Case Report

Mystery in the mediastinum: Rare case of indolent primary thoracic amyloids

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ABSTRACT

A 53-year-old African American male smoker presented with epigastric pain, tarry stools, and laboratory results indicative of acute pancreatitis. Chest X-ray showed a right perihilar mass with pleural effusion. Computed tomography scan showed multiple large right paratracheal and hilar nodes with internal calcification. The patient underwent a fiberoptic bronchoscopy with biopsies which were negative for malignancy. Mediastinoscopy was performed and revealed amyloidosis. Evaluation for multiple myeloma showed elevated kappa and lambda light chains and diffuse polyclonal gammopathy, but there was no monoclonal spike on serum protein electrophoresis. Bone marrow and abdominal fat pad were negative for amyloid, and the patient continues to lack chronic underlying systemic disease with no symptoms on cardiac or pulmonary examination.

KEY WORDS: Amyloidosis, mediastinoscopy, multiple myeloma

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INTRODUCTION

Amyloidosis is misfolded protein deposition localized to one organ or systemic in nature. Etiology of amyloidosis includes inflammatory, infectious, and neoplastic processes.[1] Localized amyloidosis is usually a benign process. Systemic amyloidosis is due to underlying neoplastic or inflammatory processes which may require treatment.[2] The World Health Organization classify amyloidosis as primary (AL) and secondary (AA). In primary amyloidosis, amyloid is composed of intact light chain which is made by monoclonal plasma cells. AL amyloidosis is associated with plasma cell disorders. In secondary amyloidosis (AA), amyloid is acute-phase protein serum amyloid. Secondary amyloidosis (AA) is associated with chronic inflammatory processes. Heritable amyloidosis involves the production of mutated amyloid protein by the liver. Typically, AL amyloidosis has a worse prognosis compared to AA amyloidosis.[3]

Clinical manifestations of amyloidosis are dependent upon the organ of its involvement. Kidneys, lungs, joints, and gastrointestinal system are the most involved organs. Approximately 75% of patients with primary and secondary amyloidosis involving the chest also involve mediastinal lymph nodes. Localized amyloidosis involving mediastinal lymph nodes without pulmonary involvement is extremely rare, with less than dozen cases reported in literature.[4] Computed tomography (CT) imaging of lymph nodes may show slowly enlarging, homogenously low attenuating, and smooth contour. Amyloid involving lymph nodes have calcifications, but its significance is not well elaborated.[5] The diagnosis of amyloidosis requires
tissue biopsy in the setting of clinical suspicion. Once the diagnosis of amyloidosis is made then the next step is to evaluate the patient for type of amyloidosis. Treatment options include immunotherapies and drugs to control symptoms of the affected organ. Asymptomatic patients are followed over time without any treatment. The prognosis depends upon the affected organ, type of amyloidosis, and duration of the diseases.

**CASE REPORT**

A 53-year-old African American male smoker with a history of hypertension presents with sharp epigastric pain extending to the lower abdomen, lower extremity swelling, shooting pain down the right arm, and black stools. Initial laboratories showed normal prothrombin time, international normalized ratio, hemoglobin, and hematocrit. Chest X-ray shows right perihilar mass with right pleural effusion [Figure 1]. Amylase and lipase levels are slightly elevated. A nasal gastric tube is guaiac negative, whereas rectal examination is stool guaiac positive.

Bronchoscopy for right hilar adenopathy shows narrowed airway, external compression of the anterior right upper lung, and erythematous right middle lung. The right upper and middle lobe biopsies and bronchoalveolar lavage are negative for malignancy. Mediastinal biopsy of 2R station mass showed that the sclerotic tissue is possible for amyloid. The scattered lymphocytes show no evidence of clonality on CD20 and CD3 immunostaining. The CT scan showed thickening of the parietal pleura and mediastinal mass with cuffing of the pulmonary artery and main stem bronchus [Figure 2]. To categorize the type of amyloid, Congo red staining with and without permanganate was ordered. Abdominal fat and bone marrow specimens displayed Congo red negative for amyloid. Sclerotic tissue from the mediastinal mass was positive for Congo red with and without permanganate digestion, leading to the initial diagnosis of amyloidosis [Figure 3]. Resistance of amyloid to the use of permanganate digestion would indicate an origin from a hematopoietic malignancy and light chain excess. Flow cytometric evaluation of mediastinal mass reveals predominantly T-cells with few polyclonal B-cells and no aberrant immunophenotype. Positron emission tomography scan shows uptake in right supraclavicular, paratracheal, and hilar region. Further serum protein testing reveals moderately increased gamma fraction. Light chain assay showed elevated kappa and lambda light chains. Serum protein electrophoresis and urine protein show no monoclonal spike, though there is diffuse polyclonal gammopathy. Diagnosis of AL amyloidosis of mediastinal nodes is made.

**DISCUSSION**

Amyloidosis has variable presentations and cannot be diagnosed clinically. Diagnosis of amyloidosis relies on histopathology. If systemic amyloidosis is suspected, an abdominal fat pad biopsy may be ordered. Apple-green birefringence on Congo red staining is a characteristic finding. If amyloid deposits are identified without chronic inflammatory disease, primary amyloidosis must be ruled out. Testing for monoclonal protein on electrophoresis is done to identify plasma cell dyscrasias, and bone marrow biopsy may be used to aid in diagnosis.

Considering amyloidosis as a diagnosis is highly dependent on the clinical scenario. In a patient with mediastinal lymphadenopathy, mediastinal amyloid...
should be considered, as thoracic amyloidosis can also involve the mediastinal lymph nodes. However, primary mediastinal amyloidosis without pulmonary involvement is exceedingly rare. Accordingly, other more common causes of mediastinal lymphadenopathy should be ruled out, such as primary lung cancer, metastatic cancer, sarcoidosis, interstitial lung disease, drug reactions, and histoplasmosis. Other diagnostic tools may provide limited utility in aiding the diagnosis. Mediastinal calcifications on radiography may be present, but the specificity and sensitivity of such findings are unclear. Unfortunately, any radiographic findings associated with mediastinal amyloid often mimic other lung pathology, decreasing diagnostic utility.

Treatment of mediastinal amyloidosis is dependent on the extent of deposition and the type of amyloidosis. Asymptomatic individuals with limited deposition do not require treatment and should be routinely monitored. Current treatment methods involve addressing the underlying plasma cell dyscrasia or inflammatory state in AL and AA amyloidosis, respectively. Utilizing tumor necrosis factor-alpha inhibitors provides benefit in patients with AA complications. Liver transplantation may be indicated for heritable amyloidosis. Newer agents, such as inotersen, are RNA-targeted therapies preventing translation of TTR amyloid. Others, such as tafamidis, stabilize and prevent release of TTR monomers responsible for pathological deposition. Other forms of treatment have instead focused on reducing the amount of amyloid that has already deposited. In a small study of patients, administration of CPHPC followed by anti-SAP antibodies was shown to trigger the depletion of amyloid deposits from several organs. Specifically, the drug miridesap (CPHPGC) removes circulating SAP. Some SAP is left in amyloid deposits, which serves as a target for Dezamizumab, an anti-SAP antibody that specifically allows for amyloid clearance. Despite the advancements, no curative treatment for amyloidosis exists.

All in all, primary mediastinal amyloidosis remains an uncommon clinical condition. Obtaining a definitive pathologic diagnosis and ruling out causes of secondary amyloidosis remain the standard approach, frequently requiring multiple diagnostic procedures. It may be diagnosed following workup of an incidental finding as was the case in this patient.

**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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