

Hairy Cell Leukemia - A Rare Case Report

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Abstract: Hairy cell leukemia (HCL) is a rare clonal chronic lymphoproliferative disorder commonly seen in males in the middle years of life. It is a rare form of leukemia characterized by pancytopenia, moderate to massive splenomegaly and bone marrow infiltration by atypical cells with circumferential abundant cytoplasm which spreads in to shaggy hairy cytoplasmic projections. A 60 year old male presented with shortness of breath, pedal oedema. On examination there was pallor, and moderate splenomegaly. Peripheral smear was diagnosed as chronic lymphoproliferative disorder (? hairy cell leukaemia). Bone marrow aspiration was a dry tap so bone marrow biopsy was done and was reported as hairy cell leukemia because of its characteristic fried egg appearance and increased reticulin on retic stain. Immunohistochemistry showed CD20, cyclinD1 positive cells in the marrow. Flow cytometry was positive for hairy cell markers including CD19, FMC 7, and CD103. Based on the clinical, peripheral smear, bone marrow, immunohistochemistry, flow cytometry findings, a diagnosis of hairy cell leukaemia was made.

Keywords: flow cytometry, Hairy cell leukaemia, lymphoproliferative disorder, splenomegaly.

INTRODUCTION

Hairy cell leukaemia (HCL) is a rare and an indolent form of a small, mature, B-cell leukaemia, which accounts for 2% of all leukemias. It is characterized by oval or indented (bean shaped) nuclei and abundant "hairy" cytoplasm, which involves the peripheral blood, bone marrow and the spleen [1]. The term hairy cell leukaemia was coined by Schrek and Donely in 1966 to emphasize the irregular cytoplasmic projections of the abnormal cells observed in the peripheral blood or bone marrow [2]. It was first identified as leukemic reticuloendotheliosis. The patients generally presents with cytopenias and splenomegaly without prominent peripheral lymphadenopathy. These cells show tartrate resistant acid phosphatase (TRAP) positivity and strongly expresses CD 103, CD19, CD 20, CD11c, FMC 7. Careful attention to morphological details is important for an early diagnosis of hairy cell leukaemia to ensure that patients obtain maximum benefit from new therapeutic agents.

CASE REPORT

A 60 years old male presented with shortness of breath, weight loss, pedal oedema. On examination mild pallor was present. Abdominal examination revealed enlarged firm, non tender splenomegaly 10cm below the costal margin. On ultrasonography the spleen measured 18x10x 7cm. No lymphadenopathy was noted. His haemogram showed haemoglobin

4.1gms/dl, white blood cells (WBC)-3100 cells/cumm, platelets-6000 cells/cumm. The differential count showed 30% neutrophils, 45% small lymphocytes, 3% eosinophils, 2% monocytes, and 20% atypical lymphocytes. These atypical lymphocytes showed villous hairy cytoplasmic projections and small round nuclei with condensed chromatin and a distinct nucleoli. His peripheral smear was reported as chronic lymphoproliferative disorder (? Hairy cell leukaemia). Bone marrow aspiration was attempted but it was dry tap, so bone marrow biopsy was done. The diagnosis of chronic lymphoproliferative disorder-Hairy cell leukaemia was made based on typical "fried egg" appearance. Reticulin stain was done to demonstrate fibrosis in the marrow, which showed increased reticulin. Immunohistochemistry markers showed CD20, strongly positive and CD10 negative. Flow cytometry showed CD 19, FMC7 moderately positive and CD103 strongly positive. Based on the clinical, morphological features on peripheral smear, bone marrow, immunohistochemistry markers, and flow cytometry, diagnosis of hairy cell leukaemia was confirmed.

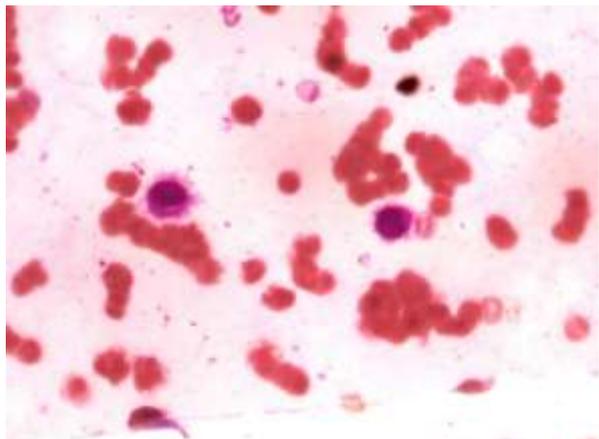


Fig-1: A peripheral blood smear demonstrating atypical cells with cytoplasmic hairy projections. (Leishman stain x 1000)

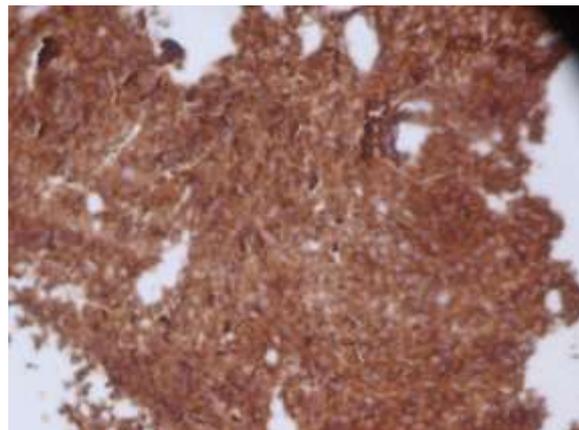


Fig- 4: A bone marrow biopsy showing CD 20 Positive B- Lymphocytes

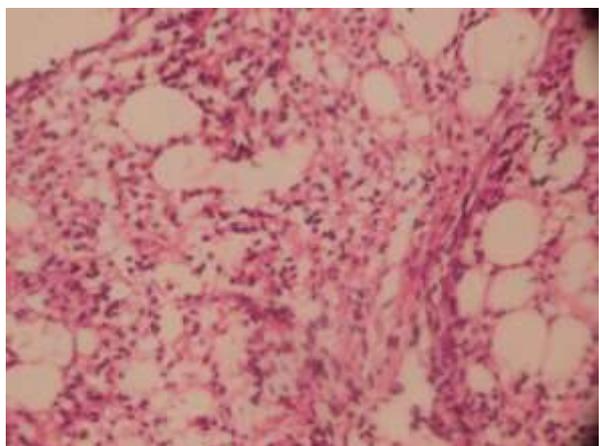


Fig-2: A bonemarrow biopsy showing the typical Fried egg appearance of hairy cells. (haematoxyline and Eosin x 40)

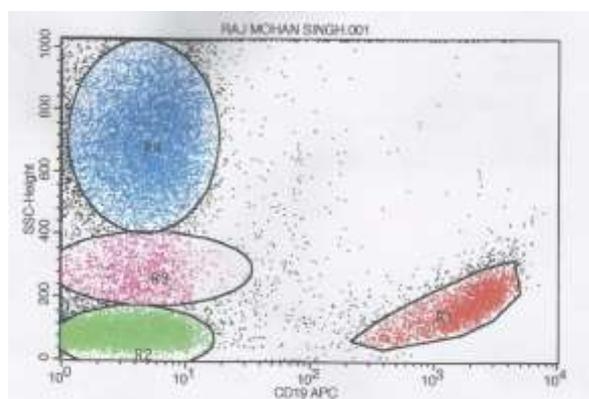


Fig-5: Flow cytometric dot plots show the cells with expression of CD19.

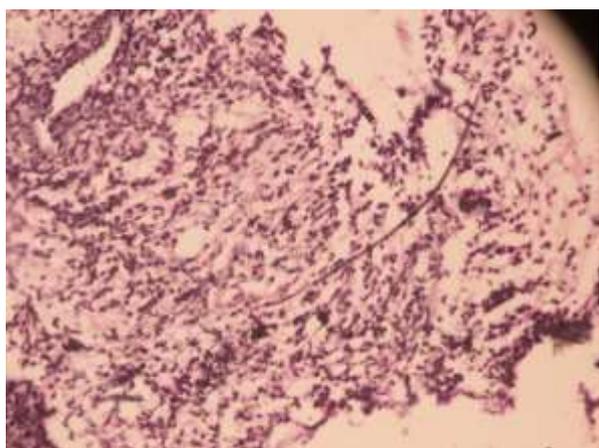


Fig- 3: A bonemarrow biopsy Reticuline stain showing increased reticuline.

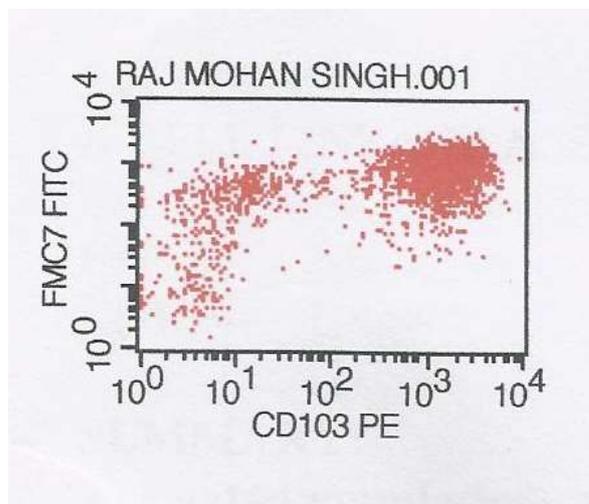


Fig- 6: Flow cytometric dot plots showing moderately positive FMC7, and Strongly positive CD 103.

DISCUSSION

Hairy cell leukemia is a rare lymphoproliferative disorder accounting for 2% of all leukemias . HCL was first recognized by Ewald in 1923 who described the condition as leukemic

reticuloendotheliosis. [3]. The name HCL was coined in 1954 by Shrek and Donnelly .HCL has been classified into three types HCL- classic,variant-HCL (HCL –V), and Japanese variant HCL (HCL – J). Middle aged people are more affected by HCL with a male to female ratio of 4:1 as noted in our case. . Characteristic presentation is with pancytopenia in 50% of patients , moderate to massive splenomegaly in 85% with or without hepatomegaly in 40% and bonemarrow infiltration , All these features were present in our case ..Morphological evaluation of a peripheral blood smear is an extremely valuable tool in screening for HCL . the disease may go undetected when very low counts of hairy cells are present in the peripheral smear[4].The basic mechanism involved in the pathogenesis of HCL are poorly understood. Recent studies have demonstrated that the hairy cells are mature Bcells , they are mutated IgH genes suggesting post germinal center antigen acquired memory cells. They have low mitotic cycling rates and has a protracted clinical course,but a highly activated cytokine transcription apparatus including a cytokine storm which is responsible for diverse clinical and morphological features[5-6] . Differential diagnosis of HCL include, B-chronic lymphocytic leukemia (CLL),Prolymphocytic leukemia and T-cell lymphoproliferative disorder such as hepatosplenic gamma, delta T-cell lymphoma and splenic B-cell lymphoma including splenic B-cell with villous lymphocytes(SLVL). The cells of CLL differ from HCL as they have more coarsely clumped chromatin and round or ovoid nuclei [7]. Hairy cells are intermediate sized lymphocytes that possess round to oval nuclei and abundant light blue agranular cytoplasm with characteristic micro filaments (“hairy”) projections. They strongly express CD103 CD 19,CD20 ,FMC7 and CD11C .In our case CD19, CD20,CD103, was strongly positive , cyclin D1,FMC7 moderately positive and ,CD10 was negative These cells typically infiltrate the bone marrow, spleen and to a lesser extent the liver lymphnodes and skin Recently immunohistochemical demonstration of Annexin - A has been reported to be a 100 % specific marker for HCL[8] . Prolymphocytic leukaemia occurs in elderly male individuals with a median age of 70 years .patients usually present with peripheral lymphadenopathy leukocytosis tartrate resistant acid phosphatase (TRAP) in activity CD5+,CD19+,CD25- and CD10- [9]. Cytochemistry and histochemistry play an important role in the diagnosis of HCL . Cytochemistry on the hairy lymphocytes in blood or bone marrow aspirate with Acid Phosphatase is resistant to tartrate (TRAP) .This is also done as immunohistochemistry Annexin – A and DBA44 on the trephine biopsy . Thus morphology , cytochemistry , flowcytometry are useful tools in

diagnosis of this uncommon lymphoma in its leukemic phase . The current treatment of HCL is with the purine analogues cladribine and pentostatin . Treatment is indicated for patients with significant cytopenias , symptomatic splenomegaly , recurrent and constitutional symptoms[10].

CONCLUSION

Careful attention to morphological details are important for an early diagnosis particularly when low percentages of hairy cells are present in the peripheral blood and bone marrow . Early diagnosis is important to ensure that patients obtain maximum benefit from new therapeutic agents that have greatly improved prognosis in this rare disease.

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