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Hairy Cell Leukemia: A Case Report

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ABSTRACT

We report a case of a middle aged male diagnosed as Hairy cell leukemia. Clinicohematologic features were fever, weight loss, splenomegaly, anemia and thrombocytopenia. Bone marrow and spleen were infilterated by Hairy cells. An unusual feature was high TLC with large number of Hairy cells resembling superficially Hairy cell Variant. But the Flow cytometric analysis confirmed that immunophenotype was that of classic Hairy cell leukemia.Patient responded to Cladarabine therapy and had an uneventful recovery.

CASE REPORT

Forty seven years old male presented with history of weakness, easy fatiguability and heaviness in left hypochondrium. There was history of significant weight loss and fever in last two to three months. Physical examination revealed mild splenomegaly (1cm below costal margin).

CBC revealed Hb 10 gm/dl. TLC $32x10^9/l$, and platelet count $35x10^9/l$. Differential count showed neutrophils 15% and atypical lymphocytes showing cytoplsmic projections 85% (Fig. 1).Bone marrow aspiration and biopsy was performed. Aspirate was hemodiluted showing atypical lymphocytes which comprised 86% of nucleated marrow cells. These cells had abundant cytoplasm, condensed nuclear chromatin and circumferential cytoplasmic projections. Trephine biopsy showed that erythropoiesis and myelopoiesis were hypoplastic. Megakaryocytes were reduced. More than 90% of marrow cellularity was replaced by a diffuse lymphocytic infiltrate with round, oval and slightly angulated nuclei with clear cytoplsm (fried egg appearance). A diagnosis of extensive bone marrow involvement by Hairy Cell Leukemia was made.

Peripheral blood Flow-cytometry for lymphocyte subset analysis was advised. Result (from SKMH) revealed that lymphoid population was 76%.B lymphocytes(60%) were CD45+, CD19+, CD20+, CD22+, CD25+, CD11c+ and CD103+. These cells were negative for CD5, CD10, CD23, CD38 and CD56. T cells were phenotypically normal and were CD2+, CD3+, CD5+ and CD7+. Myeloid population was 16% of total cellular events. Monocyte population was reduced. Result were consistent with the diagnosis of Hairy Cell Leukemia.

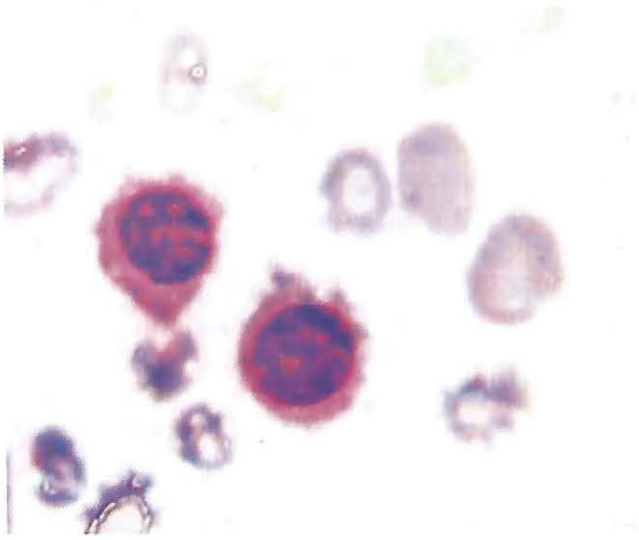

Fig. 1. Hairy cells seen in peripheral blood film.

He was admitted in SZH for treatment. Baseline biochemical profile revealed normal LFTs, RFTs, Uric acid and Serum electrolytes. LDH was moderately elevated. Ultrasound abdomen revealed normal liver (14.5 cm),enlarged spleen (16.8cm) and no enlarged para aortic lymphnodes.

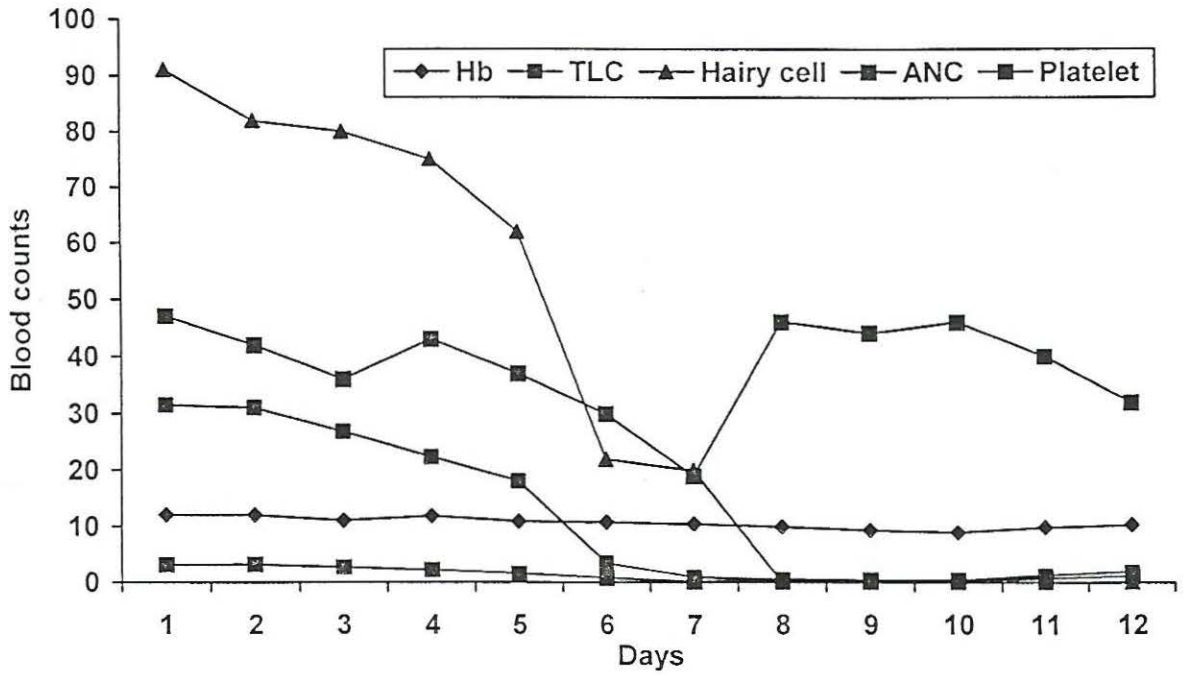

Fig. 2. Serial blood counts, hairy cells and ANC in Hairy cell leukemia patient during treatment.

Pre-treatment work up also included, chest X-ray and ECG and echo-cardiography. No abnormality was detected.

Cladarabine was chosen as single chemotherapeutic agent. Infusion Cladarabine 0.09 mg/kg/day was given as slow IV infusion over 24 hours for 7 days. Ani-sickness premedication (avil, ondanesetrone, and solucortef injections), Tab Allopurinol (300mg OD) and Cap Omeperazole (20mg BD) were also given.

Daily blood counts alongwith manual leucocyte differential were done. LFTs, creatinine, uric acid and LDH were monitored and remained stable. During first four days of treatment patient had fever up to 101°F which responded to tab Paracetamol. At this time absolute neutrophil count (ANC) was normal. However in next 1 week, there was a progressive fall in hemoglobin, leukocyte count, platelet count and Hairy cells in blood (Fig. 2). On 7th day of treatment patient developed grade IV neutropenia (ANC 180 /µl) with fever .Platelet count dropped to 19x10^9/l. One mega unit of platelet transfusion (irradiated) were given. Broad spectrum intravenous antibiotics were started after taking cultures from blood, throat and urine. Injection Meronem (1 gram BD), levofloxacin (500mg BD), metronidazole (500 mg TDS) were given for 1 week. Fever subsided on next day but neutropenia persisted at ANC 300/µl. So GM-CSF 300 µg as subcutaneus injection was given for 2 days. There was a rise in TLC to 2 x10^9/l and ANC was 1100 after 2 days. Platelet counts remained between 35x10^9/l to 50x10^9/l but patient was haemostatically stable and afebrile, so further platelet transfusions were not given..

Patient was discharged on 13th day. On discharge, patient was afebrile. No disease related signs and symptoms were seen. Serum creatinine, LFTs and uric acid levels were normal. On abdominal ultrasound splenic size was 11cm. Hb was 10.4 gm/dl, TLC 2x10^9/l with no Hairy cells on peripheral smear, ANC 1100/µl and platelet count 32x10^9/l. As MCV was high at this time Folic acid and Vitamin B12 were added in treatment on discharge. Prophylaxis for Pneumocystis Carini Pneumonia was given as absolute lymphocyte count (ALC) was still less than 1000/µl.

On follow-up after 1 month and 2 months,

peripheral counts and biochemical profile were normal. Bone marrow biopsy performed after 3 months revealed normal morphology. Splenic size was normal on ultrasound abdomen. Patient seems to be in remission. Further follow up is planned at 3 monthly intervals.

DISCUSSION

The case reported had a typical presentation in a middle aged male .Sign and symptoms were also similar to those reported previosly[1]. Bone marrow and spleen were infiltrated by Hairy cells. There was no lymph node involvement. An unusual feature was high TLC with large number of Hairy cells resembling superficially Hairy cell Variant. But the Flow cytometric analysis confirmed that immunophenotype was that of classic Hairy cell leukemia.Patient responded to Cladarabine therapy and had an uneventful recovery.

HCL is an uncommon, but distinct, lympho-proliferative disorder of B cell origin with an indolent clinical course[1]. The incidence has been estimated as 2% of all forms of leukaemia and 8% considering only leukaemias of mature B and T cells, including also low/intermediate-grade non-Hodgkin's lymphomas with lymphocytosis more than 5 x 10^9/l.

HCL is 6–10 times less frequent than chronic lymphocytic leukaemia. HCL affects middle-aged men more commonly than women; the male:female ratio is 4.5:1.

Main laboratory findings are cytopenias, usually affecting two or three lineages.

Monocytopenia is a consistent feature. Leucocyte counts tend to be low (usually less than 5x10^9/l and very rarely over 10x10^9/l), except in HCL-variant, in which leucocyte count is 30x10^9/l to 50x10^9/l. Hairy cells are often seen in peripheral blood films but their proportion is variable[2]. Less common sites of involvement by HCL include deep-seated lymph nodes, liver, bone, retroperitoneum, thyroid, etc[1].

An accurate diagnosis of HCL depends on clinical features, as well as morphologic examination of peripheral blood smears, bone marrow and other tissues These patients generally present with anemia, neutropenia, monocytopenia, and splenomegaly. Abdominal lymph adenopathy is unlikely to occur at the time of initial presentation; however, up to 15% of patients may develop abdominal lymphadenopathy during the course of their disease[1].

Estimation of cell reactivity with four McAbs (CD11c, CD25, CD103, and HC2) is useful to distinguish HCL from other disorders with circulating villous cells, such as SLVL and HCL variant. Cells from HCL are positive for three or four of these markers. Whereas cells from SLVL and HCL variant are positive for one or at the most two of these markers.[3]

The immunophenotype of the HCL-variant cells[3,4] differs from that of HCL in that CD25 and HC2 are, as a rule, negative in HCL-variant, CD103 is infrequently expressed, and CD11c is nearly always positive[3]. Recently another McAb CD123 is seen to be consistently positive in HCL and negative in SLVL and HCL variant. Therefore CD123could replace HC2 in routine setting because the latter McAb is not commercially available.[5]

A great interest in this disease has evolved in parallel with the development of useful therapeutic agents: alpha-interferon and pentostatin in the 1980s and cladribine in the 1990s[2]. The mainstay of the treatment of HCL comprises the two nucleoside analogues pentostatin[6] and cladribine[7–9]. Both agents induce a high rate (> 80%) of complete remissions. There may still be some role for interferon-alpha and splenectomy in the management of HCL. However, neither these nor pentostatin or cladribine have been tested in large randomized trials. Most of the available information derives from published series[6–10]. Because overall survival in HCL is nowadays 95–98% at 5 years, the end points to assess the value of any treatment should be disease-free interval (DFI; remission duration) and event-free survival (EFS)[10]. Cotrimoxazole should be started once treatment is completed, to prevent pneumocystis infections. Patients receiving pentostatin or cladribine should receive irradiated blood components to prevent transfusion-associated graft-versus-host disease[11].

The rare HCL variant[12,13] is important from the point of view of differential diagnosis and because it is generally resistant to interferon-alpha and rarely achieves CR with either pentostatin or

cladribine. It differs from the classic form in the lack of monocytopenia and the elevated WBC, in the range of $40–60x10^9/l$[14]. CD25 and HC2 are, as a rule, negative in HCL-variant. CD103 is infrequently expressed, and CD11c is nearly always positive[3].

The development of extremely effective therapy for HCL results in a high incidence of complete remission. However, a significant percentage of patients continue to harbour minimal residual disease that can be revealed with immunohistochemical and flow cytometric studies[15].

Justin et al[16] recommended that flow cytometric immunophenotyping is useful after treatment for the detection of minimal residual disease in HCL. It can detect HCL when the disease is present in very low levels (<1%) in the peripheral blood and in leukopenic patients[16].

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