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Localized Primary Thymic Amyloidosis Presenting as a Mediastinal Mass – A Case Report –

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We herein describe a case of a 55-year-old healthy woman with localized primary thymic amyloidosis presented as a mediastinal mass, found incidentally by chest radiography. Computed tomography revealed a 4.1 cm soft tissue lesion with nodular calcification in the left anterior mediastinum. The resected specimen was a well-defined lobulating mass with calcification. Microscopically, the mass was consisted of amorphous eosinophilc hyalinized substances involving the thymus and intrathymic lymph nodes. These eosinophilic substances showed apple-green birefringence under polarized light after staining with Congo red. In immunohistochemical study, they were positive for kappa and lambda light chains and negative for amyloid A. There was no evidence of systemic amyloidosis in clinical investigations. A final diagnosis of localized primary thymic amyloidosis was made.

Key Words: Thymoma; Amyloidosis; Mediastinum

Localized primary amyloidosis is uncommon and distinguishable from systemic amyloidosis by its benign course, which generally involves the upper respiratory tract, lip, colon, skin, nails, and the orbit.[1] Reports on amyloidosis presented as a mediastinal mass are very rare.[2] Although several cases involving the mediastinal lymph nodes have been reported, including two cases in Korea,[3,4] localized primary amyloidosis involving the thymus has not yet been reported. We herein report a rare case of localized primary thymic amyloidosis presented as a mediastinal mass.

CASE REPORT

A 55-year-old woman was referred to our hospital with a mediastinal mass found by routine chest roentgenogram. Chest computed tomography scan showed a soft tissue mass with nodular calcification, 4.1 cm in size, in the left anterior mediastinum (Fig. 1). She had no past medical history and did not experience subjective symptoms. Pre-operative investigations, including pulmonary function test, electrocardiogram, echocardiogram, hematological and biochemical studies, showed no specific abnormalities. Based on the clinical impression of thymoma, tumor resection with total thymectomy was performed.

The resected tumor was a relatively well demarcated and lobulated mass, measuring 7×4×2 cm (Fig. 2A). The cut section was yellow to gray tan, firm, and calcified. Additionally, 5 nodules showing the same features with the main mass were found. Microscopically, the mass was consisted of amorphous eosinophilc hyalinized substances involving the thymus, intrathymic adipose tissues, and lymph nodes (Fig. 2B). Perivascular infiltration with calcification, ossification, and peripheral lymphoplasmacytic infiltration were its characteristics (Fig. 2C-E). These eosinophilic substances showed apple-green birefringence under polarized light after staining with Congo red. In immunohistochemical study, they were positive for kappa and lambda light chains and negative for amyloid A. These pathologic findings were consistent with light chain amyloidosis. Serum IgG, IgA, and IgM were within the normal limits. The ratio of kappa and lambda in the serum was also within the normal limits. Monoclonal immunoglobulin protein was not detected by electrophoresis immunofixation for IgG, IgA, and IgD in serum and

urine. Serum protein electrophoresis revealed no abnormal band. Based on these findings, we made a diagnosis of localized primary amyloidosis.

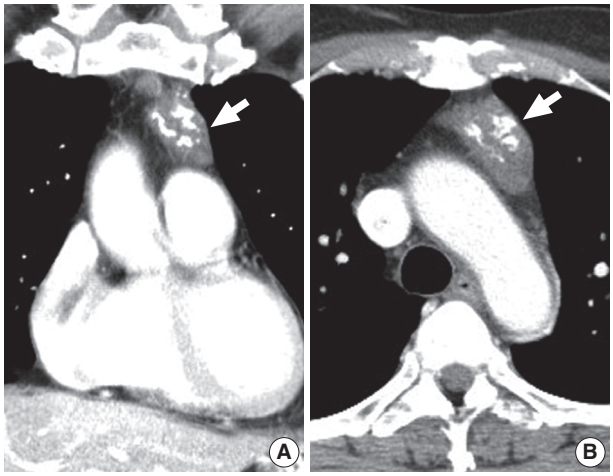

Fig. 1. (A, B) Computed tomography reveals a soft tissue mass with nodular calcification in the left anterior mediastinum.

DISCUSSION

Amyloidosis is a heterogeneous group of diseases that generally have extracellular accumulation of insoluble polymeric protein fibrils in tissues and organs. Amyloid is defined by the biochemical nature of the protein in fibril deposits, and is classified into systemic and localized, acquired and inherited, and by their clinical patterns.[1,5] The two most common types are light chain amyloidosis (also called primary amyloidosis) and amyloid A amyloidosis (also called secondary or reactive amyloidosis). The former is associated with an underlying monoclonal plasma cell disorder and can be systemic (80-90%) or localized (10-20%). The latter is associated with chronic inflammatory conditions, such as rheumatoid arthritis, chronic sepsis, periodic fever syndrome, Crohn's disease, and is mostly systemic.[1,4,5]

Localized primary amyloidosis involving mainly the upper respiratory tract, lip, colon, skin, nails, and orbit has been documented. The clinical course is generally benign, and surgical excision is the treatment of choice.[1]

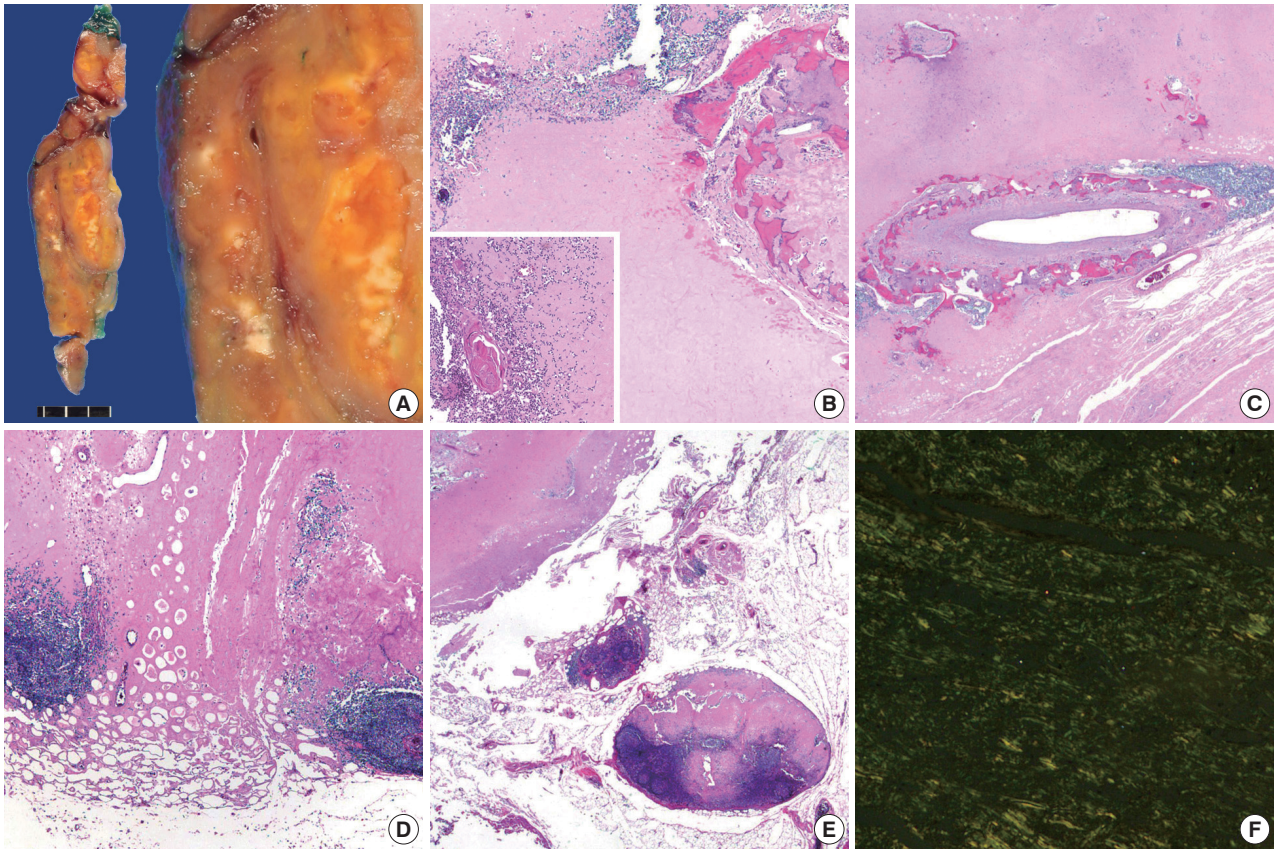

Fig. 2. (A) The tumor is firm and has a lobulated contour. The cut surface of the tumor is yellow tan colored with chalky calcification. (B) The mass is consisted of amorphous eosinophilic hyaline materials with calcification and ossification. Involvement of thymic Hassal's corpuscle is noted (inset). (C-E) There are perivascular ossification, extension to the intrathymic adipose tissue and involvement of the intrathymic lymph nodes. (F) The deposition shows apple-green bi-refringence under polarized light after staining with Congo red.

Table 1. Cases of amyloidosis presented as mediastinal mass

Reference	Age/ Sex	Symptom	Past history or underlying disease	Size (cm)	Calcification/ Ossification	Lympho-plasma cell infiltration	Amyloid type	Involving organ	Other involving site
Osnoss and Harrell[6]	49/M	Ankle pain	(-)	8.5	(-)/(-)	(+)	NA	Lymph node	Ankle bone, rectum
Melato *et al*.[7]	66/M	Recurrent broncho-pneumonia	Multiple myeloma (diagnosed at autopsy)	10	(-)/(-)	(+)	AL(+)	Lymph node	All organs
Shaw *et al*.[8]	53/F	Dyspnea, cough	Plasma cell dyscrasia	NA	(+)/(-)	(+)	AL(+)		Neck, bronchus, lung
Jenkins and Potter[9]	53/F	Airway obstruction	Extramedullary plasmacytoma	8	(+)/(-)	(-)	AL(+)	Lymph node	No
Hiller *et al*.[10]	66/M	Dyspnea, cough/sputum	DM with nephropathy	NA	(-)/(-)	(+)	NA		Rectum
Conaghan *et al*.[11]	64/M	Laryngeal nerve palsy	Unproven sarcoidosis (diagnosed by X-ray)	NA	(-)/(-)	(+)	AL(-) AA(-)		No
Takeshita *et al*.[12]	71/F	Dry cough	Expose to radiation (atomic bomb survivor)	4	(-)/(-)	(+)	AL(+)	Lymph node	No
Ordrmann *et al*.[13]	61/M	Chest pain pneumonia	(-)	8-10	(+)/(+)	(+)	NA		No
Takamori *et al*.[2]	33/F	No	Rheumatoid arthritis	8.3	(+)/(+)	(-)	AA(+)	Thymus	No

M, male; F, female; NA, not available; AL, light chain amyloid; DM, diabetes mellitus; AA, amyloid A.

Although very rarely, amyloidosis presented as an isolated mediastinal mass has been reported. Since the first report by Osnoss and Harrell[6] in 1980, only nine cases have been reported in the English literature (Table 1).[2,6-13] Several cases of amyloidosis presenting as mediastinal lymphadenopathy have been reported. However, these cases were excluded, because most of them revealed multiple lymphadenopathy and were distinguishable from the mediastinal mass on radiologic examination. Isolated mediastinal mass not involving other organs was observed in only five out of nine cases.[2,9,11-13] Despite the common presentation as mediastinal mass, the involved organ was not common in each case. The thymus was only involved in one case,[2] whereas lymph node involvement was noted in four cases.[6,7,9,12] In the other four cases, no definite organ involvement was seen. These cases could probably be categorized into amyloidosis arising in soft tissues, according to Krishnan *et al.*,[14] who reported tumor presentation of amyloidosis in soft tissues. The type of amyloidosis was different in each case. Four cases were shown to be light chain amyloidosis upon immunohistochemical study, three of which were associated with plasma cell disorders.[7-9,12] One case was proved as amyloid A amyloidosis in a patient with rheumatoid arthritis.[2] One case showed negative immunohistochemical stain for kappa/lambda light chain and amyloid A.[11] This type of amyloidosis was not evaluated in the other three cases.[6,10,13] Histologically, lymphoplasma cell infiltration with occasional multinucleated giant cells characterized in seven cases.[6-8,10-13] Clinically, respiratory symptoms such as cough, sputum, dyspnea, chest pain, and airway obstruction were observed in six cases.[7-10,12,13] Radiologically, calcification or ossification was marked in four cases.[2,8,9,13]

The diagnosis of localized amyloidosis is based on exclusion. Shah *et al.*[15] emphasized the importance of complete screening for amyloid fibril type and systemic conditions in amyloidosis of the respiratory tract. Our patient showed positivity for kappa and lambda light chain in areas of Congo red positivity but negativity for amyloid A protein. In addition, no tangible proof on the involvement of other organs was found. Furthermore, no evidence of plasma cell dyscrasia, normal serum IgG, IgA and IgM, normal ratio of kappa and lambda in the serum, no abnormal band on serum protein electrophoresis and immunofixation for IgG, IgA, and IgM were found. According to Palladini *et al.*,[16] the combination of serum and urine electrophoresis immunofixation and free light chain assay with kappa and lambda ratio enables the detection of amyloidogenic light chain with 100% sensitivity.

To the best of our knowledge, this is the first case report on localized primary thymic amyloidosis presented as an isolated mediastinal mass. Although extremely rare, the mediastinum could be a site for localized amyloidosis. Therefore, amyloidosis should be considered as a differential diagnosis of mediastinal mass.

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