Case Report

Challenges in diagnosing concurrent acute leukemia in an immunosuppressed patient with systemic lupus erythematosus: A case report

Shaily Agrawal[1], Amit K. Jangir[1], Yogesh M[2], Rohankumar Gandhi[2]

[1]Second-Year MBBS Student, Shri MP Shah Medical College, Jamnagar, Gujarat, India, [2]Department of Community Medicine, Shri MP Shah Medical College, Jamnagar, Gujarat, India

Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by damage to organs and cells, initially mediated by tissue-binding autoantibodies and immune complexes. Lymphomas have been frequently reported, but the association of SLE with acute leukemia is rare and likely coincidental. We report a case of a 40-year-old female admitted for an etiological diagnosis of fever and dyspnea with peripheral edema. She had a history of SLE diagnosed 2 years prior and had been on immunosuppressive therapy since then. Hematological investigations showed leukocytosis, anemia, and thrombocytopenia. Further diagnostic testing could not be done as she passed away 3 days after acute leukemia was diagnosed. This case highlights the challenges of diagnosing hematological malignancies in immunosuppressed SLE patients where symptoms may be obscured.

Keywords: Acute leukemia, blast cell, co-occurrence, SLE, thrombocytopenia

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by loss of tolerance to self-antigens. Hematologic abnormalities are common in SLE at diagnosis and throughout the disease course, partly due to immunosuppressant use.[1] Though life expectancy has improved with therapeutic advances, mortality risk remains elevated.[2] There are few published reports on the association between SLE and acute leukemias, likely due to rarity. We present a case of the rare co-occurrence of acute leukemia and SLE to provide insights into this association.

Address for correspondence: Dr. Rohankumar Gandhi, Department of Community Medicine, Shri MP Shah Medical College, Jamnagar, Gujarat, India.
E-mail: drrohangandhi92@gmail.com

Received: 21-05-2024 **Revised:** 24-07-2024
Accepted: 29-07-2024 **Published:** 18-11-2024

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_874_24

Case Presentation

A 40-year-old woman presented with fatigue, pallor, headache, palpitations, and intermittent fever. She had a history of SLE diagnosed 2 years prior and managed with immunosuppressive therapy (Prednisone: 10 mg daily maintenance dose, with occasional increases to 40 mg daily during flares, Mycophenolate mofetil: 1000 mg twice daily, Hydroxychloroquine: 200 mg twice daily). On examination, she was conscious and oriented but had pallor, lower limb edema, fever (39.4°C), blood pressure 90/60 mm Hg, respiratory rate 21/min, and pulse 120/min. Cardiac and respiratory exams were unremarkable. No lymphadenopathy or organomegaly was found.

Lab investigations showed anemia (hemoglobin 5.1 g/dL), elevated ESR (>150 mm/hr), and thrombocytopenia (platelets 18,000/mm3), The relative lymphocytosis (32%) is not

How to cite this article: Agrawal S, Jangir AK, Yogesh M, Gandhi R. Challenges in diagnosing concurrent acute leukemia in an immunosuppressed patient with systemic lupus erythematosus: A case report. J Family Med Prim Care 2024;13:5402-6.

uncommon in some types of acute leukemia, particularly acute lymphoblastic leukemia (ALL). The neutropenia (10%) is consistent with bone marrow infiltration by leukemic cells and is common in acute leukemia. Small percentages of monocytes (3%) and eosinophils (1%) have been included for a more complete picture, as these are typically present in small numbers. leukocytosis, and macrocytic red cells [Table 1]. Blood biochemistry shows elevated urea, creatinine, and elevated direct bilirubin [Table 2]. On urine analysis, elevated pus cells and the presence of protein in the urine were detected [Table 3]. Peripheral smear demonstrated 54% blast cells concerning acute leukemia [Table 4]. Flow Cytometry-Although not completed due to the patient's rapid decline, blood samples were sent for flow cytometry to identify the immunophenotype of the blast cells and determine the lineage (myeloid vs lymphoid) of the leukemia.

Figure 1 shows the presence of blast cells in peripheral blood smear.

SLE was diagnosed 2 years ago based on malar rash, weight loss, joint pain, and positive ANA. Serologies for hepatitis B, C, and HIV were negative. The patient passed away 3 days after acute leukemia diagnosis before additional testing could be performed.

Discussion

Hematologic manifestations are common in SLE, estimated to occur in over 50% of patients during the disease course.[1] Anemia of chronic disease, leukopenia, thrombocytopenia, and pancytopenia are frequently seen and result from autoantibody-mediated peripheral destruction, bone marrow suppression by cytokines, medications, and comorbidities.[2] While lymphomas have been frequently reported in lupus, co-occurrence with acute leukemias is very rare, with limited cases documented in the literature.[3-5]

The development of hematologic malignancies can be multifactorial in SLE. First, patients are immunocompromised due to the disease itself and cytotoxic therapies used for treatment like cyclophosphamide, impairing immune surveillance mechanisms.[6] Second, chronic inflammation promotes malignant transformation through the production of DNA-damaging reactive oxygen species.[7] Genetic factors, viral infections, and environmental exposures may also contribute.[8] High-dose glucocorticoids used long-term in SLE further increase risk through direct DNA damage and inhibition of apoptosis.[9]

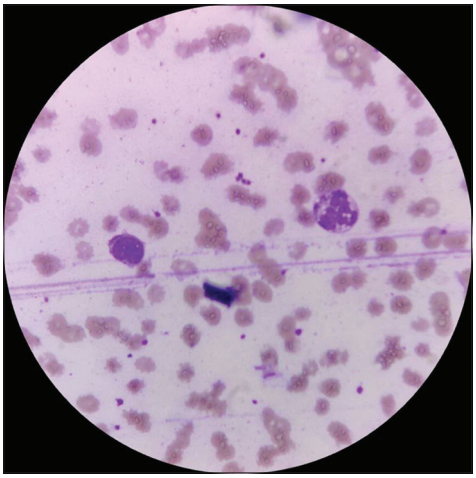

Figure 1: Shows the peripheral blood smear shows the blast cells

Table 1: Complete blood count of the patient

	Patient Value	Reference Value
Red blood cell	1.61 * 10^6/cumm	3.8–6.5 * 10^6/cumm
Hemoglobin	5.1 gm/dL	11.5–17gm/dl
Mean cell volume	97 μm^3	80–100 μm^3
Platelet	18 * 10^3/cumm	150–500 * 10^3/cumm
White blood cell	23.3 * 10^3/cum m	4.0–10.0 * 10^3/cumm
Neutrophils	2.33 * 10^3/cumm	2–7.5 * 10^3/cumm
Lymphocytes	7.4 * 10^3/cumm	1.00–4.00 * 10^3/cumm
Monocytes	0.699 * 10^3/cumm	0.20–1 * 10^3/cumm
Nucleated red blood cells	20/100 WBC	

Table 2: Blood biochemistry profile of the patient

Test	Result	Reference Range
Total Protein	6.7 g/dL	6.0–8.0 g/dL
Albumin	3 g/dL	3.5–5.0 g/dL
Urea	98 mg/dL	20–40 mg/dL
Creatinine	3 mg/dL	0.7–1.4 mg/dL
Bilirubin (Total)	0.8 mg/dL	0.2–1.0 mg/dL
Bilirubin (Direct)	0.4 mg/dL	0.0–0.02 mg/dL
Bilirubin (Indirect)	0.4 mg/dL	0.2–0.8 mg/dL
Sodium	141.2 mEq/L	135–145 mEq/L
Potassium	4.34 mEq/L	3.5–5.5 mEq/L

Table 3: Urine analysis of the patient

Parameter	Result
pH	Acidic
Protein	Positive
Glucose	Negative
Pus Cells	10–12/HPF
RBC	Not Seen
Epithelial Cells	Occasional
Casts	Hyaline
Amorphous Deposits	Present

Table 4: Peripheral blood smear report of the patient

Parameter	Result
Total WBC Count	23.3 cells/cumm
Differential Count	
Blasts	54%
Metamyelocyte	3%
Myelocytes	2%
Atypical Lymphocytes	8%
Neutrophils	10%
Lymphocytes	32%

Our patient had been on immunosuppressive medications including steroids for 2 years before acute leukemia diagnosis. Her non-specific constitutional symptoms of fatigue, fever, and dyspnea were likely dismissed as SLE flare or infection initially. Thrombocytopenia was possibly attributed to SLE itself or drug effect. Without a high index of suspicion for concurrent malignancy, the diagnosis of acute leukemia was missed until severe pancytopenia prompted peripheral smear evaluation. This delay in diagnosis due to obscuring symptom overlap negatively impacted prognosis.

Earlier case reports of concurrent acute leukemia and SLE also describe initial cytopenias being assigned to lupus, with leukemia detected late.[10,11] SLE management presents a dilemma once malignancy is identified, as discontinuing immunosuppression can lead to disease flare but continuing it risks infection and poorer cancer outcomes.[12] Chemotherapy is also challenging in immunocompromised lupus patients.[13]

Screening high-risk SLE patients could enable early leukemia detection at a treatable stage. Those on prolonged cytotoxic drugs or with unexplained cytopenias should be monitored closely with frequent blood counts, smear reviews, and bone marrow examinations if concerned.[14] Flow cytometry analysis of peripheral blood can also detect leukemia cells.[15] Treatment-wise, conservative chemotherapy regimens may be appropriate to limit toxicity in frail patients.[16] Infection prophylaxis and transfusion support are key.[17]

A major limitation of this report was the Incomplete diagnostic workup: Due to the patient's rapid decline, we were unable to complete a full diagnostic workup, including bone marrow biopsy and cytogenetic studies. This limits our ability to provide a comprehensive characterization of the leukemia and Lacks molecular data: Without detailed genetic and molecular analyses, we cannot comment on specific pathogenic mechanisms linking SLE and acute leukemia in this case.

Recommendations for Clinicians:

1. Screening and Monitoring:
    - Perform regular complete blood counts (CBC) with differential in SLE patients, at least quarterly or more frequently if clinically indicated.
    - Consider annual bone marrow examination for patients with persistent unexplained cytopenias or other hematological abnormalities.
    - Implement a low threshold for peripheral blood smear examination when CBC shows significant changes or unexplained results.
2. Diagnostic Approach:
    - Maintain a high index of suspicion for hematological malignancies in SLE patients presenting with atypical or worsening cytopenias.
    - Consider flow cytometry analysis of peripheral blood when leukemia is suspected, even before bone marrow biopsy.
    - Perform comprehensive molecular and cytogenetic studies to aid in diagnosis and prognosis when a hematological malignancy is confirmed.
3. Interdisciplinary Collaboration:
    - Establish regular communication channels between rheumatologists and hematologists for prompt consultation and joint management.
    - Consider creating multidisciplinary clinics for complex cases of SLE with hematological complications.
4. Patient Education:
    - Educate SLE patients about the potential increased risk of malignancies and the importance of regular monitoring.
    - Encourage patients to report new or worsening symptoms promptly, emphasizing that not all changes are related to SLE.

Treatment Strategies for Concurrent SLE and Acute Leukemia:

1. Individualized Approach:
    - Tailor treatment plans to each patient's specific SLE manifestations, leukemia subtype, and overall health status.
    - Consider the potential interactions between SLE medications and chemotherapy agents.
2. SLE Management:
    - Aim to achieve SLE remission or low disease activity before initiating intensive chemotherapy if possible.
    - Consider tapering immunosuppressive medications, especially cytotoxic agents, while maintaining minimum necessary doses to prevent severe SLE flares.
3. Leukemia Treatment:
    - Adapt standard chemotherapy protocols to account for the patient's SLE status and prior immunosuppression.
    - Consider less intensive regimens or targeted therapies in patients with significant organ damage from SLE.
    - Closely monitor for infections and autoimmune complications during treatment.
4. Supportive Care:
    - Implement aggressive infection prophylaxis given the dual risk from SLE and leukemia treatment.
    - Provide careful transfusion support, considering the risk of alloimmunization in SLE patients.
    - Offer psychological support to help patients cope with the dual diagnosis.
5. Clinical Trial Consideration:
    - Explore the possibility of enrolling patients in clinical trials specifically designed for individuals with autoimmune diseases and hematological malignancies.
6. Long-term Follow-up:
    - Develop a comprehensive long-term follow-up plan to monitor for both SLE flares and leukemia recurrence.
    - Consider the increased risk of secondary malignancies in survivorship care planning.

These strategies highlight the need for a delicate balance between managing SLE and treating acute leukemia, emphasizing the importance of a personalized, multidisciplinary approach to care.

This case highlights several areas for future research:

1. Prospective cohort studies: Long-term follow-up of large SLE cohorts to better quantify the risk of acute leukemia and identify specific risk factors.

2. Genetic profiling: Investigation of shared genetic susceptibilities between SLE and hematological malignancies.
3. Biomarker development: Identification of novel biomarkers that could predict the development of leukemia in SLE patients.
4. Optimal screening protocols: Development and validation of cost-effective screening strategies for early detection of hematological malignancies in SLE patients.
5. Tailored therapies: Exploration of immunosuppressive regimens that effectively control SLE while minimizing the risk of secondary malignancies.
6. Immunotherapy approaches: Investigation of whether newer immunotherapies for SLE might have a lower risk of promoting malignancy compared to traditional immunosuppressants.

These research directions could significantly advance our understanding of the SLE-leukemia association and improve patient care.

Conclusion

In conclusion, though rare, clinicians should be alert about concurrent hematologic malignancies in SLE patients presenting with atypical symptoms or worsening cytopenias. Early suspicion and evaluation with marrow studies facilitate prompt diagnosis and treatment. Individualized chemotherapy regimens, infection control, and optimal lupus management are needed to improve the otherwise poor prognosis. Further research into pathophysiologic mechanisms can help identify those at the highest risk for the development of leukemia.

Key Learning Points:

- Acute leukemia, though rare, should be considered in SLE patients presenting with atypical or worsening cytopenias.
- The symptom overlap between SLE flares and hematological malignancies can lead to diagnostic delays, emphasizing the need for a high index of suspicion.
- Long-term immunosuppressive therapy in SLE patients may contribute to an increased risk of hematological malignancies.
- Regular hematological monitoring, including peripheral blood smears and flow cytometry when indicated, is crucial for early detection of malignancies in SLE patients.
- A multidisciplinary approach involving rheumatologists, hematologists, and other specialists is essential for optimal management of concurrent SLE and acute leukemia.

Acknowledgments

We acknowledge and are grateful to all the patients who contributed to the data collection for this study. We are also thankful to Dr. Nandini Desai (Dean and Chairman of MDRU), and Dr. Dipesh Parmar (Professor and Head, Department of Community Medicine) - Shri M P Shah Government Medical College, Jamnagar, India.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Hara A, Wada T, Kitajima S, Toyama T, Okumura T, Kitagawa K. *et al.* Combined pure red cell aplasia and autoimmune hemolytic anemia in systemic lupus erythematosus with anti-erythropoietin autoantibodies. American Journal of Hematology 2008;83:750-2. doi: 10.1002/ajh.21241.
2. Keeling DM, Isenberg DA. Haematological manifestations of systemic lupus erythematosus. Blood Rev 1993;7:199-207.
3. Liang Y, Zhang L, Gao J, Hu D. Coexistence of acute myeloid leukemia with systemic lupus erythematosus in the absence of cytotoxic therapy: Coincidence or correlation?. Leuk Lymphoma 2009;50:1384-7.
4. Au WY, Lie AK, Chim CS, Choy C, Loong F, Lie AK, *et al.* Clinicopathologic features and treatment outcome of mature B-cell lymphomas in patients with dermatomyositis and polymyositis. Am J Med 2003;114:188-95.
5. Mirrakhimov AE. Malignancy risk in systemic lupus erythematosus: A review of the role of immunosuppressive therapy. Curr Rheumatol Rep 2021;23:16.
6. Zhang Y, Li W, Zhang P, Guo J, Sun J, Lu J. *et al.* Hematological malignancies in systemic lupus erythematosus: clinical characteristics, risk factors, and prognosis—a case-control study. Arthritis Research &Amp; Therapy 2022;24. doi: 10.1186/s13075-021-02692-8.
7. Thomas G, Mancano MA, Thomas K. Lupus erythematosus and systemic lupus erythematosus: A comparison of cutaneous manifestations in two different age groups. Int J Womens Dermatol 2017;3:40-4.
8. Lin Y, Yen J, Chang S. The age-risk relationship of haematologic malignancies in female patients with systemic lupus erythematosus: a nationwide retrospective cohort study. Lupus 2012;21:1250-6. doi: 10.1177/0961203312451783.
9. Katarzyna PB, Wiktor S, Ewa D, Piotr L. Current treatment of systemic lupus erythematosus: a clinician's perspective. Rheumatol Int 2023;43:1395-407. doi: 10.1007/s00296-023-05306-5.
10. Au W, Ma S, Chim C, Choy C, Loong F, Lie A. *et al.* Clinicopathologic features and treatment outcome of mature T-cell and natural killer-cell lymphomas diagnosed according to the World Health Organization classification scheme: a single center experience of 10 years. Annals of Oncology 2005;16:206-14. doi: 10.1093/annonc/mdi037.

11. Randrianarisoa R, Andrianiaina A, Sendrasoa F, Ramily S, Razafimaharo T, Ratovonjanahary V. *et al.* Association of systemic lupus erythematosus and acute myeloid leukemia: a case report. Medicine: Case Reports and Study Protocols 2023;4:e0279. doi: 10.1097/md9.0000000000000279.
12. Löfström B, Backlin C, Sundström C, Hellström-Lindberg E, Ekbom A, Lundberg I. Myeloid leukemia in systemic lupus erythematosus--a nested case-control study based on Swedish registers. Rheumatology 2009;48:1222-6. doi: 10.1093/rheumatology/kep204.
13. Moder KG, Tefferi A. Hematologic malignancies and the use of immunosuppressive therapy in lupus erythematosus: A critical review of clinical evidence. Leuk Lymphoma 2001;42:467-80.
14. Giannouli S, Voulgarelis M. Anaemia in systemic lupus erythematosus: From pathophysiology to clinical assessment. Ann Rheum Dis 2006;65:144-8.
15. Strati P. and Shanafelt T. Monoclonal b-cell lymphocytosis and early-stage chronic lymphocytic leukemia: diagnosis, natural history, and risk stratification. Blood 2015;126:454-62. doi: 10.1182/blood-2015-02-585059.
16. Ramadan S, Fouad T, Summa V, Hasan S, Lo-Coco F. Acute myeloid leukemia developing in patients with autoimmune diseases. Haematologica 2011;97:805-17. doi: 10.3324/haematol.2011.056283.
17. Siegel C. and Sammaritano L. Systemic lupus erythematosus. Jama 2024;331:1480. doi: 10.1001/jama.2024.2315.