



CASE STUDY

Unusual cystic presentation of pulmonary nodular amyloidosis associated with MALT-type lymphoma

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ABSTRACT: The case reported herein consists of nodular pulmonary amyloidosis presenting with unusual cystic radiological features which reveal a pulmonary localisation of an extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma).

The present case is the first to report a radiological presentation of nodular pulmonary amyloidosis in the absence of Sjögren's syndrome.

Although transthoracic fine-needle biopsy was helpful for the diagnostic of amyloidosis, final diagnosis of associated MALT-type lymphoma required an open lung biopsy.

This emphasises the importance of performing surgical investigations in pulmonary nodular amyloidosis in order to depict the presence of underlying lung tumours or lymphoproliferative disorders.

KEYWORDS: Amyloidosis, cystic, lung, lymphoma, mucosa-associated lymphoid tissue, nodular

Association of pulmonary amyloidosis with lymphoma is a classical albeit rare finding [1–4], reported mainly with extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) of gastrointestinal [5, 6] or pulmonary origin [1, 2]. Pulmonary nodular amyloidosis is a localised form of pulmonary amyloidosis, in addition to tracheobronchial and diffuse alveolo-septal amyloidosis, characterised histologically by extracellular deposits of amyloid-type AL protein, homologous to the variable portion of immunoglobulin light chains, predominantly of λ type. Pulmonary nodular amyloidosis mainly occurs in elderly patients who harbour an indolent clinical presentation; incidentally, nodules are most frequently found on chest radiographs or at *post mortem* examination. Prognosis is usually excellent, although nodular pulmonary amyloidosis can obscure underlying lymphoproliferative disorders, including lymphoma. Whereas pulmonary amyloid deposit demonstrated using fine-needle biopsy [7], the present study reports a case of nodular pulmonary amyloidosis presenting with unusual cystic features on the computed tomography (CT) scan, which, in relation to a pulmonary localisation of MALT-type

lymphoma, could only be demonstrated by surgical lung biopsy.

CASE HISTORY

A 50-yr-old female ex-smoker (20 pack-yrs) was referred to the present authors' institution (Dept of Pathology, CHU A Michallon, Grenoble, France) in April 2004 for multiple pulmonary nodules discovered on a systematic chest radiograph. Past history included epigastralgias 1 month previously, with gastric biopsies favouring a gastric MALT-type lymphoma related to *Helicobacter pylori*. A bone marrow biopsy performed as a result showed bone marrow involvement by the same lymphoid proliferation and confirmed its λ monoclonality. A high-resolution CT scan 1 month later revealed eight ill-defined nodules of different sizes associated with cysts, and distributed through both lungs. Some of them were calcified and bronchiolocentric (fig. 1). A fine-needle transthoracic biopsy was performed and showed amorphous eosinophilic material suggestive of amyloidosis engulfed by giant cells and surrounded by a few crushed lymphocytes. This amorphous material was revealed by thioflavine T staining under UV light, but remained negative with anti-serum

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STATEMENT OF INTEREST

None declared.



FIGURE 1. High-resolution computed tomography scan (1 mm slice thickness) at the level of the heart shows thin-walled cysts (arrow) within the right lung and one pulmonary nodule of soft tissue density that contains eccentric nodular calcifications (arrowhead).

amyloid A (SAA) protein immunostaining. No evidence of lymphoid proliferation was noticed.

Two partially cavitated nodules were surgically resected because the high suspicion of a pulmonary localisation of lymphoma requires a more aggressive treatment. At histology, the nodules were widely composed of amyloid deposits, with foci of calcification and ossification (fig. 2). Amyloid deposits were again positively stained with thioflavine T (fig. 3) and remained negative with anti-SAA antibody. They were surrounded by sheets of small plasmacytoid lymphocytes admixed with large lymphocytes expressing CD20, but not CD5, CD10, CD43 and CD23 antigens at immunohistochemistry (fig. 4). These lymphocytes focally invaded the pleura and surrounded bronchovascular bundles, infiltrating bronchiolar epithelium to form typical lymphoepithelial lesions (fig. 5).

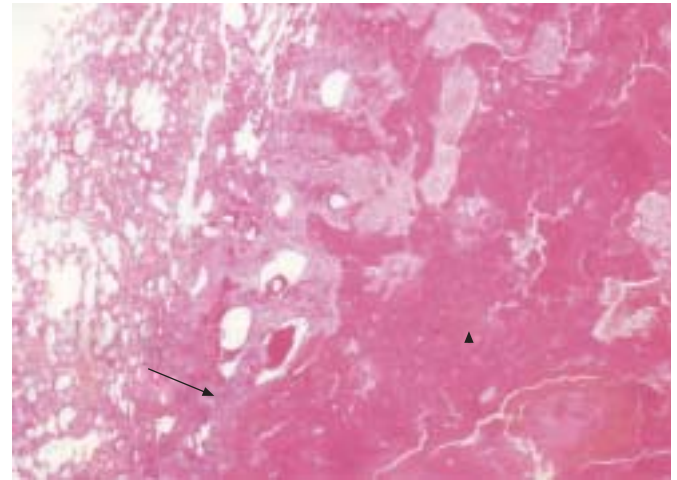


FIGURE 2. Histological examination of one nodule, mainly composed of amyloid deposits (arrowhead), surrounded by a lymphoplasmacytoid proliferation extending to the adjacent normal lung (arrow; haematoxylin-eosin-saffron stain).

Cystic lesions corresponded to dilated bronchioles infiltrated by amyloidosis (fig. 6). Overall, the diagnosis of a stage IV marginal zone lymphoma of MALT-type with gastric, bone marrow and pulmonary involvement was established and the patient was treated by rituximab chemotherapy and bone marrow transplantation. The patient is alive and well 17 months on, with no modification of the volume of the nodules and the cysts on the radiological controls.

DISCUSSION

The present authors report a case of a pulmonary localisation of MALT-type lymphoma associated with pulmonary nodular amyloidosis presenting with unusual findings on the CT scan. Radiological patterns of pulmonary MALT-type lymphoma are numerous, often found in combination, and consist of localised alveolar opacities, nodules and/or interstitial infiltrates. In

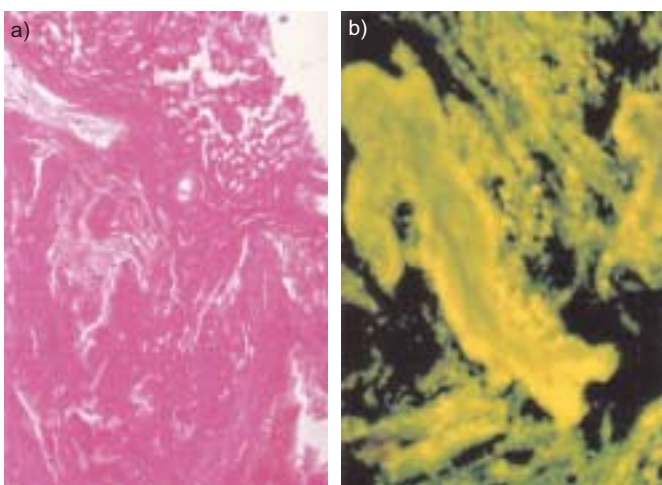


FIGURE 3. a) Amyloid deposit at high magnification consisting of a solid mass of amorphous eosinophilic extracellular material (haematoxylin-eosin stain). b) Amyloid deposits strongly fluorescing with thioflavine T stain under UV light.

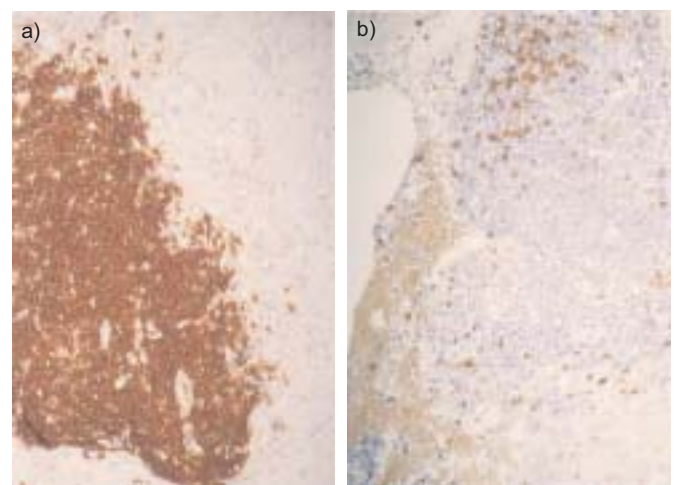


FIGURE 4. Strong expression of the lymphoid proliferation of (a) CD20, whereas only T-cell lymphocytes, and no malignant cells, expressed CD5 (b; immunoperoxidase stain).

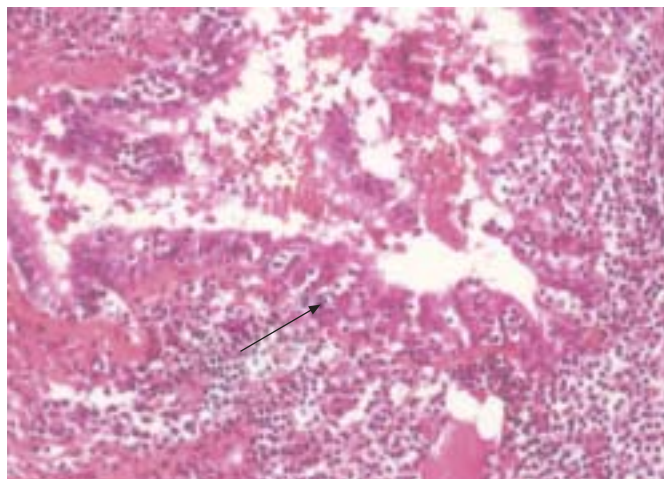


FIGURE 5. At higher magnification, small lymphoplasmacytoid lymphocytes infiltrate the bronchiolar epithelium, forming classical lymphoepithelial lesions (arrow; haematoxylin–eosin–safran stain).

contrast, pulmonary nodular amyloidosis predominantly presents with tumour-like nodules, bilateral but asymmetrical in distribution, and is often located in the lower lobes. They range in size from 0.4–5 cm [8], and they classically contain calcification or bone formation. Very occasionally, pulmonary nodular amyloidosis may present with bronchiolocentric nodules abutting large thin-walled cysts with internal septae. These findings have been described in patients with Sjögren's syndrome, either with or without lymphoid interstitial pneumonia [9, 10] or in association with lymphoproliferative disease [11]. One case of nodular amyloidosis with bullae has also been observed without any underlying inflammatory or proliferative disorder [12], and one case was reported in association with alveoloseptal amyloidosis [13]. The present case is the first to document cystic pulmonary nodular amyloidosis related to MALT-type lymphoma in the absence of Sjögren's syndrome, as the patient did not present any of the revised diagnostic criteria from the American–European Consensus Group for this disease [14].

As the authors' first diagnosis based on fine-needle biopsy was restricted to pulmonary nodular amyloidosis, it must be kept in mind that the amyloidosis may be isolated or may accompany either benign or malignant lymphoproliferations, including nodular lymphoid hyperplasia, lymphoid interstitial pneumonia and lymphoma, in addition to connective tissue diseases and HIV infection [1, 4]. Other malignant lung tumours can also exhibit amyloid deposits, such as carcinoids, which may contain an amyloid stroma, which is likely to be composed of calcitonin-related gene peptide or to be neuropeptide derived [15], or squamous cell and bronchioloalveolar carcinomas, where amyloid deposits are more related to systemic amyloidosis [16, 17]. In addition, metastatic renal cell carcinoma may exhibit an SAA-rich stroma [18], and pulmonary localisation of light-chain disease can masquerade as amyloidosis by tissue deposition of nonamyloid κ chains [19].

The mechanism of cyst formation in pulmonary nodular amyloidosis remains unknown, but is thought to be due to a ball-valve mechanism, responsible for air trapping within

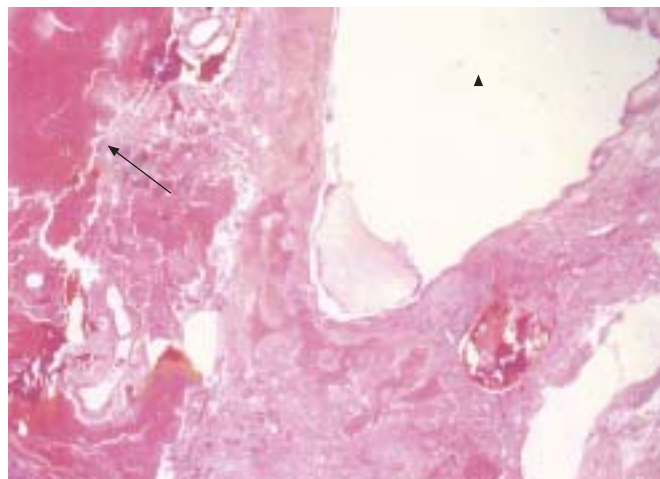


FIGURE 6. Cystic lesions formed by dilated bronchioles (arrowhead) infiltrated by amyloid deposits (arrow).

narrowed airways infiltrated either by amyloid deposits and/or malignant lymphoid proliferation, as in the present case. Another hypothesis is that amyloid deposits within bronchioalveolar structures and around alveolar capillaries could favour an ischaemic process leading to disruption of alveolar walls [13].

In conclusion, the present authors report a case of pulmonary localisation of mucosa-associated lymphoid tissue-type lymphoma associated with pulmonary nodular amyloidosis presenting with unusual cystic features on computed tomography. The present case study illustrates the fact that, although a fine-needle biopsy may be sufficient for the diagnosis of pulmonary nodular amyloidosis, the presence of an associated tumour must be considered in the differential diagnosis of amyloid deposits and may justify additional surgical investigations for diagnosis and staging.

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