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Pulmonary MALT lymphoma with underlying interstitial lung disease: A case report and rewiev of the literature

Cem Mirili [a, *], Semra Paydas [a], Ali Ogul [a], Serkan Gokcay [b], Mahmut Buyuksimsek [a], Evren Yetisir [a], Ismail Hanta [c], Melek Ergin [d], Emine Bağır Kılıç [d], Isa Burak Guney [e]

[a] Çukurova University, Department of Medical Oncology, Adana, Turkey
[b] Sanliurfa Training and Research Hospital, Department of Medical Oncology, Sanliurfa, Turkey
[c] Çukurova University, Department of Respiratory Medicine, Adana, Turkey
[d] Çukurova University, Department of Pathology, Adana, Turkey
[e] Çukurova University, Department of Nuclear Medicine, Adana, Turkey

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ABSTRACT

Marginal zone lymphoma (MZL) is low grade lymphoma and accounts about 5% of all lymphomas and 5–10% of MZLs are localized in the lung. Interstitial Lung Disease (ILD) is a group of systemic diseases characterized by diffuse inflammation in lung and there is a long list for differential diagnosis. Here we represent a 53 years old man who had been followed as ILD by the department of chest diseases for 1,5 years. Biopsy taken by wedge resection was reported as MZL.

1. Introduction

Extranodal Marginal Zone lymphomas (EN-MZL) belong to low grade Mucosa-associated B-cell lymphoma (MALT lymphoma) originating from post-germinal center B lymphocytes and constitute 5% of Non-Hodgkin's Lymphomas (NHL).[1] MALT Lymphomas are seen most frequently in stomach (50%) and followed by salivary glands, lung, small bowel, thyroid.[2,3] Interstitial Lung Disease (ILD) is a group of diseases causing diffuse inflammation, fibrosis and structural deterioration at variable degrees in the lung parenchyma including alveols, septa, perivascular, perilymphatic and peribronchovascular tissue.[4] Some cases are associated with systemic diseases and some are related with environmental occupational or radiation exposures, infections, collagen tissue diseases, sarcoidosis and vasculitis. In some cases, the cause can not be identified and they are categorized as idiopathic.[5] Here, a case with EN-MZL lymphoma suggesting ILD has been presented and discussed in the light of the available data.

2. Case report

A 53 years old male had been followed as ILD by the department of chest diseases for 1,5 years. High resolution computed tomography (HRCT) showed mosaic pattern in lung parenchyma, subpleural localized bilateral diffuse frosted infiltration, subpleural honey pattern and fibrotic masses (Fig. 1). He had no evidence of viral and autoimmune diseases including hepatitis B and C virus, human immunodeficiency virus, anti nuclear antibody, rheumatoid factor, anti neutrophil cytoplasmic antibody, anti-Ro-La, anti-cyclic citrunillated peptide antibodies, anti-double stranded DNA antibody. He had been treated by oral corticosteroids but there was no evidence of improvement (Fig. 2). Lung biopsy taken with wedge resection was performed due to progressive signs and symptoms. Microscopic examination of specimen was reported as MZL characterized by small-to-medium sized centrocyte-like lymphocytes with irregular nuclei and nucleolus infiltrated lung parenchyma (Fig. 3A H&Ex40). Immunohistochemically, tumor cells were found to be positive for CD20 (Fig. 3B IHCx100), CD43 (Fig. 3C IHCx100),

* Corresponding author.
E-mail addresses: cmirili@cu.edu.tr (C. Mirili), sepay@cu.edu.tr (S. Paydas), mdaliogul@gmail.com (A. Ogul), drsgok@hotmail.com (S. Gokcay), mahmutbuyuksimsek@gmail.com (M. Buyuksimsek), evrenyetisir@hotmail.com (E. Yetisir), ismailhnt@gmail.com (I. Hanta), erginm@cu.edu.tr (M. Ergin), ebagir@cu.edu.tr (E.B. Kılıç), isaburak@gmail.com (I.B. Guney).

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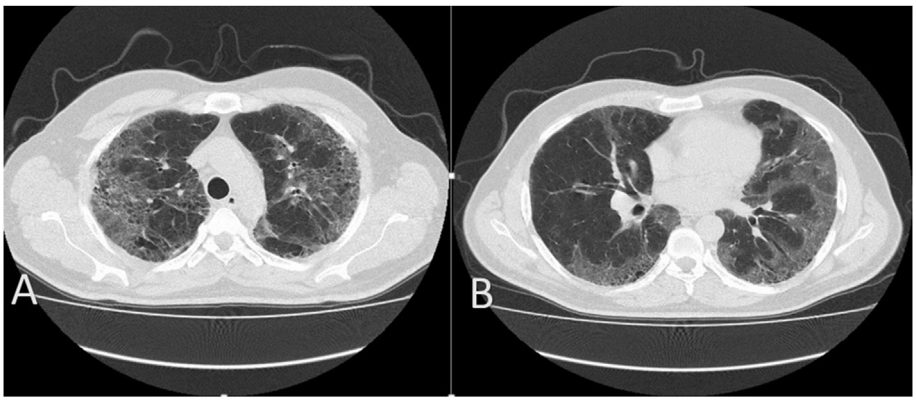

Fig. 1. Interstitial lung disease findings (mosaic pattern, ground glass opacity, honey comb pattern) in HRCT at the initial admittance.

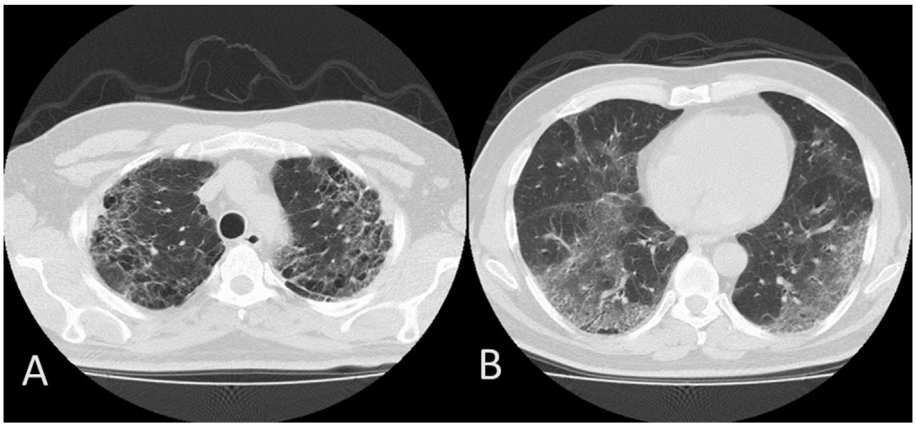

Fig. 2. Control HRCT findings (progression with the honey comb pattern and pulmonary fibrosis added to Fig. 1 findings).

CD38 and CD5 (Fig. 3D IHCx100). He had no fever, night sweats and weight loss. Positron emission tomography-computed tomography (PET-CT) showed multiple cervical lymph nodes and diffuse (disseminated) irregular densities in the lung parenchyma (Fig. 4). There was no evidence of lymphoma infiltration in bone marrow. Immuno-chemotherapy containing rituximab + bendamustine was prescribed for advanced and symptomatic disease. After 4 cycles PET-CT showed partial regression. Chemotherapy was completed with 6 cycles. However his symptoms deteriorated and repeated lung biopsy showed fibrosis in lung parenchyma and he died due to respiratory distress within 11 months.

3. Discussion

ILD is a group of diseases starting from interstitium in the lung and progressing to alveoli and bronchi. Symptoms are dry cough and shortness of breath, and it is difficult to distinguish from other causes of respiratory disorders. Diagnostic procedures are pulmonary function tests including diffusion capacity of lung for carbon monoxide (DLCO), bronchoalveolar lavage (BAL), HRCT and serologic tests for infections and autoimmune disorders. However generally specific cause is not detected. Lung biopsy can reveal specific diagnosis only in a limited number of cases, and biopsy is indicated in cases not-responding to nonspecific treatment.

Pulmonary MALT lymphomas are seen in some cases presenting with ILD. Approximately 50% of the patients are symptomatic and 50% have cough and dyspnea (Table 1). B symptoms are present in about 20% of these patients. Our patient had been followed with respiratory symptoms without B symptoms for 1,5 years with the diagnosis of ILD. Lung biopsy was done due to no response to steroid treatment.

ILD is characterized by bilateral basal and peripheral reticular opacities, bronchiectatic areas, honey comb pattern and ground glass opacity in HRCT. As seen in Table 1, bilateral nodular or patchy opacities suggesting ILD are seen in approximately 50% of cases with pulmonary lymphoma and differential diagnosis can be done only with lung biopsy.[6–9] For this reason, although the HRCT has become a standard test for the evaluation of patients with possible ILD, imaging methods alone can not be reliable due to similarity of radiological findings.[10]

In a study conducted by Borie et al., 5 years survival rate has been found to be more than 90% in pulmonary lymphomas with a relatively indolent clinical course. In this study 58.7% of the patients have been treated with chemotherapy.[3] Progression-free and overall survival in this study has not been found to be related with age, gender, performance score, delayed diagnosis or patterns of pulmonary involvement. In our patient, fibrosis was detected in second lung biopsy after immunochemotherapy. We predict it can be proposed that the clinical outcome of our case will not be favorable because of the fibrotic process in lung parenchyma which is an irreversible status.

60-80% of EN-MZLs are seen in early-localized stage and preferred therapies in these cases local modalities such as surgery and/or radiotherapy.[11] However there is no consensus in cases with advanced stage disease ve it is proposed to make analogy from follicular lymphoma for the managmenet of cases with advanced

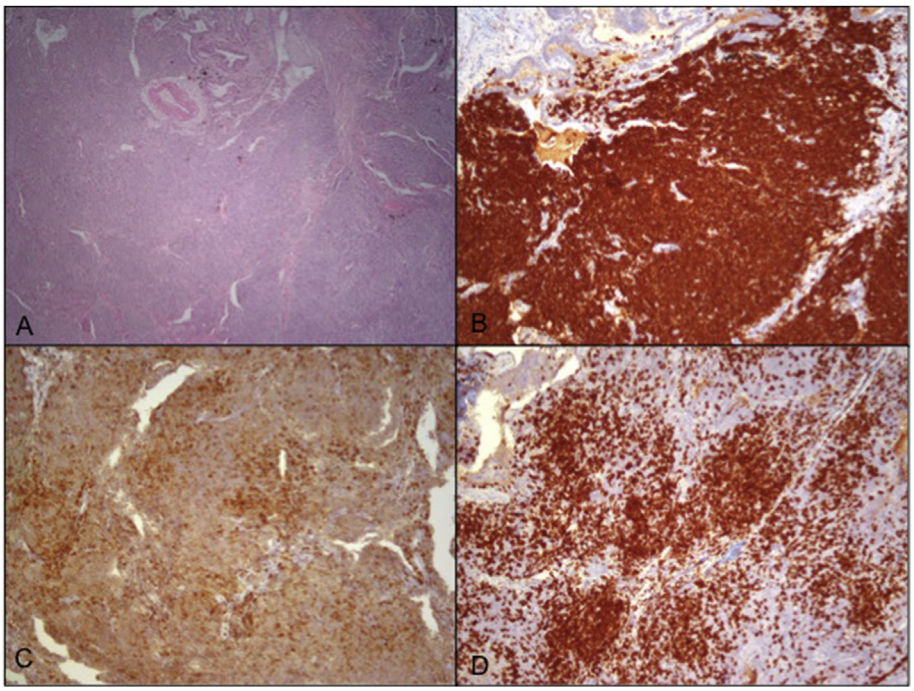

Fig. 3. Microscopic examination of the wedge resection specimen; small-to-medium size centrocyte-like lymphocytes with irregular nuclei slightly nucleolus infiltrated lung parenchyma (figüre 3A H&Ex40). Immunohistochemically, tumor cell were positive CD20 (Fig. 3B IHCx100), CD43 (Fig. 3C IHCx100), CD38 and CD5 (Fig. 3D IHCx100), kappa and lambda staining were polyclonal.

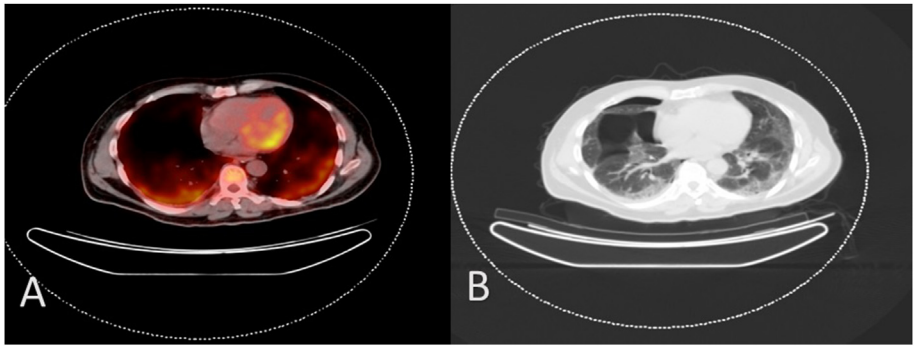

Fig. 4. PET-CT findings (dissemated lymphoma lung). PET fusion (Fig. 4A) and PET Lung parenchyma (Fig. 4B).

Table 1
Literature rewiev Pulmoner Lymphoma.

References	3	6	7	8	9
Authors	Borie	Huang	Zinzani	Kurtin	Kocaturk
Number of patients	63	23	12	41	8
Asypmptomatic	% 36	% 44	% 50	% 56	% 0
Cough	%41	%44	%50	%28	%50
Dsypne	%35	%35	%40	%25	
B Sypmtom	%22	%26		%5	%40
Unilateral pattern[a]	%52	%43	%75	%73	%50
Bilateral pattern[a]	%48	%57	%25	%27	%50
Noduler pattern[a]	%55	%65		%80	%20
Patchy pattern[a]	%35	%35		%15	%60

[a] HRCT findings.

stage and/or symptomatic disease. Initial therapy is changes from watch and wait to single agent rituximab or immunochemotherapy like R + CHOP (rituksimab, cyclophosphamide, doxorubicin, vincristine, and prednisone), R + CVP (rituksimab, cyclophosphamide, vincristine, and prednisolone), R + BENDAMUSTIN (BR).[12–15] BR has been found to be preferred therapy with good efficacy and low toxicity profile in cases with symptomatic and/or advanced stage indolent lymphoma. Additionally BR has been found to be similar PFS in cases with MZL.[16] We used BR in our symptomatic and advanced stage disease with the advantage of this regimen.

In conclusion lymphoma must be considered in the differential diagnosis of ILD in addition to many diseases including autoimmune diseases, sarcoidosis, asbestosis, chemicals, drugs, genetic disorders (Niemann-Pick, Gaucher). Lymphoma can not be diagnosed unless lung biopsy is performed. EN-MZL lymphomas show variable outcome but prognosis is bad in cases with fibrotic process in lung parenchyma.

References

1. Armitage James O, Weisenburger Dennis D. New approach to classifying non-Hodgkin's lymphomas: clinical features of the major histologic subtypes. Non-Hodgkin's Lymphoma Classification Project. *J Clin Oncol*. 1998;16(8):2780–2795.
2. Thieblemont Catherine, Berger Francoise, Dumontet Charles, et al. Mucosa-associated lymphoid tissue lymphoma is a disseminated disease in one third of 158 patients analyzed. *Blood*. 2000;95(3):802–806.
3. Borie R, Wislez M, Thabut G, et al. Clinical characteristics and prognostic factors of pulmonary MALT lymphoma. *Eur Respir J*. 2009;34(6):1408–1416.
4. Nici L, Donner C, Wouters E, et al. American thoracic society/European respiratory society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med*. 2006;173(12):1390–1413.
5. Demedts M, Wells AU, Anto JM, et al. Interstitial lung diseases: an epidemiological overview. *Eur Respir J*. 2001;18(32 suppl):2s–16s.
6. Huang H, Lu ZW, Jiang CG, et al. Clinical and prognostic characteristics of pulmonary mucosa-associated lymphoid tissue lymphoma: a retrospective analysis of 23 cases in a Chinese population. *Chin Med J*. 2011;124(7):1026–1030.
7. Zinzani PL, Tani M, Gabriele A, et al. Extranodal marginal zone B-cell lymphoma of MALT-type of the lung: single-center experience with 12 patients. *Leuk Lymphoma*. 2003;44(5):821–824.
8. Kurtin PJ, Myers JL, Adlakha H, et al. Pathologic and clinical features of primary pulmonary extranodal marginal zone B-cell lymphoma of MALT type. *Am J Surg Pathol*. 2001;25(8):997–1008.
9. Kocatürk Cİ, Seyhan EC, Günlüoğlu MZ, et al. Primary pulmonary non-Hodgkin's lymphoma: ten cases with a review of the literature. *Tuberk. ve Toraks*. 2012;60(3):246–253.
10. Kanne JP. Interstitial lung disease (ILD): imaging finding, and the role of imaging in evaluating the patient with known or suspected ILD. *Semin Roentgenol*. 2010;45(3). https://doi.org/10.1053/j.ro.2009.09.001.
11. Teckie S, Qi S, Chelius M, et al. Long-term outcome of 487 patients with early-stage extra-nodal marginal zone lymphoma. *Ann Oncol*. 2017;28.5:1064–1069.
12. Raderer M, Kiesewetter B, Ferreri AJ. Clinicopathologic characteristics and treatment of marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma). *CA A Cancer J Clin*. 2016;66(2):152–171.
13. McLaughlin P, Grillo-López AJ, Link BK, et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. *J Clin Oncol*. 1998;16(8):2825–2833.
14. Coiffier B, Haioun C, Ketterer N, et al. Rituximab (anti-CD20 monoclonal antibody) for the treatment of patients with relapsing or refractory aggressive lymphoma: a multicenter phase II study. *Blood*. 1998;92(6):1927–1932.
15. Conconi A, Martinelli G, Thiéblemont C, et al. Clinical activity of rituximab in extranodal marginal zone B-cell lymphoma of MALT type. *Blood*. 2003;102(8):2741–2745.
16. Rummel MJ, Niederle N, Maschmeyer G, et al. Bendamustine plus rituximab versus CHOP plus rituximab as first-line treatment for patients with indolent and mantle-cell lymphomas: an open-label, multicentre, randomised, phase 3 non-inferiority trial. *Lancet*. 2013;381(9873):1203–1210.