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CASE REPORT

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Concomitant manifestations of systemic lupus erythematosus flare-up and nodal marginal zone B-cell lymphoma in a 41-year-old male patient: A challenging case report

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Key Clinical Message

Malignancy may be a possible cause of systemic lupus erythematosus (SLE) flare-ups, and it is necessary to consider it in the context of treatment resistance. In this case, we present a challenging instance of concomitant nodal marginal zone B-cell lymphoma (NMZL) and SLE flare-up in a 41-year-old male patient.

Abstract

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can cause various symptoms and affect multiple organs in the body. It is also associated with the development of malignancies, especially lymphomas. This case report discusses a patient who experienced a flare-up of SLE along with hypercalcemia, which led to the diagnosis of nodal marginal zone B-cell lymphoma (NMZL). This is the first case of its kind to be reported. A 41-year-old man with a 10-year history of SLE and antiphospholipid syndrome (APS) was referred to our center due to several symptoms, including fatigue, oral lesions, dyspnea, bilateral wrist pain and inflammation, mild pericardial effusion, organ enlargement, pancytopenia, high erythrocyte sedimentation (ESR) level, high anti-double stranded DNA (anti-dsDNA) level, low complement level, resistant hypercalcemia, and high brain natriuretic peptide (pro-BNP) level. After further testing, it was discovered that the patient had NMZL, which was the ultimate diagnosis. He underwent six cycles of the R-CHOP chemotherapy regimen, and his clinical and laboratory conditions improved during follow-ups. The initial case of SLE flare-up, with concomitant NMZL is being reported as the final diagnosis. In simpler terms, it is possible for lymphoma to manifest as a potential cause of SLE flare-ups, and clinicians should be mindful that they need to consider malignant conditions when faced with treatment resistance.

KEYWORDS
autoimmune reaction, hypercalcemia, malignancy, nodal marginal zone B-cell lymphoma, systemic lupus erythematous

1 | INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune, episodic, and chronic disease that can affect many different organs in the body, particularly the joints, skin, kidneys, liver, lungs, heart, nervous system, and hematopoietic organs.[1,2] SLE patients are at increased risk of developing cancers, especially hematological malignancies.[3,4] For instance, lymphoma risk in SLE was higher in male than female patients.[5] Although the causal pathogenic mechanisms involved remain unclear, dysregulation of the immune system and chronic inflammation are recognized as causes of malignancy in SLE patients.[6] In this regard, treatment, a persistently activated immune system, viral infection, overlap syndromes, and traditional lifestyle cancer risk factors are the factors that could contribute to the increased cancer risk in SLE patients.[7,8] In this study, a case of nodal marginal zone B-cell lymphoma (NMZL) in a patient with SLE flare-up is reported.

2 | CASE HISTORY/EXAMINATION

A 41-year-old man with a 10-year history of SLE was referred to Beheshti Hospital, affiliated with Kashan University of Medical Sciences. He met the American College of Rheumatology (ACR) criteria for SLE, including photosensitivity, malar rash, thrombocytopenia, low complement level, positive fluorescent antinuclear antibody (FANA) antibodies, and anti-double stranded DNA (anti-dsDNA). He also had antiphospholipid syndrome (APS), with two episodes of deep vein thrombosis (DVT), positive anti-cardiolipin antibodies, and lupus anticoagulant. The patient did not have a history or risk factors for human immunodeficiency virus (HIV); EBV (Epstein–Barr virus) was not reported (IgG and IgM antibodies were negative); and leishmaniosis also was not reported (the patient was not living in the common area for leishmaniosis). He had no family history of the disease or history of blood product transfusion. The patient was being treated with prednisolone (7.5 mg/day), azathioprine (100 mg/day), hydroxychloroquine (400 mg/day), and warfarin (5 mg/day), and he presented with fatigue, fever, arthralgia, an oral lesion, and a high ESR for 2 months. Dry mouth and dry eye were not reported.

2.1 | Methods (differential diagnosis, investigations, and treatment)

The patient's dosages of prednisolone and azathioprine were increased to 15 mg/day and 150 mg/day, respectively. However, due to the onset of dyspnea and failure to respond to the initial therapies, rituximab (1 g) was added; and azathioprine was discontinued. Two weeks later, the patient was admitted to our center due to recurrent oral lesions, increased arthralgia, dyspnea, and a new onset of pancytopenia (anemia, leukopenia, and thrombocytopenia). At the time of admission, the patient was conscious and aware, with a blood pressure of 120/80 mmHg, a heart rate of 100 beats per minute, a respiratory rate of 30 breaths per minute, an oral temperature of 38°C (100.4 F), and an oxygen saturation of 89% in ambient air. Additionally, the patient was found to have splenomegaly and cervical lymphadenopathy (1–2 cm). A peripheral blood smear (PBS) test confirmed pancytopenia (anemia, leukopenia, and thrombocytopenia).

The patient exhibited painless oral lesions, respiratory distress, and swelling in both wrists, with no limitation in range of motion. The distal pulses were normal. The laboratory test results are shown in (Table 1).

To further investigate the patient's condition, transthoracic echocardiography (TTE) was performed, which revealed mild pericardial effusion. A chest spiral computed tomography (CT) scan without contrast was conducted, but no remarkable concerns were identified. An abdominal and pelvic spiral CT scan with contrast revealed splenomegaly.

Due to the patient's oral lesions, dyspnea, bilateral wrist synovitis, mild pericardial effusion, pancytopenia (anemia, leukopenia, and thrombocytopenia), high ESR and CRP level, high anti-dsDNA level, low complement level, hypercalcemia, and high pro-BNP level, an SLE flare-up was suspected.

The patient was given a daily dose of intravenous methylprednisolone (1 g) for 3 days. Despite that, hypercalcemia persisted, and a sestemibi scan was performed to evaluate the parathyroid glands, which showed no abnormalities. Subsequently, a bone mineral density (BMD) test was conducted, which indicated that the patient had osteopenia. It was also suspected that the flare-up was triggered by an infection, which was evident from the fever and high procalcitonin level. To treat the presumed infection, the patient was given broad-spectrum

TABLE 1 The patient's laboratory data.

Test (value)	On admission	After methylprednisolone pulse	Reference value
White blood cell count ($\times 10^6$/L)	1900	6400	4000–11,000
Hemoglobin (g/dL)	8.7	8.1	12–18
Mean corpuscular volume (fL)	86	88	80–96
Platelet count (×10*3/μL)	26	34	165–415
Erythrocyte sedimentation rate (mm/h)	102	25	<20
C-reactive protein (mg/L)	187	33	<10
Blood urea nitrogen (mg/dL)	12	12	7–20
Creatinine (mg/dL)	1	1	0.5–1.4
Prothrombin time (s)	63	40	10–13
Partial thromboplastin time (s)	>120	30	25–35
International normalized ratio	5.6	3.3	<1.1
Calcium (mg/dL)	12	12	8.5–10
Phosphorus (mg/dL)	2	2.5	2.5–4.5
Vitamin D level	30	32	30–40
Probrain natriuretic peptide (pg/mL)	786	23	<250
Direct and indirect coombs	Negative	Negative	Negative
Blood culture	Negative	Negative	Negative
HIV (1, 2) antibodies	Negative	Negative	Negative
EBV IgG antibody	Negative	Negative	Negative
EBV IgM antibody	Negative	Negative	Negative
Anti-La (SSB)	Negative	Negative	Negative
Urine analysis	Trace proteinuria	Normal	-
Albumin (g/dL)	3.2	3.2	3–5
Fluorescent antinuclear antibody	1/160	-	>1/100
Complement component 3 (mg/dL)	34	-	90–180
Complement component 4 (mg/dL)	5	-	10–40
Anti-double-stranded DNA (IU/mL)	23.5	-	<12
Anti-Ro (SSA)	> 100	-	<12
Cytomegalovirus polymerase chain reaction	Negative	-	Negative
24 h urine protein (mg/day)	343	-	<100
24 h urine calcium (mg/day)	52	-	100–300
Troponin	Negative	-	Negative
Aspartate transferase (U/L)	22	22	<37
Alanine transferase (U/L)	34	34	5–41
Alkaline phosphatase (IU/L)	133	133	80–360
Procalcitonin (ng/mL)	0.65	-	<0.3
Parathyroid hormone (pg/mL)	55	-	10–65
COVID polymerase chains reaction	Negative	-	Negative

intravenous antibiotics, including 1 g meropenem (1 g) every 8 h, ciprofloxacin (400 mg) every 12 h, and vancomycin (1 g) every 12 h. The patient's condition improved after 3 days as his oral lesions decreased, his fever resolved, and his pancytopenia converted to bicytopenia (anemia and thrombocytopenia). Following this, methylprednisolone was stopped, and prednisolone was initiated at a dose of 1 mg/kg/day. Despite the progress, the patient's bicytopenia and hypercalcemia persisted. Even after the addition of intravenous pamidronate (60 mg), the blood calcium

concentration remained high. Due to the persistent anemia, thrombocytopenia, hypercalcemia, fatigue, and weakness, the patient underwent a hematology workup. A bone marrow malignancy was suspected, and the patient underwent bone marrow aspiration (BMA) and bone marrow biopsy (BMB), along with flow cytometry.

The bone marrow biopsy revealed fragments of bone trabecula and marrow spaces with around 70% cellularity. There was a decrease in megakaryocytes and no evidence of granuloma formation. Neoplastic lymphoid cells with round nuclei and clear diffuse cytoplasm had replaced the hematopoietic elements. An immunohistochemistry (IHC) test showed that these neoplastic cells were positive for CD20, Pax5, and BCL-2, and approximately 5% positive for ki67. However, they were negative for TdT, CD34, CD30, CD3, CD5, CD10, CD23, Cyclin D1, and BCL6.

Immunophenotyping results of bone marrow aspirate cells by flow cytometry revealed a lymphoid cell population comprising approximately 52% of the total cells analyzed. These cells were mostly composed of mature B-cells that expressed the CD45, CD19, CD20, CD22, surface kappa light chain and were negative for the CD5, CD10, CD11c, CD23, CD25, CD103, FMC7, CD34, TdT, and T-cell markers.

Both methods showed that the neoplastic cells were negative for CD5, CD10, and CD23, and these results suggest nodal marginal zone B-cell lymphoma (Figure 1).

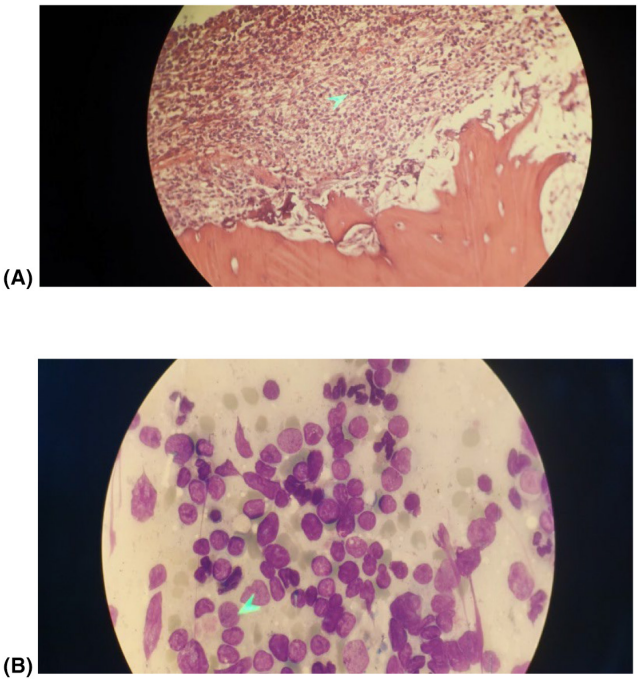

FIGURE 1 (A) H&E (×100), fragments of bone trabecula and marrow spaces with about 70% cellularity, and hematopoietic elements replaced by neoplastic lymphoid cells having round nuclei and clear cytoplasm arranged diffusely, (B) Giemsa stained bone marrow aspiration slides (×400), the arrow shows the neoplastic lymphoid cells arranged diffusely in marrow aspiration slides; in favor of nodal marginal B-cell lymphoma.

2.2 | Results (outcome and follow-up)

After undergoing six cycles of the R-CHOP chemotherapy regimen, he had his calcium levels checked. They returned to normal (8.5 mg/dL) after two cycles of chemotherapy. A follow-up bone marrow biopsy (BMB) showed that he had no remaining disease and was symptom-free. A peripheral blood smear (PBS) test showed bicytopenia, indicating anemia and thrombocytopenia. His peripheral blood counts also improved. Currently, he is taking prednisolone, azathioprine, hydroxychloroquine, and warfarin. His overall health is good.

3 | DISCUSSION

A challenging case of a 41-year-old male patient who has a history of SLE and APS is presented. He presented with multiple symptoms, including oral lesions, dyspnea, bilateral wrist arthralgia, synovitis, mild pericardial effusion, pancytopenia, high ESR, high level of anti-dsDNA, low complement level, resistant hypercalcemia, and high pro-BNP level. After conducting a thorough diagnosis, the ultimate diagnosis was NMZL.

It is believed that the aggravation of the disease was the secondary cause of cytopenia. Despite the fact that one study found that bone marrow toxicity and disease activity were the main causes of cytopenia in SLE patients.[9] BMA and BMB have typically been used in the diagnostic process for individuals with cytopenia that cannot be explained.[10] BMB revealed nodal marginal zone B-cell lymphoma in our patient.

Our patient's hypercalcemia was an uncommon finding. Numerous conditions, including malignancies, lymphoproliferative disorders, hyperparathyroidism, and renal insufficiency, can induce this disruption in calcium levels. Renal insufficiency was ruled out in our patient, nevertheless, as the urinalysis revealed only minor proteinuria and a normal plasma creatinine level. The ultrasound also revealed normal-sized kidneys. Hypercalcemia is a known complication of SLE flare-up, as mentioned in several case reports.[11] In SLE patients, hypercalcemia can also occur even when the parathyroid hormone-related protein (PTHrP) levels are normal (PTHrP is similar to PTH in terms of its sequence). It has been suggested that autoantibodies may cause hypercalcemia by triggering the PTH receptor through a cross-reaction.[12] Pathogenesis can result from high blood PTH levels, overproduction of PTHrP,

or autoantibodies against PTH receptor antibodies, commonly found during the active phase of SLE. PTHrP may be produced by nonmalignant lymphoid tissue in SLE patients. Polyclonal overactivation of B lymphocytes in SLE may result in the development of anti-PTH receptor autoantibodies, which may activate PTH receptors, bind to PTH receptors and activate PTH-mimetic effects, and block PTH and PTHrP expression, resulting in hypercalcemia. However, this phenomenon causes a low PTH level in the blood, which cannot be the reason for hypercalcemia due to the normal level of PTH in our patient.[13,14] Furthermore, some cytokines generated by active SLE patients, such as interleukin-6 (IL-6), interleukin-1 (IL-1), and prostaglandin E, may increase osteoclast bone resorption and cause hypercalcemia. However, hypercalcemia is not present in all active and remission SLE patients.[14]

SLE patients are at a higher risk of acquiring hematological malignancies[4,15]; in the general population, especially, the risk of lymphoma in SLE patients is greater for males than for females, and the risk increases with age.[16] Moreover, the majority of non-Hodgkin's lymphoma (NHL) cases among SLE patients are diffuse large B-cell lymphoma (DLBCL).[15] NHL and SLE have overlapping clinical signs and biological markers, including autoantibodies such as antinuclear antibodies (ANAs), which may present a diagnostic challenge; therefore, NHL can be misdiagnosed if the physician fails to extend the differential diagnosis.[17] In this context, marginal zone lymphoma (MZL) is the second most frequent indolent lymphoma and accounts for 7% of all non-Hodgkin lymphomas.[18] There are three subtypes: extranodal MZL (EMZL) of mucosa-associated lymphoid tissue (MALT lymphoma), which comprises 50%–70% of cases; splenic MZL (SMZL), which comprises 20%; and nodal MZL (NMZL), which comprises 10% of cases.[19,20] Infectious agents and autoimmune disorders such as sjögren syndrome, SLE, and Hashimoto thyroiditis are among the genetic and environmental risk factors for extranodal MZL.[18] In the literature, MZL, especially the nodal subtype, represents an exceedingly rare entity in SLE patients, and our case is the first such study. In one case of lymphoma with a history of SLE, a 50-year-old patient presented with fever, progressive fatigue, and pancytopenia. Like in our case, resistant pancytopenia was a notable point that supported the lymphoma diagnosis.[21] However, although antiphospholipid antibodies (APAs) are found in patients with NHL, they are rare in patients with NMZL.[22] To the best of our knowledge, only one case of NMZL associated with positive serum APAs has been described in the literature,[22] and our unique case is presented as coexistence manifestations of SLE flare-up, APS, and NMZL.

Both SLE and lymphoma possess increased levels of specific cytokines and proteins known to be associated with cell survival and proliferation, such as B-cell activating factor (BAFF), a proliferation-inducing ligand (APRIL), IL6, and B-cell lymphoma 2 (BCL2), which likely have an impact on pathogenesis.[3] Aside from the pathogenesis of the disease, a high level of suspicion of malignancy should be considered when SLE patients present with features unresponsive to treatment or unjustified with SLE presentations. In this regard, there was a possibility that exposure to some medications, such as cyclophosphamide and high-dose steroids, increased the incidence of lymphoma.[5] About other medications, previous studies, assessed the risk that azathioprine treatment predisposes to the development of malignancies[23]; in contrast, some studies reported no association between the cancer risk and the use of azathioprine.[24] In this regard, the risk of hematological malignancies associated with rituximab exposure in SLE patients was not reported.[25] Also, rituximab was reported as an effective medication in SLE patients with hematologic malignancy.[26] Whereas, our patient was not undergoing treatment with cyclophosphamide and high-dose steroids.

In addition, SLE flare-ups were considered a cause of malignancy, and there is a positive association between SLE activity and hematologic cancer.[27]

Ultimately, as both lymphoma and SLE flare-ups can present with cytopenia, hypercalcemia, and other signs that overlap with one another, it is important to be aware of the fact that both of these conditions can mimic each other's presentation.[28]

4 | CONCLUSION

Lymphoma may be a possible cause of SLE flare-ups, just like infections or other causes. It is important for doctors to understand that during flare-ups, SLE patients may display unusual symptoms and coexisting conditions, which require further examination.

AUTHOR CONTRIBUTIONS

Mohammadkian Zarafshani: Conceptualization; writing – original draft; writing – review and editing. **Ehsan Rahmanian:** Data curation; formal analysis; writing – review and editing. **Reza Manouchehri Ardekani:** Data curation; formal analysis; writing – review and editing. **Seyed Amir Hassan Matini:** Data curation; formal analysis; writing – review and editing. **Maryam Loghman:** Project administration; supervision; writing – review and editing. **Seyedeh Tahereh Faezi:** Conceptualization; supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

All data regarding this study has been reported in the manuscript. Please contact the corresponding author if you are interested in any further information.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The purpose of this research was completely explained to the patient and they were assured that their information will be kept confidential by the researcher. The present study was approved by the Medical Ethics Committee of the academy.

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REFERENCES

1. Del Porto F, Proietta M, Koverech A, Trappolini M, Aliberti G. Hypercalcaemia in systemic lupus erythematosus. *Lupus*. 2011;20(7):758-762. doi:10.1177/0961203310387182
2. Yılmaz HK, Taşar PT, Carlioglu A. Hypercalcemic crisis in systemic lupus erythematosus. *Acta Endocrinologica (Bucharest)*. 2018;14(1):102-104. doi:10.4183/aeb.2018.102
3. Klein A, Polliack A, Gafter-Gvili A. Systemic lupus erythematosus and lymphoma: incidence, pathogenesis and biology. *Leuk Res*. 2018;75:45-49. doi:10.1016/j.leukres.2018.11.004
4. Dias C, Isenberg DA. Susceptibility of patients with rheumatic diseases to B-cell non-Hodgkin lymphoma. *Nat Rev Rheumatol*. 2011;7(6):360-368. doi:10.1038/nrrheum.2011.62
5. Bernatsky S, Ramsey-Goldman R, Joseph L, et al. Lymphoma risk in systemic lupus: effects of disease activity versus treatment. *Ann Rheum Dis*. 2014;73(1):138-142. doi:10.1016/j.jaut.2012.12.009
6. Bernatsky S, Ramsey-Goldman R, Clarke A. Malignancy and autoimmunity. *Curr Opin Rheumatol*. 2006;18(2):129-134. doi:10.1097/01.bor.0000209423.39033.94
7. Bichile T, Petri M. Incidence of lymphoma associated with underlying lupus: lessons learned from observational studies. *Curr Opin Rheumatol*. 2014;26(2):111-117. doi:10.1097/bor.0000000000000026
8. Smedby KE, Baecklund E, Askling J. Malignant lymphomas in autoimmunity and inflammation: a review of risks, risk factors, and lymphoma characteristics. *Cancer Epidemiol Biomarkers Prev*. 2006;15(11):2069-2077. doi:10.1158/1055-9965.epi-06-0300
9. Barrera-Vargas A, Campos-Guzmán J, Govea-Peláez S, et al. *THU0260 Systemic Lupus Erythematosus and Cytopenias: the Key Findings in Bone Marrow*. BMJ Publishing Group Ltd; 2019. doi:10.1136/annrheumdis-2019-eular.6515
10. Desalphine M, Bagga PK, Gupta PK, Kataria AS. To evaluate the role of bone marrow aspiration and bone marrow biopsy in pancytopenia. *J Clin Diagn Res*. 2014;8(11):FC11. doi:10.7860/jcdr/2014/9042.5169
11. Zhao L, Huang L, Zhang X. Systemic lupus erythematosus-related hypercalcemia with ectopic calcinosis. *Rheumatol Int*. 2016;36:1023-1026. doi:10.1007/s00296-016-3486-3
12. Berar-Yanay N, Weiner P, Magadle R. Hypercalcaemia in systemic lupus erythematosus. *Clin Rheumatol*. 2001;20:147-149. doi:10.1007/s100670170088
13. Alaoui HB, Hamaz S, Bachir H, Eloumri AA, Berrimi M, Serraj K. Concomitant primary hyperparathyroidism and systemic lupus erythematosus: coincidence or not? A new case report. *Pan Afr Med J*. 2020;37(1):228. doi:10.11604/pamj.2020.37.228.26257
14. Xu L, Zhang J, Pu R, Yue Z, Mo Y, Jiang X. Lupus nephritis with mild asymptomatic hypercalcemia in children: a case report and literature review. *Front Pediatr*. 2019;7:507. doi:10.3389/fped.2019.00507
15. Bernatsky S, Ramsey-Goldman R, Rajan R, et al. Non-Hodgkin's lymphoma in systemic lupus erythematosus. *Ann Rheum Dis*. 2005;64(10):1507-1509. doi:10.1136/ard.2004.034504
16. Martín-López M, Galindo M, Pego-Reigosa JM, et al. Clinical characteristics and risk factors associated with lymphoma in patients with systemic lupus erythematosus: a nationwide cohort study. *Rheumatology*. 2023;62(1):217-224. doi:10.1093/rheumatology/keac258
17. Lang J, Ma K, Guo J, Zhang J, Wang Q, Sun H. Clinical significance of elevated antinuclear antibodies in patients with diffuse large B-cell lymphoma: a single center study. *J Cancer Res Ther*. 2018;14(1):213-219. doi:10.4103/0973-1482.183559
18. Cerhan JR, Habermann TM. Epidemiology of marginal zone lymphoma. *Ann Lymphoma*. 2021;5:5. doi:10.21037/aol-20-28
19. Swerdlow SH, Campo E, Harris NL, et al. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. Vol 2. International agency for research on cancer Lyon; 2008.
20. Zucca E, Bertoni F. The spectrum of MALT lymphoma at different sites: biological and therapeutic relevance. *Blood*. 2016;127(17):2082-2092. doi:10.1182/blood-2015-12-624304
21. Boddu P, Mohammed AS, Annem C, Sequeira W. SLE and non-Hodgkin's lymphoma: a case series and review of the literature. *Case Rep Rheumatol*. 2017;2017(1):1658473. doi:10.1155/2017/1658473

22. Belančić A, Vranić L, Ševeljević I, Hadžisejdić I, Načinović AD, Jonjić N. Antiphospholipid antibodies associated with nodal marginal zone lymphoma and its progression to diffuse large B-cell lymphoma—a case report. *Pathol Res Pract*. 2019;215(1):222-228. doi:10.1016/j.prp.2018.10.020
23. Nero P, Rahman A, Isenberg D. Does long term treatment with azathioprine predispose to malignancy and death in patients with systemic lupus erythematosus? *Ann Rheum Dis*. 2004;63(3):325-326. doi:10.1136/ard.2002.005371
24. Guo J, Ren Z, Li J, Li T, Liu S, Yu Z. The relationship between cancer and medication exposure in patients with systemic lupus erythematosus: a nested case-control study. *Arthritis Res Ther*. 2020;22:1-8. doi:10.1186/s13075-020-02228-6
25. Zhang Y, Li W, Zhang P, et al. Hematological malignancies in systemic lupus erythematosus: clinical characteristics, risk factors, and prognosis—a case-control study. *Arthritis Res Ther*. 2022;24:1-10. doi:10.1186/s13075-021-02692-8
26. Kosałka-Węgiel J, Pacholczak-Madej R, Dziedzic R, et al. Malignancy in systemic lupus erythematosus: relation to disease characteristics in 92 patients–a single center retrospective study. *Rheumatol Int*. 2024;1-13. doi:10.1007/s00296-024-05623-3
27. Bernatsky S, Ramsey-Goldman R, Urowitz MB, et al. Cancer risk in a large inception systemic lupus erythematosus cohort: effects of demographic characteristics, smoking, and medications. *Arthritis Care Res*. 2021;73(12):1789-1795. doi:10.1002/acr.24425
28. Gillmore R, Sin WYC. Systemic lupus erythematosus mimicking lymphoma: the relevance of the clinical background in interpreting imaging studies. *BMJ Case Rep*. 2014;2014:bcr2013201802. doi:10.1136/bcr-2013-201802

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