Clinicohematological profile of Splenic Marginal Zone Lymphomas- Case report series

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ABSTRACT

Background: Marginal zone lymphoma (MZL), an indolent B-cell lymphoproliferative disease, includes 3 entities: Mucosa-associated lymphatic tissue (MALT) lymphoma, splenic MZL (SMZL) and nodal MZL. Of these, the SMZL represents 20% of MZL, accounting for - less than 2% of all non-Hodgkin lymphomas. The median age of occurrence for SMZL is 65 years and it affects both genders equally.

Materials & Methods: We have retrospectively reviewed the clinical data of six patients diagnosed with SMZL at our institute in time duration of two years. The patients were diagnosed based on clinical history, marrow morphology along with cytochemistry and immunophenotyping (IPT).

Results: All six patients were found to have splenomegaly. All of them were positive for CD 20 and sIgM and negative for CD 5 and CD 103 while displayed variable expression for CD 11c, CD 23 and CD 25. Two of the cases were splenectomised, three of them received chemotherapy and one patient was lost to follow up. In one of the splenectomised case, normalisation of blood counts was noticed while the other four cases did not show any significant improvement in their disease manifestations..

Keywords: CLPD, IPT, Splenic marginal zone lymphoma, SLVL

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INTRODUCTION

Marginal zone lymphomas (MZLs) represent a group of lymphomas that originate from memory B lymphocytes normally present in a distinct micro-anatomic compartment called the "marginal zone" of the secondary lymphoid follicles. According to involved sites and characteristic molecular findings, the last lymphoma classification singles

out 3 subtypes of MZLs: extra nodal MZL of mucosa-associated lymphoid tissue (MALT) type, splenic MZL (SMZL), and nodal MZL (NMZL).

SMZL represents 20% of MZLs' and account for <2% of all Non-Hodgkins lymphomas [1] .

It's a B cell neoplasm consisting predominantly of small cells and involving white pulp follicles of spleen, splenic hilar lymph nodes, bone marrow and often peripheral blood.

It has got indolent clinical course, even with marrow involvement [2].Splenectomy has been recommended as first line therapy and has shown to induce hematological response. Chemotherapy is given to patients with contraindications to surgery, elderly patients or those having disseminated disease.

MATERIALS AND METHODS:

We had retrospectively analysed six cases of SMZL at our institute during the time duration of 2 years (January 2011 to December 2012) by a review of the institute database.

Our study is based on their detailed clinical findings, USG abdomen (to assess spleen, liver and presence of any lymphadenopathy), peripheral smear and bone marrow morphology after staining with Wright stain and IPT by flowcytometric studies (Canto lever 6-color flow cytometer).

The Chronic lymphoproliferative disorder (CLPD) panel comprises of following set of antibodies:

Primary panel: FMC 7,CD23, CD5,CD20,CD10,kappa,lamba,CD45, CD3, CD56,sIgM,CD22,CD79b.

Secondary panel: CD 25, CD 103, CD 11c, bcl2, CD 2, CD 4, CD8, CD 56, CD 57.

RESULTS:

Of all the six cases, two were females and four were males. Their median age of occurrence was 60 years. Clinical features ranged from being asymptomatic to low grade fever and abdominal pain/discomfort.

Clinical and radiological profile of all six cases is given in table no.1.

Table 1: Clinical and radiological profile of all cases

Cases*/8*	Age(years)/Sex	Spleen (USG)	Liver(USG)	Lymph Node
Case 1	45/F	+++ (22cm)	+	-
Case 2	60/F	+++(>20cm)	-	B/L cervical lymphadenopathy
Case 3	60/M	+++(20cm)	-	-
Case 4	61/M	+++(25cm)	++	-
Case 5	73/M	+	-	-
Case 6	75/M	+++(25cm)	-	-

The hemogram showed that of the six, five cases presented with mild to moderate anaemia, all of them had leucocytosis and four of them had thrombocytopenia. Hematological and Biochemical profile of all six cases is shown in table no. 2.

Table 2: Hematological and Biochemical profile of all cases

Cases	Haemoglobin(g/dl)	TLC(/µl)	Platelets(/µl)	Albumin(g/dl)	LDH(U/L)
Case 1	7.7	29,400	59,000	3.33	262
Case 2	11.1	39,600	22,000	2.57	3966
Case 3	9.1	1,08,000	1,26,000	3.31	746
Case 4	10.0	30,900	49,000	3.13	946
Case 5	12.2	17,800	2,14,000	3.51	235
Case 6	9.1	2,29,800	67,000	2.58	533

Bone marrow revealed lymphocytes showing villous projections in only one case , while the others showed small lymphocytes without villous projections and were diagnosed as CLPD.

Figure 1: Lymphocytes showing villous projections on peripheral smear (Wright stain 1000x)

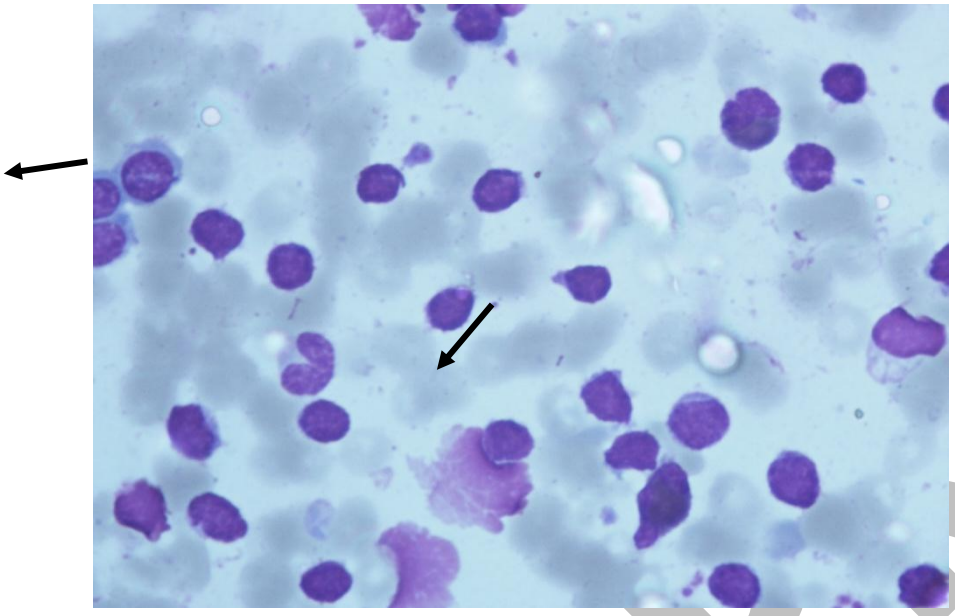

Figure 1: Peripheral smear showing small sized lymphocytes with minimal cytoplasm and condensed chromatin. Few of them showing cytoplasmic projections(arrow) , (Wright stain 1000X).

Immunophenotyping study:

All the SLVL cases showed positivity for CD 20 and sIgM while were negative for CD 103.There was variable expression of CD 11c, CD 23 and CD 25.All of them were found to be monoclonal with either kappa or lambda expression. Immunophenotypic profile of all six cases is mentioned in table no. 3.

Table 3: Immuno-phenotyping results

.	Case1	Case2	Case3	Case4	Case5	Case6
CD 5	-	-	-	-	-	-
CD 23	-	+	+	+	-	-
CD 11c	+	+	-	+	-	-
CD 20	+	+	+	+	+	+
sIg M	+	+	+	+	+	+
Kappa	-	+	-	+	+	+
Lambda	+	-	+	-	-	-
CD 25	-	-	+	+	-	-
CD 103	-	-	-	-	-	-

Treatment:

In our study, two cases were splenectomised while three of them received chemotherapy (chlorambucil) and one case was lost to follow up.

DISCUSSION AND CONCLUSION

SMZL is a rare indolent B cell lymphoma with only six cases diagnosed at our institute in a time span of two years. Median age of occurrence of SMZL is 60 years in our study which is in concordance with other studies[3].

Morphologically, only one case was diagnosed as SMZL based on presence of villous projections on lymphocytes and rest five as Chronic lymphoproliferative disorder. Sometimes morphologic differentiation of such cases from Chronic lymphocytic leukemia(CLL), Mantle cell lymphoma(MCL) and Hairy cell leukemia(HCL) may not be possible and hence IPT is necessary.

Immunophenotyping studies showed positivity of CD20 in all six cases. CD 103 was negative in all the cases differentiating it from Hairy cell leukemia. Reactivity for CD 11c, CD 23 and CD 25 was found to be variably positive.

Response criteria have been established for SMZL patients, based on blood counts (Hb, platelet count, ANC and presence or absence of circulating clonal B cells), status of organomegaly and bone marrow infiltration. On follow up hemogram, one of the case in which splenectomy was done showed complete response (defined by Hb> 12g, Platelet > 1 lac, ANC > 1500/mm^3).There was no response in the other cases[4] .

We applied the prognostic model developed by Italian Foundation of Lymphomas based on 3 factors:

Hb< 12 gm/dl, S. LDH > normal, S. Albumin < 3.5 gm/dl that categorises SLVL patients into Low risk, Intermediate risk and High risk[5] .

We found that four of the six cases were under high risk category while in the other two, one case was low risk and the other was intermediate risk. It has been postulated that patients in high risk have a five-year survival rate of 50%.

SMZL is a rare but distinct entity, having indolent clinical course, with the overall survival reported between 65-78%[6]. Therapeutic options include splenectomy, chemotherapy and immunotherapy. Spenectomy is recommended as the first line option in patients with bulky spleen, fit for surgery and without significant lymphadenopathy.Chemotherapy/Immunotherapy is indicated in patients not fit for

surgery, disseminated disease or high grade transformation. Regimens like Fludarabine or Rituximab or both can be given as single agents or can be combined with chemotherapy [7,8]. Recently, Bendamustine has also shown to have activity in SMZL [9] .

In our study, four of the five cases who were treated, did not show any significant response. Since all of them were CD 20 positive, Rituximab can be tried as an option in the treatment of SMZL. However, our cases were of lower socioeconomic status and could not afford Rituximab. As the neoplastic cells in SMZL express CD 20 strongly, response to Rituximab seems likely and can be evaluated for therapeutic efficacy. We suggest that a trial of Rituximab could be used before or after no response to chemotherapy This may improve the quality of response of such SMZL patients and eventually the disease outcome. However, the role of Rituximab and its response needs to be established by other such studies on SMZL patients.

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