

Systemic Amyloidosis with Unusual Mediastinal Involvement

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Introduction

Mediastinal lymphadenopathy as seen on Computed Tomography (CT) scan of the chest is usually caused by lymphoma, tuberculosis, sarcoidosis, metastatic cancers and granulomatous diseases. However, the differential diagnosis is broad and includes a number of rare disorders or unusual manifestations of systemic conditions including amyloidosis. We report a case of mediastinal lymphadenopathy associated with systemic amyloidosis.

Case Report

A 62-year-old African-American male with a past medical history of diabetes mellitus and hypertension was admitted with generalized fatigue and abnormal blood work up as outpatient that showed renal failure. Two months prior, he had undergone excisional biopsy of a right submandibular lymph node which had revealed immunoglobulin light chain (AL) amyloidosis. (Figure 1) and was asymptomatic beside neck swelling at that time. The procedure was done as outpatient and patient did not follow up until the time of admission when he was evaluated as outpatient and referred to our hospital. The patient had no symptoms beside fatigability; no loss of appetite or weight loss.

Physical examination was remarkable for small bilateral submandibular and left inguinal lymphadenopathy. Otherwise, no significant findings noted.

Laboratory workup was significant for elevated BUN and creatinine (99 mg/dl and 10.3 mg/dl respectively) as well as nephrotic-range proteinuria (13026 mg/24 hr). Rheumatologic work up, hemoglobin electrophoresis, and Hepatitis panel were negative.

CT scan of the chest showed conglomeration of abnormal right paratracheal lymph nodes 8.1 X 7.4cm in size, some of which had punctate calcifications (Figure 2). In addition, there were enlarged lymph nodes throughout the anterior mediastinum, left paratracheal space and azygoesophageal recess (Figure 3). There were no pulmonary nodules, abnormal interstitial markings or pleural effusion.

He underwent CT-guided core needle biopsy of the left kidney; pathology of the specimen displayed a profile consistent with

AL type amyloidosis. Because of his known diagnosis and suggestive radiological findings of systemic amyloidosis, Trans-Bronchial Needle Aspiration (TBNA) of the mediastinal lymph nodes was deemed unnecessary.

He was started on hemodialysis and discharged home in stable condition.

Discussion

Amyloidosis is defined as a group of disorders characterized by extracellular deposition of insoluble protein fibrils in a β -pleated configuration [1,2]. This condition can be acquired or hereditary, as well as being local or systemic, and is classified according to the precursor protein. Among the acquired forms of amyloidosis are primary amyloidosis (AL type), local nodular amyloidosis, secondary amyloidosis (AA type), and senile systemic amyloidosis [3].

AL amyloidosis is caused by the deposition of fibrils derived from light chains of pathologic monoclonal antibodies, and frequently involves multiple systems including the heart, gastrointestinal tract, kidneys, and skin. This type may be associated with myeloma, blood dyscrasias, and monoclonal gammopathies. [3,6,9] It usually occurs between the fifth and seventh decades of life and affects men more than women [6].

Secondary amyloidosis is associated with systemic conditions including tuberculosis, chronic kidney disease, syphilis, osteomyelitis, inflammatory bowel disease, bronchiectasis, rheumatoid arthritis, hypergammaglobulinemia, and certain malignancies. [7,9]

Thoracic manifestations of amyloidosis include lymphadenopathy, pulmonary nodules, diffuse lung disease, pleural effusions, and laryngotracheobronchial disease; such manifestations are rare but may occur with both the localized and systemic forms [2].

Systemic amyloidosis is an unusual cause of mediastinal lymphadenopathy; Lymphoma, tuberculosis, sarcoidosis, metastatic cancers, and other granulomatous diseases are often responsible for mediastinal lymphadenopathy and should be ruled out first [2,5].

Mediastinal lymphadenopathy can be unilateral or bilateral, frequently show punctate calcifications and usually accompanies parenchymal lung disease or pleural effusions; these features could be used as diagnostic clues for amyloidosis [2,8,7].

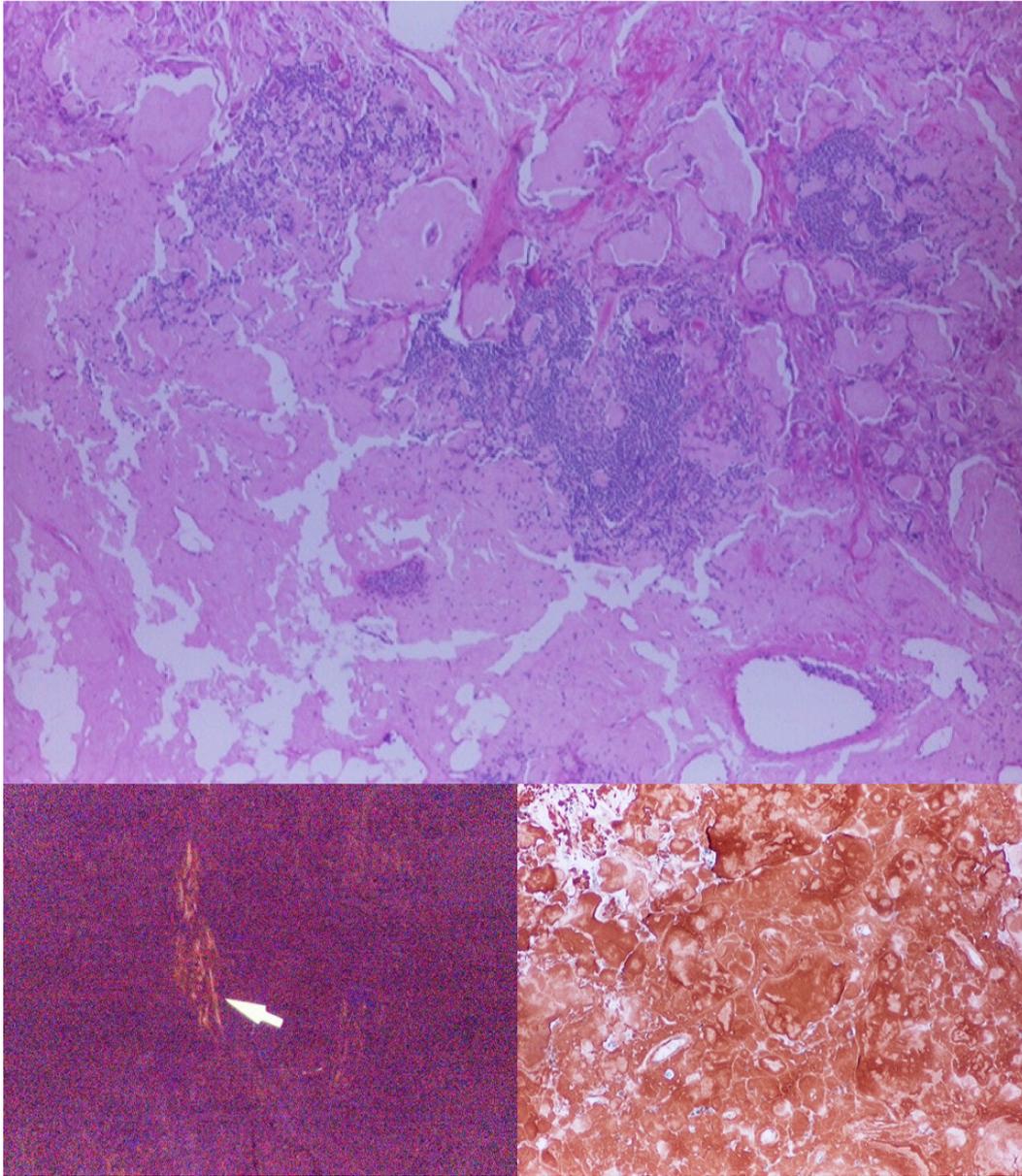


Figure 1:
 Top image: Hematoxylin and eosin stain of lymph node biopsy showing amorphous amyloid deposits.
 Bottom left image: Polarized light green birefringence of amyloid deposits.
 Bottom right image: Congo red positive amyloid deposits.

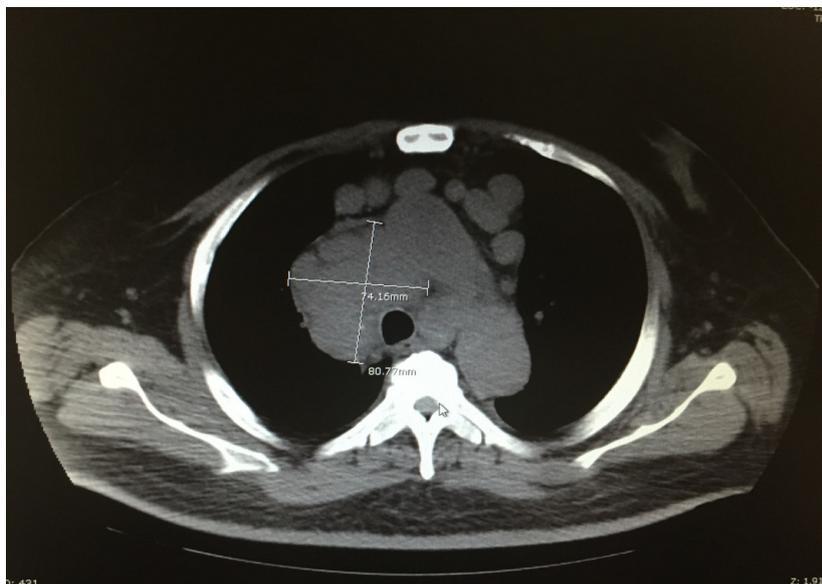


Figure 2: CT scan of the chest showing conglomeration of abnormal right paratracheal lymph nodes 8.1 X 7.4cm in size.

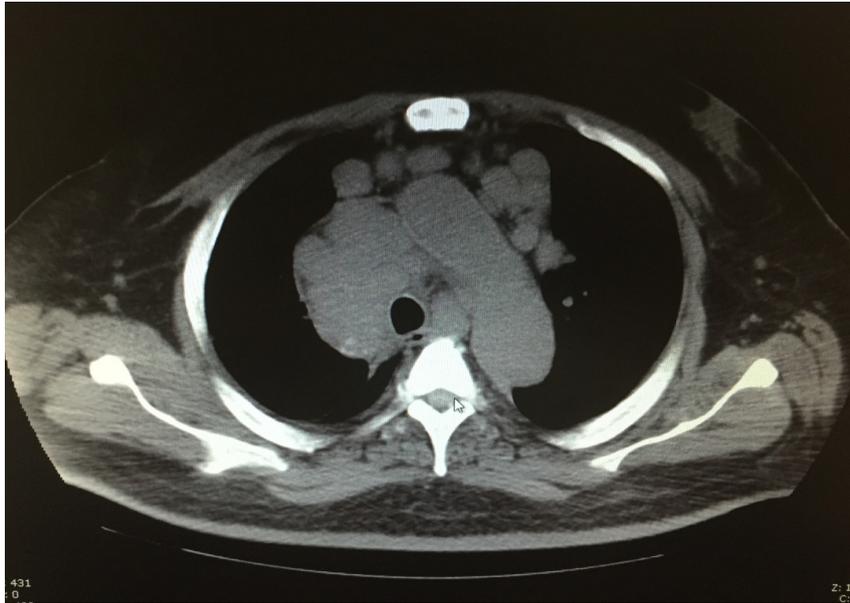


Figure 3: Enlarged lymph nodes throughout the anterior mediastinum, left paratracheal space and azygoesophageal recess.

Isolated mediastinal lymphadenopathy in the absence of pulmonary involvement is a rarer entity [4].

Diagnosis requires histological confirmation of amyloid deposition in the tissue followed by Immunohistochemical analysis to determine the fibril type [3,8]. Under light microscopy, hematoxylin & eosin staining shows homogeneous, pink amyloid protein, usually accompanied by fibrosis; and the characteristic red-green birefringence in Congo red-stained tissues under polarizing microscope [9].

The gold standard diagnostic approach for intrathoracic nodal amyloidoma is via mediastinoscopy, given that the firm consistency of amyloid deposits poses sampling difficulties. Endobronchial ultrasound with transbronchial needle aspiration (EBUS-TBNA) is another tool that has been reportedly used in tissue sampling for intrathoracic amyloidosis. Compared to mediastinoscopy, EBUS-TBNA is a minimally invasive and safe procedure, and can be performed under local anaesthesia in an outpatient setting [1,5]. Although patients with amyloidosis have an increased risk for bleeding, cases have been reported of diagnosis of pulmonary amyloid nodules by fine-needle aspiration with minimal bleeding complications [4,8,7].

The principles in the treatment of amyloidosis are to inhibit the synthesis of amyloid protein, decrease its extracellular deposition, reduce the production of amyloid precursors, and promote the degradation of amyloid. [9].

Current regimens include systemic chemotherapy for systemic AL amyloidosis and local interventions for its localized forms [8].

Systemic chemotherapy consisting of Low dose oral melphalan and prednisolone for 4 weeks (MP regimen) is one of the most commonly used treatments and is believed to inhibit the production and deposition of amyloid, but it produces a clinical response in only 20–30% of patients. Studies on more intensive chemotherapy regimens and peripheral stem cell transplantation are more promising [8,9].

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