

Splenic Lymphoma with Villous Lymphocytes: A Case Report with Review of Literature

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ABSTRACT

Splenic lymphoma with villous lymphocytes (SLVL) is a rare low-grade B cell non-hodgkin's lymphoma with distinct clinical and morphologic features.

We report a case in a 55 year old man with the diagnosis of Chronic lymphocytic leukemia. On examination patient had no peripheral lymphadenopathy, but had splenomegaly of 2cm below costal margin. Laboratory investigations revealed WBC count $27.9 \times 10^9/l$ with an absolute lymphocyte count of $22.3 \times 10^9/l$. Peripheral smear examination showed 80% lymphoid cells, 36% of which showed villous morphology, R-O nucleus, opened up chromatin and no nucleolus. Bone marrow aspirate and biopsy also showed involvement by these villous lymphocytes. These cells were negative for all cytochemical stains including tartrate-resistant acid phosphatase. On flow cytometric immuno-phenotyping these lymphoid cells were highly positive for CD19, CD20, FMC-7, moderately positive for CD10 and negative for CD5, CD23, CD25, CD103 and surface immunoglobulins (SIg). Based on these findings a diagnosis of SLVL was suggested

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Introduction

Splenic Lymphoma with Villous Lymphocytes (SLVL) is a low-grade B cell non-Hodgkin's lymphoma with distinct clinical and morphologic features that include splenomegaly without lymphadenopathy, lymphocytosis rarely exceeding $100 \times 10^9/L$, and a discrete monoclonal band in the serum in one third of patients [1-3]. According to WHO 2008, it is considered as the leukemic counterpart of Splenic marginal zone lymphoma (SMZL) that comprises less than 2% of lymphoid neoplasm [4,5]. Because of the considerable overlap of clinical and morphological features between various chronic lymphoproliferative disorders (CLPDs) it requires immuno-phenotyping to distinguish from others and therefore is under diagnosed, as most centers in India lack this facility. As the treatment modalities and prognosis differ from those of the more common lymphoproliferative disorders, it is imperative to diagnose this condition for its proper management.

We report a case in a 55 year old man who presented in the outpatient department with the diagnosis of Chronic lymphocytic leukemia (CLL).

Case Report

A 55 year married male, farmer by occupation, resident of Bihar was referred to GTB hospital in August 2011 as a case of CLL. Patient had complaint of self healing recurrent pruritic skin lesions especially on foot and palm and abdominal discomfort for last two years. Patient also had significant weight loss of 10kg in past 6 months. On examination patient had no peripheral lymphadenopathy, had splenomegaly 2cm below costal margin. Laboratory investigations revealed hemoglobin of 12.1gm%, WBC count $27.9 \times 10^9/l$ with an absolute lymphocyte count of

$22.3 \times 10^9/l$. Peripheral smear examination showed 80% lymphoid cells identified, with R-O nucleus, opened up chromatin, no nucleolus and moderate amount of cytoplasm, many of the cells show (36%) cytoplasmic projections which were broad based and circumferential and in some projections were confined to the poles (fig 1). These cells were negative for all cytochemical stains including tartrate-resistant acid phosphatase.

Bone marrow aspirate and biopsy showed atypical lymphoid cells interspersed in between normal hematopoietic cells with similar villous morphology as described in peripheral smear along with large no of bare nuclei (fig 2). Protein electrophoresis demonstrate polyclonal band in α region.

Flow cytometric immunophenotyping was performed on peripheral blood and the gated lymphocytes were highly positive for CD19, CD20, FMC-7, moderately positive for CD10 and negative for CD5, CD23, CD25, CD103 and SIg.

Based on clinical presentation, morphology, bone marrow involvement & flow cytometry, a diagnosis of SLVL was suggested.

Discussion

SLVL, a low grade B-cell lymphoma described in detail by Melo et al [1]. According to WHO classification system, marginal zone B-cell lymphomas are classified into three clinically distinct subtypes: nodal marginal zone lymphomas, extranodal marginal zone B-cell lymphomas of mucosa-associated lymphoid tissue (MALT lymphomas), and SMZL. Now it is considered to be the variant of SMZL [4,5].

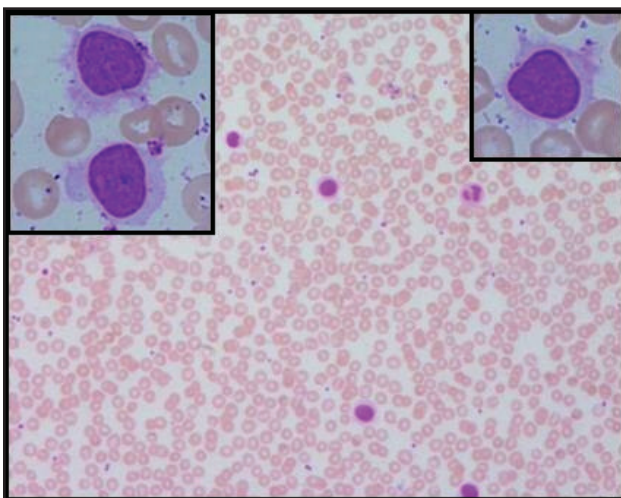


Fig. 1: Peripheral smear showing villous lymphocytes

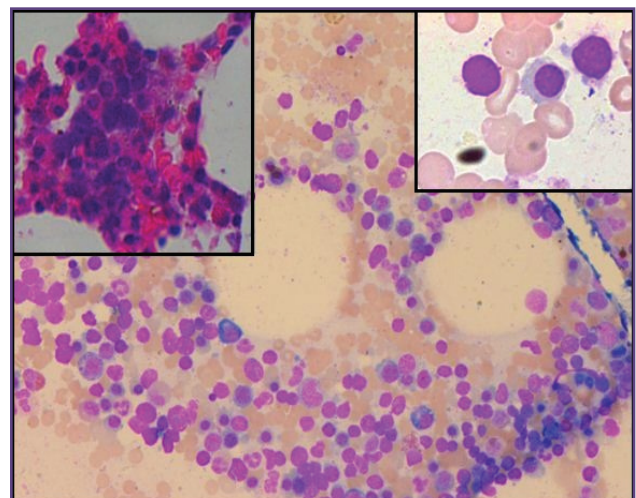


Fig. 2: Bone marrow aspirate and biopsy showing infiltration by villous lymphocytes

It is a rare neoplasm and in western literature few case series has been reported and comprised less than 2% of all lymphoid neoplasm^[6] however from India only few anecdotal case reports have been published^[7]. Most patients of SLVL are over 50 years and there is an equal sex incidence. SLVL is considered to be of B-cell origin of unknown differentiation stage, however presence of Ig gene somatic hypermutation in 50% of cases suggests exposure to antigen in the germinal centre microenvironment.

Although SLVL is specific disease, the villous lymphocytes are biologically related to neoplastic cells of other types of chronic lymphoproliferative disorders (table 1).

Of these, CLL and PLL can be distinguished on the basis of clinical presentation, cell morphology and characteristic immunophenotypic profile. However others such as HCL and HCL-V and SLVL pose some difficulty as all three present with villous lymphocytes in peripheral blood^[1,8]. Morphology of villous lymphocytes shows a distinct pattern of villous distribution as well as the nuclear characteristics and nucleoli which may sometimes help in distinguishing these three entities. Thus villous lymphocytes of hairy cells and HCL-V are typically circumferential and homogenously distributed whereas those of SLVL characteristically have preferential polar distribution of short and thin villi or are sometimes long and broad based. Beside this HCL and HCL-V have centrally located nucleus with abundant cytoplasm. HCL-V also shows a distinct nucleolus not seen in SLVL^[1, 9]. In some cases the distinction between the three

types of cells may not be immediately apparent by light microscopic examination alone, and electron microscopic studies, or cell volume measurements, may be needed^[1].

In the present case we observed villous lymphocytes in 36% of total peripheral lymphocytes and in 25% of bone marrow aspirate. These lymphocytes had round to oval nucleus, opened up chromatin, no nucleolus and moderate amount of cytoplasm showing cytoplasmic projections which were broad based and in some of the cells these projections were confined to the poles. The bone marrow showed a characteristic nodular interstitial infiltration with no reticulin fibrosis unlike the fine reticulin fibrosis seen in HCL^[10]. In addition to morphological features, SLVL differs from HCL as it lacks tartrate resistant acid phosphatase staining which is a hallmark of HCL^[7]. Moreover, in one third of cases, peripheral blood may show a monoclonal band in serum protein electrophoresis^[3]. Present case was negative for TRAP and no monoclonal band in protein electrophoresis could be demonstrated. Immunophenotypically, SLVL cells have variable profile of antigen expression. No surface marker in isolation is characteristic of SLVL, and therefore a complete panel of markers is required to differentiate it from other chronic lymphoproliferative disorders (table 2).

In the present case, mature B-cell markers (CD19, and CD20) were highly positive however the absence of CD5& CD23 ruled out the diagnosis of CLL^[1,8]. There was high positivity for FMC-7 in our case. As FMC-7 is also highly positive in HCL and HCL-V, the negative expression of CD25 and CD103 were helpful in ruling out HCL^[1, 6].

Table1: Clinical and haematological presentation of chronic lympho-proliferative neoplasms.

Parameters	CLL	PLL	SMZL/SLVL	HCL	HCL-V
Clinical Presentation	Asymptomatic	B symptoms +	Insidious	B symptoms	B symptoms
Age (Yr)	>65	>60	>50	40-70	40-70
Organomegaly	Moderate to Massive Spleen & liver,	Massive spleen,	Spleen	Massive spleen	Moderate spleen
Lymphadenopathy	Present	minimal	nil	nil	Nil
Course & Prognosis	>10yrs, indolent	Poor (3-5 yrs)	Indolent, poor response to therapy	>10yrs, responsive to IFN- α & Cladribine	No response to IFN- α & purine analogues
Type Of Cell	Mature Ag expressing B cell	prolymphocytes	B cell of U/K Differentiation stage	Late activated memory B cell	activated memory B cell, late stage
TLC	>100x10 ⁹ /L	>100x10 ⁹ /L	<1 Lakh	<10,000 (usually pancytopenia)	>35,000
Bone Marrow Involvement	diffuse	diffuse	Intrasinusoidal, Interstitial, nodular	Diffuse, fried egg appearance, reticulin fibrosis	Nodal interstitial, No significant fibrosis

Table 2: Comparison of immunophenotypic features in various chronic lymphoproliferative disorders

	CD5	CD19, CD20	CD23	CD10	CD25	C103	CD123	Annexin-A1	FMC-7	Smlg
CLL	++	++	++	-	-	-	-	-	-/+	Weak
PLL	-/+	++	-	-/+	-	-	-	-	++	Strong
FL	-	++	-/+	+	-	-	-	-	++	Strong
SLVL	-	++	-/+	-/+	-/+	-	-	-	-/+	Strong
HCL	-	++	-	-	++	++	++	++	++	Strong to moderate
HCL-V	-	++	-	-/+	-	-/+	-	-	+	Weak to strong

+ expressed, ++strongly expressed, - not expressed, -/+may be expressed,

Immunophenotypic profile of SLVL and HCL-V shows considerable overlap, CD11c is one marker which shows positivity in HCL-V as opposed to SLVL where it is variable. However the diagnosis cannot be solely confirmed based on immunophenotype alone and therefore taking a holistic view based on the clinical presentation, morphology, bone marrow involvement and immunophenotypic profile a diagnosis of SLVL was considered over HCL-V.

Conclusion

The clinical course of SLVL is indolent, even with bone marrow involvement. These patients are usually non responsive to usual chemotherapy regimens, typically effective in other chronic lymphoid leukaemias. These patients typically have haematologic responses to splenectomy with long term survival, hence it is important to diagnose it as a separate entity.

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Competing interest

None declared

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