

## Kemik iliğinde Splenik Marjinal Zon Lenfoma: Bir Olgu Sunumu ve Literatürün Gözden Geçirilmesi

### Splenic Marginal Zone Lymphoma In Bone Marrow: A Case Report And Review of the Literature

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#### Öz

Marjinal zon lenfomalar (MZL), sekonder lenfoid foliküllerin marjinal bölgesinde B lenfositlerinden kaynaklanan nadir görülen düşük dereceli B lenfomalarıdır. Nodüler Hodgkin lenfomalarının (NHL) %1'inden azını oluştururlar. Nadir bir vakayı literatür eşliğinde sunmayı amaçladık. 51 yaşında erkek hasta hematoloji kliniğinde değerlendirildi. Periferik yaymada atipik lenfositler görüldü. Kemik iliği aspirasyonunda atipik küçük B-lenfosit infiltrasyonu ve kemik biyopsisinde interstisyel tutulum izlendi. Dünya Sağlık Örgütü'nün sınıflamasına göre marjinal bölge lenfomalar üç gruba ayrılır: Ekstranodal MALT lenfoma, dalak MZL (SMZL) ve nodal MZL. Her üç grupta da kromozomal, genetik ve immünofenotibik benzerlikler vardır. SMZL, genellikle kemik iliği ve dalak hilar lenf düğümleri tutan bir lenfomadır. Dalak periferik kan ve bazen karaciğer infiltrasyon gösterir, genellikle yaşamın altıncı on yılında ortaya çıkar. Tedavi için standart bir yaklaşım yoktur. Hastaların üçte ikisi tanı sırasında asemptomatiktir ve hastaların önemli bir kısmı başarılı bir şekilde splenektomi ile tedavi edilir.

**Anahtar Kelimeler:** *B-lenfosit, marjinal zon B-hücreli lenfoma, kemik iliği*

#### ABSTRACT

Marginal zone lymphomas (MZL) are rare low-grade B lymphomas that originate from B-lymphocytes in the marginal zone of the secondary lymphoid follicles. They comprise less than 1% of nodular Hodgkin lymphomas (NHL). We aimed to present a rare case with the literature. A 51-year-old male patient was evaluated in the hematology clinic. Atypical lymphocytes were observed in peripheral smear. Atypical small B-lymphocyte infiltration in aspiration cytology and bone marrow interstitial involvement were observed in bone marrow biopsy. According to the World Health Organization's classification, marginal zone lymphomas are divided into three groups: Extranodal MALT lymphoma, splenic MZL (SMZL), and nodal MZL. All three groups have chromosomal, genetic, and immunophenotypic similarities. SMZL is a lymphoma that typically involves the bone marrow and hilar lymph nodes of the spleen. The spleen shows infiltration to peripheral blood and sometimes the liver, and usually occurs in the sixth decade of life. There is no standardized approach for treatment. Two-thirds of patients are asymptomatic during diagnosis, and a significant proportion of patients are successfully treated with a splenectomy.

**Keywords:** *B-lymphocyte, marginal zone B-cell lymphoma, bone marrow*

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## INTRODUCTION

Splenic marginal zone lymphoma (SMZL) is a slow-growing B-cell non-Hodgkin lymphoma. SMZL is a disease with peripheral blood and bone marrow involvement. It is characterized by splenomegaly (1). In two-thirds of cases, SMZL is diagnosed based on histopathological and flow cytometry examination of lymphoma cells found in peripheral blood, without spleen histology or bone marrow biopsy specimens, as in our case. Extranodal involvement and peripheral lymph node involvement are very rare (1,2).

## CASE REPORT

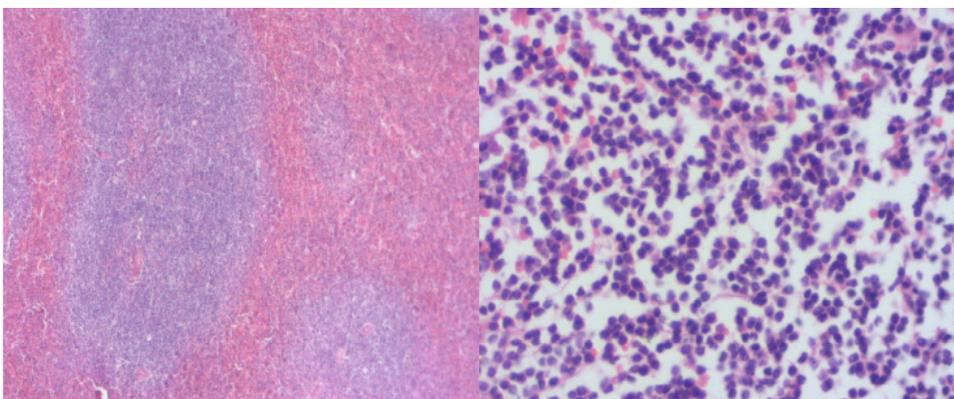
A 51-year-old male patient was admitted to the internal medicine polyclinic with complaints of asthenia, fatigue, and loss of appetite. No pathology was found except sple-

nomegaly during an abdominal computed tomography (CT) scan for anemia and splenomegaly etiology. The patient was referred to the hematology polyclinic. Atypical lymphocytes were observed in the peripheral smear. There was atypical small B-lymphocyte infiltration in bone marrow aspiration and atypical small B-lymphocyte infiltration of the interstitial type in bone marrow. The results of the bone marrow biopsy and the flow cytometric studies were consistent with SMZL, so the patient was diagnosed with chronic B-lymphoproliferative neoplasm, marginal zone lymphoma involvement. A splenectomy was performed. The splenectomy material measured 28×18×9 cm and weighed 2660 g. It formed nodular structures in the cross-section and there was a gray-beige color infiltration (Figure 1).



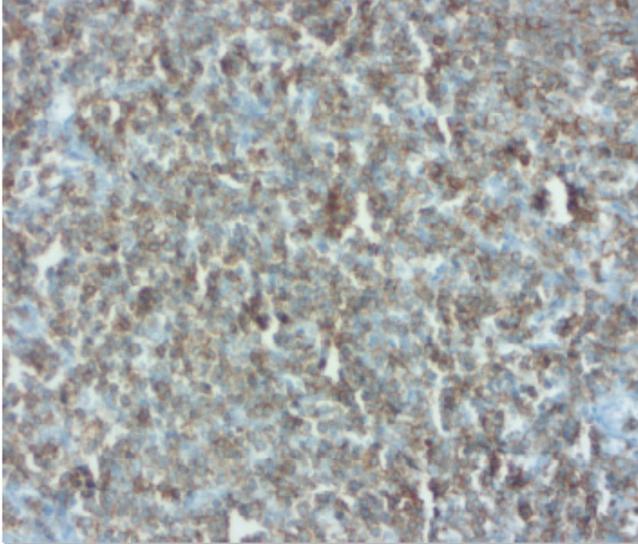
**Figure 1.** Splenic marginal zone lymphoma. Gross photography of spleen showing marked expansion of the white pulp, as well as infiltration of the red pulp (H&E;×100).

Microscopic examination revealed a small to medium lymphoid infiltration that formed nodules that removed the “mantle” region around reactive germinal centers in the white pulp and spread into the red pulp (Figure 2).



**Figure 2.** a) SMZL showing infiltration of white and red pulp (H&E;×100). b) White pulp nodule showing the small lymphocytes (H&E;×100).

In immunohistochemical staining, CD20 (Figure 3) and Bcl2+, CD3, CD23, CD43, CD38, CD5, CD10, Bcl6, and Cyclin D1 were negative, and the case was diagnosed as SMZL.



**Figure 3.** Infiltration is CD20 positive (IHC;×200).

## DISCUSSION

SMZL, a B-cell neoplasm that is predominately formed by small cells, involves white pulp follicles of the spleen, splenic hilar lymph nodes, bone marrow, and often peripheral blood (1,2). It is a rare low-grade lymphoma subtype forming less than 1% of NHLs (3). The term SMZ-cell lymphoma was first used in 1992 by Schmid in a study of four female patients with primary splenic low-grade lymphoma with morphological and immunophenotypic features reminiscent of SMZ cells (3). The entity that was first described in 1979 by Neiman et al. was characterized in detail in a series of 22 patients in 1987 by Melo et al. and was called Splenic Lymphoma with Villous Lymphocyte (SLVL) due to the presence of villous protruding lymphoid cells in the peripheral blood and were considered to be the leukemic form of SMZLs (4,5). SLVL is regarded by pathologists as a homogeneous entity with the same histology as SMZL.

Both are characterized by the presence of cytoplasmic protruding lymphoid cells in the peripheral blood as well as splenic and bone marrow involvement. Since they are different clinicopathologic entities and may require different approaches in treatment, differential diagnosis is important from similar chronic lymphoproliferative diseases, especially splenic MZL and classical hairy cell leukemia. Although morphological examinations of bone marrow smears are useful in lymphoma/leukemia infiltration, it is insufficient to diagnosis SMZL.

Bone marrow biopsy is more meaningful in terms of both

morphological evaluation and the involvement patterns of marrow areas (such as intertrabecular nodular, intrasinusoidal). Accompanying morphological examination with immunophenotyping (primarily by immunohistochemical flow cytometry) is essential for differential diagnosis.

The most common immune profile of SZL is CD20+,CD3-,CD23-,CD43-, CD38-,CD5-,CD10-,Bcl6-, Bcl2+, Cyclin D1-, IgD+, p27+, and Annexin A1-. Morphological and immunohistochemical examination of bone marrow biopsy specimens is diagnostic in most SMZL cases. However, the morphological and immunohistochemical evaluation of splenectomy and spleen for diagnosis (also a treatment option) is an another approach option, for example, in cases with different immune profiles or cases that lacking adequate lymphoma infiltration sites in the bone marrow biopsy specimen. In our case, CD20 and Bcl2+, CD3, CD23, CD43, CD38,CD5, CD10, Bcl6,and Cyclin D1 were negative in immunohistochemical staining.

SMZL is observed almost equally in both sexes and more commonly in adults over fifty years of age. Our patient was a 51-year-old male patient. Patients are usually asymptomatic, but splenomegaly was detected during the examination. Almost all patients have middle or large splenomegaly on the left upper quadrant that can lead to stiffness and discomfort (2,7). The presence of splenomegaly exceeding the rib ring by seven cm was reported in 70% of patients (6). Our case had splenomegaly and anemia. Hepatomegaly is rare. Although splenic hilar lymphadenopathies can be observed, superficial lymphadenopathy is not common (5-7). Apart from symptoms associated with splenomegaly, the most common symptom is usually mild to moderate anemia, as in our case. Leucocytosis with lymphocytosis accompanied by thrombocytopenia with or without anemia is the most commonly defined peripheral blood abnormality (3,5-7). In our case, cytopenia with 23.08. 103/ $\mu$ l (normal value 4.5-10.103/ $\mu$ l), white blood cells, neutrophil was 33.1% (normal value 41-75%), and lymphocyte was 57.0% (normal range: 12-48%) are usually associated with hypersplenism. Anemia with hemoglobin below 11g/dl is observed in 30-50% of cases, and thrombocytopenia below 100,000/ $\mu$ l is observed in about 20% of cases (6). The hemoglobin in our case was 14g/dl, and the platelets were 623×103/ $\mu$ l (normal range: 150-450×103/ $\mu$ l). Despite the presence of leukocytosis with lymphocytosis in a significant proportion of patients, leukopenia may also be present during the diagnosis (6). The incidence of severe neutropenia is quite rare. In two-thirds of cases, splenic villous lymphocytes with typical features constitute more than 25% of leukocytes in the peripheral blood (3). In cytological examination, the

SLVL cells are slightly larger than the chronic lymphocytic leukemia (CLL) lymphocytes and most are round nucleated cells with a dense chromatin structure and a single nucleolus. The cytoplasm is usually broad and irregular with a short, thin villus, the edges of which are spread around the cell or concentrated at one point (3).

Clinically, there is no symptom except for localized or systemic lymphadenopathy in the majority of cases. In particular, cervical lymph node involvement is more frequent. Although different infiltration patterns of SMZL are present in the spleen, nodular structures that delete the “mantle” region around reactive germinal centers in the white pulp and show marginal zone differentiation are regarded as typical, as in our case. SMZL also infiltrates the red pulp in micronodule clusters.

## CONCLUSION

SMZL is a disease that involves peripheral blood and bone marrow cells and is characterized by splenomegaly. In two-thirds of cases, SMZL diagnoses are based on histopathological and flow cytometry examination of lymphoma cells in peripheral blood without a spleen histology and/or bone marrow biopsy specimens, as in our case. Extranodal involvement and peripheral lymph node involvement are very rare.

**Informed Consent:** Written informed consent was obtained from patient who participated in this study.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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