CASE REPORT

A Peculiar Case of Splenic Marginal Zone Lymphoma and Review of Literature

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INTRODUCTION

The term splenic marginal zone lymphoma (SMZL) was first coined by Schmid and colleagues in 1992 who used it to describe four cases of primary low grade B cell lymphomas of the spleen with distinct clinical, morphological and immunophenotypic features (1). It is now clear that SMZL and splenic lymphoma with villous lymphocytes (SLVL) have the same pathologic features but different expressions of circulating cells (2,3). After the recognition of an unusual intrasinusoidal bone marrow infiltration definitive diagnosis can be made by bone marrow biopsy alone (4), avoiding an unnecessary splenectomy (5).

CASE REPORT

A 44-year-old educated lady presented in outdoor clinic with complaints progressive fatigue and dragging sensation in the abdomen over several months and fever for 20 days. Physical examination revealed a febrile condition, moderately severe pallor, marked splenomegaly extending up to the left iliac fossa and mild hepatomegaly – 3 cm below the right costal margin. During follow up in OPD, the patient was found to have fluctuating splenomegaly as documented on clinical and ultrasonographic examination during routine follow up of the patient. This was further confirmed by computerized tomography (CT) scan. Complete blood count examination (CBC) showed that the patient had hemoglobin of 6.8 g/dl, total leukocyte count of 2400 cell/µl with 55% neutrophils, 50% lymphocytes, 2% monocytes, 3% eosinophils and platelet count of 28,000 cell/µl. Peripheral blood smear showed moderate normocytic normochromic anemia and CBC findings were validated.

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Computed tomography scan of abdomen and thorax confirmed presence of massive splenomegaly with prominent splenic hilar lymph nodes, hepatomegaly and absence of mediastinal or other retroperitoneal lymph nodes.

Common possible causes of massive splenomegaly such as Kala Azar, Malaria and CML were excluded on the basis of absence of fever, the fact that the patient was from a non-endemic area for Leishmaniasis and lack of myeloproliferation features in the peripheral blood examination. Flowcytometry was done early during the course of workup and provided definite clue to the diagnosis which was confirmed by histopathological examination. Splenectomy was done for definitive management. The splenectomy specimen measured 25×16×7 cm and had five attached hilar lymph nodes with the largest measuring 1.5 cm. A wedge biopsy from the liver measuring 1.5 cm in length was also taken. Cut section of the spleen showed numerous tiny nodules distributed diffusely over the entire surface.

Bone marrow aspirate examination showed atypical lymphoid cells and erythroid hyperplasia. Immunophenotyping of peripheral blood mononuclear cells by flow cytometry and evaluation of the cells in lymphocyte gate showed cells positivitive for CD19; negative for CD10, CD5 and CD3. Trephine biopsy showed intrasinusoidal bone marrow infiltration. Serum electrophoresis showed an M band which was shown to be immunoglobulin M (IgM) – kappa chain by immunofixation. Serum IgM levels were 760 mg/dl. Flow cytometry of peripheral blood mononuclear cells showed normal ratio of T (CD3) to B (CD19) lymphocytes which excluded leukemic spill over. The panel of antibodies used is shown in Table 1.

Table 1. Panel of antibodies used for flow cytometry examination and results of bone marrow aspirate.

Antibody Combination	Result
IgG1 FITC/ IgG2 PE	As isotype controls
CD3 FITC/ CD19 PE	CD3 (14%) CD19 34%
CD3 FITC/CD16+56	CD3- and CD16+56PE -1.27%
CD5 FITC/CD19 PE	0.86 %
CD10 FITC/CD19 PE	< 1%
CD8 FITC/CD3 PE	CD3 -14%, CD8 &CD3+ 5%
CD3 FITC/CD4 PE	Double positive – 7%
CD22 FITC/CD19 PE	Double positive –27%
CD25 FITC/CD19 PE	Double positive – 0%

IgG = immunoglobulin G; FITC = Fluroscein isothiocynate; PE = Phycoerytherin

A diagnosis of SMZL was made on the basis of clinical and laboratory investigations. Microscopy of resected specimen revealed a marginal zone pattern of proliferating smaller atypical lymphocytes which had scant cytoplasm, and slightly irregular nuclei

with inconspicuous nucleoli. Similar cells were present diffusely in the splenic hilar lymph nodes. Liver wedge biopsy showed intact hepatic architecture with mild kupffer cell hyperplasia, focal hepatocyte necrosis and similar lymphoid infiltrate in some of the portal tracts. Immunohistochemistry of paraffin sections from spleen showed the tumor cells to be CD19+ and CD3. Six months after splenectomy there was no evidence of residual disease on examination of peripheral blood, bone marrow and abdomen imaging. The patient was apparently in perfect health at the last follow up thirteen years after treatment.

DISCUSSION

SMZL is a rare non-Hodgkin's lymphoma with primary involvement of the spleen and the typical immunophenotype (IgM+; CD5, CD10 and CD23-) has recently been recognized as an entity (6). The incidence has been estimated to be less than 1% of all NHL (7) and it constitutes 8-14% of lymphoma in surgically removed spleens involved by lymphoproliferative disorder (8). The median age of patients with SMZL is 68 years (range, 22-79 years) with a male to female ratio of 1:1.8. (9). This case report is written to document special features of this case and also because the patient was worked up completely except for cytogenetics.

This case report is one of the few studies where the diagnosis was made on the basis of microscopic examination and flow cytometry of marrow aspirate before splenectomy and was confirmed by histopathological examination including immunohistochemistry of the splenectomy specimen. The patient had typical clinical and laboratory features: which was also substantiated by the indolent behavior exhibited by the tumor - a characteristic feature of SMZL (9). Diebold *et al.* mention that although it is biologically more benign, primary SMZL does not have any distinctive microscopic features to differentiate from secondary involvement of spleen (10).

This case report was submitted due to early presentation, fluctuating splenomegaly as documented by clinical examination and ultrasound followed by thirteen year symptom free survival in spite of hepatic, hilar lymph node and marrow involvement.

The case was compared with three large studies on SMZL and compared the clinical and laboratory findings with those in this study and the same is shown in Table 2.

Table 2. Review of three medical databases using descriptors for the main clinical / lab findings in this study (11-13).

Parameter	Chacon *et al.* (11)	Baseggio *et al.* (12)	Tierens *et al.* (13)	current study
Number of cases	60	66	23	1
Females (%)	37	48	48	100
Specific features	none	CD5+ (24), CD5– (42)	Ongoing mutations	Fluctuating splenomegaly
IgM paraprotein	13%	50%	Not mentioned	100%
Age median	63	62.5	67	44

Diagnosis	Splenectomy	Biopsy and FC	FC, FISH	FC, Biopsy

FC = Flowcytometry FISH = Fluroscent- in situ- hybridization

CONCLUSION

SMZL is a distinct entity with characteristic morphological, biological and immunophenotypic features from other low grade lymphomas involving the spleen. This patient had exhibited some unusual clinical features by way of fluctuating splenomegaly during follow up and was in excellent health after thirteen years follow up in spite of involvement of liver and splenic hilar lypmhnodes at surgery eight years back.

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