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Case Report

Pathology Section

Hairy Cell Leukaemia- A Rare Case Presented with Leukocytosis

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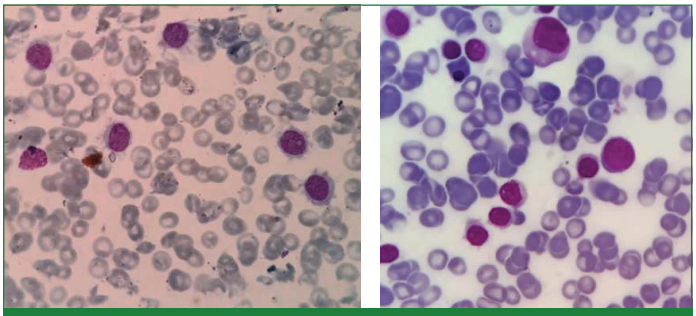
ABSTRACT

Hairy Cell Leukaemia (HCL) is an uncommon disease accounting approximately 2% of all lymphoid leukaemias. Cytologically and immunophenotypically, it is indolent neoplasm of intermediate mature lymphoid cells. The neoplastic cells have oval nuclei with abundant basophilic cytoplasm having circumferential hairy projections involving peripheral blood and diffusely involving the bone marrow and splenic red pulp. It occurs more predominantly in middle aged to elderly adults with median age of 52 years; with male predominance (M:F=4:1). HCL was firstly recognised by Ewald in 1923 and described as Leukaemische reticuloendotheliose and term HCL was coined by Schrek and Donelly in 1966. A 75-year-old male known case of diabetes and hypertension with chronic kidney disease, visited to Outpatient Department (OPD) with history of severe fatigue and weight loss of 5 kg in last one month. On physical examination; massive splenomegaly was found measuring 15 cm below left costal margin. Complete Blood Count (CBC) revealed Hemoglobin (Hb) of 10.9 gm%, Total Leucocyte Count (TLC) was 40,200/mm^3, Differential leukocyte counts were Neutrophils (N) 07, Lymphocytes (L) 11, Eosinophils (E) 01, Monocytes (M) 01 and 80% of atypical lymphoid cells and Platelets count 1.08 L/mm^3. Peripheral blood smear showed Red Blood Cells (RBCs) predominantly normocytic normochromic with mild anisocytosis and 80% of atypical lymphoid cells with hairy projections (hairy cells). On Contrast-Enhanced Computed Tomography (CECT), whole abdomen showed massive splenomegaly (size=27 cm). Bone marrow aspiration examination was done showing low cellularity and comprising of 45% cells of HCL type and suggestive of HCL. On flow cytometry, immunophenotyping showed CD19, CD20, CD79b, CD11C, CD103, FMC-7, CD123, CD200 positive abnormal cells and confirming the diagnosis of classical HCL.

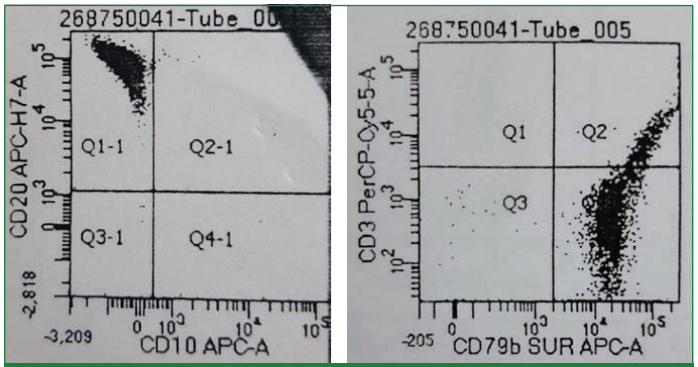
Keywords: Immunophenotyping, Leukaemische reticuloendotheliose, Massive splenomegaly

CASE REPORT

A 75-year-old male visited to the OPD with chief complaint of severe fatigue and weight loss of 5 kg in last one month. On physical examination, non tender massive splenomegaly was found 15 cm below left costal margin. The patient was a known case of type II diabetes mellitus, hypertension and chronic kidney disease. Complete blood counts revealed Haemoglobin of 10.9 gm%, Total leukocyte count of 40,200/mm^3, Differential leukocyte count showed; Neutrophils 7%, Lymphocytes 11%, Eosinophils 01%, Monocytes 01% and 80% of atypical lymphoid cells, platelets count 1.08 L/mm^3, PCV 34.30%, Mean Corpuscular Volume (MCV) 87.40 fL, Mean Corpuscular Hemoglobin (MCH) 27.40 pg, Mean Corpuscular Hemoglobin Concentration (MCHC) 31.30 g/dL. Peripheral blood smear showed RBC predominantly normocytic normochromic with mild anisocytosis and leukocytosis with 80% of atypical lymphoid cells having hairy projections [Table/Fig-1]. CECT whole abdomen showed massive splenomegaly (27 cm in size) with multiple hypodense areas scattered in splenic parenchyma and causing mass effect on stomach, left kidney and also on bowel loops and displacing them right inferio-laterally. Blood urea and serum creatinine level was 52.0 and 1.7 mg%, respectively. On bone marrow aspiration, the smears showed low cellularity due to which Myeloid to erythroid (M:E) ratio could not be accessed. Marrow showed 45% atypical cells with circumferential hairy projections [Table/Fig-2]. Bone marrow aspiration and biopsy examination was suggestive of classical HCL and HCL variant. On flow cytometry, immunophenotyping showed CD19, CD20, CD79b, CD11C, CD103, FMC-7, CD123, CD200 positive abnormal cells and confirming the diagnosis of classical HCL [Table/Fig-3-7]. Patient was given chemotherapy; cladribine along with acyclovir and cotrimoxazole from other institute. The patient was in remission for one year follow-up period.



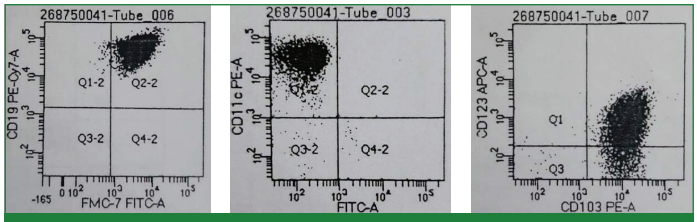
[Table/Fig-1]: Showing atypical lymphoid cells with basophilic cytoplasm having numerous hairy projections on cell surface in Peripheral Blood Smears (PBS) (MGG stain; 100X).
[Table/Fig-2]: Diluted marrow smear showing atypical lymphoid cells with hairy cytoplasmic projections (MGG stain; 100X). (Images from left to right)



[Table/Fig-3]: Flow cytometry showing Pathological cells CD20+ (99.9%).
[Table/Fig-4]: Flow cytometry showing Pathological cells CD79b+ (99.8%). (Images from left to right)

DISCUSSION

HCL is a rare disorder; accounting for 2% of all Leukaemias firstly recognised by Ewald in 1923 and described as Leukaemische reticuloendotheliose. HCL is more common in Caucasians, more frequent in males of middle age to elderly adults (median age of



[Table/Fig-5]: Flow cytometry showing Pathological cells CD19+ (100%) and FMC-7+ (99.6%).
[Table/Fig-6]: Flow cytometry showing Pathological cells CD11c+ (99.0%).
[Table/Fig-7]: Flow cytometry showing Pathological cells CD103+ (99.6%) and CD123+ (85.7%). (Images from left to right)

52 years) and overall male to female ratio of 4:1 [1]. The patients usually presents with fatigue, weight loss, moderate to massive splenomegaly and hepatomegaly in nearly 50% of the cases. Recurrent infections are a major manifestation and important cause of death [2]. Hairy cell leukemia is classified into following types: classic HCL, variant HCL (HCL-V) and Japanese variant HCL. It should be diagnosed accurately as they have different clinical and biological behaviour, particularly regarding the response to α-interferon and purine analogues [3,4]. Rituximab used to treat relapsed/refractory HCL with 80% overall response. Hairy leukemic cells are intermediate sized lymphoid cells, having round to oval nuclei and abundant basophilic clear cytoplasm with characteristic circumferential micro-filamentous (hairy) projections. The neoplastic hairy cells typically infiltrate the bone marrow, spleen and less commonly liver, lymph nodes and the skin [5]. On peripheral blood smear examination, morphological evaluation is extremely valuable for screening of HCL because very low number of hairy cells is present in the peripheral blood smears which may remain undetected [6]. Bone marrow aspirate results in dry tap due to increase in reticulin fibrosis due to hairy cells and bone marrow biopsy showing interstitial or patchy pattern with fried egg appearance due to abundant cytoplasm and prominent cell borders [6]. The leukaemic cells express B-cell markers CD19, CD20, CD22 and CD79b with characteristically positive for CD11c, CD103, CD25, CD123, TBX21, Annexin A1, FMC7, CD200 and cyclin D1 and usually negative for CD10, CD5 and CD23 [6]. The unique criterion for diagnosis of HCL is co-expression of CD103, CD25 and CD11c [7]. Recently, Annexin A1 has been reported to be a 100% specific immunohistochemical marker for hairy cell leukemia which is not expressed in any other B-cell lymphoma [8]. No cytogenetic abnormality is specific for HCL and high frequency of BRAF V600E mutation, confirmed by multiple investigators; suggest a key role in the pathogenesis of HCL [6]. The differential diagnosis of hairy cell leukemia include B-Chronic Lymphocytic Leukemia (CLL), Prolymphocytic leukemia and T-cell lymphoproliferative disorders like Splenic B-cell lymphoma with villous lymphocytes (SLVL) and Hepatosplenic γ δ T-cell lymphoma [9]. An incorrect diagnosis of other lymphoreticular disorders can lead to aggressive chemotherapy, which is contraindicated and harmful for patients with hairy cell leukemia. So, careful observation of microscopic features are important for initial diagnosis, particularly when less percentage of hairy cells present in the peripheral blood and the bone marrow [1]. The diagnosis of HCL is usually made by examining the morphologic features of the hairy cell on Peripheral Blood Smears (PBS) and Bone Marrow Aspiration (BMA) in conjunction with the characteristic immunophenotyping by flow cytometric analysis [7].

CONCLUSION(S)

Hairy Cell Leukaemia (HCL) with leukocytosis is a rare presentation. Immunophenotyping/flow cytometry plays a pivotal role in confirmation of diagnosis. It is important to thoroughly follow proper diagnostic work up in such cases.

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