

# Exceptional Cause of Massive Lymph Node Enlargement: Primary Localized Amyloidosis

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**Abstract** Amyloidosis is very rarely the cause of lymph node enlargement. In the localized form of the disease, amyloidosis commonly attains the bladder, the lung and the skin. Lymph node amyloid deposition is very unusual in the localized form of the disease. In particular, cervical and mediastinal sites are uncommon. We report an exceptional case of primary localized AL amyloidosis presenting as generalized lymph node enlargement. Our patient was initially treated by colchicine but in front of disease progression, a treatment with prednisone and melphalan was necessary for stabilization. Clinician should consider primary amyloidosis in the check-list of etiologies causing lymph node enlargement.

**Keywords:** amyloidosis, lymphadenopathy, Localized

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## 1. Introduction

Cervical and mediastinal massive lymph node enlargement are usually often caused by infection, lymphoma, metastasis cancers and granulomatous diseases, but amyloidosis is very rarely the cause.

Localized amyloidosis resulting in deposit of amyloid on individual organs, is rare [1] and cervical and mediastinal lymph node localizations, are uncommon [2]. AL amyloidosis, due to deposit of immunoglobulin light chains, is more often related to plasma cell dyscrasia [3]. We showcase in this paper an exceptional case of primary localized amyloidosis presenting as generalized lymph node enlargement.

## 2. Case Report

A 56-year-old Tunisian man with no pre-existing medical problem has experienced progressive and massive bilateral enlargement of cervical and axillary lymph nodes. He did not show any particular symptoms such as fever and weight loss. He only complained of recent weakness. He was a nonsmoker and did not have a record of infectious diseases, such as tuberculosis, in family history. Cervical examination revealed bilateral and massive cervical lymph nodes, with submandibular and retroauricular lymphadenopathies (Figure 1). These nodes were poorly mobile, firm and non painful. Physical examination

of the other systems revealed peripheral bilateral axillary and inguinal lymph nodes, with no other abnormalities. Splenomegaly and liver enlargement weren't noted on abdominal palpation. Dysautonomia and neuropathy were not seen in neurological examination.



**Figure 1.** Physical examination showing gross adenopathy

Laboratory data showed normal values for leucocytes, hemoglobin, platelet count, creatinine, calcium, liver enzymes and uric acid. The erythrocyte sedimentation rate was 56 mm/h and C reactive protein was normal. Serum immunoelectrophoresis revealed monoclonal elevation of immunoglobulin (Ig) M/Kappa (1200 mg/dL, normal

value: 50 -250mg/dL). Urine electrophoresis showed positive kappa free light chains. A contrast whole-body computerized tomography (CT) scan showed generalized, lymph node enlargement including cervical (Figure 2), mediastinal (Figure 3), axillary, retroperitoneal and inguinal group localizations with sizes of up to 3x3x3 cm.



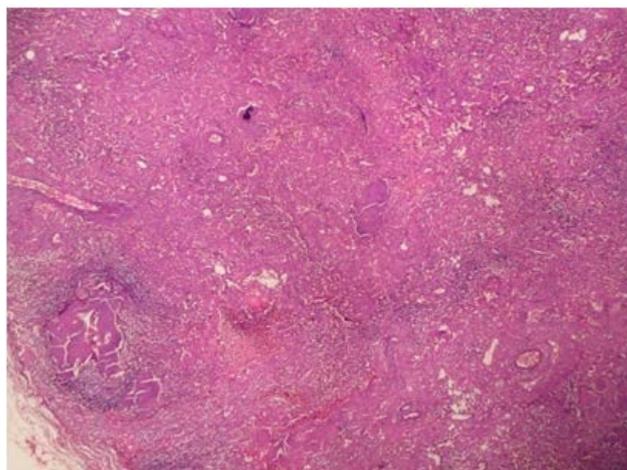
**Figure 2.** CT scan with medium contrast, showing inhomogeneous enhancement of the masses



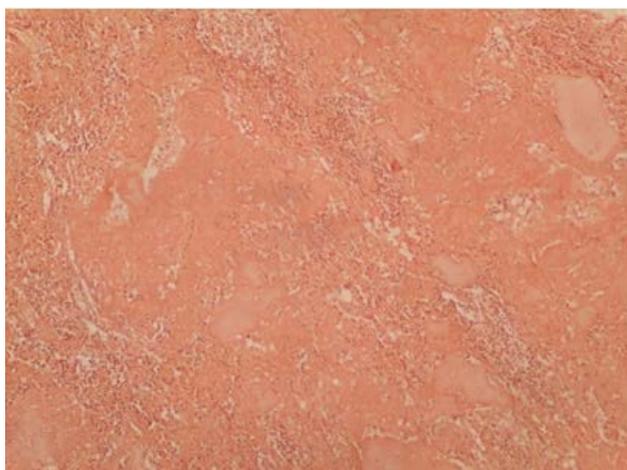
**Figure 3.** Chest CT showed mediastinal and hilar lymphadenopathy

Lymphadenopathies enlargement due to infection, neoplasmand granulomatuous diseases were considered. Infectious investigations including sputum for acid-fast stain, quantiferon test, tuberculin skin reaction and bone marrow culture were negatives. Endobroncho-alveolar fluid tested negative for acid-fast bacilli. No caseating granulomas in bone marrow and lymph nodes biopsies were found. Further investigations, including research of

infectious diseases such as brucellosis, toxoplasmosis, viral hepatitis, Epstein-Barr virus, cytomegalovirus, parvovirus B19and HIV were all negatives. The angiotensin-converting enzyme (ACE) level was normal. Bronchoscopy did not show any signs of bronchial lesions. Gastroduodenal endoscopy revealed normal biopsies. Colonoscopy didn't reveal any abnormalities. Rhinolaryngologic endoscopy was normal. Biopsy and histological study of two distinct cervical lymph nodes, showed amorphous materials that were pink on Congo red staining (Figure 4, Figure 5), with a birefringence under polarized microscopy. Immunohistochemical studies of these samples were found to be negative for amyloid A protein (AA), and positive for amyloid light chains (AL). Examination of bone marrow aspiration and bone marrow biopsy revealed no abnormalities; there weren't lymphoplasma cells proliferation and no tumoral or atypical cells. Cranial, vertebral and limbs x-ray were normal. A diagnostic of primary and localized AL-amyloid lymph nodes, without myeloma, was made. Electrocardiogram and echocardiogram didn't show any abnormalities. Cardiac troponin I was at normal value. Rectal biopsies were negatives for amyloid deposits.



**Figure 4.** Hyaline-like amorphous deposits stained with hematoxylin-eosin (HE X 200)



**Figure 5.** Extracellular deposits positive for Congo-Red staining (original X 100)

The patient was treated at first with colchicine. Follow-up examination and computed tomography 6 months later showed growth in size of lymph nodes, being painful. A

combination of melphalan and prednisone was administered with stabilization of disease. Evolution one year later didn't record new lymph node enlargement. An easy way to comply with the journal paper formatting requirements is to use this document as a template and simply type your text into it.

### 3. Discussion

We reported a new case of primary and localized lymph nodes amyloidosis with massive cervical, mediastinal, axillary and abdominal localizations. Amyloidosis can be classified as localized or systemic disease and into primary or secondary amyloidosis [1]. In systemic amyloidosis, lymph node localization is infrequent and very rare. In the localized form of the disease, amyloidosis commonly attains the bladder, the lung and the skin [4]. Lymph node amyloid deposit is very unusual in the localized form of the disease. Cervical and mediastinal lymph node sites, as described in this case, are uncommon. Prior to 2010, studies focusing on cervical lymph nodes amyloidosis, have recorded only nine such cases [5]. In a study analyzing around 80,000 lymph nodes specimens, amyloid deposit was seen in 18 cases; among which there were 3 cervical localizations and one mediastinal location [2].

In this case, localized amyloidosis was retained after searching and screening for systemic amyloid deposits. Patients with the systemic form of amyloidosis often have renal, cardiac, digestive, liver, neurological or skin problems [4]. For our patient, proteinuria was negative. Electrocardiogram, echocardiogram and cardiac troponin were normal. Gastroduodenal endoscopy with biopsies, colonoscopy and rectal biopsies didn't reveal any abnormalities. Neurological and skin examinations were normal.

As lymph nodes localization in amyloidosis is very rare, other diseases causing massive lymphadenopathy were searched. In this case, tuberculosis and other infectious disease causing lymphadenopathies were eliminated. Sarcoidosis was ruled out. Lymphoma was suspected. However, histological examination of lymph nodes specimens and bone marrow biopsy were normal. For metastasis searching, lymph nodes biopsies didn't detect suspect cells. Whole body CT, digestive, respiratory and rhinolaryngologic endoscopies were normal.

AL amyloidosis is more often related to plasma cell dyscrasia [3]. In this case, primary amyloidosis without myeloma was retained. Examination of bone marrow aspiration and bone marrow biopsy didn't reveal abnormal plasma cells. Cranial and peripheral skeletal x-ray were normal. Serum calcium, creatinine and hemoglobin levels were within normal limits. Serum immunofixation for this patient revealed high monoclonal IgM/kappa while AL amyloidosis related to monoclonal IgM was extremely rare. It has been reported that IgM-AL amyloidosis can be described as a pathology causing less systemic organ damages [6], as noted for this patient. In this IgM-AL amyloidosis form, more rates of lymph-node involvement and Kappa light chains association were reported [6].

Because AL amyloidosis is due to deposits of immunoglobulin light chains, administration of drugs effective against plasma-cell dyscrasias, is beneficial in AL amyloidosis [7]. Therapy associating melphalan and prednisone is recommended to improve responses and survival in systemic amyloidosis [8,9]. Treatment of localized forms of amyloidosis such as generalized lymph nodes deposits remain unclear. It is still a subject of debate whether patients with localized amyloidosis should be treated with the same chemotherapy protocol. Some authors consider the surgical excision in lymph nodes amyloidosis [10]. Our patient was initially treated by colchicine but in front of disease progression, a treatment with prednisone and melphalan was necessary for stabilization.

### 4. Conclusion

Lymph node amyloidosis is rare, cervical and mediastinal localizations are uncommon. Clinician should consider amyloidosis when discussing etiologies of lymph node enlargement. AL amyloidosis is due to deposits of immunoglobulin light chains. Therefore, administration of drugs effective against plasma-cell dyscrasias, is highly recommended.

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