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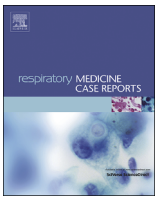

Case Report

Isolated pulmonary amyloidoma: A rare cause of solitary pulmonary nodule

Danielle DeCicco [a, *], Esra Alshaikhnassir [b], Vishal Deepak [c], Sarah Hadique [c], Rahul Sangani [c]

[a] Department of Medicine, West Virginia University, Morgantown, WV, 26505, USA
[b] Department of Pathology, West Virginia University, Morgantown, WV, 26505, USA
[c] Section of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, West Virginia University Morgantown, WV, 26505, USA

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ABSTRACT

Pulmonary nodules are a frequent finding on imaging, especially given screening guidelines for lung cancer with low dose computed tomography (CT) scan. Here, we report a case with a single pulmonary nodule in a patient exposed to coal dust and asbestos. The nodule had benign features, but it showed an increase in size on repeated imaging. A CT-guided biopsy followed by mass spectrometry of the sample identified the nodule as the AL subtype of amyloidoma. A bone marrow biopsy was without evidence for malignancy including lymphoma. Nodular pulmonary amyloidosis (NPA) is rare, and a biopsy is required to establish the diagnosis. NPA generally does not affect lung function or impact survival; thus NPA does not require specific therapy. This case is the first documented case associated with coal-dust exposure. High-risk patients need to be followed longitudinally due to association of amyloidosis with lymphoma and other systemic conditions.

1. Introduction

A single nodule discovered on chest computed tomography (CT) imaging typically requires a broad work-up for a large differential diagnosis, especially in patients with a history of tobacco use [1,2]. One benign cause of such a nodule is localized nodular pulmonary amyloidoma (NPA) which is a rare condition without systemic symptoms of amyloidosis [3,4]. Amyloidosis is a heterogenous disease characterized by misfolded proteins deposited extracellularly [1,3,5]. This leads to cell death and eventually organ damage [1]. It is histologically associated with Congo Red stain with apple-green birefringence under polarized light [5]. Amyloidosis has four general subtypes depending on the type of amyloid protein involved [5]. The AL protein is an immunoglobulin-derived light chain protein, and AL-amyloidosis can affect the heart, lungs, kidney GI, and nervous system [5]. It is also associated with plasma cell dyscrasias and most often associated with lung pathology [5]. Pulmonary amyloidosis is rare type of amyloidosis with three subtypes recognized including NPA, diffuse alveolar-septal amyloidosis and tracheobronchial amyloidosis [1,2]. Here we present a case of a single pulmonary nodule with biopsy-proven AL amyloidosis.

2. Case

A 76-year-old male with past medical history significant for type 2 diabetes, hypertension, and hyperlipidemia presented to pulmonary clinic for evaluation of a lung nodule and chronic shortness of breath. He started feeling short of breath about six months

* Corresponding author. PGY-2, Department of Medicine, PO Box 9168, 4th Floor HSC-N, 1 Medical Center Drive, Morgantown, WV, 26506, USA.
E-mail address: dd0013@hsc.wvu.edu (D. DeCicco).

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prior to presentation which has since worsened. He denied any constitutional symptoms except fatigue. He was exposed to coal dust and asbestos while working as a miner for nine years and as a welder for twenty years. He had a five pack-year smoking history, and he quit 50 years ago.

Before presenting to pulmonary clinic, he had a chest radiograph performed which showed a right lower lobe nodule. Subsequently, CT imaging of his chest showed a 2.0 × 1.5 cm elongated, partially calcified nodule along the posterior aspect of the right major fissure without any significant mediastinal and hilar lymphadenopathy (Fig. 1). Serial imaging survey showed a stable nodule at the 3-month interval, however, at 9-month follow up, the nodule showed growth in size to 3.0 × 1.7 × 1.5 cm with the anterior border abutting the fissure (Fig. 2). The patient underwent CT guided biopsy of the mass showing the presence of amyloid protein (Fig. 3). Meanwhile, the patient's pulmonary function tests showed mild obstruction with significant bronchodilator response, and he was started on maintenance inhalers in addition to as-needed albuterol.

Further work up ruled out systemic amyloidosis including normal serum and urine protein electrophoresis (SPEP and UPEP) and serum immunoglobulins profile, normal findings on transthoracic echocardiogram excluding cardiac amyloidosis, and a bone-marrow biopsy without evidence of abnormal deposition or malignancy. Flow cytometry was performed without evidence of malignancy. The final diagnosis of NPA was made. The patient maintained symptomatic stabilization with use of long-term bronchodilators. Follow up CT chest imaging revealed stable size of the nodule.

3. Discussion

Three forms of pulmonary amyloidosis have been recognized in the literature: diffuse alveolar septal, nodular, and tracheobronchial [6–8]. The most common form is nodular amyloidosis, a rare disease which is usually found incidentally on chest radi-

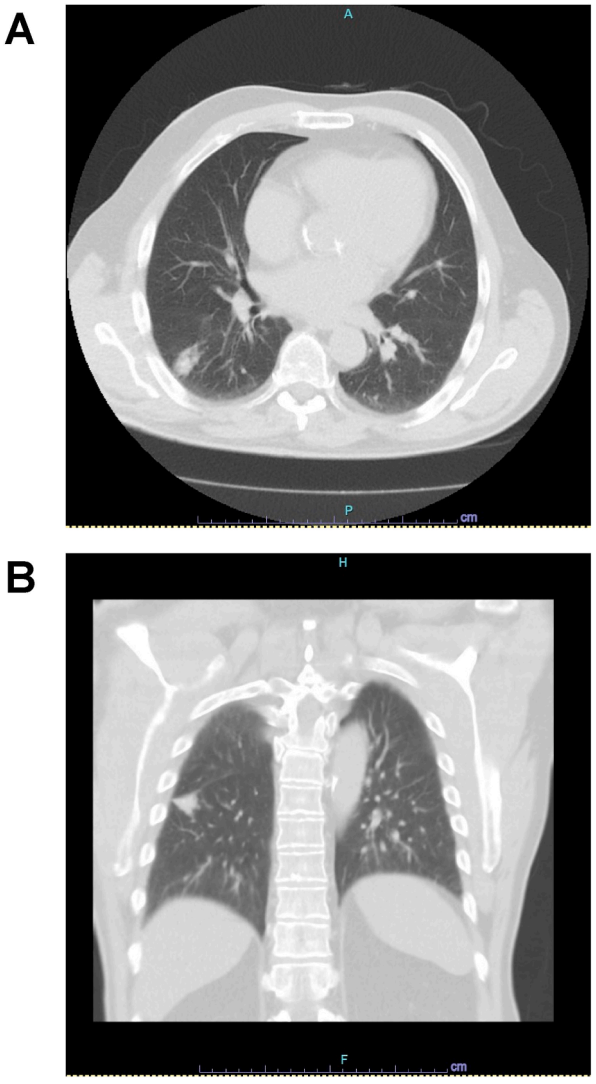

Fig. 1. CT Chest at the time of presentation depicting a 2.0 by 1.5 cm right lower lobe nodule in axial (A) and coronal views (B).

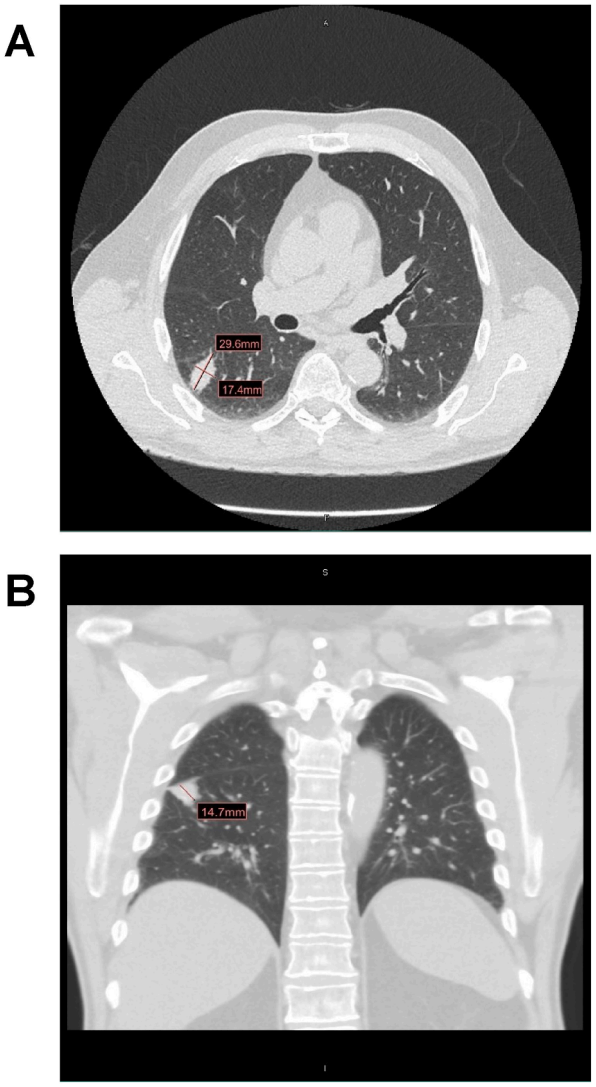

Fig. 2. CT Chest at nine-month interval depicting a 3.0 by 1.7 cm right lower lobe mass in axial (panel A) and coronal views (panel B).

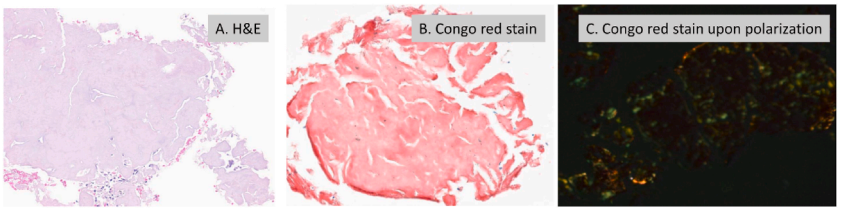

Fig. 3. Pathological sections of biopsied tissue with a section of the lung showing eosinophilic amorphous material (A). Congo red stain is positive for waxy amyloid deposit (B). There is apple-green birefringence upon polarization consistent with amyloid deposition (C). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

ographs in asymptomatic, elderly individuals [9,10]. The respiratory system is involved in 50–70% of primary amyloidosis, but the localized type, or radiographically demonstrable involvement, is considerably less common [10]. These lesions cannot be radiographically distinguished from malignant or benign neoplasms, chronic inflammatory or granulomatous lesions [10,11]. These nodules have been associated with several other systemic lymphoproliferative disorders, both benign and malignant conditions, ranging from Sjögren's syndrome and systemic amyloidosis to marginal zone lymphoma and pulmonary mucosa-associated lymphoid tissue lymphoma [1,12,13].

Literature suggests that pulmonary amyloidosis is the result of an underlying lymphoproliferative disorder or a reaction to chronic inflammatory conditions affecting the lung such as connective tissue disorders, tuberculosis, or HIV infection [12]. In a study of all

patients with amyloidosis seen in Mayo Clinic before 2001, queried by electronic medical record, six cases of NPA were found without systemic amyloidosis [14]. Those six cases were associated with pulmonary marginal zone lymphoma [14]. Therefore, executing the workup for an underlying lymphoproliferative disorder is crucial. SPEP and UPEP were performed along with flow cytometry from the bone marrow biopsy in this case, all without indication for malignancy including lymphoma.

Some cases of amyloidomas have not been associated with systemic symptoms or systemic amyloidosis [1,2]. NPA has been shown to have differences in AL composition and subtype ratios on histology compared to systemic amyloidosis [15]. In NPA, a subtype kappa derived amyloid chain exists at higher levels than the gamma-derived amyloid protein in systemic amyloidosis [15]. Also, deposition in tissues of heavy chains of the AL protein is more common in NPA than systemic amyloidosis [15]. In a longitudinal study from the Mayo Clinic over thirteen years, eleven out of fifty-five pulmonary amyloidosis cases were identified to be localized without systemic symptoms [16]. Of those eleven cases, seven were amyloidomas of the type described in this case, while the rest were of a different amyloid protein type, ATTR, associated with age-related amyloidosis or of the tracheobronchial amyloidoma subtype. The largest nodule described was 15 cm [16].

Interestingly, there has been some association of occupational exposures with amyloidosis. One case report described systemic amyloidosis following silicosis [17]. It is hypothesized that silica or other particulate exposure can increase inflammatory processes and contribute to amyloidosis. There have been two cases where exposure history was directly associated with nodular pulmonary amyloidoma with silica exposure and asbestos exposure [17,18]. In these cases, it was proposed that the frequent inhalational exposure served as a nidus for granuloma formation mediating amyloidoma formation [17,18]. There are several hypotheses regarding pathogenesis of exposure-related amyloidomas including repeated inflammation of the affected cells, tissue macrophages degrading the immunoglobulin light-chains in lysosomes secreting amyloid into the extracellular space or a local monoclonal proliferation essentially forming a tumor [17,18]. More work will need to be done to elucidate this mechanism. However, this case is the first reporting coal exposure associated with NPA.

Recognizing localized pulmonary amyloidoma is important due to the need for longitudinal observation [1,4]. Association with lymphomas or systemic amyloidosis are usually evident on diagnosis of the amyloidoma, and it is not clear based on the literature how many of these patients progress to having systemic amyloidosis or are eventually diagnosed with a lymphoma [1,5]. One study of localized cutaneous amyloidosis followed sixteen patients who did not have systemic amyloidosis on initial presentation [9]. One patient developed systemic amyloidosis within one year, and fourteen did not develop systemic amyloidosis at mean follow up of ten years with one patient lost to follow up [9]. However, more studies are needed to follow patients with pulmonary amyloidomas to assess outcomes. Therefore, monitoring these nodules with consistent follow-up and closely monitoring patients for development of new symptoms is key in management. Management can include surgical resection, which is often required in nodular pulmonary amyloidomas, however, there is risk of recurrence [4]. Patients with NPA typically have optimistic prognoses [19].

Author contribution statement

Danielle DeCicco wrote the manuscript. Esra Alshaikhnassir contributed by preparing the pathology slides and their descriptions. Vishal Deepak prepared CT imaging figures and assisted with early drafts of the manuscript. All authors reviewed, edited, and approved the manuscript.

Ethics statement

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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Declaration of competion interest

There are no conflicts of interest declared for all authors.

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