Pulmonary amyloidosis: A close mimic of malignancy

Sir,

A 64-year-old man first presented to polyclinic with chronic cough with phlegm for 2 months which was whitish color and without hemoptysis, fever, or night sweats. A frontal chest radiograph revealed bilateral scattered ill-defined nodular opacities [Figure 1]. This was treated as a lower respiratory tract infection with antibiotics. However, the follow-up chest radiograph revealed no significant change in appearance. In addition, patient-reported that he unintentionally lost 5 kg weight in the past 3 months, and experienced a progressive reduction in effort tolerance over the past few years. Computed tomography (CT) of the thorax was ordered that revealed multiple well-defined cysts and nodular opacities of varying sizes scattered in both lungs, with one of the nodular opacity in the right upper lobe showing a focus of calcification. The nodules and cysts were scattered diffusely in the axial and craniocaudal plane. There was diffuse upper lung predominant centrilobular nodularity. In addition, there were multiple small sub centimeter bilateral mediastinal and hilar lymph nodes, some demonstrating punctate calcific foci [Figure 2].

Based on the CT findings, the patient was electively admitted for further investigations. Blood investigations revealed pancytopenia with the rouleaux formation in red blood cells.

Serum protein electrophoresis revealed a polyclonal increase in the beta-gamma region, whereas urine protein electrophoresis revealed no paraprotein band. Immunofixation (serum and urine) detected no paraprotein band with (IgG, IgA, IgM, kappa, and lambda light chain). The lactate dehydrogenase, serum calcium, and serum creatinine levels were normal suggesting no definite evidence of plasma cell dyscrasia. Positron emission tomography (PET)-CT showed multiple lung cysts and lung nodules with mild fluorodeoxyglucose avidity (SUV max up to 3.8). No other hypermetabolic lesion was seen elsewhere to suggest metastasis. Furthermore, there were no features of cardiac amyloidosis on two dimensional-Echo study performed simultaneously.

The patient was then admitted to explore the feasibility of lung biopsy (CT guided vs. open surgery). A repeat CT of the thorax revealed bilateral multiple cysts and nodular opacities which were largely stable since the previous scan. Decision was made for CT-guided biopsy of the right upper lobe lung nodule. On histology, the cores of lung tissue showed nodular deposition of amorphous eosinophilic material which demonstrated salmon pink staining on light microscopy and apple-green birefringence on polarized light microscopy on Congo red staining. These features favor nodular pulmonary amyloidosis. The specimen was then sent to the U. S (Mayo Clinic) for amyloid typing which was consistent with ALH (lambda light chain and alpha heavy chain)-type amyloid deposition.

A month later, the patient developed right axillary lymphadenopathy with decreasing platelet and neutrophil counts. Although a rare condition, ALH-type amyloid deposition can be associated with indolent lymphoma and less common with conditions such as Sjogren's syndrome. A 6-month follow-up CT of the thorax revealed stable multiple cysts and nodular opacities in both lungs and resolution of

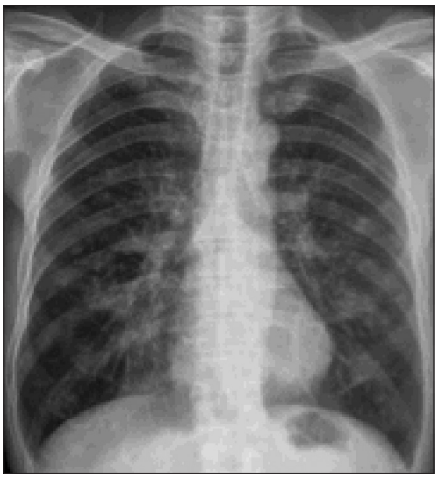

Figure 1: Initial frontal chest radiograph shows ill-defined nodular opacities scattered in both lung fields

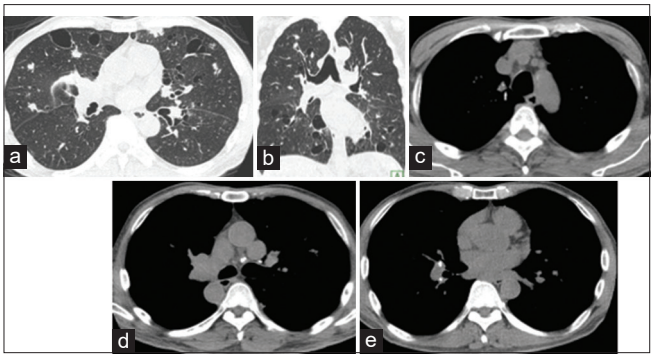

Figure 2: Initial computed tomography thorax images (a and b) reveals multiple well-defined cysts and nodular opacities of varying sizes scattered in both lungs, with one of the nodular opacity in the right upper lobe showing a focus of calcification (white arrow in c). In addition, (d and e), some demonstrating punctate calcific foci

peri-airway opacities. Meanwhile, serological examinations revealed elevated antinuclear antibodies and high Anti-Ro and Anti La levels, findings consistent with Sjogren's syndrome associated with pulmonary nodular amyloidosis. To exclude systemic amyloidosis, the patient was advised bone marrow examination and fat pad biopsy but instead, the patient opted for 6 monthly CT of the thorax follow-up for 2 years to look for progression. Since the right axillary lymphadenopathy was stable, the patient declined excision biopsy.

Amyloidosis is a rare condition caused by the pathologic extracellular deposition of abnormal insoluble proteins throughout the body. On the basis of the structure of the protein deposits, over two dozen subtypes of amyloidosis have been described. The fibrillar proteins amyloid light chain (AL) and serum amyloid A are present in the vast majority of cases. Depending on its distribution, amyloidosis may be systemic (involving multiple organ systems) or localized (involving a single organ such as the lungs or the heart). The radiologic manifestations of amyloidosis are varied and often nonspecific, making amyloidosis a diagnostic challenge for the radiologist.

In the chest, the lungs, mediastinum, pleura, and heart may be involved. The involvement of the lung is relatively common but rarely symptomatic. From the pathologist's perspective, amyloidosis can appear in the lung in three different forms: nodular pulmonary amyloidosis, diffuse alveolar-septal amyloidosis, and tracheobronchial amyloidosis.[1] Lung involvement may manifest as a diffuse reticulonodular interstitial thickening, consolidations, or solitary or multiple parenchymal nodules that may calcify, cavitate, and slowly enlarge. Pleural involvement most commonly manifests as pleural effusions. Tracheobronchial involvement may exhibit concentric airway thickening, mural and intraluminal nodules, submucosal calcification, and airway obstruction. Mediastinal and hilar lymph nodes may enlarge and frequently calcify.[2]

Many experts now believe that most cases of nodular pulmonary amyloidosis are the result of an underlying lymphoproliferative disorder in the spectrum of extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma).[3] Sjögren's disease was found to be associated with pulmonary amyloidosis and lymphoproliferative disorders.[4,5]

Histologically, the nodules are well-circumscribed and are composed of homogeneous, densely eosinophilic material. If amyloid is suspected, a Congo red stain should be performed and amyloid typing is needed. Interestingly, the light chains in nodular pulmonary amyloidosis are more frequently of the κ than the λ type, with a ratio of 3:1, in contrast to the λ predominance noted in most cases of systemic AL amyloidosis.

Differential diagnoses of nodular pulmonary amyloidosis include pneumoconioses, granulomatous infection, sarcoidosis, and malignancy.

In the majority of patients, pulmonary amyloidosis (in particular if nodular) is an incidental finding. However, each patient requires complete assessment and unequivocal amyloid typing to determine their optimal treatment. Therapy, either local or systemic, is usually effective. The prognosis of nodular amyloidosis is generally very good.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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