

Unraveling the diagnostic puzzle: Trio of lymphadenopathy, organomegaly, and lung nodules in cSLE

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Abstract

Background: Generalized lymphadenopathy with fever, pulmonary involvement, and organomegaly in children can be caused by infections, malignancies, or autoimmune disorders, with infections being the most frequent. However, childhood-onset systemic lupus erythematosus (cSLE) can present with similar features, making diagnosis challenging in the absence of classical signs.

Case presentation: A previously healthy adolescent boy presented with a two-month history of intermittent high-grade fever, progressive bilateral neck swelling, and significant weight loss. Examination showed pallor, generalized lymphadenopathy, and hepatosplenomegaly. Laboratory investigations revealed anemia, positive Coombs test, elevated ESR, and ferritin. Infectious workup was negative. Imaging showed lung infiltrates and lymphadenopathy. Lymph node biopsy was reactive, without evidence of malignancy. Autoimmune panel came as positive for ANA and anti-dsDNA, with low complements, meeting ACR/EULAR (American College of Rheumatology/European League Against Rheumatism) criteria for SLE. Although hematuria was absent, nephrotic-range proteinuria was documented with preserved renal function. Renal biopsy confirmed class V lupus nephritis. He was treated with IV methylprednisolone, oral steroids, and Tacrolimus for induction therapy. At six months, the patient was clinically stable with no systemic symptoms and showed SLEDAI 4 with proteinuria improving.

Conclusion: This case highlights the diagnostic challenge of cSLE when presenting with features mimicking infection or malignancy. Systematic exclusion of differentials enabled timely diagnosis. Despite being asymptomatic, the patient had pulmonary nodules on imaging, and renal involvement was present without hematuria—reinforcing that cSLE can affect multiple organs early. Prompt recognition and immunosuppressive therapy led to clinical stability, emphasizing the need to consider autoimmune causes in atypical pediatric presentations.

Keywords: SLE, Lupus nephritis, Generalized lymphadenopathy, Hepatosplenomegaly, Lung nodule

Abbreviations: ACR EULAR: American College of Rheumatology/European League Against Rheumatism; ANA: Anti-Nuclear Antibody; ANCA: Anti-Neutrophil Cytoplasmic Antibodies; Anti-dsDNA: Anti-double-stranded DNA antibodies; Anti-RNP: Anti-Ribonucleoprotein; Anti-CCP: Anti-Cyclic Citrullinated Peptide; BAL: Bronchoalveolar Lavage; CECT: Contrast-Enhanced Computed Tomography; cSLE: Childhood-onset SLE; EBV: Epstein-Barr Virus; ESR: Erythrocyte Sedimentation Rate; Hep-2: Human Epithelioma-2; LDH: Lactate Dehydrogenase; LL: Lupus Lymphadenopathy; LN: Lupus Nephritis; SLE: Systemic Lupus Erythematosus; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

Background

Generalized lymphadenopathy with fever is a common manifestation of several possible causes, including infections, malignancies, and connective tissue disorders, with infections being the most frequent. While not part of the diagnostic criteria for systemic lupus erythematosus (SLE), generalized

lymphadenopathy is not uncommon in SLE and may be the first symptom [1]. Childhood-onset SLE (cSLE) is a severe autoimmune disease presenting a wide range of symptoms affecting multiple organ systems and characterized by episodes of relapses and remission with varying disease activity. Sixty to eighty percent of cases can have kidney involvement at initial presentation [2]. In children, pulmonary involvement in SLE has been infrequently studied. Still, it can affect 7.6% to 75% of cSLE cases [3–6]. Here we report an interesting case of cSLE with lupus nephritis (LN) class V, presented with a range of clinical manifestations.

Case Presentation

A 16-year-old boy, developmentally normal, fully immunized, presented with a two-month history of intermittent high-grade fever spikes, with bilateral neck swelling, which was gradually progressive, without any difficulty in deglutition. The patient also reported a history of significant weight loss in this period. He had no significant past medical history or contact with tuberculosis or history of bone pain. He was hemodynamically stable and normotensive. General physical examination revealed some pallor, significant bilateral cervical and inguinal lymphadenopathy. Systemic examination demonstrated hepatosplenomegaly with no other systemic abnormalities. Differential diagnoses initially considered were infections, hematologic malignancies, and autoimmune diseases. Initially, empirical antibiotics were initiated while awaiting laboratory blood reports. Successive complete blood count showed a falling trend of hemoglobin while other cell lines were normal. Direct Coombs test was positive, although other parameters for diagnosing autoimmune hemolytic anemia, like increased LDH (Lactate dehydrogenase- 227 U/L), bilirubin, and reticulocyte, were absent. Malignancy like leukemia and lymphoma were a key concern due to the presence of generalized significant lymphadenopathy and

organomegaly however the peripheral smear demonstrated no atypical cells. For Infective workup, blood tests for Malaria, Dengue, Scrub typhus, Typhoid, Kala Azar, *Leptospira*, EBV (Epstein-Barr Virus), and Triple serology (hepatitis B, C, HIV) were negative. Blood, bronchoalveolar lavage (BAL), and urine cultures demonstrated no growth. Possibility of disseminated tuberculosis was also considered, however, Mantoux test and sputum and BAL for gastric aspirate were reported to be negative. The possibility of Hemophagocytic lymphohistiocytosis (HLH) was also considered due to prolonged fever and lymphadenopathy, but the diagnosis was not supported by other laboratory findings, and serum ferritin was only mildly elevated (236.8 ng/mL). Systemic juvenile idiopathic arthritis (sJIA) was ruled out due to the absence of arthritis, rash, or typical quotidian fever. Also, Rheumatoid factor and anti-CCP (Anti-Cyclic Citrullinated Peptide) were negative. CECT (Contrast-Enhanced Computed Tomography) thorax and abdomen showed multifocal consolidations in bilateral lungs and discrete homogeneously enhancing mediastinal nodes; discrete homogeneously enhancing cervical, supraclavicular, bilateral axillary, abdominal lymphadenopathy, and hepatosplenomegaly (**Figure 1 & 2**). Cervical lymph node biopsy revealed reactive lymphoid hyperplasia with preserved architecture and fatty hilum, without evidence of necrosis or granulomatous inflammation. These findings effectively ruled out tuberculosis (no caseating granulomas), sarcoidosis (absence of non-caseating granulomas), and Kikuchi-Fujimoto disease (no necrotizing histiocytic lymphadenitis). Given the exclusion of these differentials, autoimmune workup was planned, which showed low C3 and C4, ANA (Anti-Nuclear Antibody) on Hep2 (Human Epithelioma-2): 4+ (speckled), with anti-dsDNA (anti-double-stranded DNA antibodies) positive (908 IU/ml). ACR EULAR criteria for SLE diagnosis were established (Total score 18). Hematuria was absent; however, nephrotic-range proteinuria was documented in a 24-hour urine protein sample (2.3 grams/

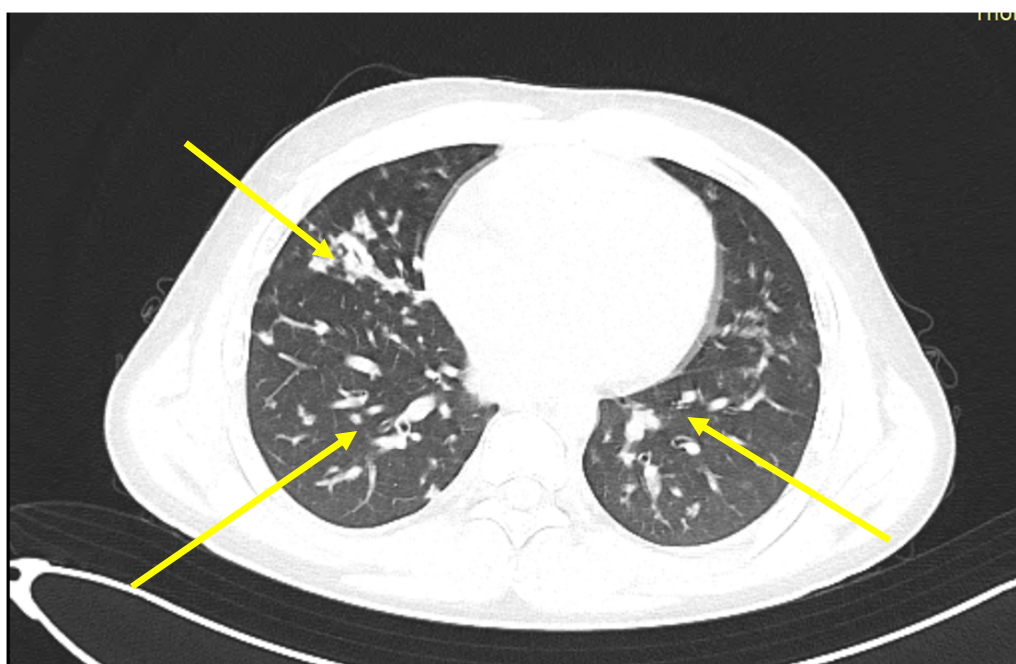


Figure 1. Centri-lobular nodules in right middle lobe, left upper lobe. Small patch of consolidation on right middle lobe.



Figure 2. Axial CT shows multiple enlarged lower deep cervical and supraclavicular lymph nodes.

day), and kidney function test remained normal throughout. Renal biopsy revealed class V lupus nephritis (Activity 0/24, chronicity 0/12). The patient was started on intravenous methylprednisolone pulse therapy, followed by oral prednisolone and Tacrolimus as the induction agent. Six months after the initiation of therapy, the patient remained clinically stable without systemic manifestations. There were no relapses, complications, or adverse events reported during this period. Laboratory evaluation at 6 months showed a 24-hour urine protein of 716 mg and stable renal function, indicating a partial renal response, and C3, C4 were within normal limits. The SLEDAI (Systemic Lupus Erythematosus Disease Activity Index) score was 4, reflecting residual renal activity in the absence of extra-renal involvement.

Discussion

SLE is known for its diverse clinical manifestations, often presenting with nonspecific constitutional symptoms such as fatigue, weakness, weight loss, and myalgia. The skin and musculoskeletal systems are the most commonly affected. Lymphadenopathy has been reported in 23%–34% of SLE cases [1]. Lupus lymphadenopathy (LL) as the primary presentation often poses a diagnostic dilemma. The estimated prevalence of LL is 5–7% at the inception of SLE and 12–15% at any point during the illness [4]. It is usually associated with more constitutional features, higher cutaneous, mucosal signs, increased incidence of organomegaly, higher anti-dsDNA titers, and low complement levels. However, there were no differences in CNS or renal manifestations [4]. Lymph node enlargement in diagnosed SLE patients can result from disease flares, infections, Kikuchi–Fujimoto disease, or lymphomas [4,8]. The commonest pulmonary involvement in SLE is pleuritis (12.5–32%) [7], which was absent in our case. Non-specific findings, such as follicular hyperplasia of lymph nodes observed in biopsies, are frequently noted, as seen in our case. Studies have identified factors such as prolonged symptom duration before diagnosis, the presence of anti-RNP (anti-ribonucleoprotein)

antibodies, and positive ANCA (Anti-Neutrophil Cytoplasmic Antibodies) as associated with an increased risk of pulmonary involvement [7]. In our case, although the child was clinically asymptomatic, CECT revealed bilateral multifocal lung nodules of consolidation, which have not been commonly reported in other cSLE case reports before [8]. This case was unusual in several aspects: the patient had pulmonary nodules without respiratory symptoms, extensive lymphadenopathy mimicking tuberculosis or lymphoma, and no typical mucocutaneous or joint features of SLE. Despite normal renal function and absence of hematuria, renal biopsy revealed Class V lupus nephritis. These findings reflect an atypical yet systemic presentation of cSLE, emphasizing the importance of high clinical suspicion and thorough evaluation.

Conclusion

This case underscores the diagnostic challenge of childhood-onset SLE (cSLE), which can initially present with nonspecific symptoms such as fever, lymphadenopathy, weight loss, and pulmonary infiltrates—features shared with infections (e.g., tuberculosis), malignancies (e.g., lymphoma), and inflammatory conditions (e.g., HLH, sarcoidosis, Kikuchi disease, sJIA). A systematic exclusion of these differentials, supported by imaging, laboratory data, and histopathology, enabled a timely diagnosis of Class V lupus nephritis. The patient responded well to immunosuppressive therapy, achieving systemic remission and partial renal response. This case highlights the need for early recognition of cSLE in children with unexplained multisystem involvement and emphasizes the clinical value of maintaining a broad differential.

Key Learning Points

- **Generalized lymphadenopathy** in children, particularly when persistent and unexplained, should raise suspicion for autoimmune conditions like cSLE—not just infections or malignancy.

- **Pulmonary nodules** in cSLE may occur even in the absence of respiratory symptoms and can easily be misinterpreted as infectious or neoplastic; careful evaluation is critical.
- **Lymph node histopathology** is a cornerstone in ruling out key differentials such as tuberculosis, sarcoidosis, lymphoma, and Kikuchi disease in febrile illnesses with nodal involvement.
- A **systematic and layered diagnostic approach**, combining clinical signs with targeted investigations (laboratory investigations, imaging, biopsy), is vital in evaluating complex multisystem presentations.
- **Early identification of atypical cSLE** presentations allows for timely immunosuppressive treatment, which can significantly influence long-term outcomes and renal prognosis.

Declarations

Ethics approval and consent to participate

The research falls under the category of less than minimal risk/minimal risk. No identifiable linked information is being collected or recorded for the study/research; therefore, ethical approval was not required.

Consent

Written informed consent was obtained from the patient's legal guardian for publication of this case report and associated clinical information and images. Consent was obtained in the participant's preferred language, and all queries were addressed before signatures were obtained.

Availability of data and material

No datasets were generated or analyzed during the current study. Therefore, data sharing does not apply to this article.

Competing interest

The authors declare no competing interests

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Authors' contributions

SM, ML: Data collection; AD: Conceptualization; ML, AD: Data extraction, drafted the manuscript; RB, RB: Conceptualization, manuscript editing; NSB, NB, SS, RS, NRM: Reviewed the manuscript, and edited the manuscript. All authors contributed to the final revision of the manuscript. AD is the guarantor.

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