CT features of primary systemic pulmonary amyloidosis mimicking pulmonary sarcoidosis

Amylose systémique pulmonaire stimulant une sarcoïdose pulmonaire en tomodensitométrie

Sarcoidosis is a common multisystem granulomatous disease that frequently involves the lungs. On CT images, the characteristic distribution of micronodules along the perihilar regions, the peribronchovascular bundles and in the subpleural zones, are relevant features in the diagnostic process. The typical features of sarcoidosis are usually well recognized and rarely confused with other granulomatous diseases like silicosis or coal worker’s pneumoconiosis, which have a similar nodular perilymphatic distribution. We report a case of a rare interstitial lung disease highly suggestive of sarcoidosis.

Case report

A 55-year-old Caucasian man was admitted to our hospital on May 2008 with a 12-month history of progressive dyspnea and a recent right spontaneous pneumothorax diagnosed on chest X-ray. He was exposed to tobacco (35 pack-years) and treated with ACE inhibitor for arterial hypertension. Chest X-ray showed diffuse reticular pattern (figure 1). Contrast-enhanced computed tomography (CT) angiography of the chest was performed after pneumothorax resolution (Somatom Definition, Siemens, Germany) which revealed multiple well-defined micronodules with a perilymphatic pattern, i.e. distributed along the interlobular septa and bronchovascular bundles, as well as beneath the visceral pleura and two small-sized intraparenchymal and thin walled cystic lesions (figure 2A and B). All of these abnormalities were particularly marked in the upper lobes of the lungs. No fibrotic changes and no tracheal abnormalities were found. Moderate lymph node enlargement was present in right paratracheal and subcarinal sites (figure 2C). The diagnosis of pulmonary sarcoidosis was suggested. Further laboratory workup revealed normal lymphocyte count, normal serum angiotensin-converting enzyme level (14 UI/L) as well as low gammaglobulin level (IgG:5 g/L). Pulmonary function tests results showed a normal value of total lung capacity (TLC; 7.70 l, i.e. 103% of predicted value), but a reduction of the other parameters including slow vital capacity (SVC; 3.54 l, i.e. 76% of predicted value), forced expiratory volume in one second (FEV1; 1.691 l, i.e. 45% of predicted value), FEV1/vital capacity (VC) at 48% (Normal > 72%), and diffusing capacity of the lung for carbon monoxide (DLCO) measured at 17 ml/min/mmHg (i.e. 50% of predicted value).

Bronchial biopsies demonstrated non-specific inflammation without granuloma. Minor salivary gland biopsy did not reveal any granulomatous lesions. Bronchoalveolar lavage cell count was normal (6% of lymphocytes, CD4/CD8 ratio: 1.9). Four months later, at the time of recurrence of the right pneumothorax, a right thoracoscopy with surgical lung biopsy was performed. By light microscopy, extensive amyloid deposits were seen in the wall of the small vessels of alveoli, bronchiolar walls and subpleural regions (figure 3A). The nodular lesions were composed of dense accumulations of amorphous eosinophilic material (figure 3B). The Congo-red stain showed apple-green birefringence to polarized light, which is indicative for the presence of amyloid fibrosis. Slight enlargement of some distal airspaces was seen in the surrounding lung; no parenchymal calcification was found. Complementary check up showed a normal echocardiography. Bone scintigraphy illustrated multiple uptakes in the lumbar spine related to joint arthrosis. A urinary Bence-Jones protein due to a monoclonal dysglobulinemia with kappa-light chain was found. On bone marrow biopsy, AL amyloid deposits were seen in the adipose tissue and in the wall of small arteries. The plasmocyte count was estimated at up to 30%, no cellular atypia was found. Immunohistochemical stains for amyloid P protein and kappa-chain were positive whereas those for amyloid A protein and lambda chain were negative. The diagnosis of amyloid light chain (AL) amyloidosis was made. Treatment with bortezomib (a proteasome inhibitor) and dexamethasone was initiated but the patient died due to massive pulmonary haemorrhage and concomitant H1N1 infection.

Figure 1
Chest X-ray. Diffuse interstitial reticular pattern
**Discussion**

The CT features of interstitial lung disease reported in this patient are characterized by a diffuse bilateral and symmetrical micronodular lung infiltrate with a perilymphatic distribution associated with thickening of the interlobular septa, predominantly in the middle-upper lung fields. These features are characteristic of diseases involving the lymphatic compartment of the lung and are highly suggestive of pulmonary granulomatosis and especially sarcoidosis, in which micronodules correspond to multiple giant cell granulomas with a peri-lymphatic distribution. Granulomas often merge and can appear on CT-scan as ground glass opacities or consolidation in the upper lobes and as pseudoplaques in the subpleural regions. In the wall of the airways, granulomas can cause bronchial and bronchiolar stenosis and air trapping, but cystic changes in the lungs are rarely found in sarcoidosis [1]. Primary systemic pulmonary amyloidosis is a common form of amyloidosis characterized by extracellular deposition of primary amyloid light (AL) chain in a wide variety of organs. Diagnosis is obtained only on lung biopsy. The most common pulmonary manifestation of systemic amyloidosis consisted of multiple pulmonary nodules, interlobular septal thickening and intra lobular opacities. It is usually associated with primary systemic amyloidosis or multiple myeloma and related to AL subtype [2,3]. In our observation as in most cases, pulmonary deposits of amyloid involve the vessel wall and therefore extend to the pulmonary interstitium of alveolar septa, subpleural regions and walls of distal airways. This suggests that the distinction proposed by some authors between arteriolar amyloidosis and alveolar septal amyloidosis is not clear [4,5]. Progressive exertional dyspnea is the most common symptom, and its severity depends on the degree of infiltration of the alveolarcapillary gas exchange zone, and thus pulmonary function tests usually show a pattern of restrictive lung disease [2,5,6]. Chest radiograph shows a non-specific diffuse interstitial reticulonodular infiltration suggestive of interstitial lung disease. As seen in our case, a perilymphatic micronodular distribution with septal thickening is often reported on CT-scan evaluation, but interstitial amyloidosis is very infrequent and the previously cited diagnoses have to be considered first [4,5,7]. Micronodules can also become confluent as diffuse inhomogeneous subpleural consolidation in which calcification or osseous metaplasia can mimic pneumoconiosis [2–4,8]. Cystic changes, typically seen in LIP, are not common in amyloidosis but have already been reported [5]. Several

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**Figure 2**

**CT angiography of the chest after re-expansion of the right pneumothorax**

A. 1-mm thick lung section at the level of the upper lobes, showing a diffuse micronodular infiltration with a subpleural (black small arrows) and peribronchovascular (white arrowheads) distribution and a nodular thickening of the interlobular septa (large black arrows). B. 1-mm thick lung section at the level of the lower lobes, showing diffuse perilymphatic micronodulation, nodular peribronchovascular thickening (white arrows) and an intraparenchymal cystic lesion in the right lower lobe (black arrow). C. 5-mm thick mediastinal image obtained at the same level as that of Fig. 1A showing right paratracheal lymph node enlargement (arrow). On figure 1A, B and C, note the additional presence of subcutaneous emphysema, secondary to the recent right sided pneumothorax.
Thus, pneumothorax. related usually amyloidosis (arrows), explanations A.

Light microscopy of lung biopsy
A. Amyloid deposits in the walls of blood vessels extending to alveolar walls (arrows), HES × 25. B. Nodular lesions composed of dense eosinophilic material typical of amyloid deposits (arrows). HES × 25.

eXplanaJons have been proposed but the relationship with amyloidosis is not clear [3]. In our case, cystic lung lesions seen on CT evaluation could correspond to some enlarged airspaces seen on pathological analysis. This can suggest the presence of subpleural cysts and could explain the episodes of spontaneous pneumothorax. The presence of hilar and mediastinal lymphadenopathy cannot discriminate well because they are often reported in most diffuse lung diseases. Lastly, haemoptysis usually occurs during the evolution of this disease, probably due to amyloid deposition within the wall of small blood vessels. Thus, the bleeding causing the death of our patient may be related to amyloidosis, H1N1 infection, or both.

Primary systemic pulmonary amyloidosis is a rare form of amyloidosis which can mimic sarcoidosis on CT-scan.

**References**


Benoit Wallaert1, Benoit Renard2, Catherine Ars2, Marie-Christine Copin1, Jacques Rémy2

1Centre of Rare Pulmonary Diseases, Hospital A. Calmette, University Lille Nord de France, Department of Pulmonology, 59000 Lille, France
2University Lille Nord de France, Hospital A. Calmette, Department of Thoracic Imaging, 59000 Lille, France
3Centre of Biology and Pathology, University Lille Nord de France, Department of Pathology, 59000 Lille, France

**Correspondence:** Benoit Wallaert, Hospital A. Calmette, Department of Pulmonology, boulevard Jules-Leclercq, 59037 Lille, cedex. France.

benoit.wallaert@chru-lille.fr

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**Malakoplakie rénale : une cause rare d’infiltration rénale pseudotumorale**

**Renal malakoplakia: A rare cause of pseudotumoral infiltration of the kidney**

La malakoplakie est une inflammation granulomateuse tissulaire d’aspect histologique caractéristique, touchant principalement le système urogénital et traduisant morphologiquement une maladie du macrophage [1,2]. Nous rapportons un cas...