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Case Report

A case report of hairy cell leukemia

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ABSTRACT

Hairy cell leukemia is a rare chronic lymphoproliferative disorder of mature B lymphocytes. Flowcytometry is necessary to arrive at correct diagnosis. It is important to differentiate HCL from other chronic B cell lymphoproliferative disorders because of the different treatment protocol and indolent course. We report a case of 48 years old male presenting with a chief complaints of fever, generalized weakness, fatigue, decrease appetite, and abdominal heaviness. Peripheral smear examination findings combined with bone marrow and flowcytometry confirmed the diagnosis of hairy cell leukemia.
Hairy cell leukemia is a very rare leukemia and immunophenotypic findings are crucial to confirm the diagnosis.

1. Introduction

Hairy cell leukemia is a rare chronic lymphoproliferative disorder of mature B lymphocytes. It is primarily a disease of middle age to elderly patients with a median age of 58 years. Peripheral blood shows pancytopenia, monocytopenia, and characteristic infrequent B cells with hair like projections on it.[1] Splenomegaly is also common. Bone marrow aspiration is difficult in most of the cases. Bone marrow biopsy shows hairy cells with a characteristic 'fried egg' appearance.[2,3] HCL is immunophenotypically characterized by bright co-expression of CD20 and CD22 along with CD103, CD11c, CD25, CD123, and annexin A1.[1,4] BRAF V600E point mutation is detected in more than 90% of cases of HCL and stable at relapse. BRAF V600E leads the activation of the RAF-MEK-extracellular signal-regulated kinase (ERK) signaling pathway which is the key event in the molecular pathogenesis of HCL. KLF2 and CDNK1B (p27) mutations may cooperate with BRAF V600E in promoting leukemic transformation. Identification of this mutation in unsuspected cases of HCL is important in confirming the diagnosis.[1,5] The epidemiologic data are multi-factorial and influenced by ethnicity, geographical factors, environmental exposures and occupational factors. Smoking has an inverse correlation with the development of hairy cell leukaemia while farming and exposure to pesticides, petroleum products, diesel and ionizing radiation have also been reported to be associated with an increased risk.[6]

2. Case Report

A 48 years old male patient presented in OPD with complaint of fever for 2 days. He had been feeling generalized weakness, fatigue, and loss of appetite for 3 months. A laboratory workup was done and the results are shown in Table 1. Abdominal ultrasound showed mild hepatomegaly of 17 cm and massive splenomegaly of 29 cm. HRCT Chest showed changes of pulmonary tuberculosis,

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interstitial lung disease, pulmonary artery hypertension, and multiple lymphadenopathies. CSF examination revealed meningitis. PCV and platelet transfusion were given.

Table 1: Laboratory findings of complete blood count

Variable	Value (references)
Haemoglobin(g/dL)	6.2 g/dL (13-17 g/dL)
Red blood cells count($x10^6$/cmm)	1.84 $x10^6$/cmm (4.5-5.5 $x10^6$/cmm)
Packed cell volume (%)	20.50% (45-50%)
Mean corpuscular volume (fL)	112 fL(83-101fL)
Mean corpuscular haemoglobin(pg)	33.8 pg (27-32 pg)
Mean corpuscular haemoglobin concentration(gm/dl)	30.3 gm/dl(31.5-34.5 gm/dl)
RDWcv(%)	15.4% (11.6 - 13.7%)
White blood cells($x10^3$/cmm)	69.5$x10^3$/cmm (4-10 $x10^3$/cmm)
Platelets(/cmm)	70000/cmm (150000-410000/cmm)
Neutrophils (%)	10% (40-80%)
Absolute neutrophil count(/cmm)	6950/cmm
Lymphocytes (%)	90% (20-40%)
Absolute lymphocyte count(/cmm)	62550/cmm

The complete blood count revealed bicytopenia, decreased Hb level and platetelet count was 70000/cumm while WBC count was 69.5$x10^3$/cmm with absolute lymphocytosis. The peripheral smear showed RBCs which were macrocytic normochromic with mild anisocytosis. There were 90% atypical lymphoid cells. Few of them were medium sized, with hair like cytoplasmic projections, reticular to clumped type chromatin and moderate amount of cytoplasm, suspicious for mature B cells of Hairy cell leukemia.

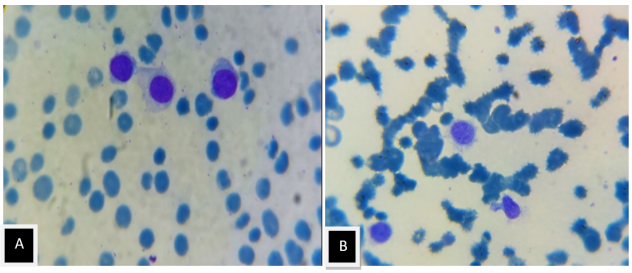

Figure 1: (**A**) Peripheral smear demonstrated macrocytic anemia with anisocytosis, polychromasia, thrombocytopenia; moderate leukocytosis with absolute lymphocytosis; (**B**): Most lymphocytes were medium-sized with coarse chromatin and moderately abundant pale basophilic cytoplasm

The bone marrow was hypercellular showing 70% of atypical lymphoid cells displaying circumferential thin cytoplasmic projection. Bone marrow biopsy showed mature bland cells with reniform nuclei and a zone of peripheral clearing (fried egg appearance) in sheets.

Flow cytometric analysis of the peripheral blood showed CD19, CD20, and CD79a positivity along with kappa light chain restriction. There was also an expression of CD11c, CD25, and CD103. There was an expression of FMC-7 and HLA-DR also. The abnormal cells did not express CD5, CD10, and CD23. The CD38, CD138, CD34, and CD117 were also negative. The markers for T Cells and NK Cells were negative. (Table 2)(Figures 2, 3, 4 and 5)

Table 2: Findings of flowcytometry

Marker	Result
CD45	Positive
HLA-DR	Positive
CD19	Positive
CD20	Positive
CD25	Positive
CD79a	Positive
CD11c	Positive
CD103	Positive
Kappa	Positive
FMC7	Positive

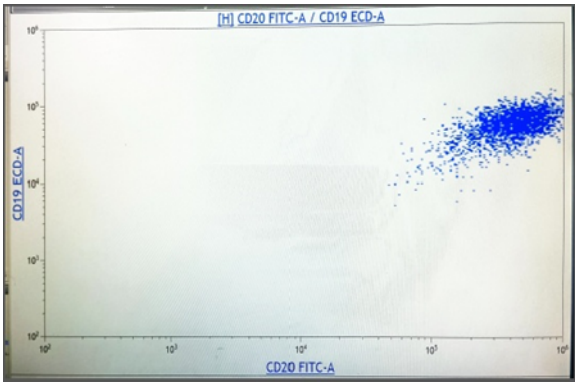

Figure 2: CD19 and CD20 positive

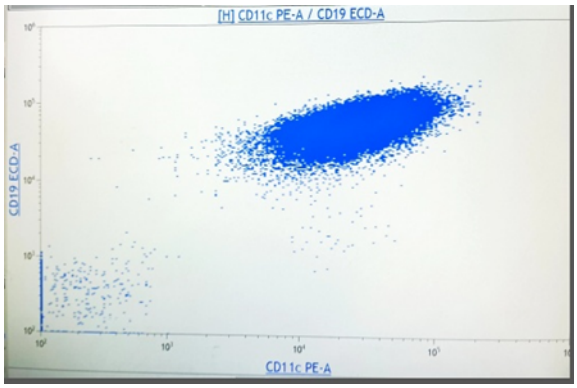

Figure 3: CD19 and CD11c positive

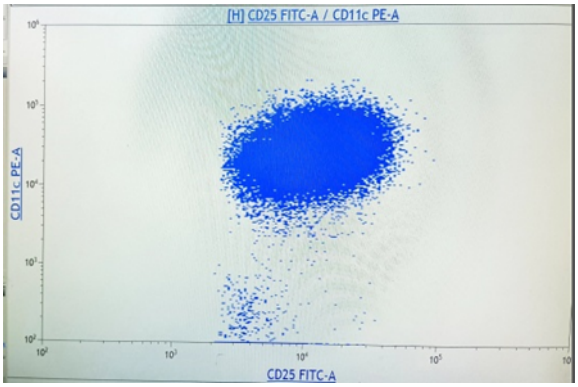

Figure 4: CD11c and CD25 positive

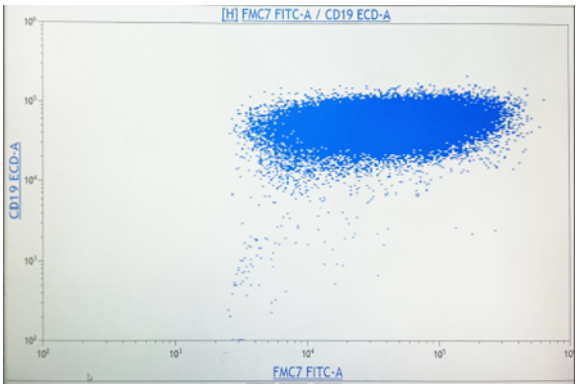

Figure 5: CD19 and FMC7 positive

Peripheral smear, bone marrow, and flow cytometry examination confirmed the diagnosis of Hairy Cell Leukemia.

3. Discussion

Hairy cell leukemia is a rare form of chronic B cell lymphoproliferative disorder representing 1-2% of lymphoid leukemia.[7] It is important to differentiate HCL from other chronic B cell lymphoproliferative disorders because of different treatment protocol and indolent course.[8,9] The median age atdiagnosis is usually around 58 years. In our case, the patient presented at 48 years which was earlier presentation. Our patient had been feeling generalized weakness, fatigue, and loss of appetite for 3 months. All of these complaints have been reported in HCL patients in the literature.[10]

Our patient presented with anemia and thrombocytopenia which is the most common hematological abnormality similar to other studies. The majority of classic HCL patients present with pancytopenia, rare cases can present with marked leucocytosis.[5,8,9] Cases of HCL with marked lymphocytosis have been reported only rarely in the literature. Our patient presented with marked lymphocytosis. In peripheral smear neoplastic hairy cells are present but at low frequency so it can be difficult to identify.

Most of the patients with HCL present with splenomegaly, our patient also presented with massive splenomegaly. A study done by Chatterjee T, et al reported 53% of cases to have hepatomegaly while Galani, et al reported 28% of cases.[10,11] Our patient had mild hepatomegaly also.

Peripheral smear examination showed 90% lymphocytes. Few of them were of medium size, with hair like cytoplasmic projections, reticular to clumped type chromatin and a moderate amount of cytoplasm, suspicious of mature B cells of Hairy cell leukemia, Splenic marginal zone lymphoma, Hairy cell leukemia variant and Splenic diffuse red pulp lymphoma.

Bone marrow examination showed hypercellular marrow with mature lymphoid cells with cytoplasmic projection. Bone marrow biopsy showed mature bland cells with reniform nuclei and zone of peripheral clearing (fried egg appearance) in sheets which ruled out the possibilities of splenic marginal zone lymphoma and Hairy cell leukemia variant. Splenic marginal zone lymphoma shows a nodular pattern of involvement on bone marrow biopsy while in Hairy cell leukemia variant and Splenic diffuse red pulp leukemia, it shows subtle infiltration of atypical lymphoid cells within the interstitial and intrasinusoidal.[1,3,12]

The diagnosis of HCL could only be confirmed based on an immunophenotyping study. Flow cytometric analysis of peripheral blood showed CD19, CD20, and CD79a positivity along with kappa light chain restriction. There was also an expression of CD11c, CD25 and CD103, FMC-7, and HLA-DR. The abnormal cells did not express CD5, CD10, and CD23. Splenic marginal zone lymphoma ,Hairy cell leukemia variant and Splenic diffuse red pulp lymphoma do not express CD 25 while variable expression for CD 103 is seen in Splenic marginal zone lymphoma and negative in Splenic diffuse red pulp lymphoma.[1] So the possibility of splenic margin zone lymphoma, Hairy cell leukemia variant and Splenic diffuse red pulp lymphoma were ruled out. There was no aberrant expression of other antigens in our case.

Patients with HCL are highly sensitive to purine analogs such as Cladribine and Pentostatin but do not respond to conventional lymphoma chemotherapy. Patients who achieve a complete response have a significantly longer disease-free survival than those who achieve a partial response. Patients with massive splenomegaly, leukocytosis ($> 10 \times 10^9$/L), high number of hairy cells in the blood have poor prognosis.[13]

4. Conclusion

Hairy cell leukemia is a rare chronic lymphoproliferative disorder of mature B lymphocytes which have a defined clinical and morphological presentation. On flow cytometry

expression of B cell markers CD19, CD20, CD22, and CD79b and 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. Flow cytometry and molecular study of BRAF600v mutation will provide an accurate diagnosis.

5. Source of Funding

None.

6. Conflict of Interest

None.

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