

Systemic Lupus Erythematosus Female with (Diffuse Large B-Cell) Non-Hodgkin's Lymphoma

Mohammed Salem¹, Omer Alharbi², Mohammed Abdaljawad³, Ahmed Alhujaliy⁴, Abeer Alharbi⁵

¹Intenal Medicine, Ibn Sina Medical College, Jeddah, Kingdom of Saudi Arabia, ²Department of Medical, King Fahad Hospital, Kingdom of Saudi Arabia, ³Department of Chest, King Fahad Hospital, ⁴Department Of Histopathology, King Fahad Hospital, Kingdom of Saudi Arabia, ⁵Head of Respiratory Division, Chest and Sleep Medicine Consultant, King Fahad Hospital-Almadina Almonwarah, Kingdom of Saudi Arabia

ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease with multisystem complications arising from both underlying disease activity and therapy-related side effects. SLE's association with lymphoma is a well-established phenomenon. Studies have reported a higher incidence of lymphoma in the SLE population compared with healthy cohorts.^[1,2] A 45-year-old woman with SLE presented with fever, cough, sputum, loss of appetite, and fatigue for 4 months. Before that time, her (SLE) symptoms had been well controlled on hydroxychloroquine, azathioprine, and small dose prednisone. Physical examination at initial evaluation was remarkable for bilateral inspiratory crackles. Laboratory investigations were normal. Computed tomography to chest showed bilateral cavitory pulmonary nodules and masses. Bronchoscopy with transbronchial biopsy was done. The histopathology showed diffuse large B-cell non-Hodgkin's lymphoma. The patient referred to oncology service, where they started her on 4 cycles of R-CHOP by followed 4 cycles of high-dose chemotherapy. She underwent hematopoietic stem cell transplantation and achieved complete remissions.

Key words: Diffuse large B-cell non-Hodgkin's lymphoma, hematopoietic stem cell transplantation, systemic lupus erythematosus

INTRODUCTION

Presenting concern

A 45-year-old married, Saudi female, with a 4-year history of systemic lupus erythematosus (SLE), and chronic hepatitis B presented in February 2017 with fever, cough, sputum, loss of appetite, and fatigue for 4 months. Before that time, her (SLE) symptoms had been well controlled on hydroxychloroquine, azathioprine, and small dose prednisone. Physical examination at initial evaluation was remarkable for bilateral inspiratory crackles. Laboratory investigations were normal. Chest X-ray and computed tomography to chest showed bilateral cavitory pulmonary nodules and masses. Bilateral innumerable lung nodules and masses some of them show cavitation and air bronchogram more predominant at the lower lobes bilaterally the largest one

seen at the right middle lobe adjacent to the heart. There is a cyst in the left lower lobe multiple enlarged mediastinal lymph nodes. Bronchiectatic changes are appreciated at the left ligula [Figures 1 and 2]. Bronchoscopy was done. Bronchoalveolar lavage for acid-fast bacilli and fungi 2 times was negative. The histopathology of transbronchial biopsy showed proliferation of round to ovoid cells with scant cytoplasm, and dense nuclear chromatin showing prominent nucleoli, arranged as diffuse dyscohesive sheets. Immunohistochemistry done, tumor cells are positive for CD45, CD20, and bcl-2 negative pan for pan CK, CD 56, bcl-6, CD 10, and Tdt. CD 3 highlights the cell population. k67 index is >80, Figures 3-5. The patient referred to oncology service, where they started her on 4 cycles of R-CHOP by followed 4 cycles of high-dose chemotherapy (HDCT). She underwent hematopoietic stem cell transplantation and achieved complete remissions.

Address for correspondence:

Abeer Alharbi, Head of Respiratory Division, Chest and Sleep Medicine Consultant, King Fahad Hospital-Almadina Almonwarah, Kingdom of Saudi Arabia. E-mail: mag414@hotmail.com

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Figure 1: Bilateral innumerable lung nodules and masses

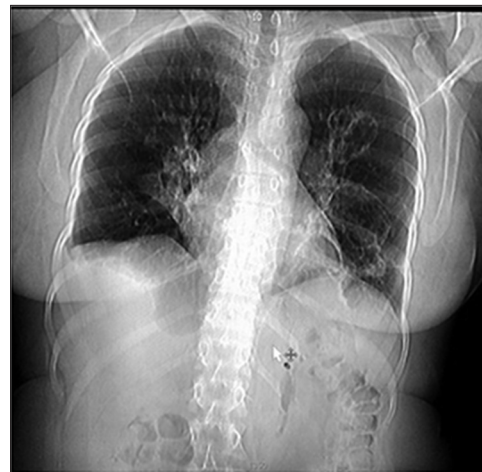


Figure 3: Follow-up X-ray after CHOP

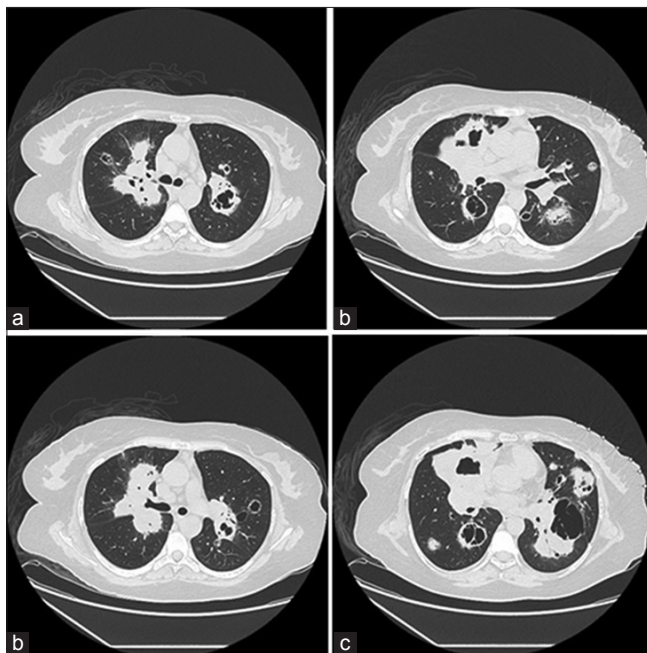


Figure 2: (a) Multiple enlarge Lymph nodes. (b) Bilateral innumerable lung nodules and masses some of them show cavitation and air bronchogram (c) Bronchectatic changes are appreciated in lingula

DISCUSSION

A recent meta-analysis which included 16 observational studies showed a mildly increased risk of overall cancer in SLE compared with the general population.^[3] This risk is most pronounced in SLE-related non-Hodgkin's lymphoma with reported relative risk estimates ranging widely from 4.39 to 44.4 in various studies.

Non-Hodgkin lymphoma (NHL) risk is determined by various factors including age, sex, and race. NHL is more common in men and among White subjects.^[4]

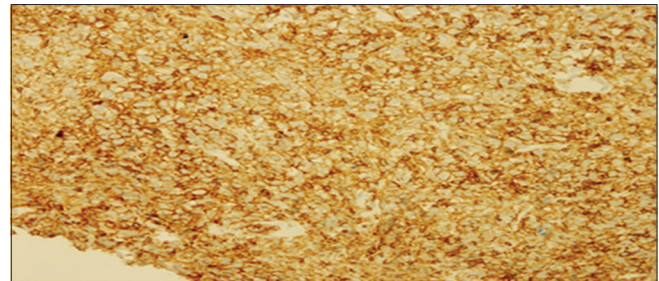


Figure 4: Section shows that tumor cells are positive for CD45 (H and E, x200)

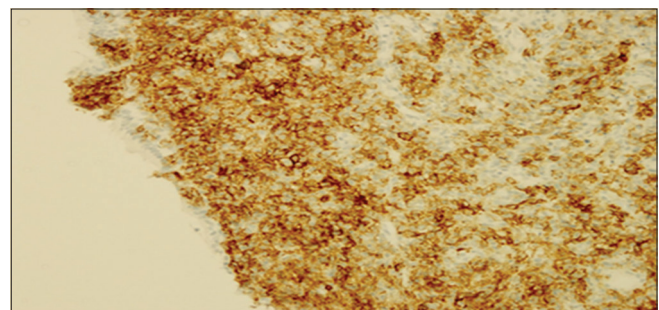


Figure 5: Section shows that tumor cells are positive for CD20 (H and E, x200)

NHL can be divided into two general prognostic groups: Indolent lymphomas and more aggressive (intermediate or high grade) lymphomas. Diffuse large B-cell and Burkitt's lymphoma. The diffuse large B-cell subtype makes up about 30% of all NHL lymphomas in the general population.^[5]

Female sex is associated with better survival for Hodgkin's disease in the general population, as is younger age at time of cancer diagnosis.^[6,7]

Data from the National Cancer Institute suggest the incidence of HL among different racial groups (i.e., White/Caucasians, Black/African Americans, and Hispanics) are similar.^[8]

There is genetic abnormalities association between SLE and NH. The presence of chromosomal abnormalities represents common pathways linking SLE and lymphoproliferative malignancies.

Chromosomal translocations, which may result from uncontrolled lymphocyte activity in active SLE, allow malignant transformation.^[9] The effect of immunosuppressive agents and viral exposures had been evaluated.

In recent small case-control study from Sweden compared 16 cases of NHL arising in SLE with 26 cancer-free control patients with SLE, the use of cyclophosphamide or azathioprine did not elevate lymphoma risk,^[10] while in another study, the relative risk of NHL after cyclophosphamide exposure was 1.1 (95% confidence interval [CI]: 0.3–3.3) and after azathioprine was 0.9 (95% CI: 0.5–2.5). The histology of the NHL cases in SLE suggests that these lesions also are derived from a lymphocyte already been exposed to antigen.^[11]

The current treatment makes the median survival for NHL exceeds 5 years.^[12]

Aggressive tumor types, late stage of presentation which more common in SLE, and therapeutic measures which may be inappropriately withheld from patients with SLE who develop cancer, these might lead to a lower than expected survival.^[13]

Diffuse large B-cell lymphomas (DLBCLs) can be divided into germinal center (GC) - DLBCL and post-GC-DLBCL groups by applying immunohistochemical antibodies.

These subgroups respond differently to chemotherapy. GC-DLBCL group shows better response to CHOP chemotherapy regimen.^[14]

The R-CHOP regimen resulted in the cure of approximately 50% of patients.^[15]

DLBCL is a highly proliferative, this makes it a suitable target for HDCT.^[16]

Of 258 patients with lupus and secondary antiphospholipid syndrome (APS), six developed lymphomas (four DLCL, one Hodgkin's, and one indolent lymphocytic lymphoma). The first five patients were treated with HDCT and achieved complete remissions (CR) with a follow-up comprised between 13 and 172 months. One patient relapsed of lymphoma and died 15 months following CR, with persistent lupus serology. One patient achieved complete remission (CR) of both diseases.^[16]

Hematopoietic stem cell transplantation can be used for severe autoimmune diseases to eradicate the last cancer stem cell.^[17]

CONCLUSION

Patients with SLE are at increased risk of developing non-Hodgkin's lymphoma (NHL).

The patient with aggressive tumor types or late stage of presentation will have lower than expected survival.

Active cancer screening is required in SLE patients with long disease duration.

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