

Hairy Cell Leukemia - A Case Report

Dr Neha Singh¹, Dr Jitender Singh Chauhan²

¹Senior Resident, Department of Pathology, BPSGMC, Khanpur Kalan, Sonipat road, Haryana, India

²Resident, Department of Surgery, PGIMS, Rohtak, Haryana, India

ABSTRACT

Hairy cell leukemia (HCL) is a relatively rare, chronic B-cell lymphoproliferative disorder characterized by splenomegaly, pancytopenia and bone marrow infiltration by hairy cells with circumferential prominent hairy cytoplasmic projections. Splenomegaly with few atypical lymphoid cells in peripheral blood lead to the examination of bone marrow for morphological findings characteristic of hairy cell leukemia (HCL) with an increased reticulin framework. Diagnosis is confirmed when flow cytometry is positive for hairy cell markers including CD11c, CD103 and FMC-7. BRAF mutation is also positive in present case which re-confirms the diagnosis.

Key words: Hairy cell Leukemia, lymphoproliferative disorder, splenomegaly.

INTRODUCTION

Hairy cell leukemia (HCL) is a relatively rare form of leukemia with an insidious onset and triad of massive splenomegaly (without lymphadenopathy), pancytopenia and monocytopenia. It has dry bone marrow aspirate.¹ Only a small number of leukemic cells are seen in the peripheral blood (PB) in a classical case. The characteristic cells are mononuclear which have abundant cytoplasm exhibiting thin projections that extend circumferentially over the cell surface with round or oval nuclei infiltrating the bone marrow diffusely and involving the red pulp of the spleen.^{2,3,4} HCL is also known as leukemic reticulo-endotheliosis, lymphoid marrow fibrosis, medullosplenic histiolymplocytosis of primitive appearance and reticulum cell leukemia, owing to confusion about its histogenesis.⁵ The term hairy cell leukemia was given by Schrek and Donnelly in 1966.⁵ The distinction between HCL and other chronic B-cell lymphoproliferative disorders is clinically important because of differing treatment protocol and an indolent clinical course. Patients with HCL are highly sensitive to purine analogues such as cladribine. Apart from morphology, HCL has a characteristic immune-phenotypic profile and light scatter characteristics. Here we report a rare presentation in an old male.

CASE REPORT

A 55 yr old gentle man presented with weakness, fatigue, intermittent gum bleeding, weight loss and abdominal lump since 2 months. He was a known case of diabetes mellitus. On examination, pallor was present. Abdominal examination revealed enlarged, firm, non tender splenomegaly, 7 cm below the costal margin. On ultrasonography, the spleen measured 15x7x4 cm with normal echotexture. Hematological examination revealed a hemoglobin (Hb) concentration of 8.3gm/dl, a total leucocyte count of $9.0 \times 10^9/L$, red blood cell count (RBC) of $3.07 \times 10^{12}/L$, platelet count of $23 \times 10^9/L$, hematocrit 26.9 l/l, red cell distribution width of 25 % CV, platelet distribution width of 77% and mean platelet volume of 10.20fl. A peripheral smear demonstrated normocytic hypochromic red cells with a differential count of 11% polymorphs, 43% lymphocytes, 2% eosinophils, 2% monocytes and 42% atypical cells. The atypical cells had light basophilic cytoplasm containing numerous hairy projections on the outer surface. The nucleus was oval and reniform with coarse chromatin (Fig. 1). Platelets were reduced in number. Repeated bone marrow aspirations demonstrated dry tap only. Trephine bone marrow biopsy revealed replacement of normal marrow particles by sheet of atypical cells and the typical fried egg appearance of hairy cells (Fig. 2a, 2b) with abnormal areas of fibrosis. Reticulin staining on a marrow biopsy demonstrated increased reticulin fibers.

Flow cytometry revealed positivity for the immuno-phenotypic markers CD 19 (bright), CD20 (bright), CD 11c (bright), CD 103 (hairy cell marker) (bright), FMC-7 (bright) and CD45 (bright), confirming the diagnosis of hairy cell leukemia.

BRAF gene mutation done outside again confirmed the diagnosis. The patient responded well to the chemotherapeutic agent 2-chlorodeoxyadenosine (Cladribine), resulting in the reduction of spleen size and normalization of blood counts.

Discussion

Hairy cell leukemia is a relatively rare form of leukemia. This is more common in Caucasians and Ashkenazi Jewish males, with an overall male predominance (5:1). The median age of onset is 50 years.⁶ It was first recognized as leukemic reticuloendotheliosis by Ewald in 1923.⁵

It has been classified into three types: HCL-classic, variant HCL (HCL-V, type II HCL) and Japanese variant HCL (HCL-J). They have different clinical and biological features, particularly regarding the response to α -interferon so it is important to diagnose these entities accurately.⁷ Morphological evaluation of a peripheral blood smear is an extremely valuable tool in screening for HCL, but the disease may go undetected when very low levels of hairy cells are present in the peripheral smears.⁸

The pathogenesis of HCL is poorly understood. Recent studies have demonstrated that the hairy cells are mature memory B cells & leukemic hairy cells differ from normal memory B cells because of altered expression of chemokine & adhesion receptors. Hairy cell morphology is influenced by overexpression & constitutive activation of members of Rho family of small GTP ases & upregulation of the growth arrest specific molecule Gas 7.⁹

Hairy cells are small to medium sized lymphoid cells with an oval or indented (bean shaped) nucleus with homogenous, spongy, ground glass chromatin that is slightly less clumped than that of normal lymphocyte. Nucleoli is inconspicuous. They have abundant light blue agranular cytoplasm with characteristic micro-filamentous (“hairy”) projections on smear. An increase in reticulin fibrosis due to hairy cells results in dry tap. The diagnosis is best made on BM biopsy. The primary pattern is interstitial or patchy with fried egg appearance due to abundant cytoplasm and prominent cell borders.⁹ These cells typically infiltrate the bone marrow, the spleen and to a lesser extent the liver, lymph nodes and skin.⁸ There are no specific chromosomal abnormalities or molecular genetic alterations that are diagnostic of this disease.¹ Thus, morphology, cytochemistry and immunohistochemistry on the trephine biopsy/flow cytometry are useful tools in diagnosis of this uncommon lymphoma in its leukaemic phase. The only cytochemical stain utilized in the diagnosis is tartrate acid phosphatase (TRAP).

The tumor cells express B cell-associated markers i.e. CD19, CD20, CD22 and CD79b. Coexpression of CD103, CD11c and CD25 is considered unique for HCL and is often used as an absolute criterion for establishing the diagnosis of HCL. However, atypical immunophenotypes have been reported in an otherwise morphologically classical HCL.¹⁰ Recently, immunohistochemical demonstration of Annexin A1 has been reported to be a 100% specific marker for HCL.¹¹ Differential diagnosis of HCL include B-Chronic Lymphocytic Leukemia (CLL), Pro-lymphocytic leukemia and T- cell lymphoproliferative disorders such as Hepatosplenic γ δ T-cell lymphoma and Splenic B-cell lymphoma including splenic lymphomas with villous lymphocytes (SLVL).

The cells of CLL differ from hairy cell leukemia as they have more coarsely clumped chromatin and round or ovoid nuclei. Pro-lymphocytic leukemia occurs in elderly male individuals with a median age of 70 years. Patients usually present with peripheral lymphadenopathy, leucocytosis, TRAP inactivity, CD5+, CD19+, CD25-, CD103- and CD10-. Splenic B-cell lymphoma including splenic lymphomas with villous lymphocytes (SLVL) is Annexin A1 negative. Until the mid-1980s, splenectomy was the predominant therapy for HCL, providing improvement of cytopenias in the majority of patients.⁵ Treatment has been revolutionized with the advent of interferon (IFN)- α and purine analogues (PA) such as pentostatin and cladribine. The overall response rate exceeds 90%. Rituximab has also been used to treat re-lapsed/refractory HCL with an overall response of 80%.^{12,13}

CONCLUSION

HCL manifests in the middle years of life, with a male predominance, characterised by pancytopenia caused by moderate to massive splenomegaly. It is an easy diagnosis to make on the morphology of well made blood smears and bone marrow biopsy. Although there are no specific markers for HCL, cytochemistry and flow cytometry readily confirm the diagnosis. The diagnosis and management was based on current guidelines. Early diagnosis of HCL is important to ensure that patients obtain maximum benefit from new therapeutic agents that have greatly improved prognosis in this rare disorder.

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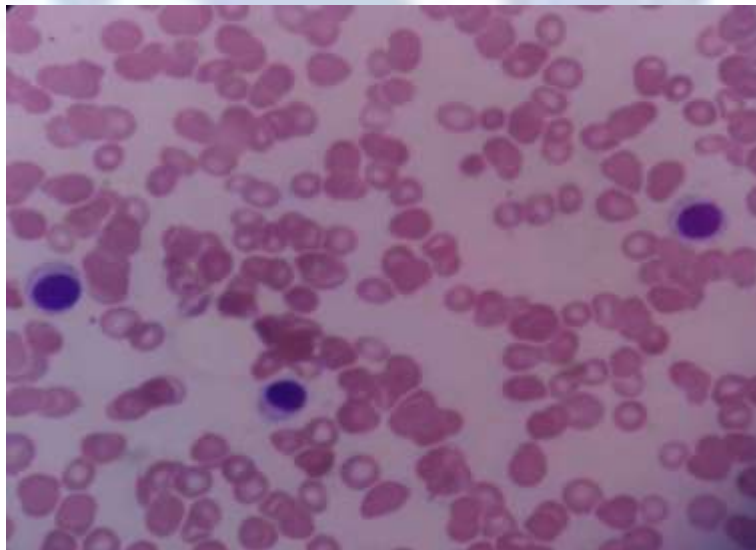


Fig. 1. A peripheral blood smear demonstrating atypical cells with light basophilic cytoplasm containing numerous hairy pro-jections on the outer surface. (Leishman's stain; x 100)

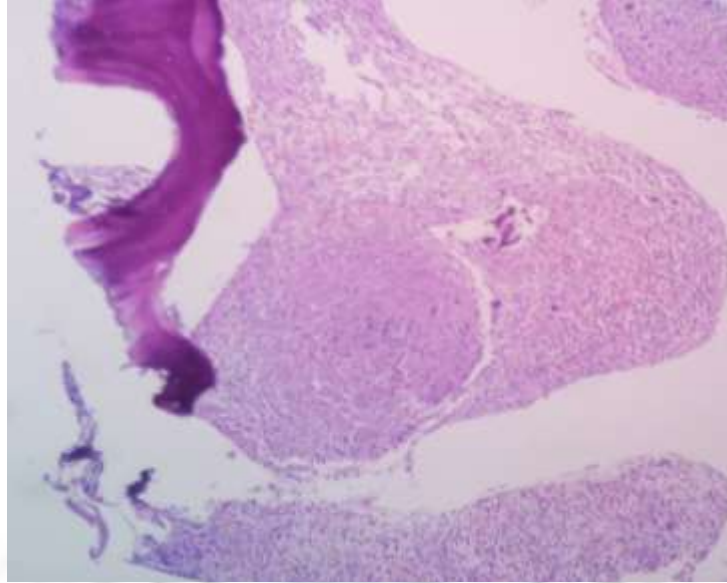


Fig. 2a. A bone marrow biopsy demonstrating replacement of normal marrow particles by sheet of atypical cells. (Hematoxylin and Eosin; x 10)

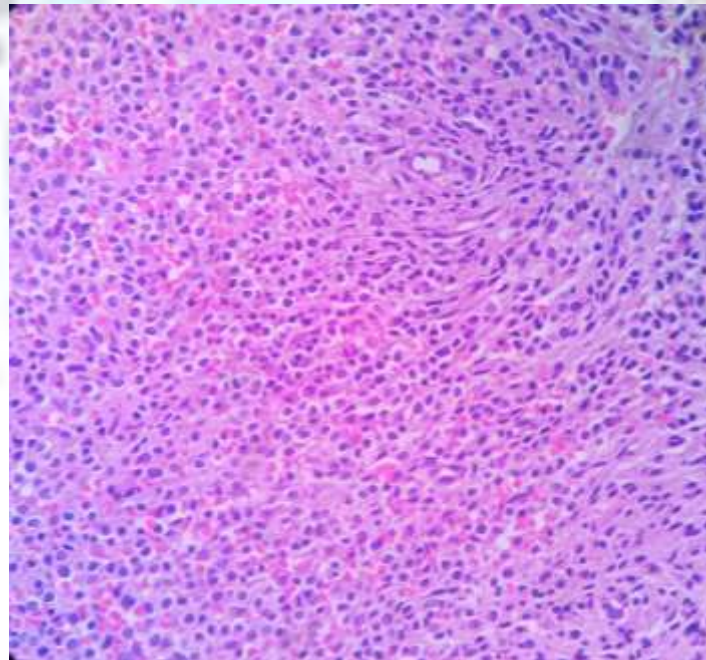


Fig. 2b. A bone marrow biopsy demonstrating the typical fried egg appearance of hairy cells. (Hematoxylin and Eosin; x 40)