

Case Report

Mediastinal lymph node amyloidosis in a patient with sarcoidosis*

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Abstract

A 27-year-old male patient presented with respiratory symptoms, bilateral enlargement of the cervical lymph nodes and enlarged liver. In the imaging studies, bilateral enlargement of the hilar nodes was observed, together with pulmonary infiltrate. The patient was submitted to lung and liver biopsies, which revealed noncaseating granulomas. The clinical, radiological, and histopathological findings were consistent with sarcoidosis and lymph node amyloidosis. The combination of sarcoidosis and amyloidosis has rarely been reported.

Keywords: Amyloidosis; Sarcoidosis; Lymph nodes.

Introduction

Sarcoidosis is a systemic disease, of unknown etiology, that affects individuals all over the world, regardless of race, gender, or age.⁽¹⁾ However, it is more common in individuals between 25 and 40 years of age and is rare in children.^(2,3) Sarcoidosis has been widely studied,⁽⁴⁻⁸⁾ as has amyloidosis, which is characterized by the deposition of fibrillary and insoluble proteins within the extracellular space, influencing the structure of tissues and organs.⁽⁹⁾

The combination of sarcoidosis and amyloidosis has rarely been described. We report a case of sarcoidosis accompanied by lymph node amyloidosis.

Case report

A 27-year-old male patient, occasional smoker for five years, presented with a 6-year history of progressive dyspnea upon moderate exertion, dry cough, and weight loss (20 kg in 6 years). The patient had been treated with systemic corticosteroid for 4 years. In the last 2 years, he

had suffered from recurrent respiratory infections and had experienced three episodes of spontaneous pneumothorax. Upon admission, he presented reactive lymph node enlargement in the anterior bilateral cervical chain and enlargement of the liver. Upon auscultation, he revealed hyperphonestosis of the second heart sound, diffusely reduced breath sounds, and rare wheezing. The blood workup showed polyglobulia (hemoglobin = 18.2 g/dL and globular volume = 54%). The results of inflammatory activity and liver function tests were normal. Sputum and bronchoalveolar lavage fluid tested negative for fungi and acid-fast bacilli (AFB). The Kveim-Siltzbach test results were negative, and the angiotensin-converting enzyme (ACE) level was 51.7 IU/L (range, 35-90 IU/L). The computed tomography of the chest showed irregular opacities surrounded by broad striations, thick interlobular septa, subpleural bullae in the upper left lobe, and bilateral enlargement of the hilar nodes, all previously seen on chest X-rays (Figures 1 and 2). Spirometry revealed

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severe obstructive respiratory disorder (forced vital capacity = 51%, forced expiratory volume in one second = 26%, and forced expiratory volume in one second/forced vital capacity = 52%) associated with air trapping (residual volume = 186% and residual volume/total lung capacity = 217%), and mild diffusion disorder (diffusing capacity of the lung for carbon monoxide = 69%). Arterial blood gas analysis revealed severe hypoxemia (arterial oxygen tension = 45.5 mmHg). Abdominal ultrasound revealed that the liver was homogeneous, albeit with signs of pronounced periportal echogenicity. A liver

biopsy showed multifocal aggregates of epithelioid cells, absence of necrosis, and no presence of AFB, which were compatible with multifocal granulomatous hepatitis. A tracheobronchial angle lymph node biopsy was performed using mediastinoscopy. Analysis of the biopsy material revealed the presence of hyaline material, which tested positive for amyloid deposition by crystal-violet staining. The patient was also submitted to open lung biopsy. The subsequent histological analysis revealed enlargement of the alveolar septa by fibrosis and lymphohistiocytic inflammatory infiltrate, as well as sparse granulomatous structures with lymphocytes, epithelioid histiocytes, and absence of caseous necrosis, consistent with sarcoidosis (Figure 3).

Discussion

Pulmonary sarcoidosis is one of the most common causes of interstitial lung disease.⁽⁴⁾ Virtually all cases of sarcoidosis affect the respiratory tract.⁽¹⁾ The lymphatic system is affected in approximately 90% of cases. Cardiac, renal, and hepatic impairment are uncommon and are rarely associated with relevant functional repercussions. Liver enlargement, cholestasis, and minimal aminotransferase alterations are the most common hepatic manifestations.⁽¹⁾ The diagnosis is based on clinical and radiological suspicion (bilateral enlargement of the hilar nodes with pulmonary infiltrate of typically perivascular distribution)⁽⁵⁾ and on histological evidence of noncaseating granuloma, as well as on

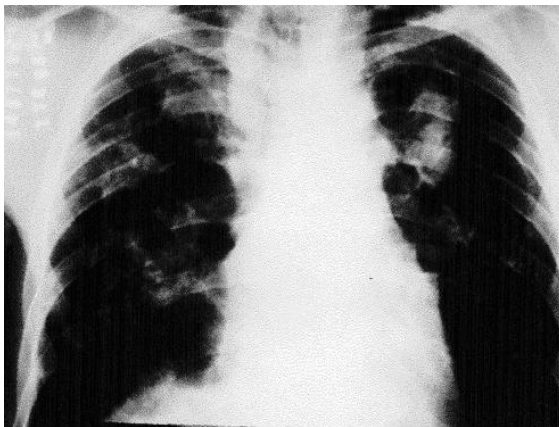


Figure 1 – Simple frontal chest X-ray showing opacities, with large nodules and irregular striations, in the upper lobes. There are bullae in pulmonary apical regions and bilateral enlargement of the hilar node.

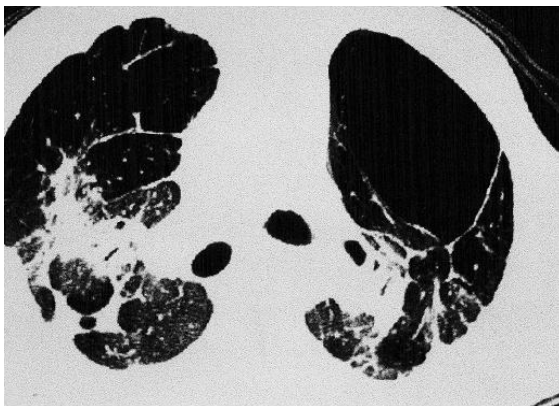


Figure 2 – Computed tomography of the chest showing irregular opacities surrounded by broad striations and containing air bronchograms. The interlobular septa are enlarged, and subpleural bullae are seen in the upper left lobe.

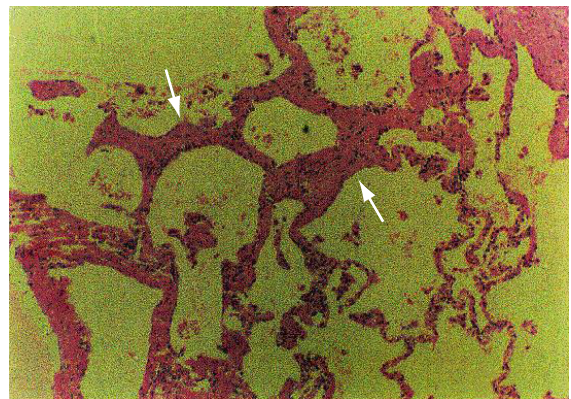


Figure 3 – Photomicrograph of lung tissue showing enlarged hyaline alveolar septa (arrows), with some lymphocytes. Presence of some morphologically preserved septa. (hematoxylin and eosin, $\times 100$).

the exclusion of other diseases capable of producing similar clinical and histological profiles.⁽⁶⁾ In patients with one of the active forms of the disease, the Kveim-Siltzbach immunologic test is positive in approximately 80% of cases.⁽⁷⁾ Although nonspecific for the diagnosis, ACE, which is present in lung tissue, is useful for evaluating treatment efficacy, since its levels are higher in patients with active sarcoidosis.⁽⁷⁾ The evolution ranges from spontaneous resolution (in 12 to 36 months) to chronicity, marked by progressive pulmonary fibrosis or the involvement of other organs.⁽²⁾ The prognosis depends on the disease staging: hilar adenopathy with no infiltration of the pulmonary parenchyma (stage I); hilar adenopathy and pulmonary infiltrate (stage II); and infiltrate without adenopathy (stage III). Remission rates are 80 and 30% in stages I and III, respectively.⁽¹⁾ Corticosteroids are indicated for the treatment of sarcoidosis, although there is no consensus on when they should be initiated, the dose to be used, and the treatment duration.⁽⁸⁾ In one systematic study, it was concluded that oral corticosteroids improve chest X-ray images and symptoms.⁽⁸⁾ However, the authors of that study found little evidence that they improve pulmonary function.

The various forms of amyloidosis are a heterogeneous group of diseases characterized by extracellular deposition of fibrillary and insoluble proteins that influence the structure and function of diverse tissues and organs. Glycosaminoglycans and the serum amyloid P protein pentraxin are nonfibrillary amyloid components that contribute to fibrillogenesis and to the stability of the amyloid deposit.⁽⁹⁾ Amyloidosis can be acquired or hereditary, as well as being local or systemic, and is defined according to the precursor protein.^(9,10) Among the acquired forms of amyloidosis are primary amyloidosis (AL type, systemic), local nodular amyloidosis, secondary amyloidosis (AA type, systemic and reactive), and senile systemic amyloidosis. Associated with myeloma, dyscrasias, and monoclonal gammopathies, AL amyloidosis is caused by the formation of fibrils from light chains of monoclonal antibodies. Local nodular amyloidosis, which primarily affects the skin, respiratory tract and urogenital tract, also originates from light chains of monoclonal antibodies. Active chronic diseases, such as chronic inflammatory diseases, chronic infections, and some malignant neoplasms, are the typical causes of AA amyloidosis, whose precursor is the serum

amyloid A protein. In addition, 25% of elderly individuals present senile systemic amyloidosis, characterized by clinically silent systemic deposits, which are occasionally more extensive in the myocardium, resulting in life-threatening fatal cardiac dysfunction. Various forms of autosomal dominant hereditary amyloidosis have also been described. Radiologically, the images are varied and nonspecific.⁽¹¹⁾ The amyloidosis diagnosis requires histological confirmation by the presence of amyloid deposition in tissue.⁽¹⁰⁾ The immunohistochemistry of the tissue determines the type of amyloidosis.⁽¹⁰⁾ Scintigraphy with serum amyloid P component can detect the involved organs, as well as allowing the evaluation of the therapeutic response.⁽⁹⁾ There is no treatment for the amyloid deposits. However, treatments that reduce the supply of amyloid precursors can improve survival and preserve the function of the affected organ.⁽¹²⁾

The combination of sarcoidosis and amyloidosis has been rarely described.⁽¹³⁻¹⁹⁾ Reports that describe the association between sarcoidosis and AA amyloidosis suggest that the sarcoidosis-related inflammatory process is implicated in the pathogenesis of amyloidosis.^(15,16,18) However, there is no consensus on whether this is an effect of the concomitance of sarcoidosis and AL amyloidosis or is merely a coincidence.^(13,14,19) We have reported here a case of systemic sarcoidosis accompanied by lymph node amyloidosis. The diagnosis of pulmonary sarcoidosis was based on the clinical profile, imaging and pulmonary function tests, together with histopathological findings and the exclusion of other granulomatous diseases through testing for fungi and AFB in sputum and bronchoalveolar lavage fluid.^(5,6) The liver enlargement led us to investigate the liver using abdominal ultrasound and biopsy. Due to the histopathological finding of granulomatous hepatitis, the history of weight loss, and the chronic nature of the condition, systemic tuberculosis was suspected. Therefore, we decided to perform a mediastinal lymph node biopsy, which revealed amyloid deposition. Since the pulmonary abnormalities were not consistent with amyloidosis, we performed a lung biopsy, through which we confirmed the diagnosis of sarcoidosis, demonstrating the fact that sarcoidosis and lymph node amyloidosis were both present. Although the Kveim-Siltzbach test results are positive in 80% of cases, negative results on this test do not rule

out a diagnosis of sarcoidosis.⁽⁷⁾ The normal ACE values suggested a favorable response to the use of corticosteroid.⁽⁷⁾ Immunohistochemical assays to determine the type of amyloidosis and scintigraphy with serial amyloid P component, which made it impossible to classify the type of amyloidosis, are not available at our facility. Considering that the reported cases of renal or cardiac amyloidosis accompanied by sarcoidosis resulted in death or lost renal function,^(13-15,18,19) we question whether the amyloid deposition in the hilar node was in any way related to the severity of the sarcoidosis progression, which was uncommonly intense. The combination described above piques the interest regarding prognosis, morbidity, mortality, and treatment response. However, the lack of data, together with the fact that amyloidosis has been found in various organs (with specific repercussions), limits our capacity to answer these questions.

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