Castleman Disease Presenting as Lymphadenopathy in a Female with Systemic Lupus Erythematosus: A rare case report

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Abstract

Background: Castleman disease is an infrequent disease that affects the lymph nodes and related tissues. The condition may manifest with lymphadenopathy, characterized by the enlargement of the lymph nodes, alongside additional symptoms such as high fever, nocturnal sweating, exhaustion, and loss of body mass. The diagnosis of Castleman disease typically entails a multifaceted approach that includes a physical examination, imaging modalities, and a biopsy of the lymph nodes that are affected. The selection of treatment modalities is contingent upon the classification and extent of the disease. Systemic lupus erythematosus (SLE) has been identified as a potential risk factor for the development of lymphoma, a condition that may manifest with lymphadenopathy resembling Castleman disease. Hence, it is crucial for individuals diagnosed with SLE and exhibiting lymphadenopathy to undergo a comprehensive assessment to exclude the possibility of any other associated disease. Although lymphadenopathy is a common symptom shared by both Castleman illness and SLE, these diseases have distinct etiologies and are treated in different ways. Seeking advice from a healthcare practitioner is crucial in order to obtain an accurate diagnosis and effective treatment.

Case presentation: A 39-year-old female patient with a history of SLE since 18 years ago and lupus nephritis since six years ago which treated with Mycophenolic Acid 2 grams daily, Hydroxychloroquine 400 mg daily, and low doses of Prednisolone. Also, Mycophenolic Acid has discontinued for him five months ago due to the reduction of proteinuria and the control of the disease

Conclusions:

Although the association of Castleman Disease with SLE is infrequent, establishing a connection between them could prove advantageous in the treatment and etiology of diseases.

Keywords:

Castleman Disease, Lymphadenopathy, Systemic Lupus Erythematosus

List of abbreviations:

SLE: Systemic lupus erythematosus

LAD: Lymphadenopathy

CD: Castleman disease

IHC: Immunohistochemistry

Introduction

Lymphadenopathy (LAD) can present features including connective tissue diseases, malignancy, and infections. A histopathological evaluation for a definitive diagnosis should be conducted in specific clinical scenarios. Systemic lupus erythematosus (SLE) is an autoimmune and chronic disease involving multi-organs (1, 2).

In approximately 60% of SLE cases, generalized or localized LAD are prevalent findings. Numerous case reports have shown that the SLE's initial clinical manifestation might be generalized LAD and is considered as an SLE non-specific feature (3, 4).

Castleman disease (CD) is a rare lymphoproliferative disorder characterized by heterogeneous manifestations from diffuse recurrent episodes of lymphadenopathy with severe systemic symptoms to asymptomatic LAD. There are some CD case reports accompanying SLE.(5-7). Hence, this article illustrates a rare CD case presenting LAD in a patient with SLE.

Case presentation

A 39-year-old female patient with a history of SLE since 18 years ago and lupus nephritis since six years ago which treated with Mycophenolic Acid 2 grams daily, Hydroxychloroquine 400 mg daily, and low doses of Prednisolone. Also, Mycophenolic Acid has discontinued for him five months ago due to the reduction of proteinuria and the control of the disease.

The patient came to the clinic complaining of fever, shortness of breath, and malar rash for a few days. His laboratory test showed 3100 mg per 24 hours proteinuria, and with diagnosed with SLE flare-up and evaluated for LAD admitted to the Rheumatology ward.

During the physical examination in the ward, blood pressure: 120/80, respiratory rate: 20, body temperature: 38.7, Pulls rate: 89, malar rash, 2+ pitting edema, and crackles in the middle and lower right lungs were detected. Also, numerous LADs were found in the bilateral axillary and cervical area, while other physical examinations were normal. Table 1 illustrates the laboratory tests.

Due to the fever and shortness of breath, a chest CT scan and Covid PCR were performed for the patient, and the CT scan findings confirmed pneumonia; also, there is no evidence of LAD in the mediastinum, and the PCR test result was negative. So, broad-spectrum antibiotics were started for the patient for two weeks, and the patient's respiratory symptoms improved. Furthermore, according to the diagnosis of SLE flare-up, Prednisolone 1mg/kg was started for the patient; hence, her edema, malar rash, and respiratory symptoms improved over time. Also, an ultrasound was performed based on LAD, which was detected during the physical examination. Multiple LADs were found in the cervical and both sides of Axillary areas; the largest was reported in the left axillary area with a size of 43mm x 19mm. Due to the suspicion of lymphoma, a CT scan of the abdomen and pelvis with oral and intravenous contrast was also performed for lymphadenopathy, but no lymphadenopathy was found.

For evaluation of the LADs, a biopsy was performed on one of the axillary lymph nodes. The pathology results and IHC (IHC results: CD20: positive in lymph nodules, Pax 5: positive in lymph nodules, BCL 6: positive in GCs, EMA: Negative, CD30: Negative, Ki 67: High in GCs, CD3: Positive in small T cells) confirmed the diagnosis of CD type Hylan vascular.(figure 1)

Discussion

SLE cases may manifest with localized or generalized LAD. Although LAD is not regarded in the SLE classification criteria, in cases with SLE, LAD is a frequent presentation. Biopsy of lymph nodes was more common in SLE cases to differentiate malignant or benign causes in recent years. The varying coagulative necrosis degrees histologically with hematoxylin bodies in lesions of the lymph node are specific to SLE. While these feature findings are found in the biopsy. Overall, nonspecific findings like hyperplasia of follicular are detected in biopsy specimens (4, 8).

The CD is a lymphoproliferative disorder polyclonal group with unclear etiology, showing two main characteristic histopathologic features: plasma-cell type and hyaline vascular type (9). Based on the disease course and clinical manifestation, CD is categorized into unicentric CD (UCD), a single lymph node involved, and is a reversible and localized disease (9, 10). Multicentric CD (MCD) is a progressive and systemic with LAD in multiple nodes, often fatal disease (11). Recently, 'regional CD' or 'oligocentric CD,' referred to as an intermediate subtype, has been described. A few lymph nodes are involved and are mostly deliberate to have a UCD-similar clinical course (12). According to these definitions and the patient's CT scan results, he can be MCD or oligocentric CD. Most cases with MCD are plasma cell type, while UCD is the hyaline vascular type like ours (1).

The CD histopathological findings have been relatively rarely reported in SLE cases. Recently, the lymph node biopsy frequency for SLE subjects exhibiting lymphadenopathy has elevated to exclude lymphoma risk, which results in case reports accumulation about the morphology of CD manifesting in SLE patients with LAD. A study showed that 26 percent of SLE cases with LAD demonstrated similar CD histological characteristics, which shows a close correlation between SLE and CD (5, 13).

A study showed SLE and CD together. In their case, only one lymph node was involved in the cervical area, while in our case, several cervical lymph nodes were involved. Also, in their cases, the onset of SLE, CD was diagnosed, and it was plasma cell type, while in our case, it was of the Hylan vascular type, and LAD was several years after initiating the SLE (7). In the study of Zhang et al. (14), another CD case of Hylan vascular type has been shown, in which the LAD was generalized and responded well to Rituximab treatment. Additionally, Simko et al. and Hu et al. reported two children with CD and SLE at 11 and 16 years, respectively.

Conclusion

In conclusion, our case presented a female with SLE who, which after 18 years, developed CD, which is a rare complication of SLE.

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Author contributions

All authors approved the final manuscript.

Availability of data and material

Considering that this study is about a rare disease availability to patients and data may hard to some extent.

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Competing interests

The authors declare that they have no competing interests

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Table 1. Laboratory parameters of the patient

Laboratory parameters	Patient's values	Normal range
Leukocyte count, per μL	21.5×10^3 (85% Neut, 8.8% Lymph)	$4\text{-}10\times10^3$
Hemoglobin, g/dL	11.7	12.3-15.3
Platelet count, per μL	374000	150000-450000
Albumin	3.3	3.5-5.2
ESR, mm/h	80	0-30
CRP, mg/L	19	< 6
AST g/dL	17	8-35
ALT, g/dL	15	8-35

Laboratory parameters	Patient's values	Normal range
Total Bilirubin	0.3	0.2-1.2
Direct Bilirubin	0.1	0-0.4
Alp	301	64-306
LDH, IU/L	525	100-300
BUN, mg/dL	53	7-20
Creatinine, mg/dL	1.25	0.5-1.1
Sodium	136	136-145
Potassium	4.3	3.7-5.5
Magnesium	1.8	1.8-2.6
24 h urine protein, mg per day	5346	< 100
ANA, IU/mL	179	< 12 Negative Equivocal > 18 Positive
Anti-dsDNA, IU/mL	5.2	< 24
C3, mg/dL	41	90-180
C4, mg/dL	6	10-40
CH50, mg/dL	80	51-150
Ferritin	37	5 - 148
HBs Ag	0.1	>1 Positive
HBs Ab	0.1	> 10 Reactive
HAV IgM	0.1	> 1.2 Positive
HCV Ab	0.1	> 1.0 Reactive
HBc Ab	0.2	> 1.1 Positive
HIV Ab	0.1	< 1.0 Positive
T.S.H	2.3	0.39-6.16

Neut, neutrophil, Lymph, lymphocyte; ESR, Erythrocyte sedimentation rate, C - reactive protein; AST, aspartate aminotransferase; ALT, aspartate alanine transferase; Alp, Alkaline phosphatase; LDH, lactic dehydrogenase; BUN, Blood Urea Nitrogen; ANA, anti-nuclear antibody; anti-dsDNA, anti-double stranded DNA; HBs Ag, Hepatitis B Surface antigen; HBs Ab, Hepatitis B surface antibody; HAV IgM, Hepatitis A virus IgM; HCV Ab, Hepatitis C antibody; HBc Ab, Hepatitis B core antibody; HIV Ab, Human Immunodeficiency antibody; T.S.H, Thyroid Stimulating Hormone

Figure 1 . IHC(A&B) and a microscopic view (histologic) of lymph node(C&D) (H&E, ×10)