

A Case of Hairy Cell Leukemia

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Abstract: Hairy Cell Leukemia is a uncommon mature B cell leukemia in adults that involves bone marrow, spleen and peripheral blood. It accounts for 2% of all leukemias. The cause is unknown but some relationship to radiation, herbicides and pesticides have been identified. Patients present with pancytopenia and splenomegaly usually. Lymphoid cells have characteristic filamentous, hair like projections on peripheral smear. We report a 36 year old male cleric presenting with malaise, fatigue and shortness of breath for two months. On examination patient had pallor, nontender splenomegaly with no hepatomegaly or lymphadenopathy. The patient had multiple dry taps on bone marrow aspiration at our institutes pathology department. On peripheral smear diagnosis of Hairy Cell Leukemia was made that was confirmed by immunohistochemistry.

1. INTRODUCTION

Hairy Cell Leukemia was initially recognized as a distinct pathological entity by Bertha Bouroncle and colleagues at The Ohio State University College of Medicine in 1958 [1]. It is a rare form of B cell leukemia and a subtype of Chronic lymphocytic leukemia. Hairy Cell Leukemia presents with massive splenomegaly, pancytopenia with no lymphadenopathy and has a dry bone marrow aspirate [2]. On peripheral smear, the lymphoid cells have characteristic filamentous cytoplasm projections that extend circumferentially over the skin surface with a round or oval nuclei and involves the bone marrow, red pulp of spleen and peripheral blood [3]. Splenomegaly is present in 80-90% of the cases of hairy cell leukemia [4]. Frequent bone marrow aspirations show dry tap because of marrow fibrosis.

Due to difference on treatment protocols between lymphoproliferative disorders, it is important to distinguish between Hairy cell leukemia and other B Cell Lymphoproliferative disorders like CLL. Bone marrow biopsy is used to diagnose HCL. The diagnosis can be confirmed by a special stain known as TRAP (Tartrate resistant acid phosphatase) but it is

now possible to definitively diagnose Hairy cell leukemia via flow cytometry. The tumor cells are larger than normal and express pan B cell markers CD19, CD22, CD20 and CD79a. Co expression of CD 103, CD11c and CD25 are unique for hairy cell leukemia. HLA DR (marker for immaturity) is also present. We report a case of hairy cell leukemia with characteristic pathologic features of peripheral blood and spleen.

2. CASE REPORT

A 36 year old male presented with fatigue, malaise and shortness of breath for two months. General physical exam revealed pallor. On abdominal examination, there was nontender splenomegaly 5 cm below costal margin with no hepatomegaly and inguinal adenopathy. No rash or infection was present on presentation. The patient had three previous dry tap at out facility which raised concerns for an underlying bone marrow pathology. Trepine imprints showed hypercellular marrow, erythropoiesis and myelopoiesis suppressed and monotonous population of lymphoid morphology. Hematological examination revealed hemoglobin 10.3 g/dl, total RBC $3.8 \times 10^{12}/L$, hematocrit 34%, Platelets $48 \times 10^9/L$, MCV 90

f1, MCH 27 pg, MCHC 30g/dl. Peripheral blood smear showed normocytic normochromic red cells. DLC had a differential count of 22% polymorphonuclear cells, 61% lymphocytes, 14% monocytes, 2% eosinophils. On peripheral smear, the lymphocytes had atypical

presentation with round to oval nuclei and moderate cytoplasm with hairlike projections (fig: 1) and trephine bone marrow biopsy showed monotonous population of lymphoid morphology with fried egg appearance and fibrosis (fig: 2)

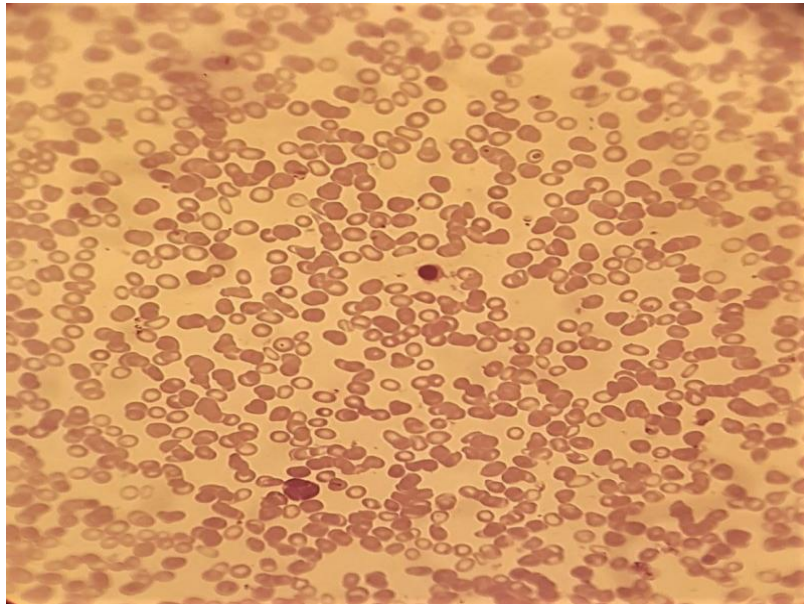


Figure1:

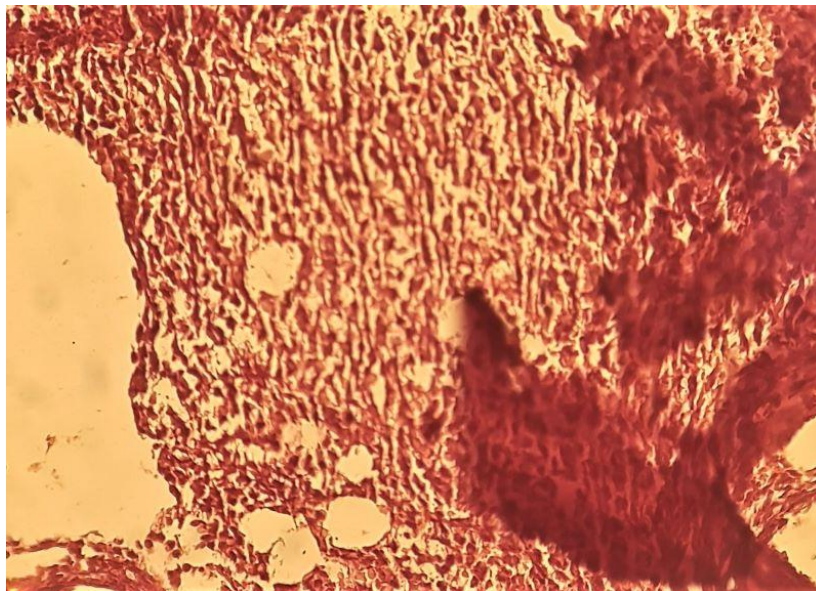


Figure2:

Flow cytometry was positive for markers CD19, CD22, CD20 and CD79a. CD103, CD11c and CD 25 confirming the diagnosis for hairy cell leukemia. Patient was prescribed chemotherapy with cladribine.

3. DISCUSSION

Hairy cell leukemia (HCL) is a rare B-cell neoplasm of middle age. It presents with a triad of pancytopenia, splenomegaly, and hairy cells in the bone marrow and peripheral smear. Hepatomegaly is present in 40% to 50% of

cases⁶. Infections in Hairy Cell Leukemia patients are a major manifestation and cause of death because of bacterial infections in neutropenia and opportunistic infections due to impaired cell mediated immunity, related prominently to corticosteroid therapy [7]. Splenectomy is indicated for those refractory to therapy or bleeding due to thrombocytopenia [8]. HCL is divided into three phenotypes: (a) typical HCL, (b) HCL variant (HCLV) and (c) Japanese type of HCL (HCLJV). In contrast to hairy cell leukemia, hairy cell leukemia variant

is a more aggressive disease and according to the new WHO classification it is no longer considered to be biologically related to its classical counterpart. Patients with hairy cell leukemia variant have an elevated white blood count versus pancytopenia in classical hairy cell leukemia, easy-to-aspirate bone marrow and weak reactivity to tartrate resistant acid phosphatase (TRAP). Immunophenotypically, Hairy cell leukemia variant cells are positive for CD103 and CD11c and negative for CD25. The HCL-V cells also express the pan B cell antigens B-cell antigens CD19, CD22 and CD20⁹. The hairy cells of the Japanese type of HCL have weak TRAP positivity with densely stained round nucleus and hairy projections¹⁰.

Differential diagnosis included splenic B cell lymphoma like splenic marginal zone lymphoma (splenic lymphoma with villous lymphocytes SLVL), prolymphocytic leukemia, chronic lymphocytic leukemia (CD10 positive), aplastic anemia, myelodysplastic syndromes and idiopathic myelofibrosis. Immunophenotypic markers are helpful in establishing diagnosis and deciding treatment options [11]. E Tiacci et al proposed BRAF V600E as hairy cell leukemia's driving mutation after they discovered that 100% of hairy-cell leukemia samples analyzed had the oncogenic BRAF mutation V600E [12]. The BRAF mutation leads to the activation of the RAF/MEK-ERK pathway, resulting in enhanced cell proliferation and survival and can be incorporated in routine diagnosed workup of Hairy Cell Leukemia [13]. However, Hairy Cell leukemia variant patients lack BRAF mutations and p53 tumor suppressor gene mutation was present in one third of these cases [14].

Several treatment options are available, single course of cladribine is potentially curable, myelosuppression and infection are prominent adverse effects [15]. Rituximab can be used as first line alternative in patients with contraindications to purine analogs and interferon alpha [16].

4. CONCLUSION

It is important to accurately diagnose SLVL, HCL-C and the Japanese variant of HCL entities, because they have different clinical and biological features, particularly with regards to their response to the purine analogue-based treatment or splenectomy. Careful assessment of morphology, immunophenotypic and cytogenetic findings is therefore important in order to deliver appropriate treatment.

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