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【 CASE REPORT 】

Localized Lymph Node Light Chain Amyloidosis

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Abstract:
The prognosis of systemic amyloid light chain (AL) amyloidosis is generally poor, hence requiring chemotherapy or hematopoietic stem cell transplantation, while the prognosis of localized AL amyloidosis without an abnormal monoclonal immunoglobulin light chain is good. Localized AL amyloidosis has been previously reported to be observed in pulmonary, urinary tract, gastrointestinal, oropharyngeal, and laryngeal sites. However, only a few cases of localized lymph node AL amyloidosis have so far been reported. We herein present a case of localized lymph node AL amyloidosis that could possibly be misdiagnosed as systematic AL amyloidosis.

Key words: localized AL amyloidosis, lymphadenopathy, PET-CT, systemic AL amyloidosis

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Introduction

Amyloidosis is a disease in which the nonbranching linear fibrils of protein are deposited in the extracellular spaces either systemically or locally (1). Localized light chain (AL) amyloidosis has a better prognosis compared to systemic AL amyloidosis. It is significantly important to establish the proper diagnosis of localized AL amyloidosis to rule out systemic AL amyloidosis. Although localized lymph node AL amyloidosis has not been sufficiently recognized because of its limited number of cases, it is important that patients be monitored to avoid a progression to systemic disease. We herein present a case of localized lymph node AL amyloidosis that was relatively similar to systemic AL amyloidosis. We also performed a literature review on AL amyloidosis, emphasizing the difference between systemic and localized AL amyloidosis.

Case Report

An 88-year-old Japanese female patient without any past medical history complained of bilateral cervical lymphadenopathy. She was conscious and had experienced painless right cervical lymphadenopathy for 1 year. She presented in our hospital following the chief complaint of a growing lymphadenopathy on both sides of her neck and inguinal regions for 2 weeks. Her lymph nodes measured approximately 1 cm in diameter and were elastic hard. However, there was no tenderness and no limits in her mobility. The results of her laboratory data including complete blood count, lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase, creatinine, soluble interleukin-2 receptor, C-reactive protein, sedimentation rate, urinalysis, globulin, antinuclear antibody, rheumatoid factor, carcinoembryonic antigen, and carbohydrate antigen 19-9 revealed no abnormalities. Furthermore, the results of her cardiology laboratory data including B-type natriuretic peptide (BNP), pro-BNP, and troponin T were within the reference values. Whole-body contrast computed tomography (CT) revealed bilateral cervical, axillary, and inguinal lymphadenopathy (Fig. 1A).

Lymph node excisional biopsy was performed from the right inguinal region. An acidophilic and unstructured substance was found inside with tissue spheres and multinucleated giant cells in the surrounding region (Fig. 2). Since the result of Congo red staining was positive, the pathological diagnosis was amyloidosis. The result of the immunostaining of commercially available antibodies against immunoglobulin light chain (IgLC) kappa type was positive. In view

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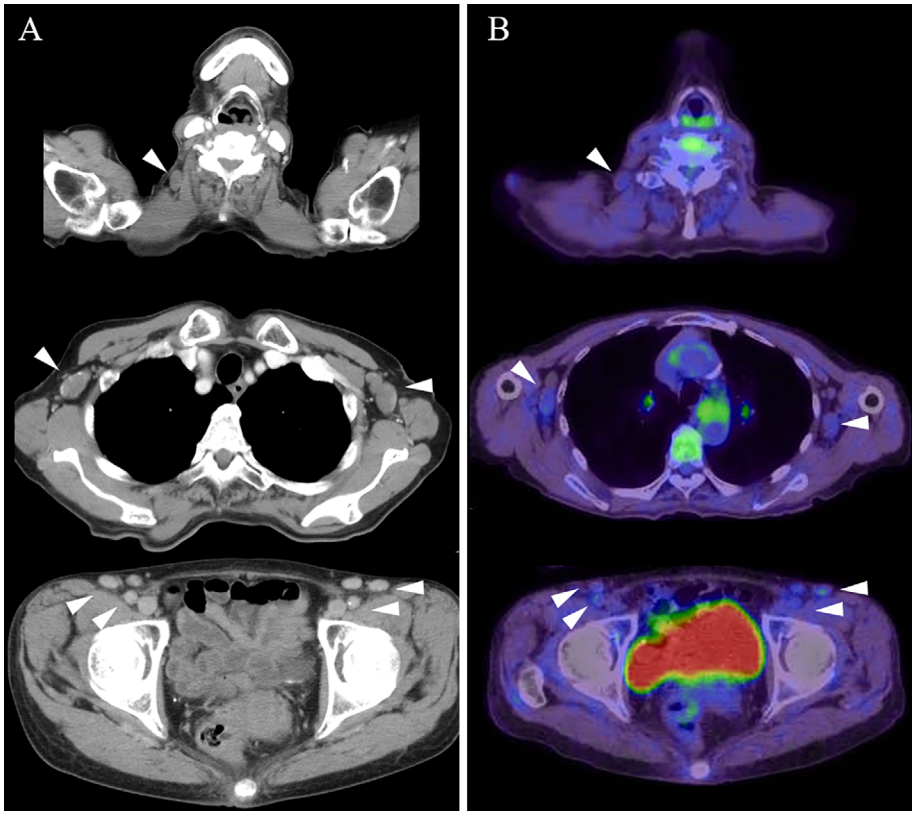

Figure 1. **A) Whole-body contrast CT scan. B) Positron emission tomography-CT scan. CT: computed tomography**

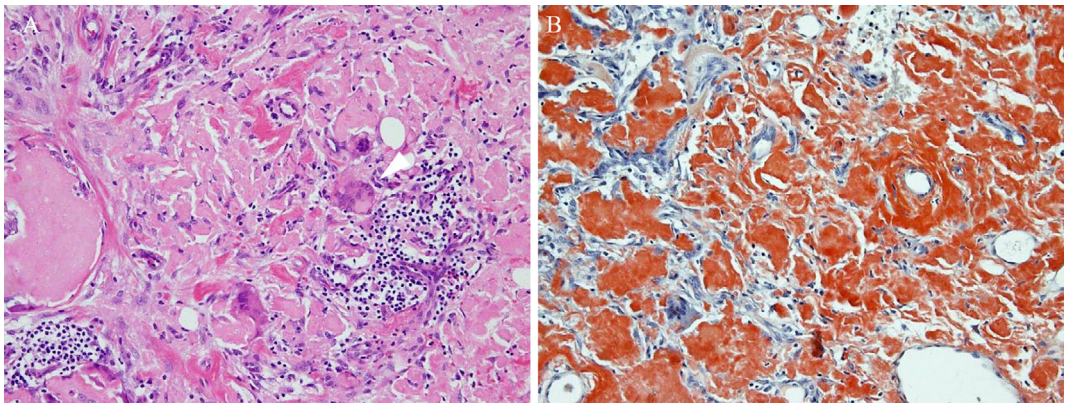

Figure 2. **A) Hematoxylin and Eosin staining of a lymph node (×40). A white arrow shows giant cells. B) Congo red stain (×40).**

of the fact that the lesions were fixed by formalin, staining for IgLC kappa-type constant region 116-133 was additionally performed to confirm the diagnosis, and the result was positive compared to anti-lambda constant region 118-134 staining (Fig. 3) (2). The results of the staining for a polyclonal antibody to transthyretin and antibody 118-134 against IgLC lambda-type constant region and a monoclonal antibody to amyloid A were negative. Considering these findings, she was diagnosed with AL kappa-type amyloidosis.

The systemic evaluation of amyloidosis in the other organs were also performed. There were no specific findings in upper and lower endoscopy, as well as for a random skin biopsy, cardiac ultrasound, cardiac contrast magnetic resonance imaging, and bone marrow aspiration and biopsy. M protein was not found in the serum or urine in immunoelectrophoresis and immunofixation. The free light chain ratio in the serum and urine was within the reference range. Positron emission tomography-CT (PET-CT) was also performed to confirm lymph node accumulation and to exclude the presence of other malignant tumors; however, there were no particular findings including the presence of lymph nodes (Fig. 1B).

Based on these negative findings, we established the diag-

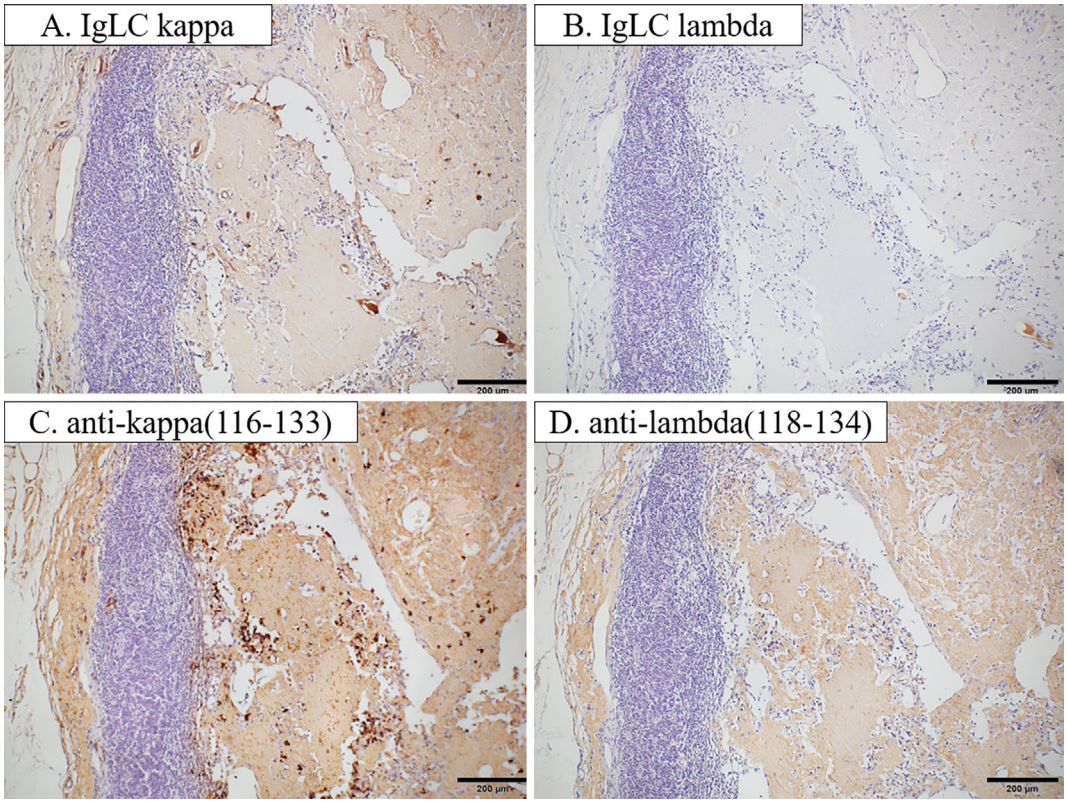

Figure 3. **Immunostaining of a lymph node. A) antibodies against IgLC kappa type, B) antibodies against IgLC lambda type, C) anti-kappa (116-133), and D) anti-lambda (118-134). IgLC: immunoglobulin light chain**

nosis of localized AL amyloidosis in the lymph nodes. She received a careful follow-up examination without any treatment and showed no disease progression for 1 year.

Discussion

It is significantly important for patients who are diagnosed with localized AL amyloidosis to continue ruling out systemic AL amyloidosis even if localized AL amyloidosis rarely developed into systemic amyloidosis (3). Systemic AL amyloidosis is characterized by the deposition of amyloid fibrils on major tissues, such as the heart, gastrointestinal tract, kidney, and nerve system, derived from monoclonal IgLC (4, 5). It is generally associated with plasma cell disorders and lymphoproliferative disorders, producing excessive and abnormal immunoglobulin chains. Moreover, in a series of amyloid cases from Boston University, a total of 2% of all patients diagnosed with all types of amyloidosis generally present with lymph node lesions (3). Regarding AL amyloidosis detected in the lymph nodes, 29 of the 47 patients were diagnosed with systemic AL amyloidosis and 2 patients were initially diagnosed with localized lymph node AL amyloidosis. These two cases eventually developed systemic disease requiring chemotherapy. Thus, AL amyloidosis accompanied with swollen lymph nodes usually indicates systemic AL amyloidosis. Additionally, it should be emphasized that localized AL amyloidosis sometimes presents with multiple nodules even in a single organ as reported in the tongue (6), larynx (7), and pulmonary (8) and urinary tract (9). Localized AL amyloidosis with multiple lymph nodes is consistent with Westermark P's review (10), "localized AL amyloidosis usually appears as one, often tumor-like lesion, although multiple nodules may occur." While several amyloidosis cases diagnosed by lymph node biopsy have been reported, only a few cases of localized AL lymph node amyloidosis have so far been reported (3, 11); the pathology of most cases of localized AL amyloidosis remains unknown and it is therefore necessary to elucidate the pathology.

It is significantly important to determine the monoclonal protein in the serum and urine and to examine the heart, intestinal tract, skin, and bone marrow to rule out systemic AL amyloidosis. While findings indicating systemic AL amyloidosis were not observed in our case, this case had multiple lymphadenopathy, which might lead to the misdiagnosis of systemic AL amyloidosis. Thus, different perspectives are significantly required.

The histopathological findings in the affected tissues are also considered to be beneficial in differentiating localized AL amyloidosis from systemic AL amyloidosis. The presence of giant cells has been reported to be one of the most important clues in the diagnosis of localized AL amyloidosis because systemic AL amyloidosis generally has no giant cells (12). However, the lymph node lesions in systemic AL amyloidosis have been reported to have giant cells. Therefore, further studies to rule out systemic AL amyloidosis

when diagnosing localized AL amyloidosis are required for patients presenting with giant cells in their lymph node lesions (10).

We ruled out the other types of amyloidosis by immunostaining. Although it is possible to make a diagnosis with a commercial-based antibody, the reaction of the antibody sometimes includes false positives and false negatives on formalin-fixed, paraffin-embedded sections. Polyclonal antibodies against the synthetic peptides corresponding to positions 116-133 of the IgLC kappa and positions 118-134 of the IgLC lambda were used to confirm the amyloidosis classification in this case (2). The former staining was stronger than the latter; hence, we classified the kappa type of AL amyloidosis (Fig. 3).

To rule out systemic AL amyloidosis and other hematologic diseases, a thorough image investigation is required. Additionally, using a PET-CT scans to distinguish systemic AL amyloidosis from localized AL amyloidosis has been reported. Fluorodeoxyglucose (FDG) accumulation was not detected in systemic AL amyloidosis by PET-CT scans, while FDG accumulation was detected in localized AL amyloidosis (13). Westermark et al. hypothesized that giant cells in localized amyloidosis are directly involved in the transformation of the soluble full-length light chains into insoluble fibrils formed from N-terminal light chain fragments (10), possibly resulting in a high FDG uptake in the surrounding giant cells and other immunoreactive cells including macrophages, monocytes, and leukocytes. While giant cells were detected in our case, no FDG accumulation was detected, which is possibly due to the low activity of localized inflammation in the affected lymph nodes. Since the number of studies assessing the differential diagnosis of systemic or localized AL amyloidosis using PET-CT is limited, physicians should be more cautious when interpreting PET-CT scans. While systemic AL amyloidosis has a poor prognosis, localized AL amyloidosis has a good prognosis and did not affect the survival of the patients compared with that expected in the British population in the case series Mahmood et al. reported (10, 14). However, they also suggested that the cases with a circulating monoclonal protein from the beginning had a high risk of progression to systemic AL amyloidosis (15). Therefore, a careful follow-up is necessary for patients with a monoclonal protein. In addition, since localized lymph node AL amyloidosis may be related to the presence of a monoclonal protein, a careful follow-up for patients with localized lymph node AL amyloidosis is also required.

Localized lymph node amyloidosis has been reported to have heavy chain (AH) or AH/AL amyloid components (16) that can be analyzed by amino acid sequencing or immunostaining of the immunoglobin heavy chain. However, we were not able to perform these assays. Thus, it is unknown whether elements of AH amyloid were present in our case.

In summary, we herein presented an extremely rare case of localized AL amyloidosis that was only deposited in multiple lymph nodes. Considering that localized AL amyloidosis is not well recognized by physicians and hematologists, its accurate diagnosis with the exclusion of systemic AL amyloidosis is significantly important.

The authors state that they have no Conflict of Interest (COI).

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