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Hairy cell leukemia with atypical presentation and hematemesis; a case report

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Abstract

Introduction: Hairy Cell Leukemia (HCL) is a rare lymphoid neoplasm categorized as a lymphoproliferative disorder being B-cell clonal neoplasm characterized by V600E *BRAF* mutation in >80% of cases, B cell expression of CD20, CD22y CD11c, and T cell expression of CD103, CD25, CD123, CD72 y FMC7. HCL classically presents with pancytopenia, bone marrow infiltration, splenomegaly and hepatomegaly with subsequent ailments due to the trilineage failure. However, several clinical rarities of the HCL have been reported frequently in the literature. **Case:** We report a 45 years old Sudanese man who presented with a history of long-standing fever, chronic generalized fatigability and dyspnea, night sweating and significant weight loss. Associated with peripheral neuropathic pain and bone pain and more recently hematemesis of fresh, non-clotted, painless blood. Physical examination of the patient was positive for jaundice, splenomegaly and hepatomegaly. Upper GI endoscopy was negative for any lesions, abdominal US showed no evidence of portal HTN nor stigmata of hepatic cirrhosis or veno-occlusive diseases. Coagulation profiles were normal, and full blood count with peripheral blood picture revealed pancytopenia with hairy cells. Bone marrow cytometry showed a heterogeneous population with strong CD45 and moderate SS (hairy cells =19.7%) The lymphocyte population was positive for B-cell marker: CD20 (strong) and negative for CD3. **Discussion:** HCL presentation with hematemesis is considered extremely uncommon and unique to encounter; several unusual presentations of HCL has been described but this one is considered a rarity. Absence of organomegaly, skeletal and neurological involvement are all considered atypical presentations and fully present in our patient's case. These variations in the clinical picture of HCL are highly associated-with by concomitant aberrancies in the immunophenotypic aberrancies which requires cytometric/immunohistochemical patterns. **Conclusion:** This report reflects the highly complexed and overlapping pathological and clinical picture of HCL which resembles a significant dilemma and challenge for early clinical recognition and pathological diagnosis of the condition. High clinical and diagnostic agilities is recommended to extract such high rarities of presentation

Keywords: Hairy Cell Leukemia, Hematemesis, Pancytopenia, BRAFp.V600E

Introduction

Hairy Cell Leukemia (HCL) is an unusual, indolent, low-grade mature B cell tumor with a typical clinical, immunophenotypic, morphological and more recently described molecular (BRAF p.V600E mutation) profile [1]. It was first described as a clear entity and received a distinct pathological description by Bouroncle and colleagues in 1958 [2,3]. Now, and with 2 to 3% representation of all leukemias types, HCL has an estimated incidence of 600 to 1600 cases per year with a male to female, Caucasian ethnicity, and middle age predominance of distribution [4,5]. Since it's recognition, several molecular and biological features have been frequently implicated in the pathogenesis, disease progression and clinical variation of HCL, specifically (*BRAF* V600E) kinase-activating mutation, which is somatically and clonally present in almost all patients through the entire disease spectrum and clinical course [6,]. By aberrantly activating the RAF-MEK-ERK signaling pathway, BRAF V600E shapes key biologic features of HCL, including its specific expression signature, hairy morphology, and antiapoptotic behavior [6,7]. Several studies have targeted the epidemiology and risk factors involved the etiology of HCL with the vast majority pointing out environmental and occupational exposures as potential contributors in the pathogenesis of the condition specifically exposure to fuel, organic dissolvent, farming pesticides and herbicide [8]. And while World Health Organization (WHO), classifies HCL as a lympho-proliferative disease within mature B-cell neoplasia, Immuno-phenotyping of HCL obtained via flowcytometry comprehends B cell expression of CD20, CD22y CD11c, and T cell expression of CD103, CD25, CD123, CD72 y FMC7. [9]

Clinically, HCL presents with symptoms and signs attributable to pancytopenia which is caused by marrow failure following infiltration of the bone marrow by leukemic cells; causing anemia, and increased frequency and severity of infections [10]. Symptoms and signs due to organs infiltration are also common to encounter and include splenomegaly, hepatomegaly (less common), with accompanying constitutional symptoms of fever, fatigability, night sweat and weight loss of varying degrees. [10,11]

The clinical picture of un-explained hematemesis, peripheral neuralgia, and generalized bone pain is considered bizarre and widely atypical for hairy cell leukemia. We aim by introducing such rare traits of a well-recognized pathology to greatly contribute to both scientific and clinical literature of leukemia, for better understanding of the disease and subsequent advancement in the preventive, diagnostic, prognostic and curative measures.

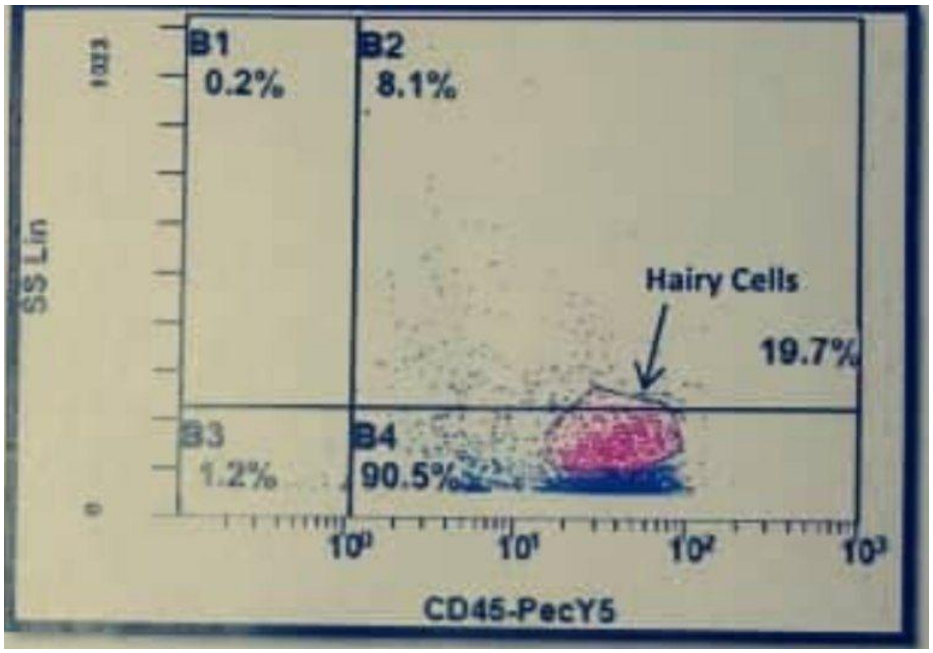
Case Presentation:

We report a 45 years old Sudanese man from Al-Alyab village in river Nile state, who presented with a history of chronic generalized fatigability associated with peripheral neuropathic pain that is paroxysmal, bricky in nature (pins and needles) and of blotchy distribution throughout the body with no associated hypoesthesia or hypoalgesia and no potentiality to be evoked nor exacerbated by any of the patient's routine activities. The patient recalls a worsening generalized fatigability up to 1 year prior to presentation, followed by development of excruciating attacks of previously outlined neuropathic pains and a concomitant bone pains for the past 6 months. Bone pain is deep, dull and core in nature. Distributed primarily over long bones of the limbs, with minimal joint involvement as with no joint effusion, redness or restriction of movement.

Constitutional symptoms resembled a significant fraction of the patients' complaints. A long-standing fever, exertional fatigability and dyspnea, night sweating and significant weight loss with multiple attacks of mild to moderate upper respiratory tract and gastrointestinal infections. The patients' complaints have followed a worsening course for the past three months period; during which the patient suffered multiple bouts of hematemesis of fresh, non-clotted, painless blood of varying amount and no associated abdominal symptoms

On examination, the patient looks wasted, pale, and jaundiced with huge splenomegaly and hepatomegaly and there are no features suggestive of liver cirrhosis or chronic liver disease. Upper Gastrointestinal endoscopy was done and revealed no gastric or peptic ulceration or esophageal varices. Abdominal ultrasound revealed moderate hepatosplenomegaly with moderate right side pleural effusion.

The viral screening was negative (HCV, HBs Ag, HIV 1 and 2), coagulation profiles were normal, and full blood count with peripheral blood picture revealed pancytopenia with hairy cells. Bone marrow examination showed MPS with a high suspension of HCL then immediately the patient was sent for flow cytometry where it showed CD45/55 histogram showed a heterogeneous population with strong CD45 and moderate SS (hairy cells =19.7%) **[Figure 1]**. The lymphocyte population was positive for B-cell marker: CD20 (strong) and negative for CD3. Diagnosis was confirmed and the patient was referred to the oncology department to initiate the standardized regimen of chemotherapy.



[Figure 1]: Flow cytometry test showed positive B-cell marker (CD 20 strong) and negative CD3 compatible to hairy cells leukemia

Discussion:

Hairy Cell Leukemia (HCL) is an uncommon, indolent lymphoid neoplasm that falls under the categorization of lymphoproliferative disorders as B-cell clonal neoplasm; making only about 2% of total leukemia cases worldwide [1,3]. There has been a considerable rise in the scientific literature and reports aiming to contemplate the pathogenesis and disease progression and modulating factors of HCL, particularly the recent discovery of the presence of the V600E *BRAF* mutation in the vast majority of cases of classic Hairy cell leukemia has suggested that the pathogenesis of this disorder lies in the RAS-RAF-MAPK signaling pathway. Constitutive activity of this pathway causes increased cellular proliferation and survival, and, ultimately, malignancy [12]. In addition, several other studies referred to *CDKN1B* to have a consistent inactivation in 16% of patients with classical HCL. Making it the second most commonly mutated gene in HCL. [6,12,13,14]

HCL classically presents with pancytopenia, bone marrow infiltration, splenomegaly and hepatomegaly with concomitant system ailments related to each (abdominal pain from organomegaly, anemia and anemic heart failure and septic

attacks and from marrow failure) [5,7]. However, splenomegaly may not be present in acute phase of the illness, and patients may not have pancytopenia. The incidence of the disease with no splenomegaly in various series ranged from 0% to 40% [7]. For these relatively significant percentages, several report and studies concluded that the mere absence of hepatosplenomegaly should not exclude or overlook HCL in the clinical differential diagnosis. [15,16]

Another HCL-associated features that are typically present in our patient and have been frequently reported in the literature are bone involvement and neuropathic pain [17,18]. Although, skeletal bone involvement is considered to some extent a rarity, such encounters have been found in 3% of cases, showing primarily lytic lesions affecting multiple sites with preferences to ends of the long bones – with an associated non-deforming arthropathy occasionally - and with almost always extensive involvement of the bone marrow [19,20]. One particular association that has been frequently reported with the atypical presentations of HCL is the low hairy cell counts obtained in peripheral picture and bone marrow aspirates; ranging from relatively low to almost scanty levels [21].

And while the patient we're reporting exhibited almost all the classical and diagnostic features of HCL, presentation with hematemesis is considered extremely uncommon and unique to encounter; especially with the uncertainty of the origin of the hematemesis having both upper GI endoscopy and coagulation studies normal with no evidence of any of the well-recognized risk factors or associations of upper GI bleeding. Such rarity could be explained by and by the well documented autoimmune phenomena that are frequently reported with HCL; including vasculitis, anti-phospholipid syndrome and thrombotic tendencies, rendering the superficial mucosal and submucosal vessels; fragile and highly prone to stress and shearing forces, and also the tumor-induced uncontrolled microvascular angiogenesis and varying states of endothelial dysfunction [22,23].

These vast variations in the clinical picture and pathological presentations of HCL are highly associated-with a strong-correlation by concomitant aberrancies in the immunophenotypic aberrancies. For this careful interpretation and special considerations should be taken when obtaining flow cytometric/immunohistochemical patterns in such cases to prevent misdiagnosis and further unwanted complications [9,17,24]

Conclusion

This report illustrates an unusual presentation of HCL with hematemesis. HCL is an indolent, low-grade mature B cell tumor with a typical clinical, immunophenotypic, morphological pattern that classically present with bone marrow infiltration, trilineage bone marrow failure and hepatosplenomegaly. Unusual or atypical clinical presentations are not uncommon to encounter in HCL and several of which have been reported; including bony involvement, asymptomatic course with ruptured viscus, neurological involvement and several others. For this, careful consideration should be taken in the management and stratification of HCL from early clinical suspicion to diagnosis and management,

Declaration of conflict of interest

No conflict of interest

Ethical approval

Obtained from federal Ministry of Health

Patient consent

Written consent was obtained from patient for the publication of this case report and any accompanying images. A copy of the written consent is available for review by Editor in chief of this journal.

Authors Contribution Statement:

Dr. Osama khder is the prime investigator, supervised the entire clinical and scientific duties; provided the framework for optimum theoretical, methodological, monitoring and evaluation approaches.

Dr. Mansour siddeeg Suraj , Dr. Abrar Almubark Abdalhafiz Abdalbasit , Dr. Afaf Ali Abdalrahim Alamin were directly responsible for data management, data acquisition and analysis and theoretical conceptualization,.

Mohammed Elmujtba Adam Essa Adam and Dr. Ahmed Babikir were responsible for data interpretation, analytical duties, manuscript preparation, initial and final draft delivery and communication with the concerned parties.

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