Case Report
Running Title: Hairy Cell Leukemia Variant Masquerading as Acute Leukemia
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Hairy Cell Leukemia Variant Masquerading as Acute Leukemia: A Rare Case Report

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Abstract
The key purpose of this report is to present an uncommon case of hairy cell leukemia variant (HCLv). HCLv is found to be a striking clinico-pathological condition which encompasses the features of classical hairy cell leukemia (cHCL) as well as B cell prolymphocytic leukemia. It is a rather rare entity accounting for 0.4% of all chronic lymphoid malignancies and about 10% of all HCL cases diagnosed worldwide. A 57-year-old man presented with pain abdomen, loss of weight, spikes of fever and massive splenomegaly to our center. Complete blood count showed leucocytosis with 60% blasts on smear. Bone marrow studies were suggestive of acute leukemia like picture. Flow cytometry revealed the markers CD11c, CD19 and CD103 to be positive. This confirmed the diagnosis of HCLv. Other differential diagnoses such as splenic marginal zone lymphoma, B cell Prolymphocytic Leukemia and cHCL should be ruled out before confirming HCLv as each of them have different responses to antimetabolites, splenectomy and BRAF inhibitors.

Keywords: Leukemia, Hairy cell, Splenomegaly, B cell leukemia**,** Case report

Introduction

Hairy cell leukemia variant (HCLv) is an uncommon B-cell lymphoproliferative disorder giving rise to 0.4% of all chronic lymphoid malignancies[1] with a clinically and biologically perspicuous entity that constitutes malignant cells that are similar in morphology to classical hairy cell leukemia (cHCL)[2]. It is predominantly associated with herbicides and also has a familial association.

Morphologically, cHCL and HCLv are characterized by mature B-cells with plenty of cytoplasm and hairy projections in the blood, spleen and bone marrow. Splenomegaly is seen usually in both these conditions as a result of the assemblage of malignant cells in the spleen. Although BRAFV600E mutation is present in >90% cHCL cases, it is not found in

HCLv. With respect to clinical presentation, HCLv presents aggressively in comparison with cHCL and is generally either resistant to therapy or has poor responses cHCL

Case Presentation

Since this is a case report, Ethics committee approval has not been taken, although informed consent has been taken from the patient.

A 57-year-old male presented to Oncology Outpatient Department with a 3-month history of abdominal swelling which was insidious in onset and gradually progressive. He also reported an 8 kg weight loss during this period associated with fever spikes. On physical examination, he was found to have a massive splenomegaly measuring 12 cm from left costal margin. No other positive findings were noted. His laboratory tests revealed the following (Table 1).

The peripheral blood smear showed 60% large blast-like hairy cells which appeared like an Acute Leukemia. He was proceeded to a bone marrow examination which revealed 40% large cells with irregular hairy cytoplasmic projections and prominent nucleoli (Figure 1).

His bone marrow was further evaluated with flow cytometry (Figure 2). This revealed:

- CD5 negative CD10 negative B cell lymphoid neoplasm consistent with a Splenic B cell lymphoma with prominent nucleoli
- CD103, CD11c, CD49d and showed Kappa light chain restriction-POSITIVE
- CD123, CD25, CD5, CD10-Negative

The immunophenotyping clinched the diagnosis of HCLv.

BRAF mutational testing was not possible as patient denied. He was offered options amongst Bendamustine+Rituximab, Rituximab+Cladribine and splenectomy. But he was lost to follow up after the diagnosis was made.

Discussion

HCLv are disorders of small B-cell lymphoproliferative system which mirror cHCL. But they vary in terms of displaying leukocytosis without monocytopenia, morphological features-neoplastic cells containing prominent blastic nuclei, flow suggesting negative TRAP, CD25, annexin A1 and refractoriness to traditional HCL therapy.[3]

Leucocytosis is one of the most striking features that differentiates HClv from cHCL where the latter presents with normal White blood cell count. TRAP activity is seen in cHCl, while it is absent in HCLv. cHCL also presents with mutated IGHV and BRAF and positive Annexin A1, while HCLv has a mutated CCND3.

Median overall survival is over 20 years in cHCL, whilst HCLv has a median survival of only about 9 years.[4] An Indian case series revealed 15 cases of HCL where clinically they presented with hepatosplenomegaly and fatigue.[5] This series showcased that Indian patients were presenting at a younger age between 32-57 years like our patient.

Responses to purine analogues like pentostatin and cladrabine amongst cHCL were >90%, encompassing majorly complete responses, while HCLv displayed inferior response rates of 40-50%, which were mostly partial responses.[6]

Conclusion

It is quintessential to accurately diagnose cHCL, HCLv and splenic marginal zone lymphoma entities, as they present with homogenous yet distinct features but their management in the form of response to

antimetabolites, BRAF inhibitors and splenectomy are quite disparate.

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Authors' Contributions
S.S: Study design, data gathering & analysis, drafting and critical reviewing of the manuscript. S.V.K: Data interpretation, drafting and reviewing the manuscript. M.N: Study design, data analysis and critical reviewing of the manuscript. V.A: Study design and data interpretation and critical reviewing of the manuscript
All authors read and approved the final manuscript version and agreed with all parts of the work in ensuring that any queries about the accuracy or integrity of any component of the work are appropriately handled.

Informed Consent
Written informed consent was received from the patient.

Conflict of Interest
None declared.

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Table 1. Complete hemogram

	Units	Patient value
White blood cell count	$10^3/\mu L$	38.5
Absolute neutrophil count	$10^3/\mu L$	2.9
Hemoglobin	g/dL	11.4
Platelets	$10^3/\mu L$	80

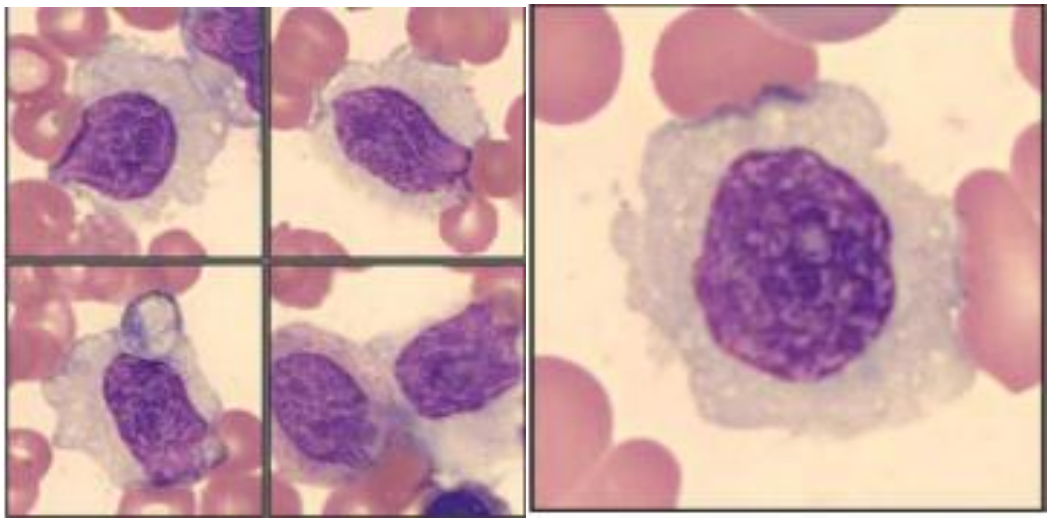

Figure 1. This figure shows the bone marrow smear showing large blastoid cells with hairy projections.

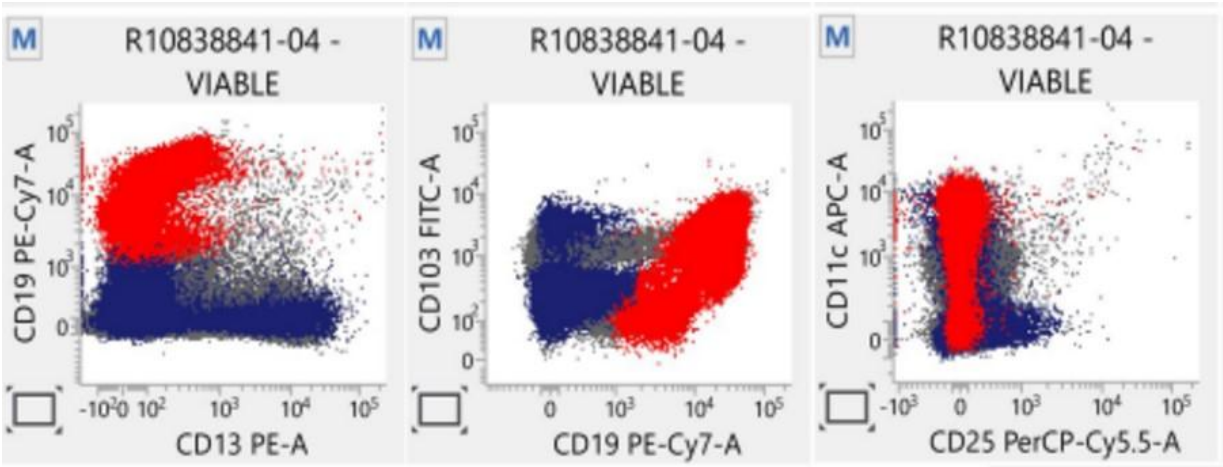

Figure 2. Flow cytometric analysis depicted neoplastic cells expressing CD19, CD103, CD11c.