Primary pulmonary systemic amyloidosis - case report

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Abstract: Pulmonary amyloidosis is a rare disease, characterized by extracellular deposition of fibrillary protein in the lungs. Primary pulmonary amyloidosis is rare disease, that present focal or systemic characteristics. The secondary systemic form is generally related to neoplastic, infectious, or chronic inflammatory processes, chronic kidney disease, syphilis, leprosy, inflammatory bowel disease, osteomyelitis, parasitic infections, rheumatoid arthritis. We present the case of patient with diffuse pulmonary amyloidosis

Key words: pulmonary amyloidosis, pathology

Amyloidosis is not a single disease but a term for diseases that share a common feature: the extracellular deposition of pathologic insoluble fibrillar proteins in organs and tissues. In the mid-19th century, Virchow adopted the botanical term “amyloid”, meaning starch or cellulose, to describe abnormal extracellular material seen in the liver at autopsy [36]. Subsequently, amyloid was found to stain with Congo red, appearing red microscopically in normal light but apple green when viewed in polarized light [1,8].

In major development was the recognition that amyloid fibrils in primary amyloidosis are fragments of immunoglobulin light chains [15]. Subsequently, it was determined that different proteins made up the amyloid fibrils in reactive [secondary] amyloidosis and familial amyloidosis [2], opening the way to specific therapies designed to target the source of fibril-precursor production [9].

Amyloidosis is characterized by deposition of abnormal protein, fibrillary proteins material in extracellular tissue, in a variety of organs [9, 13, 31, 32]. It is a generic term for a heterogeneous group of diseases, including Alzheimer’s disease and type II diabetes mellitus [28]. It can be hereditary or acquired potentially fatal or a merely accidental finding [13]. In a simplified way, the disease can be subdivided into localized or systemic form. It can also be classified as primary or secondary [23]. The respiratory system is frequently involved in patients with amyloidosis [6, 9, 17, 21, 35]. Amyloidosis of the respiratory tract was first described in 1877 by Lesser [31].
Primary multiple nodular amyloid deposition of the lung may be classified according not only to the anatomical site of involvement, based on radiographic patterns, but also in relation to the association condition that is, pulmonary amyloidosis with primary systemic amyloidosis, and nodular amyloid lesions of localized pulmonary amyloidosis [7, 14, 16]. Recently, the classification of amyloidosis has been based on the nature of the precursor plasma proteins that form the fibril deposits, with the recognition that amyloid fibrils in primary amyloidosis are fragments of immunoglobulin light chain (AL fibril protein) [6, 9, 21, 32]. AL fibrils are usually deposited systematically, but localized deposits in nodular lesions are occasionally observed in lung and skin [26, 32].

We report a case of primary pulmonary nodular amyloidosis which we examined histologically.

**Case report**

An 86-year-old man was found hanged. In personal antecedents did not exist pathological elements. Medico-legal autopsy established aortic and coronary atherosclerosis [gr. III]. The right lung of violet colored appearance with increased anthrax. In peripheral region superior lobe right lung, exist a tumoral formation with grey colour, and increase solidarity, of 3 cm diameter.
The left lung superior lobe has a tumoral formation with grey-violet colour and increased solidarity of 2 cm diameter, delimited. Histopathological examinations revealed an extensive pulmonary amyloidosis [fig.1-8].

Discussions

Pulmonary amyloidosis is frequently involved in systemic amyloidosis and causes symptoms, despite the fact that it is commonly found at necropsy [6, 9, 17, 21, 35]. Localised pulmonary amyloidosis may involve the tracheobronchial tree or pulmonary parenchyma in a localized or diffuse distribution. The tracheo-bronchial form is probably the most common, and nodular amyloid lesions are less often found [6, 17, 35]. Although AL fibrils are a common type of amyloid deposit in the lung, the amyloidosis is usually systemic [6, 9, 21, 32]. Only a few cases of AL pulmonary localized nodular amyloidosis have been reported [17, 20, 22, 25, 35].

Amyloidosis is a generic term for a heterogeneous group of disease associated with the deposition of abnormal fibrillary proteins on tissues and organs [3, 9, 27]. There are various different forms of amyloidosis [31].

Amyloidosis can be classified, through immunohistochemistry, into three types: reactive (AA type); primary idiopathic (AL type); and transthyretin related amyloidosis (ATTR type). The AA type of amyloidosis, which is derived from the serum amyloid A protein, can be hereditary or can result from chronic infectious processes, having been associated
with familial Mediterranean fever and tuberculosis. This form of amyloidosis rarely manifests as a respiratory disease. The AL type of amyloidosis [light-chain amyloidosis], which is the most common type [31], is considered a systemic process and due to the large deposition of cleaved products of immunoglobulin, manifests as a heart failure, renal insufficiency, or nephropathy [31].

The deposition-related impairment caused by idiopathic amyloidosis is also found in the non-systemic form, with the isolated involvement of organs, for example, in the nervous system or in the respiratory tract [10, 11, 31]. The involvement of the lung parenchyma caused by the AL type occurs in 28% of the patients and does not affect survival [3]. The ATTP type of amyloidosis is associated with senile systemic amyloidosis and most frequently manifests as cardiovascular dysfunction, polyneuropathy, or renal impairment [31].

The AL type has been a unanimous finding in studies of fibrillary protein sequencing. Autopsy series have confirmed that diffuse amyloidosis of the lung parenchyma is the most common histological type of systemic AL amyloidosis [28]. The clinical characteristics rarely lead to confusion with pulmonary edema or fibrosis. Advanced lung disease is not related to hereditary amyloidosis [13]. In the primary systemic form, amyloid fibrils can occur at other site, such as in the heart, kidneys, tongue, gastrointestinal tract, blood vessel walls, nerves, skin, muscles, and peri-articular structures. Of the patients with this form of the disease, 10-15% present concomitant multiple myeloma [27]. The great majority of patients with pulmonary impairment present the primary form of the disease [27, 31]. The many classification systems proposed, all of which are based on the location, clinical aspects, and chemical characteristics of the amyloid, show a limited understanding of the disease. This is true of even the most recent proposals [montessi]. In a simplified way, the disease can be subdivided into localized and systemic forms. In also can be classified as primary or secondary. Primary pulmonary amyloidosis is a rare disease that presents focal or systemic characteristics [14, 23]. The secondary systemic form is generally related to neoplastic, infectious, or chronic inflammatory processes, including tuberculosis, chronic kidney disease [especially pyelonephritis], syphilis, leprosy, inflammatory bowel disease, osteomyelitis, parasitic infections, rheumatoid arthritis, and bronchiectasis [23, 35]. In the secondary form, the incidence of clinically or radiologically significant pulmonary impairment is very low. The great majority of patients with pulmonary impairment have the primary form of the disease [33, 34]. The presence of amyloid nodules located in the lung parenchyma is a finding that needs to be distinguished from neoplasia. These nodules are typically peripheral and subpleural: occur more frequently in the lower lobe, can be bilateral, and range from 0.4 to 15 cm in diameter. They grow slowly and frequently calcify and form a cavity [13]. The nodular form is more common in patients aged 60 or older, who are typically asymptomatic, and is characterized by the presence of solitary or multiple nodules in the lung parenchyma. The nodules are frequently well-defined but are not uniform in size, number, or...
shape. In approximately half of the cases, foci of calcification or ossification can occur [29, 30].

The nodules grow slowly for years without any transient shrinkage. The differential diagnosis of the nodules form principally include: primary or metastatic neoplasia and granulomatous diaseases, especially the hyalinizing granulomas. In the nodular form, masses of amyloid, surrounded by plasma cells, lymphocytes, and giant cells, are the most common findings [16, 23].

The histopathological diagnosis is made by the finding of amyloid, which is an inert, proteinaceous, homogeneous acellular, and eosinophilic material that, when subjected to histochemical staining with Congo red, show green birefringence under polarized light [5, 9, 23, 31]. The modern classification of amyloidosis is based on the nature of the precursor plasma proteins that form the fibril deposits [3]. These plasma protein are diverse and unrelated, but all produce amyloid deposits with a common beta-fibrillar structure (table 1).

| Table 1. Characteristics of the systemic amyloidosis [9] |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Type               | Fibril composition     | Precursor protein              | Clinical features                               | Laboratory studies                |
| AL [primary]       | Mononuclear immuno-globulin light chains | A or k light chains [ratio of λ to k, 3:1] | Cardiomyopathy, hepatomegaly, macroglossia, orthostasis, autonomic and peripheral neuropathy, echymosis | Immunofixation electrophoresis of urine and serum, bone marrow biopsy with immunohistochemical staining for A and k light chains |
| ATTR [familial]   | Transthyretin           | Abnormal transthyretin [ >50] | Midlife onset of peripheral and autonomic neuropathy, cardiomyopathy, vitreous opacities | Serum isoelectric focusing for abnormal transthyretin of DNA-based test for mutant transthyretin gene |
| Other familial types | Apolipoprotein A-1 | Apo A-1                       | Polineuropathy, nephropathy | Genetic studies at special centers |
| AGel              | Gelsolin               | Gelsolin                      | Lattice dystrophy of cornea and neuropathy | |
| AFib              | Fibrinogen A α         | Fibrinogen A α                | Nephropathy, HTA | |
| ALys              | Lysozyme               | Lysozyme                      | Nephropathy, HTA | |

The epidemiology of amyloidosis is difficult to define precisely, since the disease is often undiagnosed or misdiagnosed and selection bias potentially markes data from tertiary referral centers unrepresentative. The age-adjusted incidence of AL amyloidosis is estimated to be 5.1 to 12.8 per million person-years, which means that mere are approximately 1275 to 3200 new cases annually in the United States [21]. The incidence of ATTP amyloidosis is unknown, but it is less common than AL amyloidosis, with the number of diagnosed cases in referral centers representing 10 to 20 percent of the number of cases of AL amyloidosis. A possible exception may be the recently described variant-sequence transthyretin associated with late-onset cardiac amyloidosis in blacks [18, 19], caused by the substitution of isoleucine for valine in codon 122 of the tranthyretin gene (Ile 122) [36].

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