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Hairy Cell Leukemia

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Abstract*: Hairy cell leukemia is part of the low- grade non-Hodgkin lymphoma family and represent approximately 2% of all leukemias.It occurs mostly in people aged 40-60 and is more common in men than in women.The present study describes the case of a50 yr old male whowas diagnosed with extrapulmonary tuberculosis 4 yrs back for which he took ATT for 6 months and now presented with generalized weakness, fever and cough. Liver and spleen were palpable. Complete blood count, peripheral blood film , bone marrow aspiration and biopsy was performed and the results indicated Hairy cell variant/ SLVL.*

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I. Introduction

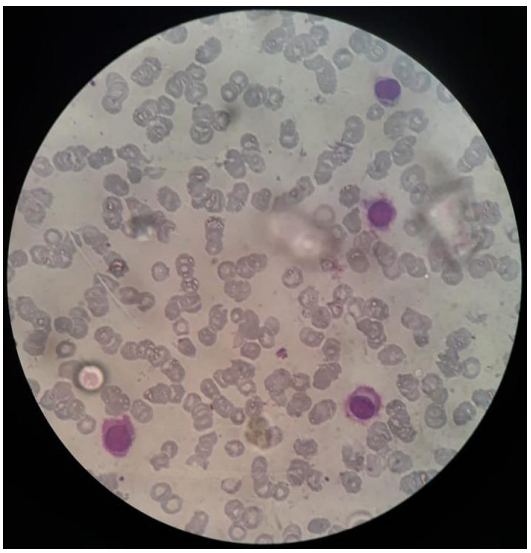
Hairy cell leukemia (HCL) is a rare mature B-cell malignancy, which was initially described by Bouroncle et al . in 1958.[1] HCL has an incidence of 0.3 cases per 100,000 individuals.[2] It occurs about four times more common in men than in women, with a median age at diagnosis of 55 years.[3]HCL cells are characterized by thin cytoplasmic hair-like projections, giving the disease its name.[4] Leukemic hairy cells accumulate in the bone marrow and cause pancytopenia, which is the most common finding at initial presentation. HCL patients report symptoms of fatigue, infections, and, occasionally, left sided abdominal pain caused by splenomegaly. In contrast to many B-cell malignancies, lymphadenopathy is rare in HCL patients.[5] A severe fibrotic reaction is usually found in the bone marrow of HCL patients to their originwhich often complicates a diagnostic bone marrow aspiration. The diagnosis is usually made on the detection of typical morphological features and a unique immubnophenotype with flow cytometry of peripheral blood and/or histological and immunohistochemical analysis(IHC) analysis of the trephine biopsies. HCL cells demonstrate a characteristic gene expression profile signature that points to their origin from memory B cells[6,7] Tiacci et al. discovered that classical HCL is characterized by a gain of function mutation of the BRAF serine/threonine protein kinase (V600E)[8,9]. In the initial validation series, all HCL patients showed this particular mutation, while a set of 195 B-cell lymphomas and leukemias did not harbor a mutated BRAF gene. The vast majority of BRAF – V600E mutations in HCL are heterozygous. Homozygous mutations are rare but have been suggested to be associated with a more aggressive couse[10]. Recurrent deletions of the BRAF gene locus on chromosome 7q34 have been described in HCL and lead to loss of heterozygosity.[11]Historically, there were two different forms of HCL: the more-common classical HCL (90%) and the less-frequent HCL variant (10%). HCL variant is characterized by a more aggressive disease course and poor response to purine analogs[12]. Most importantly, HCL variant cases are commonly negative for BRAF-V600E mutation, indicating that HCL variant is a biologically distinctive entity. A small subset of patients with bona fide classical (HCL) who also do not harbor any BRAFmutation has been reported only in a single study[13]. However, these cases are often characterized by an IGHV4-34 immunoglobulin rearrangement, which is in general absent in classical HCL and is associated with as poor a prognosis as HCL variant[13].

Case Report

A 50 yr old male was referred to a Department of Medicine, Rajindra Hospital, Government Medical College Patiala due to complaint of generalized weakness since 4 months, fever since 4 days associated with cough and breathlessness. He was diagnosed with extrapulmonary tuberculosis in 2014 for which he took ATT for 6 months. On examination –Liver was palpable 4 fingers below right costal margin and spleen was palpable 3 fingers below the left costal margin. CBC and PBF of the patient was sent in the BCL Lab, Rajindra Hospital, Government Medical College Patiala after which patient was sent to the BCL laboratory for the bone marrow aspiration and biopsy.

CBC And PBF

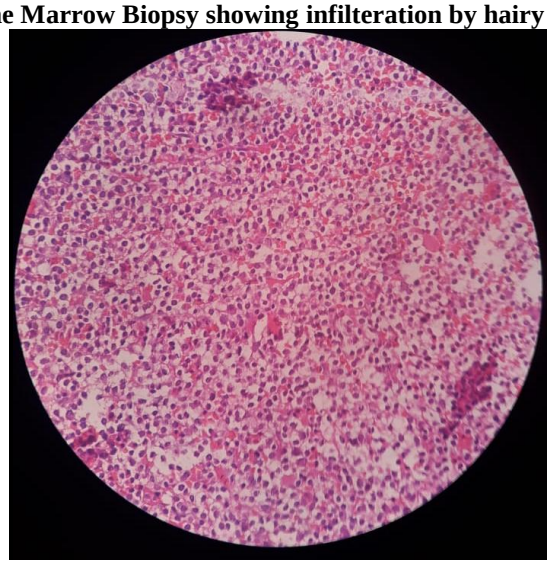
Hb-5.2 gm TLC- 20,200 DLC -Hairy cells 80% Poly 04% Lympho 16%
Platelet count-1,60,000/cmm Impression:- Hairy Cell Variant/SLVL

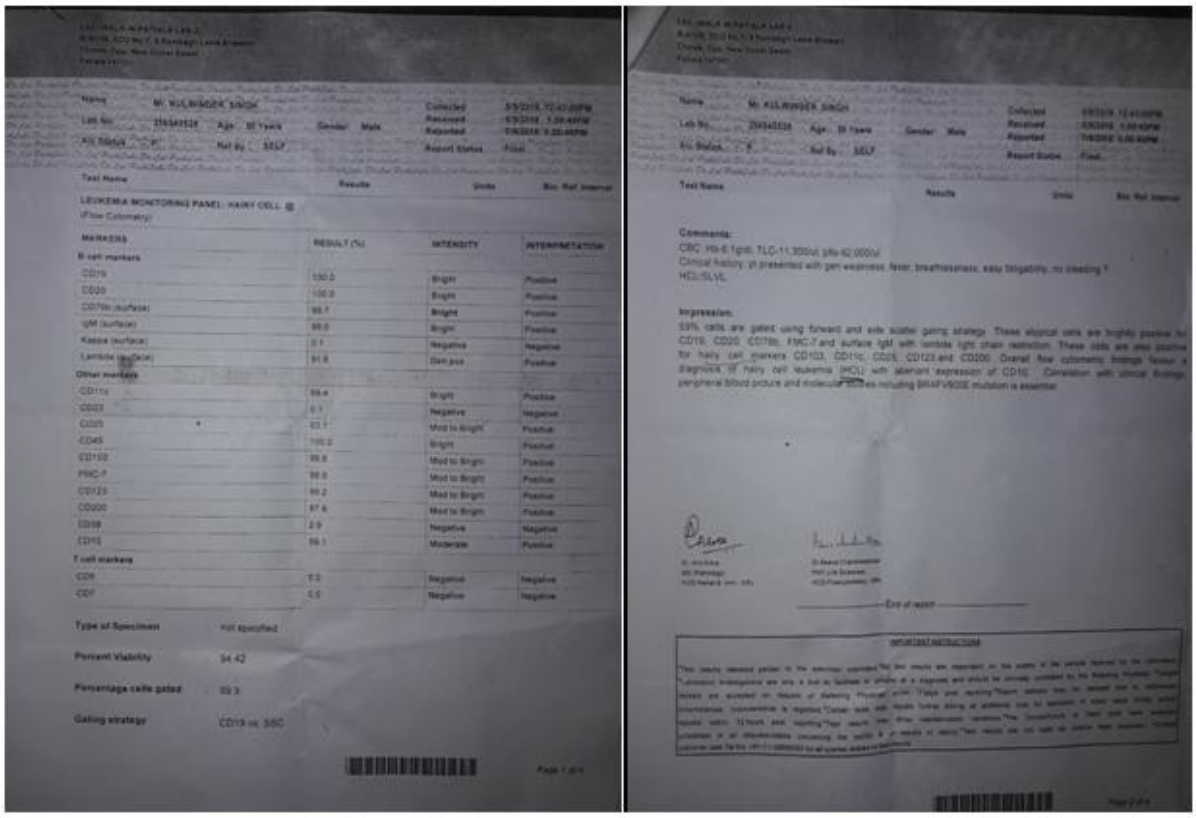


Picture above shows PBF with hairy cells.

Bone marrow aspiration and biopsy was done from Posterior superior iliac spine. Marrow was particulate and cellularity was markedly hypercellular. NE:E was 90:10(9:1). Reaction was mildly megaloblastic. Cellularity of the marrow was due to lymphoid series of cells showing 75% of hairy cells and 20% lymphocytes in non erythroid cells.Erythroid series showed intermediate megaloblasts. Megakaryocytes were adequate in number and functional in activity. No hemoparasite was seen. Differential count was – Promyelocytes 00% Myelocytes 00% Metamyelocytes00% Polymorphs00% Lymphocytes 20% Plasma cells 05% Hairy cells 75%. Impression- Hairy Cell Variant/SLVL.Bone marrow biopsy was adequate for size and evaluation. There was seen diffuse pattern of involvement by the hairy cells.Confirmation was advised from the flow cytometry CD11c, CD103, CD20 , FMC7, sIg

Bone Marrow Biopsy showing infilteration by hairy cells





II. Discussion

Almost 50% of HCL-variant and IGHV4-34-expressing HCL cases were found to harbor activating mutations in the MAP2K1 gene encoding MEK1[14]. HCL cells typically show a distinctive immunophenotype co-expressing CD19, CD20, CD11c, CD25, CD103, and CD123. In contrast, HCL variant lacks the expression of CD25 and CD123[15]. Moreover, HCL cells strongly express CD200, which can also be used as another distinctive marker to differentiate HCL[16,17]. Another distinctive feature of HCL is the expression of annexin A1, which is easily accessible by immunohistochemical staining[18]. In addition to HCL variant, the 2016 revision of WHO classification of lymphoid neoplasms recognizes two other entities resembling HCL: splenic marginal zone lymphoma (SMZL), usually associated with NOTCH2 mutations, and splenic diffuse red pulp small B-cell lymphoma (SDRPBCL), still listed as a provisional entity, whose genomic landscape has not been yet clarified[19]. In addition to CDKN1B mutations cooperating with BRAF-V600E, recurrent, inactivating mutations in KMT2C (MLL3) were identified in 15% and 13% of classical HCL and HCL variant, respectively[11]. Another study described somatic mutations or deletions of the Krüppel-like factor 2 (KLF2) in 4 of 24 (16%) HCL patients examined[20], but KLF2 mutations are more frequent in other B-cell malignancies, such as SMZL (31%) and diffuse large B-cell lymphoma (26%)[20,21]

III. Conclusion

At initial diagnosis, most patients will require treatment owing to hematopoietic insufficiency. Accepted indications to start treatment are hemoglobin <11 g/dL, platelet count <100,000/µL, or absolute neutrophil count <1,000/µL. Less frequently, increased susceptibility to infections or symptomatic splenomegaly may also serve as criteria to start treatment[5]. The introduction of the purine analogs cladribine and pentostatin into the treatment landscape of HCL significantly improved the outcome of HCL patients[22].. The first patient exposed to the BRAF inhibitor vemurafenib indeed showed an immediate and striking response, proving oncogene-dependence and clinical activity[23,24]. The dynamics of the response were notable, with a spleen size reduction of more than 6 cm in only 6 days and improvement of blood count (hemoglobin, platelets, and granulocytes) within 1 month [24]. Soon after the initial report, multiple studies confirmed the efficacy of both vemurafenib[25,26,27] and (because of availability) later dabrafenib[28]

References

[1]. BOURONCLE BA, WISEMAN BK, DOAN CA: Leukemic reticuloendotheliosis. Blood. 1958; 13(7): 609-30
[2]. Teras LR, DeSantis CE, Cerhan JR, et al.: 2016 US lymphoid malignancy statistics by World Health Organization subtypes. CA Cancer J Clin. 2016; 66(6): 443–459.
[3]. Tadmor T, Polliack A: Epidemiology and environmental risk in hairy cell leukemia. Best Pract Res Clin Haematol. 2015; 28(4): 175–9
[4]. Schrek R, Donnelly WJ: "Hairy" cells in blood in lymphoreticular neoplastic disease and "flagellated" cells of normal lymph nodes. Blood. 1966; 27(2): 199–211.
[5]. Grever MR, Abdel-Wahab O, Andritsos LA, et al.: Consensus guidelines for the diagnosis and management of patients with classic hairy cell leukemia. Blood. 2017; 129(5): 553–60.
[6]. Tiacci E, Liso A, Piris M, et al.: Evolving concepts in the pathogenesis of hairy-cell leukaemia. Nat Rev Cancer.2006; 6(6): 437–48.
[7]. Basso K, Liso A, Tiacci E, et al.: Gene expression profiling of hairy cell leukemia reveals a phenotype related to memory B cells with altered expression of chemokine and adhesion receptors. J Exp Med. 2004; 199(1): 59–68.
[8]. Tiacci E, Schiavoni G, Forconi F, et al.: Simple genetic diagnosis of hairy cell leukemia by sensitive detection of the BRAF-V600E mutation. Blood. 2012; 119(1): 192–5.
[9]. Tiacci E, Trifonov V, Schiavoni G, et al.: BRAF mutations in hairy-cell leukemia. N Engl J Med. 2011; 364(24): 2305–15.
[10]. Samuel J, Macip S, Dyer MJ: Efficacy of vemurafenib in hairy-cell leukemia. N Engl J Med. 2014; 370(3): 286–8
[11]. Durham BH, Getta B, Dietrich S, *et al.*: Genomic analysis of hairy cell leukemia identifies novel recurrent genetic alterations. *Blood.* 2017; 130(14): 1644–8
[12]. Robak T: Hairy-cell leukemia variant: recent view on diagnosis, biology and treatment. *Cancer Treat Rev.* 2011; 37(1): 3–10.
[13]. Xi L, Arons E, Navarro W, *et al.*: Both variant and IGHV4-34-expressing hairy cell leukemia lack the *BRAF* V600E mutation. *Blood.* 2012; 119(14): 3330–2
[14]. Waterfall JJ, Arons E, Walker RL, *et al.*: High prevalence of *MAP2K1* mutations in variant and IGHV4-34-expressing hairy-cell leukemias. *Nat Genet.* 2014; 46(1): 8–10.
[15]. Venkataraman G, Aguhar C, Kreitman RJ, *et al.*: Characteristic CD103 and CD123 expression pattern defines hairy cell leukemia: usefulness of CD123 and CD103 in the diagnosis of mature B-cell lymphoproliferative disorders. *Am J Clin Pathol.* 2011; 136(4): 625–30
[16]. Sandes AF, de Lourdes Chauffaille M, Oliveira CR, *et al.*: CD200 has an important role in the differential diagnosis of mature B-cell neoplasms by multiparameter flow cytometry. *Cytometry B Clin Cytom.* 2014; 86(2): 98–105.
[17]. Pillai V, Pozdnyakova O, Charest K, *et al.*: CD200 flow cytometric assessment and semiquantitative immunohistochemical staining distinguishes hairy cell leukemia from hairy cell leukemia-variant and other B-cell lymphoproliferative disorders. *Am J Clin Pathol.* 2013; 140(4): 536–43.
[18]. Falini B, Tiacci E, Liso A, *et al.*: Simple diagnostic assay for hairy cell leukaemia by immunocytochemical detection of annexin A1 (ANXA1). *Lancet.* 2004; 363(9424): 1869–70.
[19]. Swerdlow SH, Campo E, Pileri SA, et al.: The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016; 127(20): 2375–90.
[20]. Piva R, Deaglio S, Famà R, et al.: The Krüppel-like factor 2 transcription factor gene is recurrently mutated in splenic marginal zone lymphoma. Leukemia. 2015; 29(2): 503–7.
[21]. Clipson A, Wang M, de Leval L, et al.: KLF2 mutation is the most frequent somatic change in splenic marginal zone lymphoma and identifies a subset with distinct genotype. Leukemia. 2015; 29(5): 1177–85
[22]. Grever M, Kopecky K, Foucar MK, et al.: Randomized comparison of pentostatin versus interferon alfa-2a in previously untreated patients with hairy cell leukemia: an intergroup study. J Clin Oncol. 1995; 13(4): 974–82
[23]. Dietrich S, Hüllein J, Hundemer M, et al.: Continued response off treatment after BRAF inhibition in refractory hairy cell leukemia. J Clin Oncol. 2013; 31(19): e300–3.
[24]. Dietrich S, Glimm H, Andrulis M, et al.: BRAF inhibition in refractory hairy-cell leukemia. N Engl J Med. 2012; 366(21): 2038–40.
[25]. Follows GA, Sims H, Bloxham DM, et al.: Rapid response of biallelic BRAF V600E mutated hairy cell leukaemia to low dose vemurafenib. Br J Haematol. 2013; 161(1): 150–3.
[26]. Munoz J, Schlette E, Kurzrock R: Rapid response to vemurafenib in a heavily pretreated patient with hairy cell leukemia and a BRAF mutation. J Clin Oncol. 2013; 31(20): e351–2.
[27]. Peyrade F, Re D, Ginet C, et al.: Low-dose vemurafenib induces complete remission in a case of hairy-cell leukemia with a V600E mutation. Haematologica. 2013; 98(2): e20–2.
[28]. Vergote V, Dierickx D, Janssens A, et al.: Rapid and complete hematological response of refractory hairy cell leukemia to the BRAF inhibitor dabrafenib. Ann Hematol. 2014; 93(12): 2087–9.

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