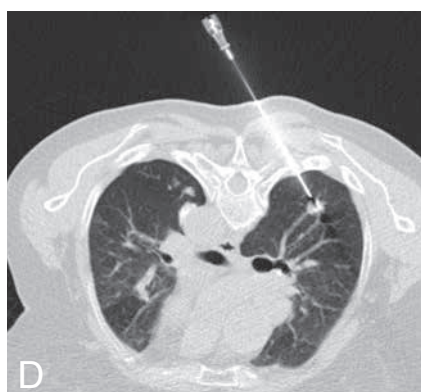
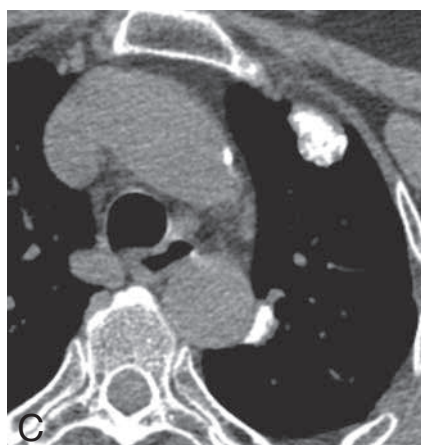
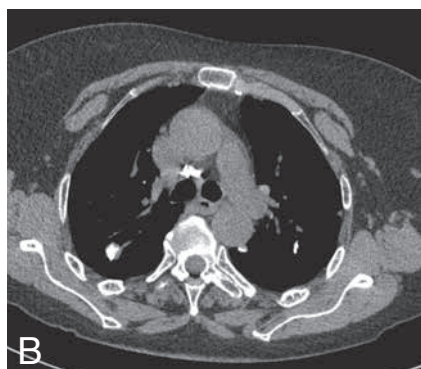
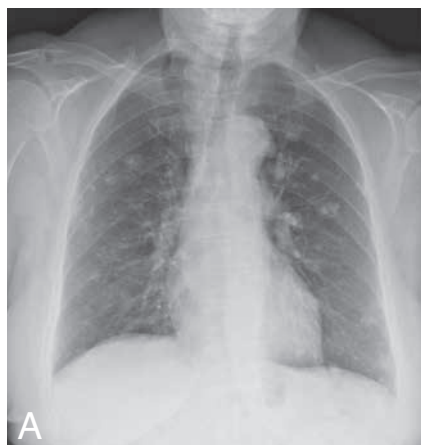


IMAGES IN CLINICAL RADIOLOGY



Multiple calcified nodules in pulmonary amyloidosis

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A 74-year-old woman was referred in the Radiology Department for evaluation of progressive dyspnea on exertion over 4 years with worsening in the last month. The patient had no cough or weight loss. She had stopped tobacco smoking more than 20 years before. She had no known history of lung disease or malignancy. Physical examination was unremarkable.

Chest radiography (Fig. A) revealed multiple pulmonary nodules scattered to both lung fields. The examination was completed by CT (Fig. B, C) which confirmed multiple partially calcified nodules with diffuse distribution and various sizes (max 23 mm). Some lesions presented hypermetabolic activity at FDG-PET. The patient underwent a CT-guided biopsy of one of the peripheral nodules (Fig. D). The pathology specimen from the left upper lobe revealed amorphous material accompanied by ossification at the periphery. The stain with Congo red produced red-green birefringence under cross-polarized light microscopy. Immunohistochemical analysis of the specimen revealed amyloid light chains deposits (AL).

Amyloid light chains can be found in localized primary amyloidosis but also in patients with primary systemic amyloidosis associated with monoclonal plasma cell dyscrasias.

In the case of this patient, work-up for multiple myeloma, including serum protein electrophoresis, bone marrow biopsy and radiographic bone survey, was negative.

Disease spread assessment showed a hyper-refracting appearance of the interventricular septum with an impaired relaxation of the left ventricle at echocardiography. This could be compatible with a secondary cardiac localization but was not proved. Other investigations were unremarkable.

Symptomatology and CT evaluation have remained stable without any treatment for 2 years now.

Comment

Differential diagnosis of multiple partially calcified nodules includes calcified metastasis, calcified granulomata, pneumoconiosis, Wegener disease, sarcoidosis, rheumatoid arthritis and pulmonary amyloidosis. Amyloidosis is a disease characterized by extracellular deposition of proteins that aggregate in insoluble beta-pleated sheets. It can be systemic (80-90%) or may be isolated to a single organ (10-20%). The classification is biochemical depending on the protein that makes the majority of deposits. The two most common forms are AA and AL amyloidosis.

Three histopathologic types of pulmonary amyloidosis have been described: tracheobronchial, nodular parenchymal and diffuse interstitial.

The tracheobronchial type can have two different patterns. Endobronchial tumor-like masses can be found. It can also be characterized by submucosal flat plaques of amyloid material in the trachea and segmental airways resulting in parietal thickening with sometimes evocative linear calcifications that do not spare the posterior membrane. This can lead to luminal narrowing or obstruction with consolidation, atelectasis, hyperinflation or bronchiectasis.

In nodular amyloidosis like in this patient, the amyloid nodules may be single or multiple. They occur more frequently in the lower lobes and vary in size and shape (range 0.5-15.0 cm). In up to 50% of cases, they may calcify, or metaplastic bone or cartilage formation may occur. They may sometimes be associated with cysts. The diffuse interstitial pattern is defined by amyloid material infiltrating alveolar walls and septa as well as around the pulmonary arterioles. This results in reticulation and interlobular septal thickening. Sometimes, subpleural scattered micronodules (2-4 mm) can be found and more rarely ground glass opacities, bronchiectasis or honeycomb images. Symptoms are similar to those of interstitial lung disease: cough and dyspnea.

The best imaging technique for the evaluation of the disease is CT. It provides a good analysis of the lung parenchyma, can suggest the diagnosis of respiratory amyloidosis mainly in the tracheobronchial pattern, plays an important role in the differentiation between localized and systemic amyloidosis and in the follow-up of the disease. The more cost-effective work-up to obtain good histologic sample appears to be biopsy under CT guidance.

Management of the patients with pulmonary amyloidosis is variable, depending upon degree and distribution of organ involvement, function, and patient functional status. The disease is incurable, but the clinical progression of the nodular form is usually slow and rarely requires intervention. In the case of obstructed airways, bronchoscopic resection, stenting, or dilatation can be done. External beam radiation therapy or chemotherapy can also be part of the treatment.

Reference

1. Lee A.Y., Godwin J.D., Pipavath S.N.J.: Pulmonary Amyloidosis. *Radiology*, 2012, 263: 929-932.

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