Hairy Cell Leukemia in a Middle-Age Patient with Pancytopenia: A Diagnostic Challenge and Case Report

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Abstract

Hairy cell leukemia (HCL) is a rare chronic B-cell lymphoproliferative neoplasm associated in most cases with the mutation BRAF V600E located in the exon 15 of proto-oncogene BRAF, which gives its morphology and immunophenotypic characteristics; HCL accounts for approximately 2% of all leukemia cases, with a median age at diagnosis of 65 years in western countries. We describe the case of a 52-year-old male patient presenting with asthenia, adynamia, unquantified progressive weight loss, hyporexia, generalized weakness, and pallor for three months, along with severe pancytopenia. The diagnosis was based on cellular morphology and flow cytometry immunophenotyping, due to the unavailability of BRAF V600E molecular testing. The patient was treated with cladribine, showing a favorable clinical evolution. The novelty of this report lies in the presentation of HCL in a patient younger than the usual demographic, emphasizing the need to consider this diagnosis even in age groups often considered atypical. Therefore, it is essential to consider this pathology even in atypical age groups and implement diagnostic aids such as the cell morphology and immunophenotyping, key for diagnosis.

Keywords: Leukemia, Hairy Cell, Pancytopenia, Proto-Oncogene Proteins B-raf, Flow Cytometry.

Introduction

Hairy Cell Leukemia (HCL) was initially described in 1958 as leukemic reticuloendotheliosis. Subsequently, with advancements in molecular diagnostic techniques, its etiology was determined to be a chronic B-cell lymphoproliferative neoplasm, accounting for approximately 2% of all leukemias[1]. The incidence is four times higher in males and predominantly affects Caucasian and Jewish populations[2]. The median age at diagnosis varies by region, being 55.5 years among Israeli Jews, 49 years among Arabs[3], and 65 years in the United States (SEER)[4]. This case report includes signed informed consent from the patient and adheres to the CARE guidelines to ensure transparency and methodological rigor.

HCL is associated with BRAF V600E mutation in up to 90% of cases, located in exon 15 of the proto-oncogene BRAF (7q34), leading to constitutive activation of the MAPK/ERK signaling pathway. This activation results in uncontrolled proliferation of leukemic B-cells, increased interactions with the extracellular matrix, characteristic cytoplasmic projections resembling hair, and resistance to apoptosis[5,6]. Splenic infiltration by neoplastic lymphocytes causes pseudosinusoid formation linked to anemia, while the presence of hyaluronate, interleukin-1 (IL-1), and platelet-derived growth factor (PDGF) in the liver and bone marrow promotes fibrosis through fibronectin production[7]. Furthermore, an imbalance between hematopoietic stimulatory and inhibitory factors, particularly elevated levels of tumor necrosis factor-alpha (TNF-α), sustains an inflammatory cycle that exacerbates marrow dysfunction[8].

Pancytopenia, defined as hemoglobin levels below 10 g/dL, leukocyte counts under 4×10^3/μL, and platelet counts below 100×10^3/μL, occurs in 60–80% of cases at the time of diagnosis. However, owing to its nonspecific nature, differential diagnosis must exclude other conditions such as myelodysplastic syndromes or

drug-induced toxicity. Currently, incidental detection of pancytopenia during blood counts serves as the initial clinical clue in 40% of HCL cases, surpassing splenomegaly, which was previously present in up to 90% of cases. The clinical triad includes: 1) increased risk of infection due to neutropenia, 2) constitutional symptoms, and 3) monocytopenia (<1×10^3/μL), with a reported sensitivity of 85% and specificity of 95% for HCL[9,10].

We report the case of a 52-year-old man diagnosed with HCL, an age group in which the incidence is uncommon, with less than 10% of cases occurring in patients under 55 years. The significance of this case lies in illustrating the diagnostic challenges posed by atypical presentations and emphasizing the importance of markers such as the CD103+/CD123+ immunophenotype and the BRAF V600E mutation. Early suspicion and diagnosis are vital to enhancing the likelihood of achieving complete remission and extending survival. This report aims to synthesize relevant clinical and academic information, highlighting the relationship between pathophysiology and clinical manifestations to facilitate timely and effective management.

Case Report

In February 2021, a 52-year-old man was referred to his hematologist with a three-month history of asthenia, adynamia, weight loss, hyporexia, weakness, and pallor, along with severe pancytopenia. He had no significant medical or family history. Vital signs were normal: blood pressure 110/80 mmHg, heart rate 72 bpm, respiratory rate 20 breaths per minute, body temperature 36.6°C, and oxygen saturation 96%. The only notable finding during the physical exam was generalized pallor without jaundice. The patient was admitted for further evaluation of his severe pancytopenia and hospitalized in isolation due to his high risk of infection.

Initially, several tests were performed. The blood count confirmed the severe pancytopenia, as illustrated in Table 1. The tests for coagulation, renal, hepatic, metabolic, autoimmune, and infectious issues were generally normal, with minor elevations in lactic acid, glucose, and bilirubin, as shown in Table 2. An abdominal ultrasound revealed splenomegaly measuring 15.2 x 6.8 cm, with no evidence of masses, the presence of cholelithiasis without cholecystitis, and normal appearance of other anatomical structures.

Table 1: Blood Count Results.

Parameter	**20/01/2021 (Prior to Admission)**	**10/02/2021 (At the Admission)**	**Reference Value**
WBC (x10^3/μL)	1,76	1,19	4-10
Lymph (%)	73,3	63	22-43
Neut (%)	14,2	16,9	50-70
Mono (%)	11,9	19,3	3-10
Eos(%)	0,6	0,8	0-5
Baso (%)	0,0	0	0-1
RBC (x10^6/μL)	2,53	2,47	3-5
Hb (g/dL)	7,8	7,6	13-15
HCT (%)	23,8	23,6	40-54
MCH (pg)	30,8	30,7	25-31
MCHC (g/dL)	32,8	32,2	32-36
MCV (fL)	94,1	95,5	86-96
RDW-(%)	20,3	20	11-16
PLT(x10^3/μL)	41	41	150-450

Table 2: Results of Clinical Chemistry Test.

Category	**Parameter**	**11/02/2021**	**12/02/2021**	**Reference Value**
Blood Chemistry	Lactic acid (mmol/L)	2.3	2.3	0.5-2.2
	Postprandial glucose (mg/dL)	142.8		80-140
	BUN (mg/dL)	16.6		7-20
	Serum creatinine (mg/dL)	0.94		0.6-1.3
	LDH (U/L)	135.2		105-335
	AST (U/L)	15		5-35

	ALT (U/L)	43		10-45
	Total bilirubin (mg/dL)	0.82		0.1-1.2
	Indirect bilirubin (mg/dL)	0.46		0.2-0.8
	Direct bilirubin (mg/dL)	0.36		<0.3
	Alkaline phosphatase (U/L)	75		20-145
	Total serum protein (g/dL)	6.76		6-8.5
	C-reactive protein (mg/dL)	0.070		<10
Hemostasis and Coagulation	PT (seconds)	10,8		10-14
	aPTT (seconds)	25,8		25-45
	INR	0,99		0,8-1,2
	Phosphorus (mg/dL)	3.39		2.5-4.5
Electrolytes	Magnesium (mg/dL)	2.09		1.7-2.2
	Sodium (mEq/L)	141		135-145
	Potassium (mEq/L)	3.7		3.5-5.5
	Chloride (mEq/L)	100.4		95-105
Autoimmunity	Complement C3 (g/L)	0.98	0.9	0.8-2
	Complement C4 (g/L)	0.18	0.18	0.16-0.48
Infectious Serology	FTA-ABS		Non-reactive	
	HIV		Negative	

For 24 days, he received daily doses of Omeprazole 20 mg, Folic acid 1 mg, and sodium chloride 0.9% at 60 cc/hr. He also had daily blood counts; a bone marrow biopsy from the right posterior iliac spine was performed, with hospitalization recommended pending results. Preventative measures for bleeding included platelet transfusions when counts were $\leq 10 \times 10^3/\mu L$ and red blood cell transfusions when hemoglobin was ≤ 7 g/dL.

The evaluation of peripheral blood evaluation revealed hairy cells on the smear, as illustrated in Figure 1. The bone marrow was deemed unsuitable for microscopic examination due to hemodilution and a limited cellular component. Flow cytometry identified a monotypic B lymphoid population consistent with hairy cell leukemia, as depicted in Figure 2 and detailed in Table 3. Consequently, a decision was made to commence a five-day course of chemotherapy with Cladribine at a dose of 9 mg daily via intravenous infusion, accompanied by prophylaxis against potential side effects with Dexamethasone at 8 mg daily and supportive antiemetic therapy with Ondansetron at 8 mg IV every eight hours. The patient was subsequently discharged with guidance to take 1 mg of folic acid daily.

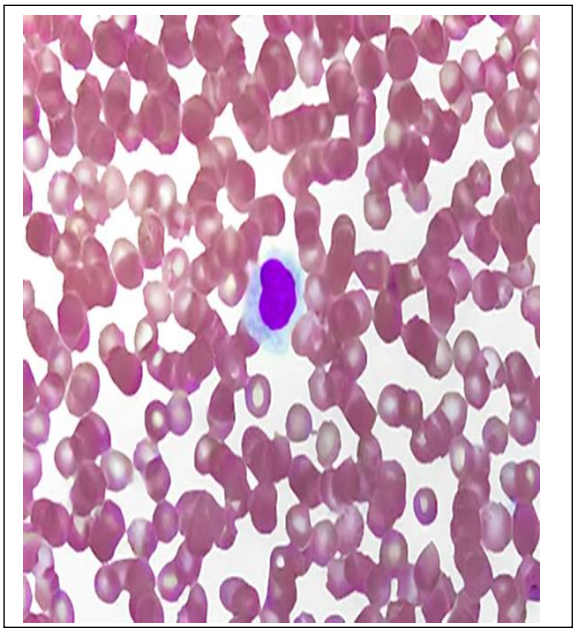

Figure 1: Peripheral blood smear showing a classic hairy cell, characterized by abundant pale blue cytoplasm with irregular, fine hair-like projections; oval to kidney-shaped nucleus with loose chromatin and indistinct nucleoli.

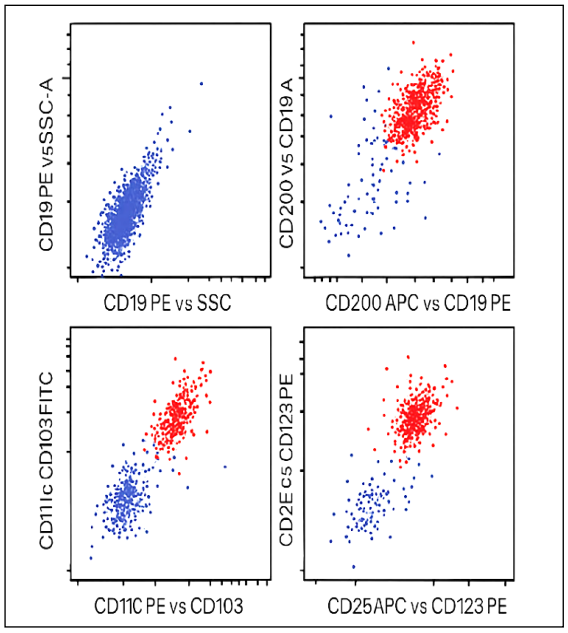

Figure 2: Flow cytometry of bone marrow showing immunomarker positivity for: CD19, CD20 (bright), CD103, CD123, CD200 (bright), CD11c (bright). Negative for: CD5, CD10, CD23, CD38. The bright co-expression of CD103/CD123/CD200 allowed to confirm the diagnosis of classic hairy cell leukemia.

Table 3: The flow cytometry immunophenotype was highly suggestive of a monotypic mature B-cell population.

Inmunomarker	**CD 19,CD 45,CD 20, CD 200, CD 103, CD 123, LAIR-1 Lambda Light Chain**	**Positive “bright”**

CD 10, CD 23, CD 38, CD 4, CD 8, CD 56, CD 3, CD 5, CD 34, MPO, Kappa Light Chain	Negative

At the evaluation 15 days after discharge the patient presented severe neutropenia in his blood count; Consequently, the following treatments were prescribed: Ciprofloxacin 500 mg (2 tablets) daily, Fluconazole 200 mg (1 capsule) daily, Trimethoprim Sulfamethoxazole 160/800 mg (1 tablet) daily for 10 days; and Pegfilgrastim 6 mg SC injectable in a single dose. One month later, a new bone marrow study was performed; the flow cytometry did not identify a monotypic population of B cells or a population of immunophenotypically aberrant T cells; the myeloid and monocytic lines were normal, and the bone marrow analysis demonstrated adequate myelopoiesis and erythropoiesis with sequential maturation and no significant dysplastic changes. The patient remains in good general condition during periodic follow-ups with blood biochemistry and blood counts.

Discussion

This case illustrates the diagnosis of hairy cell leukemia (HCL) in a 52-year-old male patient with severe pancytopenia (Hb 7.8 g/dL, platelets 41 × 10^3/μL, neutrophils 0.25 × 10^3/μL) and splenomegaly (15.2 cm by ultrasound) without splenic infiltration. The diagnosis was confirmed by flow cytometry, which revealed a monoclonal population of mature B cells. The response to cladribine treatment was favorable, with a preliminary favorable marrow response at 30 days.

Although the median age at diagnosis is in the mid-50s to mid-60s[3], depending on the population, a subset of patients presents at a younger age; roughly 10% of cases occur under age 55[4]. In its early stages, the clinical manifestations of HCL are non-specific, as in our patient's case, and include fatigue, weakness, abdominal pain, and loss of appetite. The most frequently reported physical findings are splenomegaly, hepatomegaly, and lymphadenopathy in 96%, 58%, and 35% of cases, respectively [5]. HCL is characterized by infiltration of bone marrow for neoplastic B-cells, which is associated with reticulin fibrosis and cytopenias due to normal hematopoiesis suppression[11].

Pancytopenia, although nonspecific and present in various pathologies, is observed in 70-90% of HCL cases, accompanied by monocytopenia (<0.1 x 10^3/μL), increasing its specificity and sensitivity for this disease[12]. Only 10-20% of HCL cases report moderate leukocytosis (>10 x 10^3/μL) in the complete blood count[5].

As evidenced in this case, bone marrow biopsy is a common challenge in HCL, as stromal fibrosis hinders the acquisition of adequate samples for microscopic evaluation[11]. Additionally, in 10% of patients with evaluable bone marrow, marked hypocellularity is observed[13]. In cases where the sample quality is sufficient for evaluation, fibrosis, cells with a "fried egg" appearance, and immunohistochemical positivity for CD20, TRAP, DBA-4, and Annexin A1 are typically found[14].

The classic immunophenotype of HCL by flow cytometry is characterized by restriction to a single immunoglobulin light chain type, strong positivity for CD19, CD20, CD22, and CD200, and positivity for CD11c, CD103, CD25, and CD123. In contrast, markers such as CD5, CD23, CD10, and CD27 are generally negative[6]. The immunophenotype observed in this patient is pathognomonic for HCL, particularly the intense or "bright" positivity for CD200, which is highly suggestive of the disease and allows differentiation from other types of lymphoid neoplasms, even when commonly negative markers have aberrant expression[14].

Although molecular testing was not performed in this case, the BRAF V600E mutation is present in up to 100% of HCL cases and is associated with HCL morphology and molecular characteristics[15]. This mutation is considered the "molecular signature" of HCL and is crucial in distinguishing it from other peripheral B-cell neoplasms, such as splenic marginal zone lymphoma and HCL variant, which share similar clinical and morphological features but do not present the BRAF V600E mutation[6,16].

In approximately 10% of asymptomatic patients, the diagnosis of HCL may be made incidentally, and a watchful waiting approach may be opted for over several years. A decrease in one of the hematological parameters, such as hemoglobin <11 g/dL, platelets <100,000/μL, absolute neutrophil count <1,000/μL, or severe splenomegaly, are currently indications to initiate treatment with nucleoside analogs such as cladribine or pentostatin after of HCL diagnosis is confirmed, both treatment alternatives are effective and there are no specific guidelines indicating the superiority of one over the other[12].

The complete clinical response has been defined as an interval of 4-6 months disease-free, and the near normalization of the blood count: hemoglobin >11g/dL (without transfusion need), platelets >100.000/μL and an absolute neutrophil count >1500/μL[12]; the use of continuous IV Cladribine infusion regimens has reported remission rates up to 95%. Our patient presented a preliminary favorable bone marrow response 30 days after completing the treatment. Cladribine is associated with greater myelotoxicity due to increased release of mitochondrial cytochrome C, DNA breakage, and cell apoptosis compared to pentostatin. As a result, 71% of patients treated with cladribine experience severe neutropenia (<500/μL) after one week of treatment, and 43% experience febrile neutropenia, although only 13% develop concomitant bacterial or viral infections. Therefore, prophylactic antibiotics were justified in this patient, as well as the administration of pegfilgrastim[17,18]. In cases with the BRAF V600E mutation, consideration of therapeutic options with BRAF inhibitors (BRAFi) such as vemurafenib or dabrafenib in monotherapy is warranted[6].

Conclusion

Hairy cell leukemia (HCL) is a rare B-cell malignancy with a variable average age at diagnosis depending on race and geographic location. According to the literature review, constitutional symptoms and pancytopenia are common but non-specific initial manifestations that require first ruling out other pathologies during the diagnostic workup, and the diagnosis of HCL initially may not be considered in the context of middle-aged patients with pancytopenia; its pathophysiological changes on bone marrow can difficult the diagnosis difficult through methods like biopsy, for this motive the importance of more advanced diagnosis methods like flow cytometry or the molecular testing for BRAF V600E must be highlighted. Finally, the use of nucleoside analogs like Cladribine usually leads to good outcomes despite its myelotoxicity and the possible need for infectious prophylaxis.

Disclosure

The authors declared no conflicts of interest. Written consent was obtained from the patient.

References

1. Hooper WCraig, Buss DH, Parker CL. Leukemic reticuloendotheliosis (hairy cell leukemia): A review of the evidence concerning the immunology and origin of the cell. Leukemia Research [Internet]. 1980 May 21;4(5):489–503. Available from: https://www.sciencedirect.com/science/article/abs/pii/0145212680900302

2. Swerdlow SH, Campo E, Harris NL, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. Lyon, France: World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissue; 2008, 326 pp.

3. INBAR M, HERISHANU Y, GOLDSCHMIDT N, BAIREY O, YUKLEA M, SHVIDEL L, et al. Hairy Cell Leukemia: Retrospective Analysis of Demographic Data and Outcome of 203 Patients from 12 Medical Centers in Israel. Anticancer Research [Internet]. 2018 Nov [cited 2025 Mar 4];38(11):6423–9. Available from: https://ar.iiarjournals.org/content/anticanres/38/11/6423.full.pdf.doi:10.21873/anticanres.13003

4. Chandran R, Gardiner SK, Smith SD, Spurgeon SE. Improved survival in hairy cell leukaemia over three decades: a SEER database analysis of prognostic factors. British Journal of Haematology [Internet]. 2013 Jul 24 [cited 2022 Jul 17];163(3):407–9. Available from: https://pubmed.ncbi.nlm.nih.gov/23889044/

5. Garza-Ledezma, Tellez-Hinojosa, González-López, Gómez-Almague. Hairy cell leukemia, an uncommon B-cell lymphoid neoplasia [Internet]. Elsevier.es. 2025 [cited 2025 Apr 15]. Available from: https://www.elsevier.es/en-revista-medicina-universitaria-304-pdf-S1665579616300151

6. Troussard X, Maître E, Jérôme Paillassa. Hairy cell leukemia 2024: Update on diagnosis, risk-stratification, and treatment—Annual updates in hematological malignancies. American Journal of Hematology [Internet]. 2024 Mar 5;99(4):679–96. Available from: https://pubmed.ncbi.nlm.nih.gov/38440808/

7. Zuzel M, Cawley JC. The biology of hairy cells. Best Practice & Research Clinical Haematology [Internet]. 2003 Mar 26;16(1):1–13. Available from: https://www.sciencedirect.com/science/article/pii/S1521692602000828

8. Lindemann A, Ludwig W, Oster W, Mertelsmann R, Herrmann F. High-level secretion of tumor necrosis factor-alpha contributes to hematopoietic failure in hairy cell leukemia [see comments]. Blood [Internet]. 1989 Mar 1 [cited 2023 Apr 4];73(4):880–4. Available from: https://www.sciencedirect.com/science/article/pii/S0006497120755795

9. Chew S, Kamangar M. Approach to pancytopenia: From blood tests to the bedside. Clinical Medicine [Internet]. 2024 Sep;24(5):100235. Available from: https://pubmed.ncbi.nlm.nih.gov/39159748/

10. Moustafa A, Shwaylia HM, Aldapt M, Yassin MA. Outcome of Atypical Presentations of Hairy Cell Leukemia. Blood [Internet]. 2019 Nov 13 [cited 2019 Dec 18];134(Supplement_1):5267–7. Available from: https://www.sciencedirect.com/science/article/pii/S0006497118631933

11. Grever MR. How I treat hairy cell leukemia. Blood [Internet]. 2010 Jan 7 [cited 2020 Jul 12];115(1):21–8. Available from: https://www.sciencedirect.com/science/article/pii/S0006497120301026

12. Grever MR, Abdel-Wahab O, Andritsos LA, Banerji V, Barrientos J, Blachly JS, et al. Consensus guidelines for the diagnosis and management of patients with classic hairy cell leukemia. Blood [Internet]. 2017 Feb 2 [cited 2021 Dec 2];129(5):553–60. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC5290982/#B30

13. Sherman MJ, Hanson CA, Hoyer JD. An Assessment of the Usefulness of Immunohistochemical Stains in the Diagnosis of Hairy Cell Leukemia. American Journal of Clinical Pathology [Internet]. 2011 Sep 1 [cited 2022 Sep 16];136(3):390–9. Available from: https://pubmed.ncbi.nlm.nih.gov/21846914/

14. Alex Freire Sandes, Maria, Cláudia Trindade Oliveira, Maekawa YH, Tamashiro N, Takao TT, et al. CD200 has an important role in the differential diagnosis of mature B-cell neoplasms by multiparameter flow cytometry. The Official Journal of the International Clinical Cytometry Society [Internet]. 2013 Aug 1;86(2):98–105. Available from: https://pubmed.ncbi.nlm.nih.gov/24243815/

15. Iga Hołyńska-Iwan, Karolina Szewczyk-Golec, Katarzyna Maćkowiak, Jankowiak M. Hairy cell leukemia – etiopathogenesis, diagnosis and modern therapeutic approach. Biochemia Medica [Internet]. 2024 Jun 12 [cited 2024 Nov 28];34(2):197–209. Available from: https://pubmed.ncbi.nlm.nih.gov/38882583/

16. Tiacci E, Trifonov V, Schiavoni G, Holmes A, Kern W, Martelli MP, et al. BRAF MUTATIONS IN HAIRY CELL LEUKEMIA. The New England journal of medicine [Internet]. 2011 Jun 16;364(24):2305–15. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3689585/

17. Huynh E, Sigal D, Saven A. Cladribine in the treatment of hairy cell leukemia: initial and subsequent results. Leukemia & Lymphoma [Internet]. 2009 Jan 1 [cited 2023 Sep 20];50(sup1):12–7. Available from: https://pubmed.ncbi.nlm.nih.gov/19814692/

18. Johnston JB. Mechanism of action of pentostatin and cladribine in hairy cell leukemia. Leukemia & lymphoma [Internet]. 2011 Jun;52 Suppl 2:43–5. Available from: https://pubmed.ncbi.nlm.nih.gov/21463108/