Iranian Journal of Blood & Cancer

Iran J Blood Cancer, 2024, 16(3), 14-22
https://ijbc.ir

Case Report

Development of Lymphoma in Systemic Lupus Erythematosus Patients: A Case Report and Systematic Literature Review

Raja Adib Bakhsh [1*], Khaled Saleh Dairi [1], Mohammad Hamid Alabdali [1], Sameer Mohammed Aljuhani [1], Rawan Khaled Altaib [1], Mohammed Ahmed Hasaballah [1]

[1] *King Faisal Hospital, Internal Medicine Department, 4588, Prince Majed ibn Abd Al Aziz, 7451, Al Maabdah, Makkah 24236, Saudi Arabia.*

Scan and read the article online

Citation Adib Bakhsh R, Saleh Dairi Kh, Hamid Alabdali M, Mohammed Aljuhani S, Khaled Altaib R, Ahmed Hasaballah M. Development of lymphoma in systemic lupus erythematosus patients: a case report and systematic literature review. Iran J Blood Cancer. 2024 Sep 30;16(3): 14-22.

doi 0

Article info:
Received: 02 July 2024
Accepted: 17 Sep 2024
Published: 30 Sep 2024

Keywords:
Systemic Lupus Erythematosus
Lymphoma
Vasculitis
Autoimmune
Abdominal Manifestation

Abstract

Systemic Lupus Erythematosus (SLE) is one of these conditions that presents difficult hurdles since it is a multi-systemic autoimmune condition with a wide range of implications, including an increased risk of cancer among affected people. According to recent evidence, it has been revealed that the lymphoma rate in patients with SLE can be 4 to 7 times higher than that of the general population. This increased risk is to be emphasized through stringent and attentive screening and management as the mechanism of this risk is still under research. Therefore, this section discusses a case study and literature regarding SLE and lymphoma better to comprehend the intricate correlation between the two conditions. Here, we present the case of a 53-year-old male who was just diagnosed with SLE and also suffering from abdominal pain and distention, in which the diagnosis of lymphoma is made via serial investigations. This case, therefore, gives us a lesson on the fact that Lymphoma should be considered as one of the differential diagnoses in SLE patients presenting with abdominal complaints. With the ever-changing knowledge about the basic mechanisms of SLE and appropriate screening techniques, our attention to cancer risk in SLE patients should be increased to achieve better clinical outcomes.

1. INTRODUCTION

Systemic Lupus Erythematosus, usually SLE, is a multi-system autoimmune condition associated with many symptoms, including constitutional and abdominal [1]. Due to the wide range of possible causes and intensity of the symptoms, which can range from mild to severe to possibly fatal, diagnosing the origin of abdominal symptoms in SLE patients is difficult [2]. The present case study and systematic literature delve into abdominal issues in patients with systemic lupus erythematosus (SLE), emphasizing the initial treatment steps, diagnostic techniques, and possible therapy approaches. The literature review discusses the most common causes of abdominal pain among SLE patients. It analyzes the interconnection of SLE and lymphoma, two conditions that provide various challenges in diagnosis and management, as recent studies have demonstrated an

* **Corresponding Author:**
Raja Adib Bakhsh
Affiliation: *King Faisal Hospital, Internal Medicine Department, 4588, Prince Majed ibn Abd Al Aziz, 7451, Al Maabdah, Makkah 24236, Saudi Arabia*
E-mail: **rajaa_bakhsh09@outlook.com**

[Downloaded from ijbc.ir on 2026-11-27]

[DOI: 10.61186/ijbc.16.3.14]

increased risk of developing lymphomas, primarily of the diffuse large B cell type, among patients with SLE, stressing the importance of reliable evaluation and treatment to avoid severe consequences and possible death if untreated properly. It also underlines the significance of an interdisciplinary methodology that involves clinical, radiological, and histological examination to achieve the best patient care results. Lastly, the study mentions uncommon cases where systemic vasculitis was found to be associated with lymphoproliferative diseases.

2. LITERATURE REVIEW

2.1. Abdominal Manifestations in SLE

Abdominal symptoms associated with Systemic Lupus Erythematosus (SLE) represent a significant clinical diagnostic challenge due to their undifferentiated character, variety of causes, and potentially devastating outcome. Enteritis is considered an unusual component of the gastrointestinal system involvement in SLE. Still, early recognition is critical to prevent catastrophic organ damage and other life-threatening complications such as protein-losing enteropathy, intestinal obstruction, necrosis, and perforation. LE is responsive to treatment with pulse steroids in almost 70% of the patients. Still, the differential remains wide for SLE patients with GI complaints and patients with other causes of abdominal pain, such as acute infectious gastroenteritis, peptic ulcers, acute pancreatitis, peritonitis, and other surgical causes, should be ruled out first. Lupus mesenteric vasculitis (LMV) is a unique clinical entity found in SLE patients and usually presents as acute abdominal pain with sudden onset, severe intensity, and diffuse localization. Prompt and accurate diagnosis of LMV is critical to ensure the implementation of appropriate immunosuppressive therapy and avoidance of unnecessary surgical intervention. Also, recognizing an intraabdominal thrombotic process is essential to providing the patient with the proper treatment plan by anticoagulation. A study conducted in 2023 identified an SLE patient with acute intestinal obstruction, which is a known severe complication of lupus enteritis manifested with acute abdominal pain and intestinal Vasculitis [3]. This is also shown by Chen, Long, et al. (2021), where the clinical features of lupus enteritis included ascites, hydronephrosis, and leukopenia [4].

Moreover, relapse of lupus enteritis has been pointed out by Yulistiawati (2023), showing the need for consistent and effective strategies to prevent recurrence [5] showing the need for a consistent and effective strategy to prevent recurrence. Recognizing the cause, understanding the underlying pathological mechanism, and treating the cause of the abdominal manifestations in SLE are important and lifesaving. One study illustrates the pathological mechanisms involving vasculitis and thrombosis leading to pancreatitis, protein-losing gastroenteritis, and acalculous cholecystitis [6]. Paramaiswari et al. (2023) further emphasize the difficulties of diagnosing and managing severe abdominal pain in SLE patients [7]. This highlights the complexity of abdominal presentations in SLE and the need for a multidisciplinary approach involving surgical, radiological, histological, and medical evaluation to improve patient outcomes.

2.2. Vasculitis in SLE

SLE can affect any organ system, resulting in various clinical presentations. One of these presentations is vasculitis, which can affect people with SLE at a rate of 11% to 36%, with small vessel involvement being the most frequent kind [8, 9]. It can be associated with antiphospholipid syndrome (APS) characterized by antiphospholipid antibody positivity (lupus anticoagulant, anti-cardiolipin antibodies, and anti-β2-glycoprotein−1 antibodies). It usually appears during an active disease associated with general inflammatory symptoms (fever, fatigue, and weight loss) and laboratory abnormalities (anemia, a high erythrocyte sedimentation rate, and elevated inflammatory markers). Ninety per cent of cases affect the skin. Other organs like kidneys, gastrointestinal tract, nervous system, lungs, and heart can be involved, but less frequently than skin. Kallas et al. (2020) explored the link between the SLICC/ACR Damage Index scores and cutaneous disease manifestations in SLE patients by analyzing clinical and serological characteristics, emphasizing its repetitive appearance in some patients and its association with a later disease stage [10]. In addition, Gheita et al. (2018) have also illustrated the presence of cutaneous Vasculitis in SLE patients and its association with drug rash, musculoskeletal manifestations, hypocomplementemia, and lupus nephritis [11] The results suggest that keeping a close watch on Vasculitis in SLE patients is crucial because it can have serious, even life-threatening consequences. A thorough awareness of SLE's many clinical and serological characteristics, including the

[Downloaded from ijbc.ir on 2026-11-27]

[DOI: 10.61186/ijbc.16.3.14]

possibility of vasculitic implications, is critical for providing the best patient management and improving outcomes.

2.3. Lymphoma in SLE

Klein et al. (2018) have shown that patients with SLE had a 4.7-fold higher incidence of malignancies, including non-Hodgkin lymphoma [12]. Another review by [13] examined the relationship between hematologic, lung, cervical, and vulvar cancers and Systemic Lupus Erythematosus (SLE). It was discovered that SLE patients had a marginally increased chance of developing cancer overall, with hematologic malignancies being more common. This raises serious concerns about the possibility of lymphoma development in SLE patients and underscores the need for early identification and treatment. [14] Clarified that most SLE patients had B cell-originating lymphomas, especially diffuse large B cell lymphoma. The potential association between cyclophosphamide and azathioprine use and the development of lymphoma in SLE has been widely studied in the literature. Some studies suggest an increased risk of developing lymphoma among SLE patients after exposure to immune suppressive medications, especially cyclophosphamide. On the contrary, other studies indicate that immunosuppressive do not increase the incidence of lymphoma among SLE patients. Smoking, viral infections like Epstein Barr virus infection, cytokine dysregulation, genetic polymorphisms, and disease activity are other probable factors that are considered to increase lymphoma risk in SLE patients. These findings highlight the need for further research regarding lymphoma risk in SLE and strongly advise careful monitoring of all symptoms and signs that SLE patients might exhibit during their regular clinic follow-ups and strongly encourage proper categorization of patients and staging of their disease activity.

3. METHODOLOGY

3.1. Literature Review Method

A systematic literature search was carried out to research lymphoma, vasculitis, and abdominal problems in SLE patients. Search phrases such as "SLE lymphoma," "SLE vasculitis," and "SLE abdominal complications" were used in databases such as PubMed and MEDLINE. Studies available up until May 2024 were considered in the search. Studies that addressed particular issues in patients with SLE offered perspectives on management and outcomes and contained comprehensive clinical information, which were included in **Table 6.** The final selection contained research addressing important topics such as the prevalence and management of vasculitis, the early detection of lupus enteritis, and the elevated risk and surveillance of lymphoma in individuals with SLE.

3.2. Results of the Literature Search

A total of 67 articles and case reports emphasizing abdominal challenges, vasculitis, and lymphoma in patients with SLE were identified through our systematic literature search. Fifty-five articles were excluded following a thorough screening procedure because they did not match the inclusion requirements or did not specifically address the subjects of interest. **Table 6** shows the final 12 articles that satisfied the requirements had comprehensive clinical data, addressed particular problems in SLE patients, and gave recommendations on treatment and results. Three of these articles focused on different aspects of abdominal issues associated with SLE, including lupus enteritis and acute intestinal blockage. Four articles examined cutaneous and systemic vasculitis in people with SLE. Five articles also examined the relationship between SLE and lymphoma, including incidence rates, clinical features, and risk factors related to this consequence. When taken as a whole, these studies highlight the severity and complexity of these disorders in SLE patients, highlighting the need for multidisciplinary methods, early diagnosis, and comprehensive therapeutic techniques to enhance patient outcomes.

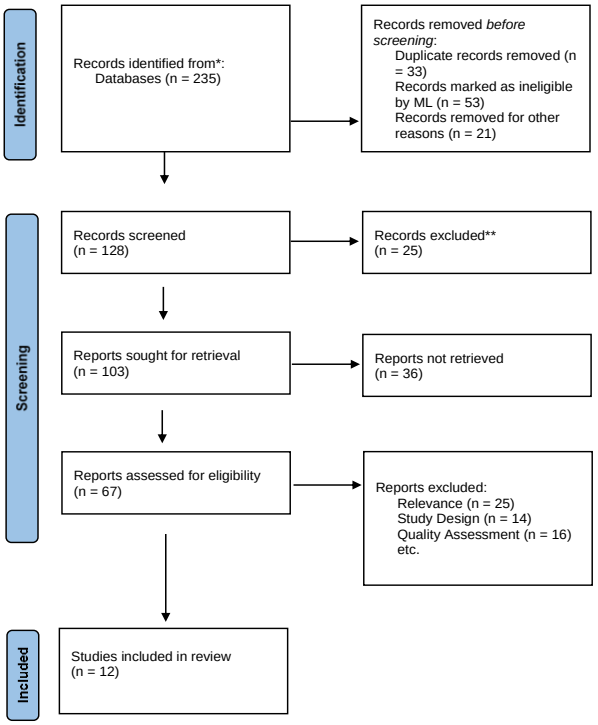


Figure 1. PRISMA Flow Diagram.

[Downloaded from ijbc.ir on 2026-11-27]

[DOI: 10.61186/ijbc.16.3.14]

4. CASE PRESENTATION

A Saudi male patient of 53 years old rushed to the emergency department of King Faisal Hospital, Makkah City, on the 2nd of April 2024. He complained of increasing fatigue and a fever that had been inconsistent over the previous two months. Additionally, the patient made complaints regarding postprandial abdominal pain, loss of appetite, abdominal distention, and unintentional weight loss of 11 kg. The patient had a noteworthy medical history of gout and was taking colchicine, febuxostat, and an oral prednisone tapering dosage due to a recent gout flare-up. In addition, he had a history of type 2 diabetes mellitus, which he had previously controlled with metformin but discontinued the medication because of a low HbA1C (glycosylated hemoglobin). The patient had hypothyroidism, which was treated with levothyroxine (100 mcg) taken orally every day and was diagnosed with Systemic Lupus Erythematosus (SLE) in December 2023 as per a positive antinuclear antibody (ANA) test with low C4 levels and is currently kept on hydroxychloroquine (200 mg), which he was taken orally every day for SLE treatment. The patient's physical exam and vitals were within the normal range except for an enlarged spleen on the abdominal examination. As seen in **Table 1**, the electrolyte and other biochemical parameters were within the normal range, indicating no electrolyte imbalance or renal issues present at that time. **Table 2** shows the results of all liver function tests, which were also in the normal range except for AST, which was slightly elevated. As per **Table 3**, the laboratory investigations show a hemoglobin level of 6.1 mg/dl with a low white blood count and platelet count. With anemia, splenomegaly, pancytopenia, and fever as the presenting symptoms, the patient was admitted to the medical ward under the internal medicine team to pursue further investigations and management and consulted both hematology and rheumatology teams. Based on the observation of hemolysis characteristics in the laboratory data, such as a high reticulocyte count and positive direct antiglobulin test (DAT), along with thrombocytopenia, the rheumatology team suspected the patient could have autoimmune hemolytic anemia with possible Evans Syndrome.

Table 1. Electrolytes Test.

Electrolytes	Ranges
Na	138.2 mmol/L
K	4.07 mmol/L
Chloride	105 mmol/L
BUN	6.7 mmol/L
CREATININE	54.2 µmol/L
CALCIUM	2.26 mmol/L
PHOSPHORUS	1.2 mmol/L
ALP	54 U/L

Abbreviations: Na (Sodium), K (Potassium), BUN (Blood Urea Nitrogen), ALP (Alkaline Phosphate)

Table 2. Liver Function Tests (LFT).

Liver Function Tests (LFT)	Ranges
BILIRUBIN	12.8 umol/L
ALT	22 U/L
AST	50 U/L
ALBUMIN	40 g/l
TOTAL PROTEIN	72 g/l

Abbreviations: ALT (Alanine aminotransferase), AST (Aspartate aminotransferase)

Table 2. Complete Blood Count (CBC).

Complete Blood Count	Ranges
WBC	1.8 x 10^3/µL (low)
Hgb	6.1 g/dl (low)
Platelet	145 x 10^9/L (low)
NEUT %	56 %
LYMPH %	27.9 %
MONO%	13.7 % (High)
EOS%	1.1%
BASO%	0.5 %
NEUT COUNT	1.04×$10^{\wedge 3}$/ µL (low)
LYMP COUNT	0.51×$10^{\wedge 3}$/ µL (low)
MONO COUNT	0.13×$10^{\wedge 3}$/ µL
EOS COUNT	0.02×$10^{\wedge 3}$/ µL
BASO COUNT	0.01×$10^{\wedge 3}$/ µL (low)
INR	0.9 Sec
PT	10.8 Sec
PTT	28.9 Sec
Peripheral blood film	RBC Agglutination seen
Direct Antiglobulin Test (DAT)	Positive

Abbreviations: WBC (White Blood Cells), Hgb (Hemoglobin), NEUT% (Neutrophil Percentage), LYMPH% (Lymphocyte Percentage), MONO% (Monocyte Percentage), EOS% (Eosinophil Percentage), BASO% (Basophil Percentage), INR (International Normalized Ratio), PT (Prothrombin Time), PTT (Partial Thromboplastin Time)

The results of the diagnostic tests, as seen in **Table 4**, show important information for the patient. A positive ANA (1:160, nuclear and speckled pattern) indicates an autoimmune disease consistent with systemic lupus

[Downloaded from ijbc.ir on 2026-11-27]

[DOI: 10.61186/ijbc.16.3.14]

erythematosus (SLE), whereas elevated CRP indicates inflammation. Reduced levels of C4 and gamma globulin signify an immune system engagement. The diagnosis of SLE is supported by the lack of particular autoantibodies (Anti-RNP, Anti-scl 70, Anti-Beta glycoprotein, Anti-Cardiolipin, Anti-ds DNA, Anti-La, and Anti-Ro), which shows that there are no active processes connected to these markers.

According to **Table 5**, the laboratory results show a negative serological pattern across a range of infectious diseases, including HIV (Human Immunodeficiency Virus), HCV (Hepatitis C Virus), HBV (Hepatitis B Virus), brucella, malaria, and leishmania. These data seem to suggest no active infection with these viruses in tested samples at the time of the study. However, in-depth screening is conducted to exclude the justifiable causes of the patient's symptoms. Nevertheless, one should be aware that the negative serologic results do not exclude the possibility of previous exposure or future infection risks. Follow-up testing or monitoring may be required if the clinician suspects it or if there are high risks.

Table 3. Diagnostic Tests.

Diagnostic Tests	Range
ESR	2 mm/H
CRP	4.83 mg/dl (high)
RF	< 8.6 IU/ML
IGG	724 mg/dl
IGA	103 mg/dl
IGM	84 mg/dl
C3	131 mg/dl
C4	<8 mg/dl (low)
ANA IF	1:160 (Positive) pattern is nuclear and speckled
Anti-RNP Abs	<3.5 CU (negative < 20)
Anti scl 70	<1 AI (negative)
Anti-Beta glycoprotein Abs (IgG)	<6.4 CU (negative <20)
Anti-beta glycoprotein Abs (IgM)	<1.1 CU (negative < 20)
Anti Cardiolipin IgG	3.0 CU (negative <20)
Anti Cardiolipin IgM	<1.0 (negative <20)
Anti-ds DNA Abs	<9.8 IU/mL (negative<27)
Anti La (SS-B) Abs	<3.3 CU (negative <20)
Anti Ro (SS-A) Abs	<4.9 CU (negative <20)
Lupus anticoagulant	Not detected
Electrophoresis Gamma globulin	0.5 g/dl (low)

Abbreviations: ESR (Erythrocyte Sedimentation Rate), CRP (C-Reactive Protein), RF (Rheumatoid Factor), IGG (Immunoglobulin G), IGA (Immunoglobulin A), IGM (Immunoglobulin M), C3 (Complement Component 3), C4 (Complement Component 4), ANA IF (Antinuclear Antibody Immunofluorescence), RNP (Ribonucleoprotein), scl (Scleroderma), Anti-La (SS-B) Abs (Anti-La (Sjogren's Syndrome-B) Antibodies, Anti-Ro (SS-A) Abs (Anti-Ro (Sjogren's Syndrome-A) Antibodies), Anti-ds DNA Abs (Anti-double-stranded DNA Antibodies)

The patient's medical examination showed various results. A 24-hour urine collection revealed proteinuria at an average of 146 mg/dl, suggesting mild non-nephrotic proteinuria. A urine screening revealed +1 protein without indicating red blood cells or casts. The echocardiogram findings were normal. Abdominal ultrasonography showed a modestly enlarged liver with a bright color, several gall bladders stones, and a greatly enlarged spleen with no specific abnormalities: the liver measured 21 cm, and the spleen 22.3 cm by 8 cm. The ultrasound also revealed functioning kidneys and pancreas.

Further imaging was performed with computed tomography (CT). The CT scan of the abdomen revealed hepatomegaly, fatty infiltration, and a large spleen. The liver had a uniform texture, while the spleen had a center footprint due to congenital lobulation with suspected areas of focal multiple small hypodensities. This could be secondary to a suspected vasculitic insult within the spleen. No aberrant lymph nodes or other vascular abnormalities were detected. A pan-computed tomography indicated a group of small-sized lymph nodes in the submandibular and deep cervical areas, and a high-resolution chest computed tomography (HRCT) indicated normal lung parenchyma and vascular mediastinal structures. The patient received an urgent 2-unit blood transfusion and planned for intravenous immunoglobulin (IVIG) treatment. It was decided that to rule out lymphoproliferative diseases, a bone marrow biopsy was required. So, after receiving the treatment mentioned above, the patient was referred to a tertiary hospital offering a bone marrow test. The findings of the bone marrow biopsy revealed unusual clusters made up of big and variable-sized B-cells. Histiocytes and reactive T-cells were also seen. Classifying the tumors seen in the biopsy proved challenging; nonetheless, nodular lymphocyte-predominant Hodgkin lymphoma (B-cell), marginal zone lymphoma, and big B-cell lymphoma were among the possible diagnoses.

Table 4. Serological Tests.

Serological Assays	Results
HIV SEROLOGY	Negative
ANTI-HCV	Negative
Brucella Serology	Negative
MALARIA KIT	Negative
Leishmania Serology	Negative
HBV PANEL	Negative

Abbreviations: HIV (Human Immunodeficiency Virus), HCV (Hepatitis C Virus), HBV (Hepatitis B Virus)

[Downloaded from ijbc.ir on 2026-11-27]

[DOI: 10.61186/ijbc.16.3.14]

Table 5. Literature Review Table.

Author	Year	Objective	Key Findings	Population	Conclusion
Mounir et al.	2023	Investigate SLE patients with acute intestinal obstruction	Identified SLE patient with acute intestinal obstruction due to lupus enteritis, highlighting severe complications such as acute abdominal pain and intestinal vasculitis	SLE patient with acute intestinal obstruction	Emphasizes the severity of complications and the need for early recognition and treatment
Chen et al.	2021	Study clinical features of lupus enteritis	Clinical features include ascites, hydronephrosis, and leukopenia	SLE patients with lupus enteritis	Highlights the need for early recognition and management to prevent severe complications
Yulistiawati	2023	Explore relapse in lupus enteritis	Points out relapse of lupus enteritis, indicating the necessity for consistent and effective strategies to prevent recurrence	SLE patients with recurrent lupus enteritis	Stresses the importance of preventive strategies and consistent management
Frittoli et al.	2021	Illustrate pathological mechanisms of abdominal complications in SLE	Pathological mechanisms involve vasculitis and thrombosis leading to pancreatitis, protein-losing gastroenteritis, and acalculous cholecystitis	SLE patients with abdominal complications	Emphasizes understanding pathological mechanisms for better management and treatment
Paramaiswari et al.	2023	Discuss diagnostic challenges in SLE patients with severe abdominal pain	Highlights difficulties in diagnosing and managing severe abdominal pain in SLE patients	SLE patients with severe abdominal pain	Stresses the need for a multidisciplinary approach for better patient outcomes
Barile-Fabris et al.	2014	Examine Vasculitis in SLE patients	Found that vasculitis affects 11% to 36% of SLE patients, with small vessel involvement being the most frequent	SLE patients with vasculitis	Emphasizes the need for vigilance in monitoring Vasculitis in SLE patients
Miyagawa et al.	2022	Study clinical and serological characteristics of Vasculitis in SLE	Association with antiphospholipid syndrome and general inflammatory symptoms	SLE patients with vasculitis	Highlights the importance of recognizing vasculitis for proper management
Kallas et al.	2020	Link between SLICC/ACR Damage Index scores and cutaneous disease manifestations	Association with repetitive cutaneous vasculitis and later disease stage	SLE patients with cutaneous vasculitis	Suggests monitoring cutaneous vasculitis to improve patient outcomes
Gheita et al.	2018	Explore cutaneous Vasculitis in SLE patients	Association with drug rash, musculoskeletal manifestations, hypocomplementemia, and lupus nephritis	SLE patients with cutaneous vasculitis	Emphasizes the serious consequences and need for thorough awareness and management
Klein et al.	2018	Examine cancer incidence in SLE patients	Found a 4.7-fold higher incidence of malignancies, including non-Hodgkin lymphoma	SLE patients with cancer	Highlights the increased cancer risk and the need for early identification and treatment
Ladouceur et al.	2020	Examine relationship between cancers and SLE	Increased risk of hematologic, lung, cervical, and vulvar cancers in SLE patients	SLE patients with various cancers	Emphasizes careful monitoring and early detection of cancers in SLE patients
Martín-López et al.	2023	Study lymphoma in SLE patients	Most SLE patients had B cell-originating lymphomas, especially diffuse large B cell lymphoma	SLE patients with lymphoma	Highlights the need for careful monitoring and further research on lymphoma risk in SLE patients

[Downloaded from ijbc.ir on 2026-11-27]

[DOI: 10.61186/ijbc.16.3.14]

Other cytogenetic investigations were asked to further help with the final diagnosis process, such as fluorescence in situ hybridization (FISH) for c-MYC, BCL2, and BCL6.

Based on the results of the bone marrow biopsy and the presence of splenomegaly with constitutional symptoms and autoimmune hemolysis related to cold agglutinins, the picture was clear that the patient has lymphoma and was educated about the disease and explained the need for prompt treatment and follow-up. Rituximab was offered for the patient as one of the best options to stop hemolysis, and he agreed. An intravenous rituximab dosage of 787 mg (lymphoma dose) was given. Regular complete blood counts (CBCs) were planned to monitor hemolysis, along with weekly rituximab injections. Additional evaluation, which entails a splenic biopsy or immune cytogenetics to make an accurate diagnosis of the lymphoma subtype, is pursued at the tertiary center to which the patient was previously referred.

5. DISCUSSION

5.1. Clinical Manifestations and Diagnostic Challenges

The clinical manifestation of SLE involves constitutional nonspecific symptoms such as fever, weakness, weight loss, anorexia, and arthralgia. Besides the clinical features classically associated with SLE, abdominal manifestations, such as bowel wall thickening (enteritis), viscus perforation, small bowel obstruction, and multiple infarctions due to mesenteric vasculitis, have been documented. On the contrary, the involvement of the liver in SLE is not common, and a careful diagnostic evaluation of the liver disease must be performed before associating it with lupus. Among the causes of liver disease in SLE, the most common differential diagnoses include drug-induced liver toxicity, fatty liver disease, viral hepatitis, and thrombotic processes. Splenomegaly, defined as an enlarged spleen of more than 12 cm long, is seen in 10 to 45% of SLE patients and is thought to be more common during active disease. Mild to moderate splenomegaly is recorded in The British Isles Lupus Assessment Group (BILAG) index [15], unlike other measures of disease activity such as the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and European Consensus Lupus Activity Measurement (ECLAM) do not account for splenomegaly. Since its prevalence is frequently linked to lymphadenopathy and hepatomegaly, it may signal several additional differential diagnoses, including neoplastic and lymphoproliferative illnesses like leukemia, lymphoma, or other hematological cytopathology. Splenic tumors, liver cirrhosis, vascular occlusive diseases such as splenic vein thrombosis, immunological diseases such as autoimmune hemolytic anemia, and infections such as viral, malarial, endocarditis, and splenic abscess can all cause splenic disease in Systemic Lupus Erythematosus.

Hyposplenism, which affects up to 5% of individuals, is seldom documented and is assumed to result from the vasculitis process and tissue microinfarctions within the spleen. Cytoskeletal abnormalities such as a hereditary sphere or elliptocytosis can also promote hyposplenism. In the present case, the patient had splenomegaly and Autoimmune Hemolytic Anemia (AIHA) with cold agglutinins that may be idiopathic or associated with various types of non-Hodgkin lymphoma like lymphoplasmacytic or marginal zone B cell lymphoma. The difference between cold agglutinin disease and secondary cold agglutinin syndrome has been gradually recognized. The latter is a rare, heterogeneous group of cold agglutinins, mediated autoimmune hemolytic anemia disorders resulting from, or associated with, other diseases such as infections (*Mycoplasma pneumonia* infection, Epstein–Barr virus infection, cytomegalovirus infection, COVID-19 lung infection) or malignancies (mostly, aggressive B-cell lymphoma). In our case, after the bone marrow result was achieved, agglutinin-associated lymphoproliferative disorder was considered the most likely cause of the disease.

5.2. Association Between SLE and Lymphoma

Non-Hodgkin lymphoma is associated with SLE, and its risk is predicted to be 4–7 times higher than that of the general population. According to a population-based study conducted across the country in Taiwan, results showed that among the 16,417 individuals diagnosed with SLE, 512 (3.1%) developed cancer, including 34 (0.2%) cases of non-Hodgkin lymphoma [16]. Based on site-specific cancer risk examination, non-Hodgkin lymphoma had the highest standardized incidence ratio (4.2, 95% CI: 2.9–5.9) [17]. Additionally, a meta-analysis conducted by [18] revealed that among individuals with SLE, the pooled standardized incidence ratio for non-Hodgkin lymphoma was 4.93 (95% CI: 3.81–6.36). Furthermore, the most prevalent subtype of lymphoma in individuals with SLE is diffuse large B-cell lymphoma, which makes up 37–62% of all lymphomas. In individuals with SLE, several mechanisms may have a role in the pathophysiology of non-Hodgkin lymphoma. Initially, persistent inflammation can cause B cells to become hyperactive and proliferate, leading to the independent growth of monoclonal populations [19]. Secondly, inadequate elimination of apoptotic cells might result from immune system dysregulation. Third, there is evidence that immunosuppressants like cyclophosphamide

[Downloaded from ijbc.ir on 2026-11-27]

[DOI: 10.61186/ijbc.16.3.14]

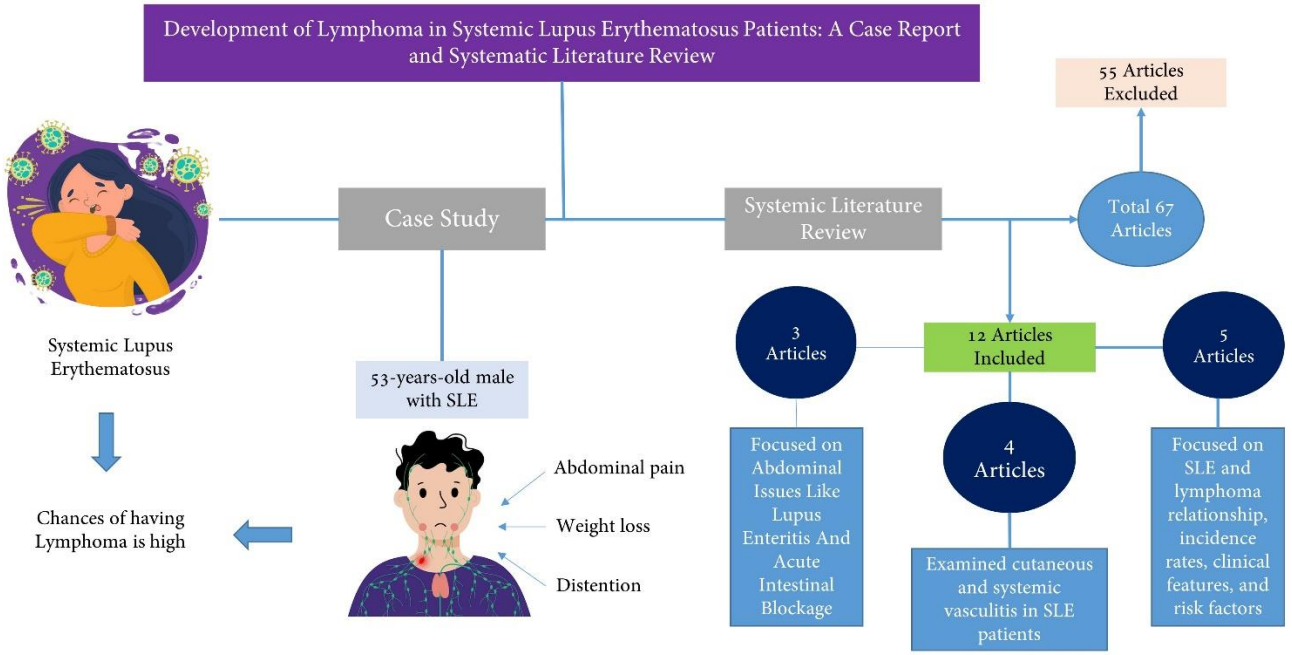


Figure 2. Graphical abstract.

contribute to the higher prevalence of lymphoma in SLE patients. Fourth, it's probable that non-Hodgkin lymphoma and SLE are frequently triggered by Epstein-Barr virus infection [20]. Prior research has demonstrated that, in comparison to healthy controls, patients with SLE had higher viral loads, higher levels of Epstein-Barr virus mRNA expression, higher levels of Epstein-Barr virus-directed antibodies, and lower levels of cell-mediated immunity towards the virus [16].

5.3. Special Considerations: Vasculitis and Lymphoproliferative Disorders

Systemic vasculitis is another autoimmune disease that poses an unusual connection to lymphoma. In particular situations, individuals develop cryoglobulinemic vasculitis, which can be related to unnoticed lymphoproliferative diseases. Cryoglobulinemia, frequently linked with diseases such as Waldenström's macroglobulinemia or lymphocytic lymphoma, can cause cryoglobulinaemic vasculitis in some systemic vasculitis. This highlights the crucial need to look for undetected lymphoproliferative disorders in those with cryoglobulinaemic vasculitis symptoms. Henoch-Schönlein purpura and lymphoma, Wegener's granulomatosis and Hodgkin's disease, granulomatous angiitis of the central nervous system and lymphoma, temporal arteritis and lymphoma, and polyarteritis nodosa and hairy cell leukemia are all unusual associations involving a systemic vasculitis plus lymph proliferative disorder. Patients with vasculitis must be examined closely for the presence of lymphoproliferative conditions, as vasculitis could be the presenting symptom of an undiagnosed lymphoproliferative disorder.

6. CONCLUSION

Cold agglutinin-related autoimmune hemolytic anemia and splenomegaly in Systemic Lupus Erythematosus (SLE) highlight the importance of considering lymphoma in the differential diagnosis. Diffuse large B cell lymphoma (DLBCL) is the most prevalent subtype, and cancer development in SLE patients should be aggressively monitored through history, physical exam, laboratory findings, or imaging. Patients with newly diagnosed autoimmune diseases should consider the risk of undiagnosed malignancy or lymphoproliferative disorder, especially in the elderly and those with constitutional symptoms. Complex and recurrent abdominal symptoms in SLE patients require prompt diagnosis and management due to serositis, enteritis, thrombosis, vasculitis, and possible malignancy. A multidisciplinary approach and collaboration between healthcare centers are crucial for accurate diagnosis and treatment plans. Adherence to future follow-up and monitoring processes is also essential to prevent recurrence.

[Downloaded from ijbc.ir on 2026-11-27]

[DOI: 10.61186/ijbc.16.3.14]

Acknowledgment
None.

Conflict of interest
All authors declare that there is no conflict of interest

Funding
No Funding was obtained for this review.

Ethical statement
Informed consent was obtained from the participant before publication.

References
1. Gergianaki, I. and G. Bertsias, *Systemic lupus erythematosus in primary care: an update and practical messages for the general practitioner.* Frontiers in medicine, 2018. **5**: p. 161.

2. Pavli, P., et al., *Acute abdominal situations as presenting or flaring manifestations of systemic lupus erythematosus: a case series.* Mediterranean Journal of Rheumatology, 2022. **33**(3): p. 339.

3. Mounir, B., et al., *Acute intestinal obstruction in systemic lupus Erythematosus: Case report and review of the literature.* Global Journal of Rare Diseases, 2023. **8**(1): p. 001-005.

4. Chen, L., et al., *Clinical features of lupus enteritis: a single-center retrospective study.* Orphanet journal of rare diseases, 2021. **16**: p. 1-8.

5. Yulistiawati, F., *A case report of a woman with SLE and lupus enteritis as the first manifestation of active systemic lupus erythematosus.* Bali Medical Journal, 2023. **12**(2): p. 1321-1237.

6. Frittoli, R.B., et al., *Gastrointestinal involvement in systemic lupus erythematosus: A systematic review.* Journal of translational autoimmunity, 2021. **4**: p. 100106.

7. Paramaiswari, A., A. Kusumawati, and D.B. Nugroho, *Severe Abdominal Pain and Multi-Organ Involvement in a Young Woman With Systemic Lupus Erythematosus.* Journal of Medical Cases, 2023. **14**(6): p. 196.

8. Barile-Fabris, L., M. Hernández-Cabrera, and J. Barragan-Garfias, *Vasculitis in systemic lupus erythematosus.* Current rheumatology reports, 2014. **16**: p. 1-6.

9. Miyagawa, F., et al., *A case of systemic lupus erythematosus with cutaneous leukocytoclastic vasculitis mimicking bullous SLE.* Case Reports in Dermatology, 2022. **13**(3): p. 464-469.

10. Kallas, R., D. Goldman, and M.A. Petri, *Cutaneous vasculitis in SLE.* Lupus Science & Medicine, 2020. **7**(1): p. e000411.

11. Gheita, T., et al., *Cutaneous vasculitis in systemic lupus erythematosus patients: potential key players and implications.* Lupus, 2018. **27**(5): p. 738-743.

12. Klein, A., A. Polliack, and A. Gafter-Gvili, *Systemic lupus erythematosus and lymphoma: Incidence, pathogenesis and biology.* Leukemia research, 2018. **75**: p. 45-49.

13. Ladouceur, A., et al., *Cancer and systemic lupus erythematosus.* Rheumatic Disease Clinics, 2020. **46**(3): p. 533-550.

14. Martín-López, M., et al., *Clinical characteristics and risk factors associated with lymphoma in patients with systemic lupus erythematosus: a nationwide cohort study.* Rheumatology, 2023. **62**(1): p. 217-224.

15. Shaharir, S. and C. Gordon, *Constitutional symptoms and fatigue in systemic lupus erythematosus*, in *Systemic Lupus Erythematosus*. 2016, Elsevier. p. 317-324.

16. Iwamuro, M., et al., *Intestinal Diffuse Large B-Cell Lymphoma in a Patient with Systemic Lupus Erythematosus.* Case Reports in Gastrointestinal Medicine, 2020. **2020**.

17. Qattan, M.Y., *The Incidence Rate of Non-Hodgkin's Lymphoma in Saudi Arabia: An Observational Descriptive Population Based Epidemiological Study from the Saudi Cancer Registry (2006–2016).* Open Access Macedonian Journal of Medical Sciences, 2023. **11**(B): p. 445-452.

18. Song, L., et al., *The risks of cancer development in systemic lupus erythematosus (SLE) patients: a systematic review and meta-analysis.* Arthritis research & therapy, 2018. **20**: p. 1-13.

19. Saadoun, D., et al., *Expansion of autoreactive unresponsive CD21–/low B cells in Sjögren's syndrome–associated lymphoproliferation.* Arthritis & Rheumatism, 2013. **65**(4): p. 1085-1096.

20. Boddu, P., et al., *SLE and non-Hodgkin's lymphoma: a case series and review of the literature.* Case Reports in Rheumatology, 2017. **2017**.

[Downloaded from ijbc.ir on 2026-11-27]

[DOI: 10.61186/ijbc.16.3.14]