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# Hairy Cell Leukemia in Sudan: A Case Highlighting Morphological Diagnosis Under Resource Constraints

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## ABSTRACT

**Background:** Hairy Cell Leukemia (HCL) is an uncommon, indolent B-cell lymphoproliferative illness distinguished by unique cytological characteristics and a generally subtle clinical progression.

**Case presentation:** We present the case of an 85-year-old Sudanese man exhibiting prominent pancytopenia, splenomegaly, and recurrent infections. A peripheral blood smear showed lymphoid cells with cytoplasmic projections, and a bone marrow biopsy revealed diffuse infiltration with lymphocytes that resembled "fried eggs." The lack of flow cytometry and cytogenetic analysis, due to infrastructural constraints intensified by ongoing armed conflict, highlights the essential need for clinical expertise and morphological observation in resource-limited settings.

**Conclusion:** The above scenario highlights the importance of maintaining a high clinical suspicion for HCL in pancytopenic patients, particularly in resource-constrained environments. It highlights the importance of immunophenotypic validation to ensure accurate diagnosis and inform treatment decisions.

**Keywords:** Hairy cell leukemia, B-cell; Lymphoproliferative disease; Lymphocytes projection; Sudan

## INTRODUCTION

Hairy Cell Leukemia (HCL) is an uncommon chronic B-cell neoplasm, initially identified in 1958 by Bouroncle et al., distinguished by lymphocytes exhibiting cytoplasmic projections that resemble hair-like extensions [1]. It comprises almost 2% of all leukemias and has a significant impact on middle-aged men (50 - 55 years), with a male-to-female ratio of nearly 4:1 or 5:1 [2]. The incidence is approximately 0.3 cases per 100,000 per year in Western populations; however, data from African populations remain sparse [3]. HCL frequently manifests clinically with weariness, recurrent infections, splenomegaly, and cytopenias, notably monocytopenia and pancytopenia [4, 5].

Hematologic malignancies, especially leukemias, provide a considerable challenge in Sudan, as population-based studies indicate that leukemia is among the most prevalent hematological tumors reported to oncology facilities [6,7]. Nonetheless, precise data regarding the incidence of HCL in Sudan are absent [6]. The disruption

of diagnostic and treatment infrastructure due to conflict further complicates the identification and treatment of rare diseases, such as HCL [8].

A combination of a peripheral blood smear, a bone marrow biopsy, and immunophenotyping using flow cytometry is the standard method for confirming a diagnosis. CD11c, CD25, CD103, and annexin A1 are some of the markers that hairy cells express, which help distinguish HCL from other B-cell neoplasms [2 - 9]. However, in places where resources are scarce, especially in areas of conflict, access to these diagnostic tools is typically limited. HCL is often not detected or misdiagnosed as other chronic lymphoproliferative diseases [10]. Sudan's healthcare system is currently grappling with significant challenges due to the ongoing war, which poses obstacles to hematologic diagnosis. In such situations, the reliance on classical morphology becomes paramount. This case report outlines the diagnostic process of HCL in a Sudanese adult, instilling confidence in the audience about the effectiveness of peripheral smear interpretation in the absence of modern laboratory resources.

## CASE PRESENTATION

An 85-year-old male from eastern Sudan exhibited a 5-month history of escalating weariness, a weight reduction of 5 kg, recurrent fever episodes, and abdominal distension. No history of nocturnal diaphoresis or hemorrhagic tendencies was noted. He had no history of chronic infections or prior hematological disease. There was no known family history of malignancy. Upon examination, he exhibited marked pallor and significant splenomegaly (6 cm beneath the costal edge) without palpable lymphadenopathy. Importantly, hepatomegaly and cutaneous abnormalities were notably absent. No skin lesions or neurological deficits were noted.

Laboratory diagnostic evaluation indicated Complete Blood Count (CBC): Hemoglobin 7.7 g/dL, White Blood Cells (WBC) 3.5 × $10^9$/L, neutrophils 1.1 × $10^9$/L, lymphocytes 2.4 × $10^9$/L, platelets 27 × $10^9$/L (Table 1). The peripheral blood smear revealed a population of atypical mononuclear cells characterized by oval nuclei, thin chromatin, and copious pale cytoplasm with fragile, hair-like projections. These physical characteristics were consistent with those of hairy cells (Figure 1). Morphologically aberrant "hairy cells" constituted about 70% of circulating white cells, primarily comprising lymphoid cells. Bone marrow aspiration: Dry tap because of fibrosis. Bone marrow trephine biopsy: Widespread infiltration by mononuclear cells exhibiting ample cytoplasm and oval nuclei, like a "fried egg".

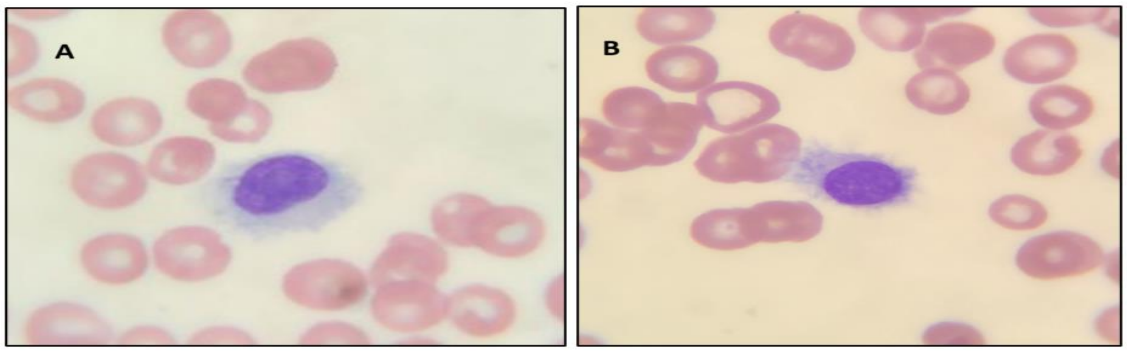


**Figure 1:** Peripheral blood picture; Panel A reveals mononuclear cells with abundant pale cytoplasm. Panel B displays atypical lymphoid cells with oval nuclei and cytoplasmic projections

**Table 1:** Hematological and Biochemical Parameters of the Patient at Presentation.

| Variable | Patients result | Reference Interval |
|---|---|---|
| White blood cells **x10$^9$/l** | 3.5 | 4 – 10 |
| Red blood cells **x10$^{12}$/l** | 2.2 | 3.5 – 5.5 |
| Hemoglobin **g/dl** | 7.7 | 12 – 16 |
| Hematocrit **%** | 22.1 | 35 – 47 |
| Mean Corpuscular Volume **fl** | 100.5 | 78 – 98 |
| Mean Corpuscular Hemoglobin **pg** | 35 | 26 – 35 |
| Mean Corpuscular Hemoglobin Concentration **%** | 34.8 | 30 – 36 |
| Absolute lymphocyte counts **x10$^9$/l** | 2.4 | 1.0 – 4.3 |
| Absolute neutrophil counts **x10$^9$/l** | 1.1 | 1.5 – 7.0 |
| Absolute monocyte counts **x10$^9$/l** | 0 | 0.1 – 1.0 |
| Platelet count **x10$^9$/l** | 27 | 150 – 400 |
| Erythrocyte sedimentation rate, 1$^{st}$ hour, **mm/h** | 90 | Up to 20 |
| Creatinine**, mg/dl** | 1.3 | 0.4 – 1.6 |
| Blood Urea**, mg/dl** | 47 | 10 – 50 |
| Blood Urea Nitrogen**, mg/dl** | 22.9 | Jul-21 |
| Uric Acid**, mg/dl** | 6 | 3.4 – 7.0 |
| Total Bilirubin**, mg/dl** | 0.8 | 0.2 – 1.3 |
| Direct bilirubin**, mg/dl** | 0.3 | Up to 0.25 |
| Total protein, **g/dl** | 6.6 | 6.6 – 8.3 |
| Albumin, **g/dl** | 3.6 | 3.5 – 5.5 |
| Alanine transaminase, **U/l** | 38 | Up to 41 |
| Aspartate transaminase, **U/l** | 43 | Up to 43 |
| Alkaline phosphatase, **U/l** | 113 | Up to 115 |
| Glycosylated Hemoglobin**, %** | 6.3 | 4.5 – 6.5 |
| C-reactive protein (quantitative), ***mg/l*** | 8.9 | < 10 |
| Direct Anit-human Globulin (DAT) | Negative | – |
| Indirect Anti-human Globulin | Negative | – |
| Hepatitis C virus screening (HCV) | Negative | – |
| Hepatitis B virus screening (HBV) | Negative | – |
| Human Immunodeficiency virus screening (HIV) | Negative | – |

## DIAGNOSTIC WORKUP AND LIMITATIONS

In optimal conditions, the diagnosis of HCL is validated using flow cytometry and cytogenetic analysis (BRAF V600E testing), which were not accessible at the first diagnosis [5]. Due to the ongoing war in Sudan, it was not possible to obtain immunophenotyping and cytogenetic services. Consequently, a provisional diagnosis was established based on characteristic peripheral smear morphology and supportive hematological indicators, with a thorough exclusion of alternative lymphoproliferative diseases.

The differential diagnoses contemplated were comprehensive, encompassing Chronic Lymphocytic Leukemia (CLL), Prolymphocytic Leukemia (PLL), Splenic Marginal Zone Lymphoma (SMZL), and Hairy Cell Leukemia Variant (HCL-v). The cytoplasmic projections, nuclear morphology, and absence of lymphadenopathy indicated a diagnosis of classical HCL as the most probable.

## MANAGEMENT AND FOLLOW-UP

Due to a strong clinical and morphological suspicion of HCL, but lacking immunophenotyping, the decision was made to postpone therapy. The patient received supportive care, including transfusion support for low blood

platelets and anemia and broad-spectrum antibiotics for febrile neutropenia episodes. The team provided support with growth factors (G-CSF) during long-term neutropenia.

Purine analog therapy (cladribine or pentostatin) was contemplated but postponed owing to the absence of confirmatory testing, high risk of profound treatment-related cytopenias in an older person, and the fact that medications are not available in the area because of war and insurance problems.

Three months later, the patient's cytopenias were still stable, and he reported that transfusion support had helped him feel better. Plans were made to send him abroad for flow cytometry and tailored therapy if possible.

## DISCUSSION

This case shows the diagnostic and therapeutic challenges of HCL in elderly patients in resource-constrained and conflict-affected environments. The patient, a remarkable 85 years old, displayed characteristic signs of HCL, including pancytopenia, splenomegaly, and recurrent infections. Despite the ongoing conflict in Sudan preventing them from undergoing confirmatory diagnostics, such as flow cytometry and testing for the BRAF V600E mutation, their resilience was truly admirable.

According to WHO guidelines on cancer care in humanitarian catastrophes [11], tailored diagnostic and treatment routes should be preferred when laboratory service is interrupted. It's worth noting that Sudanese oncology records indicate that leukemias are a significant component of adult cancers [12]. This suggests that hematology services require strengthening, particularly in areas where ongoing conflict exists.

The above scenario exemplifies three significant challenges: old age, diagnostic constraints, and healthcare obstacles associated with warfare. HCL is uncommon in those above 80 years old. In affluent nations, cladribine or pentostatin attains complete remission in 70-90% of instances; nonetheless, older adults encounter elevated treatment-related dangers [13].

Morphologically, the peripheral smear exhibited characteristic hairy cells with circumferential cytoplasmic extensions, while the bone marrow biopsy demonstrated diffuse infiltration by cells with a “fried egg” morphology; both findings align with the classical features of HCL [1,5]. The lack of monocytosis and lymphadenopathy further corroborated the diagnosis, aiding in its differentiation from HCL variant (HCL-v), CLL, and SMZL [9,10].

The patient's laboratory results indicate severe anemia (Hemoglobin 7.7 g/dL), neutropenia (Absolute Neutrophil Count 1.1 × $10^9$/L), thrombocytopenia (Platelet count 27 × $10^9$/L), and an elevated ESR (90 mm/h). These results indicate that the marrow is being infiltrated and that persistent inflammation persists. The lack of viral markers (HBV, HCV, HIV) and negative Coombs tests excluded infectious and autoimmune etiologies of cytopenia. In the case of HCL, our assessment of the peripheral blood smear with a differential count typically indicates pancytopenia, accompanied by normocytic-normochromic anemia, neutropenia, monocytopenia, and thrombocytopenia [1, 3, 5]. Monocytopenia is a unique and sensitive indicator of classic form HCL. A diagnostic feature of HCL is the presence of medium-sized cells with pale blue cytoplasm, which are moderately numerous, a key component in identifying HCL. It has "hair-like" projections that are serrated around the edges and a spherical, well-defined nucleus [10]. You may observe this cell on a peripheral blood smear and in the bone marrow; your keen observation is essential in this process.

The trephine bone marrow biopsy with aspirate is typically performed to confirm the diagnosis of HCL and to assess the extent of bone marrow involvement. A "dry tap," or failure to obtain a successful bone marrow aspirate, is a commonly observed occurrence [2], indicating the presence of extensive fibrosis in the bone marrow. You can use immunohistochemical stains for CD20, Annexin-A1, cyclin D1, and VEI/BRAFV600E to see how many leukemic cells have gotten into the bone marrow [5]. The typical flow cytometry markers for HCL are CD11c+, CD25+, CD103+, and CD123+. The typical B-cell markers are CD19+, CD20+, or CD22+ [5,10].

Management was cautious due to the hazards associated with aging and the difficulty in obtaining purine analogs. Cladribine and pentostatin are first-line treatments that are effective in more than 85% of people [13]. However, they should be used with caution in older people because they can cause long-term immunosuppression and increase the risk of opportunistic infections [14]. The use of transfusions, G-CSF, and antibiotics aligns with the general guidelines for treating HCL in vulnerable populations, providing a supportive framework for treatment [5]. HCL is linked to a higher chance of getting other cancers, like melanomas, prostate and gastrointestinal cancers, and non-Hodgkin lymphomas. With prompt medical care, the median survival can be as long as the average life expectancy [15].

The current guidelines for therapy for HCL suggest primary nucleoside analog induction therapy with either cladribine or pentostatin, provided there is no renal impairment or active infection. Conversely, asymptomatic patients do not necessitate immediate treatment but require vigilant clinical monitoring [4 - 9]. In general, at least one of the following hematological indicators indicates that treatment is needed: The hemoglobin level must be below 11 g/dL, the platelet count must be below 100,000/μL, or the absolute neutrophil count must be below 1000/μL, or there must be significant systemic symptoms [5,9].

The current scenario highlights the crucial role of morphological expertise in detecting hematologic malignancies, particularly in the absence of advanced diagnostic tools. It also stresses how important it is for global health programs to help keep cancer care going in conflict zones, where delays in diagnosis can have a significant effect on outcomes [11].

## CONCLUSION

Hairy cell leukemia can affect the elderly and may provide diagnostic and treatment challenges in resource-constrained or conflict-affected environments. Even without flow cytometry, clinical suspicion supported by blood film and bone marrow morphology can aid in initial care. To make confirmatory testing and treatment available, countries need to work together.

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