

CASE REPORT

Castleman disease presenting as lymphadenopathy in a female with systemic lupus erythematosus: A rare case report

Alireza Khabbazi¹ | Amirreza Khalaji^{1,2}  | Omid Pourbagherian² | Amir Vahedi³ | Mehdi Jafarpour¹ 

¹Connective Tissue Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

²Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

³Department of Pathology, Tabriz University of Medical Sciences, Tabriz, Iran

Correspondence

Mehdi Jafarpour, Connective Tissue Diseases Research Center, Tabriz University of Medical Sciences, Flat 1, Imam Reza Hospital, Tabriz, Iran.
Email: jafarpourmehdi1360@gmail.com

Key Clinical Message

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. A 39-year-old female patient with a history of SLE since 18 years ago and lupus nephritis since 6 years ago which treated with Mycophenolic Acid 2 g daily, Hydroxychloroquine 400 mg daily, and low doses of Prednisolone. Also, Mycophenolic Acid has discontinued for her 5 months ago due to the reduction of proteinuria and the control of the disease. 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

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1 | 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.

2 | CASE PRESENTATION

A 39-year-old female patient with a history of SLE since 18 years ago and lupus nephritis since 6 years ago which treated with Mycophenolic Acid 2g daily, Hydroxychloroquine 400mg daily, and low doses of Prednisolone. Also, Mycophenolic Acid has discontinued for her 5 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 3100mg per 24h 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, Pulse 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 2 weeks, and the patient's respiratory symptoms improved. Furthermore, according to the diagnosis of SLE flare-up, Prednisolone 1 mg/kg was started for the patient; hence, her edema, malar rash, and respiratory symptoms improved over time. Also,

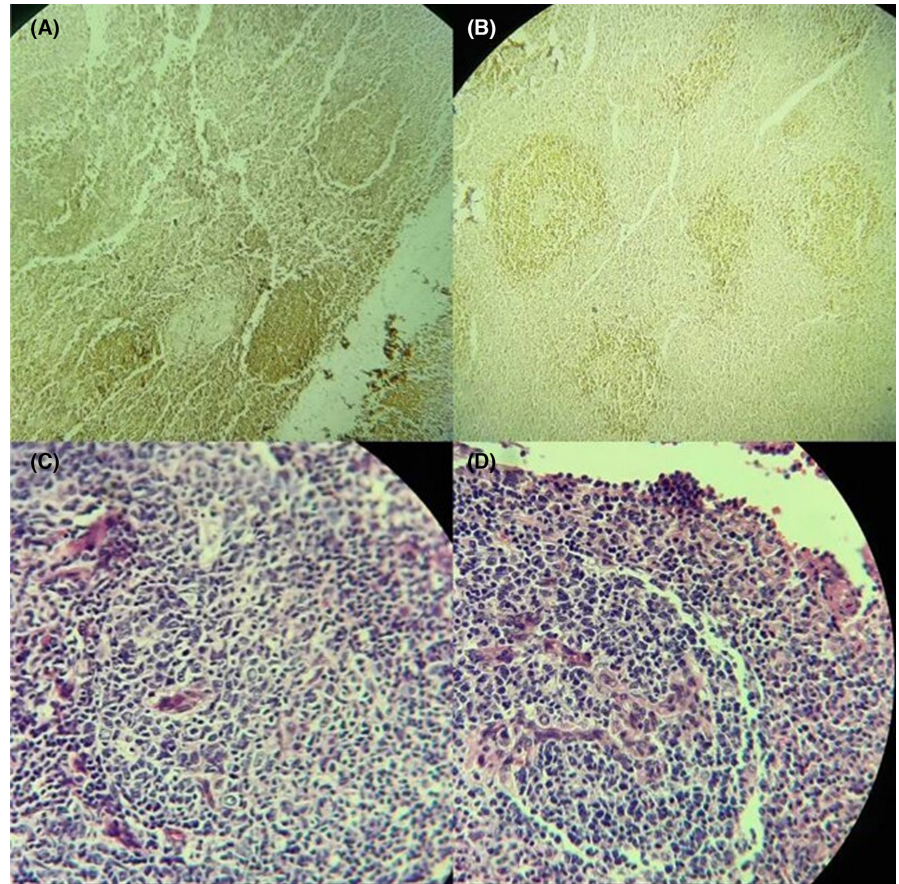
TABLE 1 Laboratory parameters of the patient.

Laboratory parameters	Patient's values	Normal range
Leukocyte count, per μL	21.5×10^3 (85% Neut, 8.8% Lymph)	$4\text{--}10 \times 10^3$
Hemoglobin, g/dL	11.7	12.3–15.3
Platelet count, per μL	374,000	150,000–450,000
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
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
24h urine protein, mg per day	5346	<100
ANA, IU/mL	179	<12 Negative 12–18 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

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

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 43×19 mm. Due to the suspicion of lymphoma, a CT

FIGURE 1 IHC (A and B) and a microscopic view (histologic) of lymph node (C and D) (H&E, $\times 10$).



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 Hyaline vascular (Figure 1).

3 | DISCUSSION

Systemic lupus erythematosus 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 “oligo-centric 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 oligo-centric 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.

4 | CONCLUSION

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

AUTHOR CONTRIBUTIONS

Alireza Khabbazi: Data curation; formal analysis. **Amirreza Khalaji:** Project administration; validation. **Omid Pourbagherian:** Writing – review and editing. **Amir Vahedi:** Data curation; investigation. **Mehdi Jafarpour:** Funding acquisition; investigation; project administration.

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FUNDING INFORMATION

Not applicable.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

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



ETHICAL APPROVAL

This study has been performed according to the Declaration of Helsinki.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Amirreza Khalaji  <https://orcid.org/0000-0001-9909-1683>
Mehdi Jafarpour  <https://orcid.org/0009-0008-3555-8908>

REFERENCES

- Demirkan FG, Doğan S, Kalyoncu Uçar A, Sönmez HE, Aktay AN. Systemic lupus erythematosus complicated with Castleman disease: a case-based review. *Rheumatol Int.* 2021;41(2):475-479.
- Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum.* 2012;64(8):2677-2686.
- Gillmore R, Sin WY. Systemic lupus erythematosus mimicking lymphoma: the relevance of the clinical background in interpreting imaging studies. *BMJ Case Rep.* 2014;2014:bcr2013201802.
- Scott GD, Kumar J, Oak JS, Boyd SD, Raess PW, Gratzinger DA. Histology-independent signature distinguishes Kikuchi-Fujimoto disease/systemic lupus erythematosus-associated lymphadenitis from benign and malignant lymphadenopathies. *Am J Clin Pathol.* 2020;154(2):215-224.
- Xia JY, Chen XY, Xu F, Yang Y, Wang HY, Xue J. A case report of systemic lupus erythematosus combined with Castleman's disease and literature review. *Rheumatol Int.* 2012;32(7):2189-2193.
- De Marchi G, De Vita S, Fabris M, Scott CA, Ferraccioli G. Systemic connective tissue disease complicated by Castleman's disease: report of a case and review of the literature. *Haematologica.* 2004;89(4):Ecr03.
- Van de Voorde K, De Raeye H, De Block CE, et al. Atypical systemic lupus erythematosus or Castleman's disease. *Acta Clin Belg.* 2004;59(3):161-164.
- Kojima M, Nakamura S, Morishita Y, et al. Reactive follicular hyperplasia in the lymph node lesions from systemic lupus erythematosus patients: a clinicopathological and immunohistological study of 21 cases. *Pathol Int.* 2000;50(4):304-312.
- Keller AR, Hochholzer L, Castleman B. Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. *Cancer.* 1972;29(3):670-683.
- Castleman B, Towne VW. Case records of the Massachusetts General Hospital: case No. 40231. *N Engl J Med.* 1954;250(23):1001-1005.
- Kessler E. Multicentric giant lymph node hyperplasia. A report of seven cases. *Cancer.* 1985;56(10):2446-2451.
- van Rhee F, Oksenhendler E, Skralovic G, et al. International evidence-based consensus diagnostic and treatment guidelines for unicentric Castleman disease. *Blood Adv.* 2020;4(23):6039-6050.
- Kojima M, Nakamura S, Itoh H, et al. Systemic lupus erythematosus (SLE) lymphadenopathy presenting with histopathologic features of Castleman' disease: a clinicopathologic study of five cases. *Pathol Res Pract.* 1997;193(8):565-571.
- Zhang L, Jiao L, Wang SJ. Successful treatment with rituximab in a patient with Castleman's disease complicated by systemic lupus erythematosus and severe autoimmune thrombocytopenia. *Chin Med J (Engl).* 2015;128(18):2551-2552.

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