case warrants it, with the aim of diagnosing the disease and offering adequate treatment for the patient.

Conclusion

Pulmonary amyloidosis is a rare condition. Diffuse interstitial lung disease associated with amyloidosis is uncommon and occasionally, amyloid infiltration of the arterioles may mimic lymphangitic carcinomatosis and should be considered in the differential diagnosis of perilymphatic micronodularity.

Patient Consent Statement

This case report corresponds to a retrospective selection of cases from the San José hospital, in Bogotá, Colombia. As it is a histopathological diagnosis in a deceased patient, the informed consent of the patient could not be obtained. However,

the family allowed his study and subsequent publication of the results, presented in this manuscript.

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