

# Systemic Lupus Erythematosus Revealing Splenic Marginal Zone Lymphoma. A Case Report

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**Abstract** Autoimmune manifestations are common in splenic marginal zone lymphoma (SMZL) and are sometimes the presenting feature of the disease. We report Herein the case of a 72-year old woman presenting with systemic lupus erythematosus revealing SMZL. To our knowledge, there are only 3 case reports of SLE associated to SMZL. In case of authentic autoimmune disease with unusual clinical features Physician awareness is recommended, to rule out associated lymphoproliferative syndrome.

**Keywords:** *systemic lupus erythematosus, splenic marginal zone lymphoma*

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## 1. Introduction

Autoimmune manifestations are common in splenic marginal zone lymphoma (SMZL) and are sometimes the presenting feature of the disease [1]. Autoimmune cytopenia (anemia, thrombocytopenia) are the most frequently reported autoimmune conditions. However, other immunological manifestations may be associated with SMZL. We report hereby the case of a 72-year-old woman presenting with a systemic lupus erythematosus (SLE) revealing a SMZL.

## 2. Case Report

A 72-year-old female patient without medical history presented with prolonged fever and pallor. The patient's symptoms had begun 6 months before and worsened progressively. She complained of fever (>39°C) spiking once a day, usually in the evening, with undefined abdominal pain; she also reported recent palpitations, dyspnea and vertigo. Physical examination showed, besides fever (>39°C), blood pressure of 110/70 mmHg, heart rate of 120 beat per minute, mucocutaneous pallor, malar rash, proteinuria on urine dipstick, bilateral axillary, and cervical lymph node enlargement. Pulmonary examination revealed dullness on the right basis and abdominal palpation concluded to a liver and spleen enlargement. Cell blood count revealed bicytopenia with normochromic normocytic anemia of 6 g/dl, low platelet count of 77000 elements/mm<sup>3</sup>, and lymphopenia of 600 elements/mm<sup>3</sup>. Liver tests revealed anicteric cholestasis

and transaminases elevated twice the normal range. Creatinine rate was 6 mg/l and 24-hour proteinuria was 0.7 g. Serum protein electrophoresis showed monoclonal type hypergammaglobulinemia of 27 g/l, and serum immune-electrophoresis confirmed Ig M kappa type. Direct Coombs's test was positive IgG type. Immunological investigation revealed positive antinuclear antibodies with a level of 1/1280, anti-DNA and antiphospholipid antibodies were negative. Infectious investigations including repeated bacteriological and fungal blood cultures, Mycobacterium tuberculosis throat examination, and viral serological investigations (Hepatitis C virus, Hepatitis B virus, Epstein-Barr virus, and Cytomegalovirus) were negative. Chest X-ray revealed right pleural effusion. Echocardiography was normal. Thoracic and abdominal computed tomography scan revealed diffuse lymph node enlargement on cervical, mediastinal and hepato-splenic hilar adenopathy associated to right mild pleural effusion. Bone marrow and liver biopsies concluded to lymphoid infiltrate, and immunohistochemical study showed that tumor cells stained positive with CD20<sup>+</sup>, CD3<sup>+</sup>, CD5<sup>+</sup> phenotype thus, concluding to a splenic marginal zone lymphoma (SMZL). The diagnosis of SLE revealing stage 4 SMZL was retained. The treatment was as follows: 1 mg/kg/day of prednisone with progressive tapering associated to 375 mg/m<sup>2</sup> of body surface of rituximab once weekly during 4 weeks. The patient's outcome was favorable and the decline was 12 months.

## 3. Discussion

Splenic marginal zone lymphoma (SMZL) was reported for the first time in 1992 [2] and is considered to be a non-Hodgkin-B-lymphoma (NHBL) with a primitive splenic localization [3]. Its prevalence varies between 1 and 2 % of NHBL [3] and is often associated to hepatitis C virus infection [4]. Its clinical presentation is often limited to a spleen enlargement associated to hilar spleen adenomegaly and liver enlargement and multiple lymph node enlargement are reported in only 15 % of cases [5,6]. Autoimmune disorders associated to SMZL are reported in 20% of cases, which is often limited to biological abnormalities such as positive rheumatoid factor, auto immune cytopenia, positive antinuclear antibodies and antiphospholipid antibodies [1,5,7]. To our knowledge, there are only 3 case reports of SLE associated to SMZL [1,8,9] and SLE was inaugural in only one case [1] (Table 1). In fact, in a national Swedish systemic lupus erythematosus cohort including 6438 patients, 16 patients developed NHBL and only 2 patients developed SMZL [10]. In the previous reports, SMZL occurred 3 and 7 years after lupus diagnosis [8,9]. These patients had not previously received immunosuppressive agents [8,9]. Our

patient had some unusual features such as her advanced age at onset, the tumor syndrome and the monoclonal gammopathy. These abnormalities have made us look for a possible association with a lymphoma. In our case, the SMZL diagnosis was based on liver and bone marrow histological findings; in fact, marrow biopsy was contributive because of a medullar invasion reported in 95% of cases [5]. Furthermore, in our case, HCV serology was negative as in the case reported by Voinchet et al [1]. In the other cases, HCV serology was not mentioned [8,9]. Splenectomy, chemotherapy, and anti viral agents (for HCV related SMZL) are the alternatives used to treat SMZL. In our case, a combined treatment of rituximab-prednisone was successful, with a favorable outcome concerning the two conditions. In previous data, the treatment was reported in only one case and consisted of a splenectomy with a chemotherapy associating cyclophosphamide, adriamycine, vincristine, and prednisone, with a favorable outcome [8]. Further studies with larger effectives are needed to conclude about the appropriate treatment. SMZL associated to SLE is extremely rare.

**Table 1. Clinical, immunological features, and outcome in patients with SLE and SMZL.**

	Case 1 (9)	Case 2 (8)	Case 3 (1)	Our case
Age at SLE onset (year)	Uns	66	66	72
Age at SMZL onset (year)	Uns	69	66	72
Delay (year)	7	3	0	0
Clinical features of SLE	Alopecia, discoid lupus, polyarthritis, proteinuria, lymphopenia	Polyarthritis, pleuropericarditis, lymphopenia	Polyarthritis, pleural effusion, lymphopenia, hemolytic anemia, thrombocytopenia	Malar rash, hemolytic anemia, thrombocytopenia, lymphopenia, proteinuria, pleural effusion
immunological features	Positive ANA	Positive ANA (1/1000), positive anti-DNA	Positive ANA (1/32 000), positive anti-platelet antibodies,	Positive ANA (1/1280)
Clinical presence of lymphoma	Uns	Hepatosplenomegaly, lymph nodes, monoclonal gammopathy (Ig G kappa)	General symptoms, splenomegaly, lymph nodes, monoclonal gammopathy (Ig G kappa)	General symptoms, hepatosplenomegaly, lymph nodes, monoclonal gammopathy (Ig M kappa)
Treatment	Uns	Splenectomy + chemotherapy (cyclophosphamide, adriamycine, vincristine, and prednisone)	Uns	Rituximab+prednisone
Outcome	Uns	Favorable	Uns	Favorable
Decline (months)	Uns	6	Uns	12

ANA: antinuclear antibodies, Uns: unspecified

## 4. Conclusion

SMLZ can be associated to auto-immune abnormalities and more rarely to auto-immune diseases such as SLE which may be inaugural at clinical presentation. SMLZ associated to SLE is a rare condition.

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