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A Rare Case of Hairy Cell Leukemia with COVID Infection: A Case Report

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Abstract

Hairy cell leukemia (HCL) is a distinct subset of chronic lymphoid leukemia, presents with unique features, including the characteristic "hairy" projections seen in neoplastic B cells. We reported a case on hairy cell leukemia (HCL), emphasizing the challenges posed by this rare hematological malignancy, especially in the context of concurrent health crises such as the COVID-19 pandemic. This malignancy, though uncommon, necessitates comprehensive diagnostic methodologies, such as peripheral blood studies, flow cytometry, and bone marrow biopsy.

Treatment strategies for HCL involve tailored approaches based on symptomatic presentations. Purine analogs, cladribine and pentostatin, stand as first-line interventions, showcasing efficacy in inducing and sustaining remission. However, the prolonged immunosuppression resulting from these treatments warrants vigilant monitoring for potential infectious complications. Emerging therapies, such as the BRAF inhibitor vemurafenib, provide additional options for refractory or progressive cases.

The post-treatment phase demands meticulous follow-up, with an emphasis on regular blood work assessments by an oncology nurse and primary care physician.

Our case further highlights the need for heightened awareness among healthcare professionals, particularly in the post-COVID-19 phase, where persistent symptoms led to the discovery of an underlying hematological disorder.

Keywords: Hairy cell leukemia, Evan syndrome, Covid-19.

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1. Introduction

Hairy cell leukemia (HCL) is an infrequent form of chronic leukemia originating from B lymphocytes, predominantly affecting the bone marrow, spleen, and peripheral blood. Characterized by the accumulation of neoplastic B cells with distinctive "hairy" projections, HCL causes splenomegaly and various cytopenias, leading to systemic implications. The diagnostic evaluation involves bone marrow biopsy, immunophenotyping, and flow cytometry, with peripheral blood and bone marrow exhibiting characteristic features such as "hairy" cells and a "fried egg" appearance

2. Main Results

A 43-year-old male, employed as a teacher, sought medical attention with symptoms including fever, cough, and headache persisting for one week. Three days into his illness, he developed difficulty breathing, prompting a COVID-19 test on 19th January 2021, confirming positive results on 20th January 2021. Following contact with Dubai Health Authority, he was transported to Canadian Specialist Hospital via ambulance.

The patient had no known medical conditions, was a non-smoker, and had no history of asthma. Upon examination, his temperature was 38°C, his respiratory rate was 24/min, a blood pressure of 142/83 mmHg, and a saturation level of 91%. On examination, bilateral basal crepitations were observed. Initial treatment involved administering 10 liters of oxygen via NRBM (Non-rebreather mask) to maintain saturation at 96%.

The diagnosis upon admission was severe bilateral pneumonia attributed to COVID-19 infection. The treatment plan included high-flow oxygen, remedesivir, clexane, steroids, zinc, vitamin C and D and broad-spectrum antibiotics.

Over the subsequent two days, the patient's condition deteriorated, complaining of increased shortness of breath. Oxygen inhalation was adjusted to 15 liters via NRBM, with consideration that ICU transfer has to be done if further deterioration occurred. However, the patient maintained oxygen saturation at 90-92%.

Antibiotics were adjusted due to elevated inflammatory markers and procalcitonin, transitioning from ceftrixone to cefepime and levofloxacin. A positive turn in the patient's condition was observed over a period of 10 days, facilitated by chest physiotherapy and spirometry.

- All laboratory parameters showed improvement, leading to the patient's discharge after 12 days with supportive medication and a continuation of spirometry at home.

3. Labs During Hospital Admission

Additionally, inflammatory markers are elevated, with C-reactive protein (CRP) at 114 mg/dL, procalcitonin at 10 ng/mL, and ferritin at 346 ng/mL. Cardiac markers, including CKMB and high-sensitive Troponin T, show values within normal range. Blood sugar as well as magnesium and calcium levels were within normal ranges, Prothrombin time (PT) is slightly prolonged at 16.7 seconds, as well as APTT is prolonged at 43 seconds corresponding to an international normalized ratio (INR) of 1.28. Notably, a COVID PCR test returned positive, and imaging studies, including a chest X-ray and CT, reveal classic features of COVID-19 infection, with bilateral multifocal pneumonia and ground glass haziness in the lungs.

CT pulmonary angiogram was planned to rule out pulmonary thrombus, which yielded normal results with no evidence of thrombus. ECG showed normal findings. Following discharge, the patient exhibited improved breathing but reported persistent fatigue. On a follow-up visit, he appeared pale, prompting investigations that revealed a drop in hemoglobin and platelets. Initially attributed to post-COVID effects, further workup for anemia and low platelets showed a reticulocyte count of **3%**, positive Coombs test, and negative ANA profile. Vitamin B12 and iron studies were normal. Abdominal ultrasound was done to rule out any liver disease. · there was significant Splenomegaly with measurement across the splenic hilum more than 21.8 cm and the maximum AP diameter was 14.3 cm. The liver appeared normal and there was no portal vein thrombosis and no periportal or perisplenic collaterals was seen.

Given the unexplained course, a diagnosis of Evan syndrome (thrombocytopenia with hemolysis) was considered, marked by septicemia. Evan syndrome in a young patient is unexplained without chronic medical problems.

The patient's complete blood count reveals a white blood cell count (WBC) of 7.14 x 10^9/L, erythrocytes (RBC) count low at 3.82 x 10^12/L, and a hemoglobin level of 11.8 g/dL which is low. Other hematological parameters include a low hematocrit (HCT) of 37.0%, mean corpuscular volume of 96.9 fL which is normal and a high red cell distribution width (RDW) of 20.2%. Platelet count is markedly reduced at 50 x 10^9/L, with a normal mean platelet volume (MPV) of 8.8 fL. Differential counts show elevated monocytes at 44.4% and elevated lymphocytes at 43.3%, with decreased neutrophils at 11.6%. Normal electrolytes and renal function was present. Despite a steroid course, the patient's platelet count dropped to 45,000x10^9/L, and hemoglobin was at 12.5 g/dl. Fatigue and bruising persisted over 3-4 months after the initial COVID infection.

Referral to a hematologist was made, leading to a bone marrow examination. The bone marrow biopsy was mildly hypercellular for patient age (70% cellularity/30% marrow cells). The myeloid series was suppressed but there were no dysplastic features. There is diffuse interstitial infiltrate of cells with clear cytoplasm that shows strong expression of CD20, weak cytoplasmic expression of Annexin A and focal expression of CD79a. The tumor cells also express CD10, Bcl2, Cyclin D1 and PAX5. It showed that there was infiltration by low grade B cell lymphoma /

leukemia which supports the diagnosis of Hairy cell leukemia.
The Peripheral Blood Smear Report shows RBCs within normal size, chromasia and morphology. WBCs were normal in count with few lymphocytes showing atypical features and cytoplasmic projection suggestive of HCL. The Platelets were decreased in number but normal in morphology. There was no platelets clumping or satellitism seen.
The examination and associated markers pointed towards hairy cell leukemia. Chemotherapy, including cladribine and four cycles of Rituximab, was initiated on 11 July 2021. A repeat bone marrow aspiration on 21st July 2022 revealed findings consistent with trilineage hematopoiesis and hematological remission.

4. Labels of figures and tables

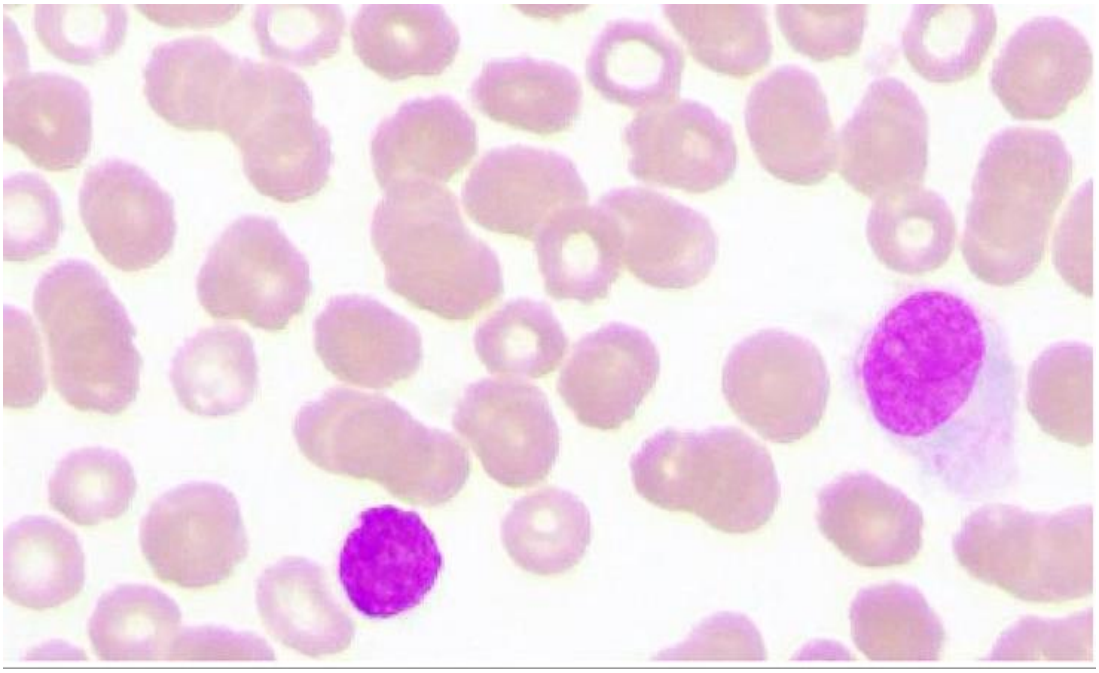

Figure 1: Bone marrow biopsy reveals infiltration by low grade B- cell lymphoma indicating hairy cell leukemia

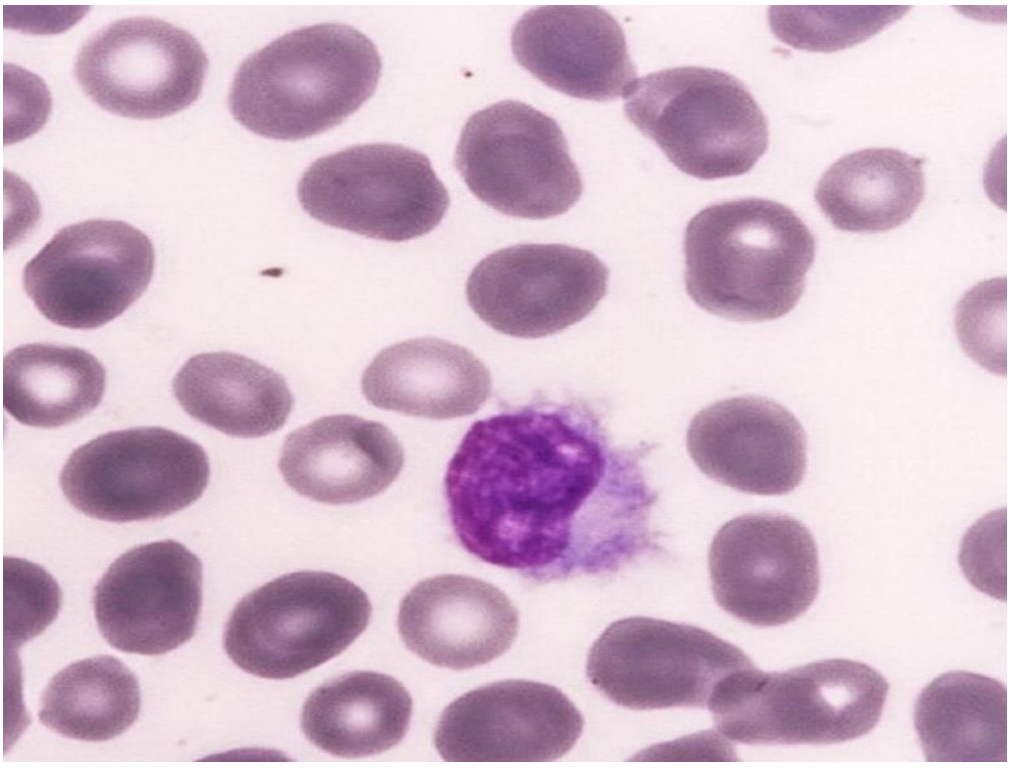

Figure 2: The peripheral smear report is showing relative lymphocytes with few atypical lymphocytes with cytoplasmic projection.

5. Discussion

Hairy cell leukemia (HCL) stands as a chronic lymphoid leukemia, initially characterized by hairlike cytoplasmic projections discernible on abnormal B-cells. The clonal B-cell lymphocyte, the hallmark of HCL, infiltrates the reticuloendothelial system, disrupting bone marrow function and causing bone marrow failure or pancytopenia. This infiltration extends to the liver and spleen, resulting in organomegaly.

Hairy cell leukemia is relatively uncommon, constituting 2% of all leukemia cases, with approximately 1100 new cases reported in the United States in 2016. Predominantly affecting middle-aged men, HCL presents with a median age of 49-51 years and a male-to-female ratio ranging from 4:1 to 5:1.[1]

Despite its recognized impact, the precise cause of hairy cell leukemia remains elusive, with potential links to past exposure to various chemicals. Such as ionizing radiation, farming, and pesticides. [2,3] The majority of cases are believed to stem from a V600E BRAF gene mutation in late-activated memory B cells. The pathophysiology of HCL, classified as a lymphoproliferative neoplasm, has been further elucidated by the discovery of the V600E BRAF mutation, predominantly present in classic HCL cases. This mutation implicates the RAS-RAF-MAPK

signaling pathway, leading to heightened cellular proliferation, survival, and eventual malignancy. CDKN1B inactivation, the second most common mutation in HCL, as revealed by Sascha Dietrich et al., further adds complexity to the understanding of HCL's genetic underpinnings.[4]

Histopathologically, the diagnosis of HCL relies on the morphological evidence of hairy cells observed through microscopic examination. These mononuclear cells, typically 1 to 2 times the size of mature lymphocytes, display distinctive features such as ovoid nuclei, variable cytoplasm, and characteristic "hairy" projections. The identification of these cells in peripheral blood films, stained with Romanowsky, provides valuable diagnostic insights. Hairy cell leukemia's complex interplay of genetics, morphology, and clinical manifestations emphasizes the need for comprehensive approaches in its diagnosis and understanding.

Patients with hairy cell leukemia often experience non-specific symptoms, such as fatigue and weakness. The clinical presentation of HCL commonly involves splenomegaly or cytopenias, leading to symptoms like anemia, thrombocytopenia, neutropenia, monocytopenia, along with weakness, fatigue, and varying severity of infections. Hemorrhagic findings such as gingival bleeding, ecchymoses, epistaxis, or menorrhagia may also manifest. Notably, 80% of patients display significant cytopenias at the time of diagnosis, with severe pancytopenia observed in less than 10% of cases. While splenomegaly is a predominant feature, the occurrence of massive, symptomatic splenomegaly is less frequent, possibly due to earlier detection through routine complete blood count (CBC). Hairy cell leukemia may uncommonly coexist with autoimmune thrombocytopenia and hemolytic anemia. The heightened susceptibility to infectious complications arises from the dual impact of underlying immunosuppression due to cytopenias and myelosuppressive therapy. This clinical profile underscores the complexity and diverse presentations associated with hairy cell leukemia, demanding a comprehensive approach to diagnosis and management.[5]

Establishing a diagnosis of hairy cell leukemia involves a comprehensive approach, combining studies on peripheral blood, flow cytometry assessment, review of peripheral smear, and bone marrow biopsy. While a "dry tap" – the inability to perform bone marrow aspiration – is a common challenge encountered in hairy cell leukemia, it is not observed in HCL-V. The characteristic-appearing mononuclear cells of hairy cell leukemia are notably large, featuring circumferential hair-like cytoplasmic projections and a distinct, round nucleus.[6]

Flow cytometry serves as a crucial diagnostic tool, revealing positive markers for hairy cell leukemia, including CD11c, CD25, CD103, and CD123, alongside typical B-cell markers like CD19, CD20, or CD22. Notably, cyclin-D1 expression is typically present, although weak or focal compared to mantle cell lymphoma. In the case of HCL-V, there is a negative expression for CD25 and CD123. The V600E BRAF mutation is a prominent feature, observed in nearly all classic hairy cell leukemia cases, differentiating it from HCL-V.[6] Complementary to these diagnostic methods, computed tomography (CT) is recommended for assessing the degree of lymphadenopathy. Annexin A1 expression in B cells is a specific but not highly

sensitive marker for HCL diagnosis. [7]

This multifaceted diagnostic approach ensures accurate identification and differentiation of hairy cell leukemia, allowing for targeted and effective management.

In addressing the inherent challenges of hairy cell leukemia, treatments is selectively given to symptomatic patients, targeting those with significant fatigue, symptomatic splenomegaly, and notable cytopenias (hemoglobin less than 12 g/dL, platelets less than 100,000/mcL, ANC less than 1000/mcL). Asymptomatic individuals undergo close monitoring for disease progression through regular history, physical examinations, and CBC every 3 to 6 months.

The primary therapeutic approach involves purine analogs, specifically cladribine and pentostatin, acknowledged as first-line treatments due to their equal effectiveness in inducing and sustaining remission. It's crucial to recognize that patients subjected to these therapies experience prolonged immunosuppression, necessitating vigilant attention to potential infectious complications. Vemurafenib, while demonstrating efficacy, is typically reserved for refractory or progressive cases.

Splenectomy becomes a consideration in patients with symptomatic massive splenomegaly and severe pancytopenia due to splenic sequestrations, serving as a temporary measure for symptomatic pregnant women. For relapsed disease, another course of purine analog may be an option if relapse occurs more than a year from the initial treatment. However, response rates and remissions tend to be lower and shorter after relapse. Diverse alternatives for relapsed or refractory cases encompass a combination of cladribine or pentostatin with rituximab, fludarabine alone or in combination with rituximab, bendamustine, and interferon-alpha. The BRAF mutation in hairy cell leukemia can be specifically targeted using the oral BRAF inhibitor vemurafenib, demonstrating efficacy in both relapsed and refractory settings.[8]

To complement these treatments, supportive care measures, such as antimicrobial prophylaxis for viral and pneumocystis pneumonia, should be considered for individuals with significant cytopenias. In cases requiring transfused blood products, irradiation is imperative to prevent transfusion-associated graft-versus-host disease. This comprehensive approach aims to manage hairy cell leukemia effectively while addressing potential complications and ensuring the well-being of affected individuals.

6. Conclusion

Hairy cell leukemia (HCL), is a rare hematological malignancy affecting the spleen, bone marrow, and peripheral blood. Patients commonly present with general complaints like fatigue and weakness, along with symptoms associated with cytopenias. Although not curative, many individuals can attain lasting remissions with extended periods free of treatment, with subsequent therapy initiated upon symptomatic relapse. Close monitoring by an oncology nurse and primary care physician, along with regular blood work assessments, is essential post-treatment. This demands a comprehensive and inter-professional approach for optimal management.

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