Human Pathology (2010) 41, 1040–1045

Human PATHOLOGY

www.elsevier.com/locate/humpath

Case study

Nodular senile pulmonary amyloidosis: a unique case confirmed by immunohistochemistry, mass spectrometry, and genetic study

Anja C. Roden MD[a], Marie-Christine Aubry MD[a], Kai Zhang MD[b], James O. Brady MD[b], David Levin MD, PhD[c], Ahmet Dogan MD, PhD[a], Eunhee S. Yi MD[a,*]

[a]*Department of Laboratory Medicine and Pathology, Mayo Clinic Rochester, MN 55905, USA*
[b]*Geisinger Health System, Danville, PA 17822, USA*
[c]*Department of Radiology, Mayo Clinic Rochester, MN 55905, USA*

Received 18 September 2009; revised 29 November 2009; accepted 30 November 2009

Keywords:
Amyloidosis;
Senile;
Nodular;
Transthyretin;
Immunohistochemistry;
Mass spectrometry;
Molecular study

Summary Nodular pulmonary amyloidosis, characterized by solitary or multiple parenchymal nodules, is primarily composed of amyloid immunoglobulin light chain protein. Pulmonary involvement by senile amyloidosis has been reported as an incidental finding with scattered or diffuse interstitial deposition of amyloid protein transthyretin mostly in patients with cardiac senile amyloidosis in a small number of autopsy cases. We report a unique case of pulmonary senile amyloidosis presenting with conglomerated nodular deposition of amyloid protein transthyretin as the main clinical manifestation. The patient was an 82-year-old man who presented with recurrent pleural effusions and nodular replacement of pulmonary parenchyma on a chest computed tomographic scan. He underwent a wedge resection of the lesion. Histologic examination revealed a massive deposition of Congo red–positive amyloid identified as amyloid protein transthyretin by both immunohistochemistry and mass spectrometry using formalin-fixed, paraffin-embedded tissues. Molecular testing did not show any mutation associated with familial amyloidosis in the *TTR* gene, further supporting the diagnosis of senile amyloidosis. To our knowledge, this is the first documented case of nodular senile amyloidosis of the lung that was confirmed with the current state-of-the-art methods.

1. Introduction

In 1853, Rudolph Virchow used the term *amyloid* to describe tissue deposits that showed chemical reactions with iodine similar to cellulose [1,2]. Since then, various methods have been introduced to determine the nature of amyloid in different types of amyloidosis. Immunohistochemical staining methods have been widely used for subtyping, but the results can often be inconclusive for any specific type. Accurate typing of the amyloid present in the tissue is very important for the appropriate management, which may involve high-risk modalities such as high-dose chemotherapy and/or stem cell transplantation for amyloid immunoglobulin light chain (AL)–type amyloidosis and liver transplantation for hereditary amyloid protein transthyretin (ATTR) amyloidosis. Mass spectrometry has been recently introduced to characterize the various stromal substances in the tissue including amyloid and proven to be a highly accurate and effective method applicable to routinely processed paraffin block [3].

* Corresponding author.
E-mail address: yi.joanne@mayo.edu (E. S. Yi).

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doi:10.1016/j.humpath.2009.11.019

Localized amyloidosis confined to the lung is uncommon [4]; a Mayo Clinic series encompassing a 14-year period reported that only 17 of 55 amyloidosis cases involving the lung were diagnosed as localized pulmonary amyloidosis [4]. Although it has been suggested that localized pulmonary amyloidosis is usually either AL or AA type, detailed information on the types and distribution patterns of amyloid deposits in localized pulmonary amyloidosis is scanty, probably because of the relative rarity of this condition.

Pulmonary amyloid deposits are usually a manifestation of systemic amyloidosis. Systemic amyloidosis affecting the lungs includes immunoglobulin light-chain restricted idiopathic (primary) amyloidosis (AL type), reactive (secondary) amyloidosis caused by deposition of amyloid A protein (AA type), amyloidosis associated with chronic dialysis (β-2-microglobulin type), and familial and senile amyloidosis characterized by deposition of transthyretin/prealbumin protein (ATTR type). Pulmonary involvement by systemic senile amyloidosis is usually a mild and incidental finding that has been reported in only a few autopsy cases [5].

Herein, we report a unique case of confluent nodular amyloidosis mimicking a localized type but confirmed as senile ATTR type by comprehensive ancillary studies including mass spectrometry (MS). To our knowledge, this is the first case to document a senile amyloidosis presenting as a nodular pulmonary amyloidosis.

2. Report of a case

An 82-year-old white man of Middle Eastern descent presented with recurrent left pleural effusions requiring multiple thoracenteses. He had chronic dyspnea without hemoptysis or pleuritic chest pain. A chest computed tomographic (CT) scan revealed a nodular lesion in a background of ground glass opacities and interstitial thickening involving the left lower lung lobe but sparing the rest of the left lung field (Fig. 1). He underwent a wedge biopsy of the left lower lung lobe for the evaluation of these abnormal radiologic findings. Urine and serum protein immunoelectrophoresis performed 8 months before the lung biopsy did not reveal any monoclonal gammopathy. His past medical history was quite complex and involved many major organ systems: recently started hemodialysis for chronic renal failure, atherosclerotic cardiovascular disease, cardiac arrhythmia requiring a permanent pacemaker and surgical repair of multiple heart valves 3 years prior, chronic shoulder disability, pulmonary hypertension, recent onset of mild confusion and memory difficulties, unilateral hearing loss and mild dysphagia of unknown etiology, chronic anemia, diabetes mellitus, and hyperparathyroidism. He also had cardiomyopathy of unknown etiology. His family history was significant for a sister with congestive heart failure, renal failure, and diabetes mellitus.

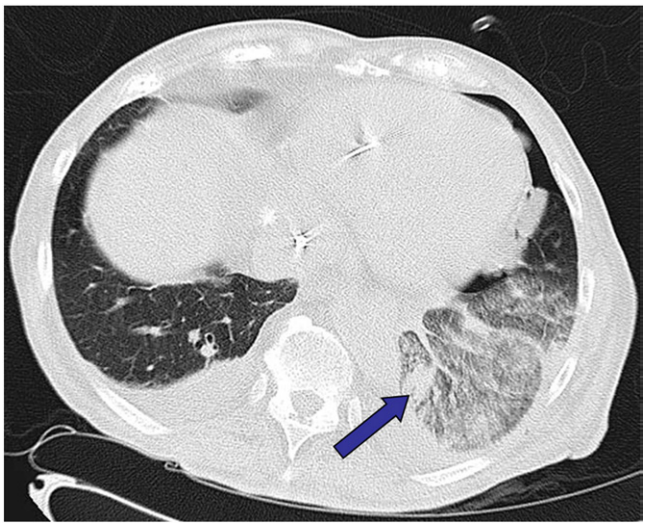

Fig. 1 Chest CT scan reveals a nodular lesion (arrow) in the periphery of the left lower lobe in a background of ground glass opacification and septal thickening. Bilateral pleural effusions are present on imaging study despite the clinical presentation as left pleural effusion. The remaining left upper lobe and the right lung are unremarkable.

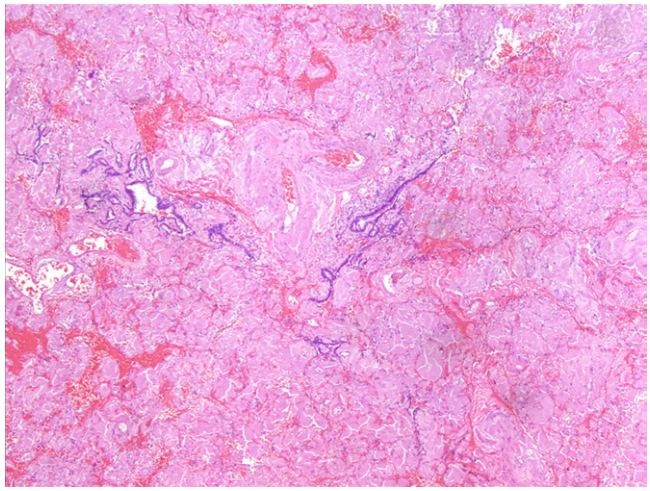

Fig. 2 Eosinophilic deposition comprising the left lower lobe nodule (hematoxylin and eosin, 100× original magnification).

Hematoxylin- and eosin-stained sections of the wedge biopsy showed the lung parenchyma mostly replaced by amorphous eosinophilic materials (Fig. 2). Pulmonary arteries were present within the lesion and revealed mural accumulations of similar-appearing amorphous eosinophilic materials involving focally or circumferentially the vessel walls. These deposits were confirmed as amyloid by the apple-green birefringence on a Congo red stain (Fig. 3). A panel of immunohistochemical stainings [3] revealed that the amyloid in the tissue was positive for serum amyloid P component (SAP) (Fig. 4A) and TTR (Fig. 4B), but negative for SAA (Fig. 4C). Expression of immunoglobulin κ and λ light chains was similar (Fig. 4D). Lymphoplasmacytic infiltrates were seen not only in the amyloid deposits but also in the adjacent visceral pleura. The plasma cells within these infiltrates were polytypic.

To confirm the ATTR type of amyloid as shown by immunohistochemical study, we performed liquid chroma-